EMERGE

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ENTREMED

CREATING A NEW GENERATION OF TARGETED THERAPIES

FORM 10−K

ENTREMED INC − ENMD

Filed: March 16, 2005 (period: December 31, 2004)

Annual report which provides a comprehensive overview of the company for the past year

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FORM 10−K

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D. C., 20549

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

For the fiscal year ended December 31, 2004

Commission file number 0−20713

ENTREMED, INC.

(Exact name of registrant as specified in its charter)

Delaware	58−1959440
(State of Incorporation)	(I.R.S. Employer Identification No.)
9640 Medical Center Drive, Rockville, MD	20850
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code: (240) 864 − 2600

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

Title
Common Stock, Par Value $.01 Per Share

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 ☐

As of June 30, 2004, the aggregate market value of the shares of common stock held by non−affiliates was approximately $76,237,348.

As of March 10, 2005, 42,815,284 shares of the Company's common stock were outstanding.

Documents incorporated by reference

See Part III hereof with respect to incorporation by reference from the registrant's definitive proxy statement to be filed pursuant to Regulation 14A under the Securities Exchange Act of 1934 and the Exhibit Index hereto.

ENTREMED, INC.
FORM 10−K − FISCAL YEAR ENDED DECEMBER 31, 2004

Contents and Cross Reference Sheet

SPECIAL NOTE REGARDING FORWARD−LOOKING STATEMENTS

This report contains and incorporates by reference certain forward−looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended. These statements may be identified by forward−looking words such as “may,” “will,” “expect,” “anticipate” or similar words. These forward−looking statements include, among others, statements regarding our business strategy, the timing of our clinical trials and the expected increases in our expenses.

Our forward−looking statements are based on information available to us today, and we will not update these statements. Our actual results may differ significantly from those discussed in our forward−looking statements due to, among other factors, our history of operating losses and anticipation of future losses; the value of our common stock; uncertainties relating to our technological approach; uncertainty of our product candidate development; our need for additional capital and uncertainty of additional funding; our dependence on collaborators and licensees; intense competition and rapid technological change in the biopharmaceutical industry; uncertainties relating to our patent and proprietary rights; uncertainties relating to clinical trials; government regulation and uncertainties of obtaining regulatory approval on a timely basis or at all; our dependence on key personnel, research collaborators and scientific advisors; uncertainties relating to health care reform measures and third−party reimbursement; risks associated with product liability; and other factors discussed in our other filings with the Securities and Exchange Commission. You are encouraged to review the risk factors included in this report.

PART I

ITEM 1. BUSINESS

OVERVIEW

EntreMed, Inc. (“EntreMed” or “the Company”) (Nasdaq: EMND) is a clinical−stage pharmaceutical company focused on developing the next generation of multi−mechanism oncology and anti−inflammatory drugs that target disease cells directly and the blood vessels that nourish them. We are focused on developing drugs that are safe and convenient, and provide the potential for improved patient outcomes. Panzem® (2−methoxyestradiol or 2ME2), our lead drug candidate, is currently in clinical trials for cancer, as well as in preclinical development for non−oncology indications.

EntreMed’s goal is to develop and commercialize new compounds based on our expertise in the science of angiogenesis, cell cycle regulation and inflammation — processes vital to the treatment of cancer and other diseases. Our expertise has led to the identification of new molecules, including analogs of 2ME2, modulators of fibroblast growth factor−2 (FGF−2) activity, tissue factor pathway inhibitor (TFPI) peptides, and proteinase activated receptor−2 (PAR−2) antagonists. We are developing these potential drug candidates for either in−house advancement or external partnering. In order to advance EntreMed’s commercial objectives, we intend to seek strategic alliances, licensing relationships and co−development partnerships with other companies to develop compounds for both oncology and non−oncology therapeutic areas.

We were incorporated under Delaware law in 1991. Our principal executive offices are located at 9640 Medical Center Drive, Rockville, Maryland 20850, and our telephone number is (240) 864−2600.

SCIENTIFIC FOUNDATION

We developed our initial drug pipeline based upon comprehensive research into the relationship between malignancy and the process of angiogenesis (the growth of new blood vessels). This research led EntreMed scientists to focus on drug candidates that act on the cellular pathways that affect biological processes important in multiple diseases, specifically angiogenesis, inflammation and cell cycle regulation. Our drug candidates have potential applications in oncology and other diseases because they are involved with one or more of these pathways.

Angiogenesis. Angiogenesis is a multi−step process in which preexisting blood vessels send out capillary sprouts to produce new blood vessels. This tightly regulated process involves the migration, proliferation and differentiation of endothelial cells. In normal physiology, angiogenesis is a necessary component of menstrual cycling and wound healing, where the process is tightly regulated through appropriate shifts in the balance of pro−angiogenic and anti−angiogenic signals. However, this tight regulation of angiogenesis in normal physiology is absent or aberrant in multiple disease settings that are characterized by persistent, inappropriate blood vessel development.

Angiogenesis occurs in more than 80 disease states, particularly in various forms of cancer where the growth of new blood vessels is necessary to sustain tumor growth. Other diseases dependent on angiogenesis include arthritis (where inflammation triggers new blood vessel growth and erosion of joints), cardiovascular disease (where the growth of atherosclerotic plaques blocks blood vessels), age−related macular degeneration (where newly formed vessels damage retinal cells), and psoriasis (where vessel growth sustains excessive proliferation of skin cells). EntreMed scientists, who have studied the process of angiogenesis in−depth for over a decade, are developing drug candidates to inhibit blood vessel formation and, in turn, control or stop diseases resulting from inappropriate blood vessel growth.

Cell Cycle Regulation. Cell cycle regulation is the replication, differentiation and death of cells. One specific aspect of cell cycle regulation is the programmed control of cell death (apoptosis). In certain disease states, such as cancer, atherosclerosis and endometriosis, the balance between cell proliferation and cell death is altered, resulting in inappropriate cell growth. EntreMed’s compounds impact biochemical pathways in cells that result in their death via apoptosis. We believe that the selective induction of apoptosis through drugs that block cell−cycle activities can either stabilize or cause the regression of cancer, inflammation and other disease processes

characterized by inappropriate cell growth. Our preclinical studies have demonstrated induction of endothelial cell and tumor cell apoptosis without significant toxicity.

Inflammation. Inflammation is the process involving the reaction of tissue to injury or disease. The condition may be either local or systemic and can be divided into acute (immediate) and chronic (prolonged) patterns. The endothelial cell responses involved in angiogenesis (formation of new blood vessels) and homeostasis (physiological equilibrium) are central to inflammatory diseases. In contrast to acute inflammation, which is manifested by vascular changes, edema, and largely neutrophil infiltration, chronic inflammation is characterized by infiltration with mononuclear leukocytes, tissue destruction, angiogenesis, and fibrosis. As a result, the cellular pathways involved in acute and chronic inflammation can be overlapping or distinct. Inflammation is a process that is associated with many pathologies, including cancer, cardiovascular disease and arthritis. Many of EntreMed's compounds have demonstrated both anti−inflammatory and anti−tumor properties in preclinical models.

EntreMed is developing compounds that we believe have broad therapeutic potential and significant commercial opportunity. These compounds can be formulated for local or systemic delivery. Our initial formulation of our clinical drug candidate, Panzem® Capsules (2−methoxyestradiol, 2ME2), has been administered to more than 165 patients in six Phase I and II oncology trials and has shown an excellent safety profile with no dose limiting toxicities reported to date. Furthermore, investigators have reported tumor regression and disease stabilization in some patients with advanced cancers.

Based on preclinical research and data from healthy human subjects, we have developed a new formulation of 2ME2 in an orally−administered liquid suspension that is designed to enhance drug bioavailability (plasma drug levels). In July 2004, we entered into a clinical manufacturing and supply agreement with Elan Drug Delivery, Inc. to optimize and produce the new liquid suspension formulation using Elan's NanoCrystal® Colloidal Dispersion (NCD) technology. Panzem® NCD is now being used in EntreMed's clinical trials in advanced cancer patients, which commenced in January 2005. 2−methoxyestradiol is also in preclinical testing for potential applications in rheumatoid arthritis.

In addition to 2ME2 (Panzem® Capsules and Panzem® NCD), EntreMed's scientists have discovered a number of compounds that are at various stages of development:

ENMD−1198 (2ME2 Analog). By modifying the chemical structure of 2−methoxyestradiol (2ME2), we have identified a number of 2ME2 analogs with improved anti−angiogenesis and anti−tumor activity. We have selected a lead compound, ENMD−1198, and IND−directed studies are ongoing.

ENMD−0996 (FGF−2 Vaccine). EntreMed scientists are currently developing a peptide vaccine directed against fibroblast growth factor−2 (FGF−2), a naturally−occurring protein that stimulates angiogenesis. We are conducting further preclinical oncology studies and evaluating internal and external co−development opportunities.

Proteinase Activated Receptor−2 (PAR−2) Inhibitors. The EntreMed research team has designed the first compounds known to block PAR−2, a receptor that plays an important role in inflammation. This project has potential therapeutic applications in oncology and other diseases associated with inflammation and angiogenesis.

Tissue Factor Pathway Inhibitor (TFPI). We have identified a peptide fragment of TFPI, a naturally occurring anti−coagulant protein that blocks tumor growth and angiogenesis. This peptide does not appear to affect normal blood clotting. EntreMed researchers are using the peptide as a template to design therapeutic peptides with similar, but improved, properties.

In October 2004, we entered into a research collaboration with Affymax, Inc., a leader in the discovery and development of novel peptide drugs. Under the terms of the collaboration, EntreMed and Affymax are combining their expertise in peptide design and drug development with the goal of identifying lead anticancer drug candidates for further development.

PIPELINE STRENGTH

We believe that our pipeline offers promising candidates for successful commercialization for the following reasons:

Multiple Mechanisms of Action. Unlike many therapeutic compounds that affect only one cellular activity, compounds work through multiple mechanisms of action (MOA). Therefore, a single compound can attack a disease through several pathways, as well as impact different diseases. For example, 2ME2's MOAs include the inhibition of: 1) angiogenesis; 2) microtubule (cell skeleton) formation; 3) hypoxia inducible factor−1 alpha (HIF−1∝), a protein required for cell survival under stress. Apoptosis (cell death) can also be induced by 2ME2.

Working through multiple mechanisms of action, 2ME2 has the potential to attack cancer cells through multiple pathways that affect the formation and replication of tumor cells, as well as interrupt the formation of blood vessels that nourish tumor cells and sustain tumor growth.

Versatility. Our compounds are versatile in terms of possible therapeutic applications. While our preclinical and clinical efforts continue to focus on oncology and inflammatory disease, we believe that other diseases characterized by angiogenesis represent future opportunities. However, at the present time, we are concentrating almost entirely on our core cancer and inflammation therapy areas. Non−core programs will be evaluated on a case−by−case basis.

Convenient Dosing. We are developing drug candidates that we believe will be easy to use with minimal interruption to the patient's daily routine as compared to other modes of drug administration. We are focusing specifically on oral and local drug delivery technologies, as well as other convenient administration routes. For the Phase 1b studies, cancer patients will take a few teaspoons of Panzem® NCD every six hours and store the liquid drug candidate in their refrigerators at home.

Intellectual Property Position. All EntreMed compounds, with the exception of 2ME2, were discovered and developed internally and, as a result, are EntreMed's sole property. Our in−house discoveries reduce significantly our obligation to make future milestone, royalty and/or licensing payments. We plan to continue supporting our internally−generated pipeline and development efforts.

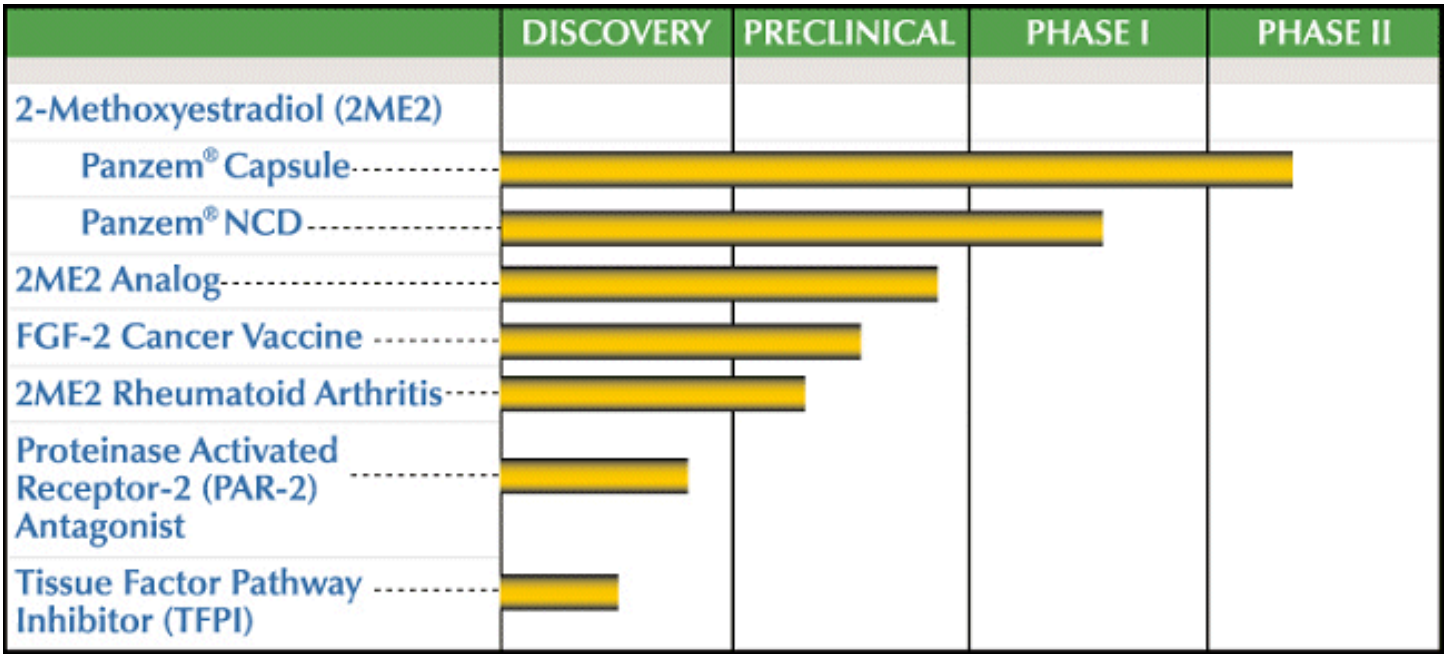
Economic Viability. We believe that our compounds will be economical to develop and have versatile potential applications. The development pathway for our products does not require the creation of novel technology. In addition, our product candidates can be manufactured synthetically and scaled from clinical to commercial quantities. We believe that these features will translate into lower product development, process development, and other associated costs when compared to biological products. Additionally, greater economic potential may be possible because each of our compounds may offer several therapeutic applications.

BUSINESS DEVELOPMENT STRATEGY

Oncology is EntreMed's principal clinical and commercial focus. Our scientific research, however, has provided data that support the preclinical development of our compounds in certain non−oncology applications, such as rheumatoid arthritis. These results increase the potential value of our drug candidates without substantial additional development expense. Therefore, our strategy is to continue developing compounds for oncology and inflammatory diseases, while opportunistically exploring strategic alliances for these compounds in other therapeutic areas.

We intend to pursue co−development partners for our core pipeline product candidates to help accelerate their development and strengthen the development program with complementary expertise. Likewise, we can provide our co−development partners with substantial know−how relating to small molecules, peptides and mimetics that inhibit angiogenesis and inflammation, as well as regulate cell−cycle pathways.

ENTREMED PRODUCT PIPELINE
(As of March 10, 2005)



CLINICAL PIPELINE

2ME2. 2−methoxyestradiol (2ME2) is the molecule from which our lead clinical candidate, Panzem®, has been developed. 2ME2 has multiple mechanisms of action (MOA), including inhibiting angiogenesis, disrupting microtubule (cell structure) formation, down regulating hypoxia inducible factor one−alpha (HIF−1∝, a survival protein), and inducing apoptosis (cell death). The 2ME2 mechanisms that are particularly relevant to the treatment of cancer involve inhibiting endothelial cell growth (anti−angiogenic activity) and killing tumor cells directly (pro−apoptotic activity). Additionally, preclinical models show that 2ME2 has potential therapeutic applications in inflammatory diseases such as rheumatoid arthritis.

Although it is a naturally occurring estrogen metabolite, 2ME2 has little estrogenic activity because it binds poorly to known estrogen receptors. 2ME2 has activity in cell lines that are resistant to various chemotherapy agents including taxanes (microtubule stabilizing agents), etoposide, adriamycin and methotrexate, (DNA synthesis interfering agents), and tamoxifen (anti−estrogen agent).

Panzem® Capsules. Panzem® Capsules, EntreMed's trade name for its initial 2ME2 clinical product candidate, has been administered in capsule form to more than 165 advanced cancer patients to date and has exhibited an excellent safety profile with some patients receiving over two years of therapy. Panzem® Capsules have been tested in cancer patients as a single agent, as well as in combination with an approved chemotherapeutic agent. Clinicians have reported indications of clinical benefit in patients with advanced cancer, including objective responses and stable disease.

Panzem® NCD. EntreMed has recently completed reformulating 2ME2 to increase plasma levels in patients. In April 2004, we completed a Phase 1a clinical trial in healthy human volunteers to evaluate the pharmacokinetics (blood levels after oral administration) and safety profiles of several new oral dosage forms of 2ME2. The most robust of these formulation approaches – an orally−administered liquid suspension – resulted in significantly higher peak blood levels of 2ME2 than those achieved with Panzem® Capsules. In preclinical toxicity studies, the liquid suspension formulation demonstrated no additional toxicity.

The liquid suspension of Panzem® has now been improved as a NanoCrystal® Colloidal Dispersion (NCD), a proprietary technology of Elan Drug Delivery, Inc. (Elan) that is being used successfully in marketed pharmaceuticals. The NCD technology produces nanometer−sized particles that are up to 50 times smaller than particles manufactured by conventional pharmaceutical milling techniques. In July 2004, EntreMed entered into a clinical supply agreement with Elan to produce Panzem® NCD for use in our Phase 1b clinical trials in patients with advanced cancer. Clinical data from these trials will determine the specific cancer indications to be pursued in subsequent Panzem® NCD trials. Specific cancer indications currently under consideration for clinical testing include breast, prostate, ovarian, renal cell, glioma, multiple myeloma and lung (NSCLC).

In January 2005, we announced commencement of two Phase 1b clinical studies for Panzem® NCD in patients with advanced cancer. The studies are being conducted at the University of Wisconsin Comprehensive Cancer Center and Indiana University Cancer Center. Panzem® NCD will be supplied to cancer patients as a liquid in bottles, much like over−the−counter medications. Patients will take the equivalent of a few teaspoons of Panzem® NCD every six hours, and store the product in their refrigerators at home. Based on past clinical experience with Panzem® Capsules, we expect that patients should not experience the side effects associated with many chemotherapeutic agents.

Clinical Trials

PRODUCT CANDIDATE	CLINICAL SITE LOCATION	INDICATION	PHASE	STATUS
Panzem® NCD	University of Wisconsin Comprehensive Cancer Center, Madison, WI	Advanced Cancer`	Ib	Open
Panzem® NCD	Indiana University Cancer Center, Indianapolis, IN	Advanced Cancer	Ib	Open
Panzem® Capsules	Mayo Clinic, Rochester, MN Dana−Farber Cancer Institute, Boston, MA	Multiple Myeloma	II	Open
Panzem® Capsules*	National Cancer Institute, Bethesda, MD	Advanced solid tumors	I	Open
Panzem®*	Mayo Clinic, Rochester, MN	Advanced solid tumors	I	Closed
Panzem® Capsules w/ Taxotere	Indiana University Cancer Center, Indianapolis, IN	Metastatic breast cancer	I	Complete
Panzem® Capsules	University of Wisconsin, Madison, WI Indiana University Cancer Center, Indianapolis, IN	Prostate Cancer	II	Complete
Panzem® Capsules	Indiana University Cancer Center, Indianapolis, IN	Metastatic breast cancer	I	Complete

PRECLINICAL PIPELINE

Analogs of 2ME2. We have discovered new compounds that inhibit tumor growth. Specifically, EntreMed scientists have modified the chemical structure of 2−methoxyestradiol (2ME2) to increase its anti−tumor and anti−angiogenic properties and decrease its rate of metabolism. We have identified three molecules that demonstrate improved pharmacokinetic parameters, a reduced rate of metabolism, and enhanced anti−tumor activity in preclinical animal models.

We are evaluating various formulation technologies to optimize absorption, distribution and metabolic properties, as well as anti−tumor activities of these molecules. A lead compound has been selected, ENMD−1198, and Investigational New Drug (IND)−directed studies in oncology are ongoing. Since 2ME2 has multiple mechanisms of action and therapeutic potential in both oncology and non−oncology indications,

we may seek out− licensing or co−development opportunities for our 2ME2 analogs in other applications. All of these 2ME2 analogs have been discovered in−house and the intellectual property belongs exclusively to EntreMed.

FGF−2 Cancer Vaccine (ENMD−0996). EntreMed scientists are currently developing a cancer vaccine that targets fibroblast growth factor−2 (FGF−2), a potent stimulator of angiogenesis. ENMD−0996 consists of a specific peptide fragment of FGF−2 in an adjuvant formulation. In preclinical studies, ENMD−0996 inhibited tumor development of both B16BL6 melanoma and Lewis lung carcinoma by up to 90% in animal models.

To date, ENMD−0996 has demonstrated no evidence of toxicity in preclinical models, nor have there been any negative effects on wound healing or reproduction. Currently, EntreMed scientists are conducting further preclinical oncology studies with ENMD−0996. The goal of these studies is to advance ENMD−0996 into IND−directed studies that are expected to commence in the second half of 2005. ENMD−0996 was discovered internally and the respective intellectual property belongs exclusively to EntreMed.

2ME2 Rheumatoid Arthritis. The activities ascribed to 2ME2, namely anti−angiogenesis, pro−apoptosis, down regulation of HIF−1∝, and inhibition of bone resorption, have implicated its use in diseases with inflammatory components, such as rheumatoid arthritis. EntreMed is currently in preclinical testing to determine the therapeutic potential of 2ME2 in rheumatoid arthritis.

Proteinase Activated Receptor−2 (PAR−2) Inhibitor. PAR−2 is a cell surface receptor that is known to play a critical role in acute and chronic inflammation. We discovered a peptide that blocks PAR−2, the first such compound identified as an antagonist of PAR−2. The anti−PAR−2 peptide inhibits tumor growth and formation of new blood vessels in preclinical models. Our PAR−2 antagonist has also been shown to be an inhibitor of inflammation in preclinical models.

Multiple small molecule PAR−2 antagonists have been synthesized to identify compounds with increased activity, and we are currently studying PAR−2's potential therapeutic applications in oncology and inflammatory diseases. EntreMed exclusively owns all intellectual property associated with the PAR−2 antagonist program and its resulting compounds.

Tissue Factor Pathway Inhibitor (TFPI). TFPI is a naturally occurring anticoagulant protein that has been shown to inhibit tumor progression in preclinical models. We identified a peptide fragment of TFPI that blocks tumor growth and angiogenesis in animal models. In preclinical studies, the peptide does not affect normal blood clotting, a risk long associated with the development of coagulation inhibitors for oncology applications. In addition, we also identified the TFPI peptide's anti−angiogenic mechanism of action, which has now been shown to be independent of TFPI's anticoagulant activity. The TFPI peptide binds to a very low density lipoprotein receptor and induces apoptosis (cell death) in endothelial cells, the cells that form blood vessels.

We have used the peptide and its target as templates to design additional compounds with improved properties. The resulting new compounds will subsequently be screened for their therapeutic potential in oncology, as well as inflammatory diseases. We have entered into a research collaboration with Affymax, a leader in the discovery and development of novel peptide drugs, to identify lead drug candidates for the treatment of cancer.

EMPLOYEES

As of December 31, 2004, we had 35 full−time employees and one part−time employee. Twenty−six employees work in our research and development department. We may hire additional personnel in addition to utilizing part−time or temporary consultants on an as−needed basis. None of our employees are represented by a labor union, and we believe our relations with our employees are satisfactory.

RELATIONSHIPS – CORPORATE AND NON−PROFIT

Corporate Transactions.

- Celgene. In December 2002, we sold our thalidomide analog programs to Celgene. Prior in 1998, we licensed thalidomide to Celgene for angiogenesis−related uses only. The analog program was specifically excluded from the 1998 license agreement.

- Oxford BioMedica. In September 2003, we licensed the localized delivery of the Endostatin and Angiostatin genes for ophthalmology to Oxford BioMedica.

- Alchemgen Therapeutics, Inc. In February 2004, we transferred the licenses for Endostatin and Angiostatin to Alchemgen, who holds exclusive rights to develop, make and market Endostatin and Angiostatin in Asia.

- Children's Medical Center Corporation (CMCC). As part of our three−way agreement with Alchemgen Therapuetics, Inc. executed in February 2004, CMCC holds the licenses for Endostatin and Angiostatin for all markets outside of Asia.

- Affymax, Inc. In October 2004, we entered into a research collaboration with Affymax, Inc. to identify lead tissue factor pathway inhibitor (TFPI) drug candidates for the treatment of cancer.

Contract Manufacturing. The manufacturing efforts for the production of our clinical trial materials are performed by contract manufacturing organizations. Established relationships coupled with supply agreements have secured the necessary resources to ensure adequate supply of clinical materials to support our clinical development program. We believe that our current strategy of outsourcing manufacturing is cost−effective and allows for the flexibility we require.

2ME2 is currently bulk manufactured by Akzo Nobel and Panzem® NCD is currently manufactured by Elan Drug Delivery, Inc. We do not anticipate any challenges in securing contract manufacturing capacity at either of these facilities to produce Panzem® NCD.

Sponsored Research Agreements. To complement our in−house research and development efforts, we have entered into sponsored research agreements with outside scientists to conduct specific projects as outlined below. Under these agreements, we have secured the rights to intellectual property and to develop under exclusive license any discoveries resulting from these collaborations. The funds provided by us in accordance with these agreements partially support the scientists' laboratory, research personnel and research supplies.

Children's Hospital, Boston
2−year agreement effective November 1, 2003
"2ME2 Analog Program and Melanocyte Secreted Angiogenesis Inhibitor Program"

Emory University
1−year agreement effective October 1, 2004
"Investigation of the Molecular Mechanism of Antitumor and Antiangiogenic Effect of 2ME2 and 2ME2 Analogs"

Purdue University
1−year agreement effective June 1, 2004
"Design and Synthesis of 2ME2 Analogs"

Southwest Foundation for Biomedical Research
1−year agreement effective July 1, 2003
"Synthesis of 2ME2 Analogs"

University of Colorado Health Sciences Center
1−year agreement effective February 1, 2004
"*In vivo* Efficacy Studies of 2ME2 in Combination with Taxotere in Orthotopic Lung Tumors in Athymic Nude Rats"

European Institute of Oncology
1.5−year agreement effective February 1, 2004
"Preclinical Efficacy of Panzem in Lymphoma and Leukemia"

University of Maryland
1−year agreement effective November 1, 2004
"Aim #1: To determine if various VLDL receptor isoforms have different functional responses when incubated with TFPI and TFPIc23 and to establish a cell model system to explore the functional properties of the VLDL receptor."
"Aim #2: To confirm the involvement of the VLDL receptor in TFPI/TFPIc23 actively using genetic models in which the VLDL receptor gene has been deleted."

University of Paisley (United Kingdom)
3−year agreement ($30,000/year) to support post−doctoral fellow
"Evaluation of PAR−2 Antagonist"

Cooperative Research and Development Agreements (CRADAs). We extended one existing CRADA with the National Cancer Institute:

– Preclinical and Clinical Development of 2ME2 (Panzem®)" (Expires April 2005).

Clinical Trial Centers. As of March 10, 2005, we are conducting clinical trials at the following institutions:

– Dana−Farber Cancer Institute

– Indiana University Cancer Center

– Mayo Clinic

– Wisconsin Comprehensive Cancer Center

PATENTS, LICENSES AND PROPRIETARY RIGHTS

Our success will depend in part on our ability to obtain patent protection for our products, both in the United States and abroad. The patent position of biotechnology and pharmaceutical companies, in general, is highly uncertain and involves complex legal and factual questions.

Following the February 2004 transfer of the licenses for endostatin and angiostatin, we own or have licensed on an exclusive basis a total of 43 patent applications and issued patents in the United States for our product candidates. We have a total of 99 pending patent applications and issued patents in the United States and other countries.

We have exclusively licensed technology from Children's Hospital, Boston, which covers the use of steroid−derived small molecular weight compounds such as Panzem® that are antimitotic and antiangiogenic agents. A patent application has been filed covering purified Panzem® as a composition of matter. There are 6 pending United States patent applications and 11 allowed or issued United States patents covering this technology. Patent applications also cover estrogen−related compounds with anti−fungal activity and the treatment of localized atherosclerosis. The terms of the licenses for Panzem® extend until the underlying patents expire.

We own the technology associated with our 2ME2 analogs, PAR−2 inhibitors, TFPI peptides, NCEs for oncology and inflammation and the ENMD 0996 immunomodulator.

Many patent applications corresponding to the above−described United States patent applications have been filed in Europe, Japan, Canada, Australia, and other selected countries.

We have registered the trademarks ENTREMED, PANZEM® and THE ANGIOGENESIS COMPANY in the U.S. Patent and Trademark Office and have applied for registration of the marks in selected foreign countries.

GOVERNMENT REGULATION

Our development, manufacture, and potential sale of therapeutics are subject to extensive regulation by United States and foreign governmental authorities.

The Food and Drug Administration (FDA) will regulate our product candidates currently being developed as drugs or biologics. New drugs are subject to regulation under the Federal Food, Drug, and Cosmetic Act, and biological products, in addition to being subject to certain provisions of that Act, are regulated under the Public Health Service Act. We believe that drug products developed by us or our collaborators will be regulated either as biological products or as new drugs. Both applicable statutes and the regulations govern, among other things, the testing, manufacturing, safety, efficacy, labeling, storage, record keeping, advertising and other promotional practices involving biologics or new drugs, as the case may be. FDA clearances or approvals must be obtained before clinical testing, and before manufacturing and marketing of biologics or drugs.

Preparing drug candidates for approval has been historically a costly and time−consuming process. Generally, in order to gain FDA permission to test a new agent, a developer first must conduct preclinical studies in the laboratory and in animal model systems to gain preliminary information on an agent's effectiveness and to identify any safety problems. The results of these studies are submitted as a part of an investigational new drug (IND) application for a drug or biologic, which the FDA must review before human clinical trials of an investigational drug can begin. The IND includes a detailed description of the clinical investigations to be undertaken.

In order to commercialize any products, we or our collaborators must sponsor and file an IND and conduct clinical studies to demonstrate the safety and effectiveness necessary to obtain FDA approval of such products. For INDs sponsored by us or our collaborators, we or our collaborators will be required to select qualified investigators (usually physicians within medical institutions) to supervise the administration of the products, and ensure that the investigations are conducted and monitored in accordance with FDA regulations, including the general investigational plan and protocols contained in the IND.

Clinical trials of drugs or biologics are normally done in three phases, although the phases may overlap. Phase I trials for agents to be used to treat cancer patients are concerned primarily with the safety and preliminary effectiveness of the drug, involve a small group ranging from 15 − 40 subjects, and may take from six months to over one year to complete. Phase II trials normally involve 30 − 200 patients and are designed primarily to demonstrate effectiveness in treating or diagnosing the disease or condition for which the drug is intended, although short−term side effects and risks in people whose health is impaired may also be examined. Phase III trials are expanded clinical trials with larger numbers of patients which are intended to evaluate the overall benefit−risk relationship of the drug and to gather additional information for proper dosage and labeling of the drug. Phase III clinical trials generally take two to five years to complete, but may take longer. The FDA receives reports on the progress of each phase of clinical testing, and it may require the modification, suspension, or termination of clinical trials, if it concludes that an unwarranted risk is presented to patients, or, in Phase II and III, if it concludes that the study protocols are deficient in design to meet their stated objectives.

If clinical trials of a new product are completed successfully, the sponsor of the product may seek FDA marketing approval. If the product is classified as a new drug, an applicant must file a New Drug Application (NDA) with the FDA and receive approval before commercial marketing of the drug. If the product is regulated as a biologic, the FDA will require the submission and approval of a Biologics License Application (BLA) before commercial marketing of the biologic. The NDA or BLA must include detailed information about the product and its manufacture and the results of product development, preclinical studies and clinical trials.

The testing and approval processes require substantial time and effort and there can be no assurance that any approval will be obtained on a timely basis, if at all. Although it is the policy of the FDA to complete the review of the initial submission of BLAs and NDAs within six to twelve months, the entire FDA review process may take several years to receive approval. Notwithstanding the submission of relevant data, the FDA may ultimately decide that the BLA or NDA does not satisfy its regulatory criteria and deny the approval. Further, the FDA may require additional clinical studies before making a decision on approval. In addition, the FDA may condition marketing approval on the conduct of specific post−marketing studies to further evaluate safety and effectiveness. Even if FDA regulatory clearances are obtained, a marketed product is subject to continual regulatory requirements and review relating to GMP, adverse event reporting, promotion and advertising, and other matters. Discovery of previously unknown problems or failure to comply with the applicable regulatory requirements may result in restrictions on the marketing of a product or withdrawal of the product from the market, as well as possible civil or criminal sanctions.

Based on the current FDA organizational structure, Panzem®, its 2ME2 analogs, and other compounds in our small molecules programs are expected to be regulated as new chemical entities by the FDA's Center for Drug Evaluation and Research. Generally, as new chemical entities are discovered, formal IND−directed toxicology studies will be required prior to human testing.

COMPETITION

Competition in the pharmaceutical, biotechnology and biopharmaceutical industries is intense and based significantly on scientific and technological factors, the availability of patent and other protection for technology and products, the ability and length of time required to obtain governmental approval for testing, manufacturing and marketing and the ability to commercialize products in a timely fashion. Moreover, the biopharmaceutical industry is characterized by rapidly evolving technology that could result in the technological obsolescence of any products that we develop.

We compete with many specialized biopharmaceutical firms, as well as a growing number of large pharmaceutical companies that are applying biotechnology to their operations. Many biopharmaceutical companies have focused their development efforts in the human therapeutics area, and many major pharmaceutical companies have developed or acquired internal biotechnology capabilities or made commercial arrangements with other biopharmaceutical companies. These companies, as well as academic institutions, governmental agencies and private research organizations, also compete with us in recruiting and retaining highly qualified scientific personnel and consultants.

Our competition will be determined in part by the potential indications for which our product candidates may be developed and ultimately approved by regulatory authorities. We may rely on third parties to commercialize our products, and accordingly, the success of these products will depend in significant part on these third parties' efforts and ability to compete in these markets. The success of any collaboration will depend in part upon our collaborative partners' own competitive, marketing and strategic considerations, including the relative advantages of alternative products being developed and marketed by our collaborative partners and our competitors.

Many of our existing or potential competitors have substantially greater financial, technical and human resources than we do and may be better equipped to develop, manufacture and market products. In addition, many of these competitors have extensive experience in preclinical testing and human clinical trials and in obtaining regulatory approvals. The existence of competitive products, including products or treatments of which we are not aware, or products or treatments that may be developed in the future, may adversely affect the marketability of products that we may develop.

RISK FACTORS

We Have a History of Losses and Anticipate Future Losses

To date, we have been engaged primarily in research and development activities. Although we have received license fees and research and development funding from a former collaborator, limited revenues on royalties from sales of THALOMID® and certain research grants, we

have not derived significant revenues from operations.

At December 31, 2004, we had an accumulated deficit of approximately $245,434,600. Losses have continued since December 31, 2004. We will also be required to conduct substantial research and development and clinical testing activities for our proposed products. We expect that these activities will result in operating losses for the foreseeable future before we commercialize any products, if ever. In addition, to the extent we rely on others to develop and commercialize our products, our ability to achieve profitability will depend upon the success of these other parties. To support our research and development of certain product candidates, we also may rely on cooperative agreements from governmental and other organizations as a source of support. If our cooperative agreements were to be reduced to any substantial extent, it may impair our ability to continue our research and development efforts. Even if we do achieve profitability, we may be unable to sustain or increase it.

Development of Our Products is at an Early Stage and is Uncertain

Our proposed products and research programs are in the early stage of clinical development and require significant, time−consuming and costly research and development, testing and regulatory clearances. In developing our products, we are subject to risks of failure that are inherent in the development of products and therapeutic procedures. For example, it is possible that any or all of our proposed products will be ineffective or toxic, or otherwise will fail to receive necessary FDA clearances. There is a risk that the proposed products will be uneconomical to manufacture or market or will not achieve market acceptance. There is also a risk that third parties may hold proprietary rights that preclude us from marketing our proposed products or that others will market a superior or equivalent product. Further, our research and development activities might never result in commercially viable products.

Our product candidates are at the clinical and preclinical stages of development. Although several of our product candidates have demonstrated some success in early clinical (human) trials and preclinical (animal) studies, they may not prove to be effective in humans.

Testing on animals may occur under different conditions than testing in people. There are many regulatory steps that must be taken before any of these product candidates will be eligible for FDA approval and subsequent sale, including the completion of preclinical and clinical trials. We do not expect that these product candidates will be commercially available for several years, if ever.

We Are Uncertain Whether Additional Funding Will Be Available For Our Future Capital Needs and Commitments

We will require substantial funds in addition to our existing working capital to develop our product candidates and otherwise to meet our business objectives. We have never generated sufficient revenue during any period since our inception to cover our expenses and have spent, and expect to continue to spend, substantial funds to continue our research and development and clinical programs. Any one of the following factors, among others, could cause us to require additional funds or otherwise cause our cash requirements in the future to increase materially:

- results of research and development activities;
- progress of our preclinical studies or clinical trials;
- results of clinical trials;
- changes in or terminations of our relationships with strategic partners;
- changes in the focus, direction, or costs of our research and development programs;

- competitive and technological advances;
- establishment of marketing and sales capabilities;
- manufacturing;
- the regulatory approval process; or
- product launch.

We Must Show the Safety and Efficacy of Our Product Candidates Through Clinical Trials, the Results of Which Are Uncertain

Before obtaining regulatory approvals for the commercial sale of our products, we must demonstrate, through preclinical studies (animal testing) and clinical trials (human testing), that our proposed products are safe and effective for use in each target indication. Testing of our product candidates will be required, and failure can occur at any stage of testing. Clinical trials may not demonstrate sufficient safety and efficacy to obtain the required regulatory approvals or result in marketable products. The failure to adequately demonstrate the safety and efficacy of a product under development could delay or prevent regulatory approval of the potential product.

Clinical trials for the product candidates we are developing may be delayed by many factors, including that potential patients for testing are limited in number. The failure of any clinical trials to meet applicable regulatory standards could cause such trials to be delayed or terminated, which could further delay the commercialization of any of our product candidates. Any such delays will increase our product development costs. If such delays are significant, they could negatively affect our financial results and the commercial prospects for our products.

Panzem® NCD May Not be Successful

We have reformulated our lead product candidate, Panzem®, in order to increase its concentration in the blood stream. Through the use of NanoCrystal® Colloidal Dispersion (NCD), a proprietary technology of Elan Drug Delivery, Inc. ("Elan"), we have reformulated Panzem® as an orally−administered liquid suspension. In January 2005, we commenced Phase Ib studies using Panzem® NCD in patients with advanced cancer. Although Panzem® NCD showed increased levels in the blood in both preclinical models and in healthy humans in a Phase Ia clinical trial, it may not work as well in upcoming trials as it has in earlier testing.

We May Need New Collaborative Partners to Further Develop and Commercialize Products, and if We Enter Into Such Arrangements, We May Give Up Control Over the Development and Approval Process and Decrease Our Potential Revenue

We plan to develop and commercialize our product candidates with or without corporate alliances and partners. Nonetheless, we intend to explore opportunities for new corporate alliances and partners to help us develop, commercialize and market our product candidates. We expect to grant to our partners certain rights to commercialize any products developed under these agreements, and we may rely on our partners to conduct research and development efforts and clinical trials on, obtain regulatory approvals for, and manufacture and market any products licensed to them. Each individual partner will seek to control the amount and timing of resources devoted to these activities generally. We anticipate obtaining revenues from our strategic partners under such relationships in the form of research and development payments and payments upon achievement of certain milestones. Since we generally expect to obtain a royalty for sales or a percentage of profits of products licensed to third parties, our revenues may be less than if we retained all commercialization rights and marketed products directly. In addition, there is a risk that our corporate partners will pursue alternative technologies or develop competitive products as a means for developing treatments for the diseases targeted by our programs.

We may not be successful in establishing any collaborative arrangements. Even if we do establish such collaborations, we may not successfully commercialize any products under or derive any revenues from these arrangements. Our strategy also involves entering

into multiple, concurrent strategic alliances to pursue commercialization of our core technologies. There is a risk that we will be unable to manage simultaneous programs successfully. With respect to existing and potential future strategic alliances and collaborative arrangements, we will depend on the expertise and dedication of sufficient resources by these outside parties to develop, manufacture, or market products. If a strategic alliance or collaborative partner fails to develop or commercialize a product to which it has rights, we may not recognize any revenues on that particular product.

We Have No Current Manufacturing or Marketing Capacity and Rely on Only One Supplier For Some of Our Products

We do not expect to manufacture or market products in the near term, but we may try to do so in certain cases. We do not currently have the capacity to manufacture or market products and we have limited experience in these activities. If we elect to perform these functions, we will be required to either develop these capacities, or contract with others to perform some or all of these tasks. We may be dependent to a significant extent on corporate partners, licensees, or other entities for manufacturing and marketing of products. If we engage directly in manufacturing or marketing, we will require substantial additional funds and personnel and will be required to comply with extensive regulations. We may be unable to develop or contract for these capacities when required to do so in connection with our business.

We are currently manufacturing products for clinical trials on a contract basis. Panzem® NCD, our lead small molecule clinical drug candidate, is currently manufactured by Elan. We do not have arrangements in place with alternative suppliers if our current supplier Elan was unable to deliver the product in necessary quantities.

We depend on our third−party manufacturers to perform their obligations effectively and on a timely basis. These third parties may not meet their obligations and any such non−performance may delay clinical development or submission of products for regulatory approval, or otherwise impair our competitive position. Any significant problem experienced by one of our suppliers could result in a delay or interruption in the supply of materials to us until such supplier resolves the problem or an alternative source of supply is located. Any delay or interruption would likely lead to a delay or interruption of manufacturing operations, which could negatively affect our operations. Although we have identified alternative suppliers for our product candidates, we have not entered into contractual or other arrangements with them. If we needed to use an alternate supplier for any product, we would experience delays while we negotiated an agreement with them for the manufacture of such product. In addition, we may be unable to negotiate manufacturing terms with a new supplier that are as favorable as the terms we have with our current suppliers.

Problems with any manufacturing processes could result in product defects, which could require us to delay shipment of products or recall products previously shipped. In addition, any prolonged interruption in the operations of the manufacturing facilities of one of our sole−source suppliers could result in the cancellation of shipments. A number of factors could cause interruptions, including equipment malfunctions or failures, or damage to a facility due to natural disasters or otherwise. Because our manufacturing processes are or are expected to be highly complex and subject to a lengthy FDA approval process, alternative qualified production capacity may not be available on a timely basis or at all. Difficulties or delays in our manufacturing could increase our costs and damage our reputation.

The manufacture of pharmaceutical products can be an expensive, time consuming, and complex process. Manufacturers often encounter difficulties in scaling−up production of new products, including quality control and assurance and shortages of personnel. Delays in formulation and scale−up to commercial quantities could result in additional expense and delays in our clinical trials, regulatory submissions, and commercialization.

Failure of Manufacturing Facilities Producing Our Product Candidates to Maintain Regulatory Approval Could Delay or Otherwise Hinder Our Ability to Market Our Product Candidates

Any manufacturer of our product candidates will be subject to applicable Good Manufacturing Practices (GMP) prescribed by the FDA or other rules and regulations prescribed by foreign regulatory authorities. We and any of our collaborators may be unable to enter into or maintain relationships either domestically or abroad with manufacturers whose facilities and procedures comply or will continue to comply with GMP and who are able to

produce our small molecules. Failure by a manufacturer of our products to comply with GMP could result in significant time delays or our inability to obtain marketing approval or, should we have market approval, for such approval to continue. Changes in our manufacturers could require new product testing and facility compliance inspections. In the United States, failure to comply with GMP or other applicable legal requirements can lead to federal seizure of violated products, injunctive actions brought by the federal government, and potential criminal and civil liability on the part of a company and its officers and employees.

Manufacturing Our Product Candidates May Not Be Commercially Feasible

The manufacturing processes for several of the small molecules we are developing have not yet been tested at commercial levels, and it may not be possible to manufacture these materials in a cost−effective manner.

We Depend on Patents and Other Proprietary Rights, Some of Which are Uncertain

Our success will depend in part on our ability to obtain patents for our products, both in the United States and abroad. The patent position of biotechnology and pharmaceutical companies in general is highly uncertain and involves complex legal and factual questions. Risks that relate to patenting our products include the following:

- our failure to obtain additional patents;
- challenge, invalidation, or circumvention of patents already issued to us;
- failure of the rights granted under our patents to provide sufficient protection;
- independent development of similar products by third parties; or
- ability of third parties to design around patents issued to our collaborators or us.

For several of the products that we are developing, including Panzem®, composition of matter patents are not available because the compounds are in the public domain. In these cases, only patents covering the “use” of the product are available. In general, patents covering a new use for a known compound can be more difficult to enforce against infringers of the use claims in the patent.

Our potential products may conflict with patents that have been or may be granted to competitors, universities or others. As the biotechnology industry expands and more patents are issued, the risk increases that our potential products may give rise to claims that may infringe the patents of others. Such other persons could bring legal actions against us claiming damages and seeking to enjoin clinical testing, manufacturing and marketing of the affected products. Any such litigation could result in substantial cost to us and diversion of effort by our management and technical personnel. If any of these actions are successful, in addition to any potential liability for damages, we could be required to obtain a license in order to continue to manufacture or market the affected products. We may not prevail in any action and any license required under any needed patent might not be made available on acceptable terms, if at all.

We are a party to sponsored research agreements and license agreements that require us to make milestone payments upon attainment of certain regulatory milestones. Failure to meet such milestones could result in the loss of certain rights to compounds covered under such license agreements.

We also rely on trade secret protection for our confidential and proprietary information. However, trade secrets are difficult to protect and others may independently develop substantially equivalent proprietary information and techniques and gain access to our trade secrets and disclose our technology. We may be unable to meaningfully protect our rights to unpatented trade secrets. We require our employees to complete confidentiality training that specifically addresses trade secrets. All employees, consultants, and advisors are required to execute a confidentiality agreement when beginning an employment or a consulting relationship with us. The agreements generally provide that all trade secrets and inventions conceived by the individual and all confidential information developed or made known to the individual during the

term of the relationship automatically become our exclusive property. Employees and consultants must keep such information confidential and may not disclose such information to third parties except in specified circumstances. However, these agreements may not provide meaningful protection for our proprietary information in the event of unauthorized use or disclosure of such information.

To the extent that consultants, key employees, or other third parties apply technological information independently developed by them or by others to our proposed projects, disputes may arise as to the proprietary rights to such information. Any such disputes may not be resolved in our favor. Certain of our consultants are employed by or have consulting agreements with other companies and any inventions discovered by them generally will not become our property.

Our Potential Products Are Subject to Government Regulatory Requirements and an Extensive Approval Process

Our research, development, preclinical and clinical trials, manufacturing, and marketing of most of our product candidates are subject to an extensive regulatory approval process by the FDA and other regulatory agencies in the United States and abroad. The process of obtaining FDA and other required regulatory approvals for drug and biologic products, including required preclinical and clinical testing, is time consuming and expensive. Even after spending time and money, we may not receive regulatory approvals for clinical testing or for the manufacturing or marketing of any products. Our collaborators or we may encounter significant delays or costs in the effort to secure necessary approvals or licenses. Even if we obtain regulatory clearance for a product, that product will be subject to continual review. Later discovery of previously unknown defects or failure to comply with the applicable regulatory requirements may result in restrictions on a product's marketing or withdrawal of the product from the market, as well as possible civil or criminal penalties.

Potential Products May Subject Us to Product Liability for Which Insurance May Not Be Available

The use of our potential products in clinical trials and the marketing of any pharmaceutical products may expose us to product liability claims. We have obtained a level of liability insurance coverage that we believe is adequate in scope and coverage for our current stage of development. However, our present insurance coverage may not be adequate to protect us from liabilities we might incur. In addition, our existing coverage will not be adequate as we further develop products, and in the future adequate insurance coverage and indemnification by collaborative partners may not be available in sufficient amounts or at a reasonable cost. If a product liability claim or series of claims are brought against us for uninsured liabilities, or in excess of our insurance coverage, the payment of such liabilities could have a negative effect on our business and financial condition.

AVAILABLE INFORMATION

Through our website at www.entremed.com, we make available, free of charge, our filings with the Securities and Exchange Commission ("SEC"), including our annual proxy statements, annual reports on Form 10−K, quarterly reports on Form 10−Q and current reports on Form 8−K, and all amendments thereto, as soon as reasonably practicable after such reports are filed with or furnished to the Securities and Exchange Commission.

ITEM 2. PROPERTIES

We currently lease approximately 46,000 square feet of space (approximately 32,000 square feet of which is laboratory space) in Rockville, Maryland. The lease expires in February 2009. We believe that our existing facilities will be adequate to accommodate the implementation of our current business plan.

ITEM 3. LEGAL PROCEEDINGS

EntreMed is subject in the normal course of business to various legal proceedings in which claims for monetary or other damages may be asserted. Management does not believe such legal proceedings, except as otherwise disclosed herein, are material.

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

None.

PART II

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

Our common stock began trading publicly on the Nasdaq National Market under the symbol "ENMD" on June 12, 1996. The following table sets forth the high and low closing price for our common stock by quarter, as reported by the Nasdaq National Market, for the periods indicated:

	HIGH	LOW
2003:		
First Quarter	$ 1.49	$ 0.96
Second Quarter	6.53	0.98
Third Quarter	5.77	3.00
Fourth Quarter	5.93	3.18
2004:		
First Quarter	$ 4.37	$ 3.09
Second Quarter	4.01	2.01
Third Quarter	2.08	1.28
Fourth Quarter	3.43	1.75
2005:		
First Quarter (through March 10, 2005)	$ 4.64	$ 2.41

On March 10, 2005, the closing price of our common stock, as reported by the Nasdaq National Market, was $2.41 per share. As of March 10, 2005 there were approximately 886 holders of record of our common stock.

Since our initial public offering in 1996, we have not paid cash dividends on our common stock. We currently anticipate that any earnings will be retained for the continued development of our business and we do not anticipate paying any cash dividends on our common stock in the foreseeable future.

ITEM 6. SELECTED FINANCIAL DATA

The following selected consolidated financial data set forth below has been derived from our audited consolidated financial statements. The data should be read in conjunction with the consolidated financial statements and related notes, Management's Discussion and Analysis of Financial Condition and Results of Operations in Item 7 and other financial information included elsewhere in this annual report on Form 10−K.

	Year Ended December 31,				
	2004	2003	2002	2001	2000
STATEMENTS OF OPERATIONS DATA:					
Revenues					
Collaborative research and development	$ —	$ 667,796	$ 835,493	$ —	$ —
License fees	495,496	310,496	115,496	—	—
Grant revenues	—	508,243	131,681	358,427	401,477
Royalty revenues	5,918	2,705	38,790	1,440,070	3,117,282
Other	12,581	86,306	55,030	63,444	153,016
Total revenues	513,995	1,575,546	1,176,490	1,861,941	3,671,775
Expenses:					
Research and development	10,523,252	14,252,196	31,308,427	54,201,179	42,743,798
General and administrative	6,570,664	7,022,986	13,932,133	14,473,012	11,645,651
Interest expense	—	—	390,941	344,969	241,451
Investment income	(313,940)	(205,580)	(317,910)	(1,437,966)	(2,164,748)
Gain on discharge of liabilities	—	—	(2,174,765)	—	—
Gain on sale of asset	(124,083)	—	(2,940,184)	—	—
Gain on sale of securities	(520,000)	—	—	—	—
Gain on sale of royalty interest	(3,000,000)	—	—	(22,410,182)	—
Net loss	$(12,621,898)	$(19,494,056)	$(39,022,152)	$(43,309,071)	$(48,794,377)
Dividends on Series A convertible preferred stock	(1,005,000)	(1,005,000)	—	—	—
Net loss attributable to common shareholders	$(13,626,898)	$(20,499,056)	$(39,022,152)	$(43,309,071)	$(48,794,377)
Net loss per share	$ (0.37)	$ (0.68)	$ (1.78)	$ (2.39)	$ (3.04)
Weighted average number of shares outstanding	37,170,544	29,943,161	21,892,520	18,093,174	16,057,047

	As of December 31,				
	2004	2003	2002	2001	2000
BALANCE SHEET DATA:					
Cash and cash equivalents and short−term investments	$ 34,539,516	$ 36,941,430	$ 24,067,045	$ 41,386,300	$ 24,503,886
Working capital	34,979,936	33,405,818	7,716,002	21,257,950	15,129,183
Total assets	39,404,002	40,153,764	27,810,212	46,218,450	31,410,412
Deferred revenue, less current portion	95,496	192,993	286,488	—	—
Accumulated deficit	(245,434,572)	(232,812,674)	(213,318,618)	(174,296,466)	(130,987,395)
Total stockholders' equity	35,704,754	34,858,883	10,493,646	23,194,898	19,039,945

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

The following discussion should be read in conjunction with the Consolidated Financial Statements and Notes thereto appearing elsewhere in this report. See "Risk Factors".

OVERVIEW

Since our inception in September 1991, we have devoted substantially all of our efforts and resources to sponsoring and conducting research and development on our own behalf and through collaborations. Through December 31, 2004, all of our revenues have been generated from license fees, research and development funding, royalty payments, the sale of royalty rights and certain research grants; we have not generated any revenue from direct product sales. We anticipate our primary revenue sources for the next few years will include research grants, royalties and collaboration payments under current or future arrangements. The timing and amounts of such revenues, if any, will likely fluctuate and depend upon the achievement of specified research and development milestones. Results of operations for any period may be unrelated to the results of operations for any other period.

Historically our research and development efforts have been focused on the identification and development of new compounds for the treatment of certain diseases utilizing our understanding of the interrelationships of angiogenesis, cell cycle regulation, and inflammation – processes vital to the treatment of multiple diseases, including cancer. In 2004, our main focus was on the reformulation of 2ME2, our lead drug candidate Panzem®, which has been administered in capsule form to oncology patients in Phase I and Phase II trials. The goal of our reformulation effort was to increase the level of Panzem® in the patient's bloodstream. Based on preclinical findings and data from healthy human subjects, we have selected a new Panzem® formulation that is a liquid suspension approach that we believe will increase the Panzem® bloodstream levels in oncology patients. In July 2004, we announced that we entered into a Clinical Supply Agreement with Elan to produce reformulated Panzem®. We refer to the liquid product format as Panzem®NCD, and in January 2005 we initiated phase 1b clinical trials with this new Panzem® formulation at two sites.

In addition to our work with Panzem®, we are evaluating various analogs of 2ME2 in preclinical studies. One of these compounds, ENMD 1198, has progressed into IND−directed development with the goal of entering clinical trials in oncology. We have three additional programs with compounds in various stages of discovery and preclinical research. Our expenses will exceed our revenues as we continue the development of Panzem® and bring our other drug candidates through preclinical research to clinical trials.

With Panzem®NCD in clinical trials and other pipeline candidates moving towards IND, we are progressing from a fundamentally research organization to that of a product development and commercialization organization. We have already begun de−emphasizing early discovery activities and we reduced certain operating expenses in order to devote more resources to key preclinical development activities. We also will seek product acquisitions, co−development alliances and in−licensing opportunities to attempt to build a broader portfolio of late preclinical and clinical product candidates.

CRITICAL ACCOUNTING POLICIES AND THE USE OF ESTIMATES

The preparation of our financial statements in conformity with accounting principles generally accepted in the U.S. requires management to make estimates and assumptions that affect the amounts reported in our consolidated financial statements and accompanying notes. Actual results could differ materially from those estimates. Our critical accounting policies, including the items in our financial statements requiring significant estimates and judgments, are as follows:

Grant Revenue – In 2002 the Company received a government grant for the development of potential malaria vaccines. In 2003 we received a government grant to support financially our Phase II Endostatin clinical trial in patients with neuroendocrine tumors.

Grants are funded in specific amounts based on funding requests submitted to the grantor. Grant revenues are recognized and realized at the time that research and development activities are performed.

Collaborative Research Revenue – In 2002 and 2003 the Company received revenues for performance under commercial research and development contracts. These contracts require that the Company provide services directed toward specific objectives and include developmental milestones and deliverables. These revenues are recognized at the time that research and development activities are performed.

Licensing Revenue – The Company recognizes licensing revenues resulting from the January 2002 five−year strategic alliance with Allergan, to develop and commercialize small molecule angiogenic inhibitors for treatment and prevention of diseases and conditions of the eye. The initial net fee is amortized to income over the five−year license term. In September 2003 the Company entered into a licensing agreement with Oxford Biomedica, PLC and Oxford Biomedica (UK) Limited for the use of endostatin and angiostatin genes in the development of locally delivered gene therapy for ophthalmologic applications. Under the agreement, the Company had no continuing obligations. As such, we recorded as revenue the value of the initial net cash and shares of common stock received under the agreement. In February 2004 the Company transferred rights to the proteins, endostatin and angiostatin, in an agreement with Children's Medical Center Corporation and Alchemgen Therapeutics. Under the agreement, Alchemgen received rights to market endostatin and angiostatin in Asia. In exchange, the Company receives upfront and future cash payments and royalties. The upfront cash payment was fully amortized in 2004, as the Company has completed its obligations to transfer data and material.

Research and Development — Research and development expenses consist primarily of compensation and other expenses related to research and development personnel, research collaborations, costs associated with pre−clinical testing and clinical trials of our product candidates, including the costs of manufacturing the product candidates, and facilities expenses. Research and development costs are expensed as incurred.

Stock−Based Compensation — We have stock option plans under which options to purchase shares of our common stock may be granted to employees, consultants and directors at a price no less than the fair market value on the date of grant. We account for our stock−based compensation in accordance with the provisions of APB No. 25, *Accounting for Stock Issued to Employees* ("APB No. 25"). Under APB No. 25, compensation expense is based on the difference, if any, on the date of the grant between the fair value of the Company's stock and the exercise price of the option and is recognized ratably over the vesting period of the option. Because our options must be granted at fair market value, we recognize no compensation expense in accordance with APB No. 25. If we were to adopt SFAS No. 123, *Accounting for Stock−Based Compensation* ("SFAS No. 123"), we would recognize compensation expense based upon the fair value at the grant date for awards under the plans using the fair value method. The Company currently expects to adopt SFAS No. 123R in the quarter ended September 30, 2005, using the modified prospective method, although the Company continues to review its options for adoption under this new pronouncement. We expense equity instruments issued to nonemployees in accordance with SFAS No. 123 and EITF 96−18, *Accounting for Equity Instruments that are issued to other than employees for acquiring, or in conjunction with selling goods or services*.

RESULTS OF OPERATIONS

Years Ended December 31, 2004, 2003 and 2002.

Revenues. Revenues decreased 67% in 2004 to $514,000 from $1,576,000 in 2003 after increasing 34% in 2003 from $1,176,000 in 2002. These variations resulted from changes in collaborative research and development revenues, grant revenues, and licensing revenues. Collaborative research and development revenues, resulting primarily from work performed on commercial research and development contracts, decreased to $668,000 in 2003 from $835,000 in 2002. Collaborative research and development revenues in 2002 and 2003 primarily represent work under a NIH sponsored contract, which was completed in 2003. We did not receive collaborative research and development revenues in 2004. We also did not recognize grant revenue in 2004. We recognized grant revenues of $508,000 in 2003 compared to $132,000 in 2002. 2003 grant revenues represent a grant, sponsored by the FDA, which provided financial support for our Phase II Endostatin clinical trial in patients with neuroendocrine tumors.

2002 grant revenues were funds received from a Small Business Innovative Research, or SBIR, program of the National Institutes of Health. Licensing revenues increased to $495,000 in 2004 from $310,000 in 2003. The 2003 amount was an increase from $115,000 in 2002. The 2004 increase is attributable to the recognition of amortized licensing revenues from a February 2004 agreement with Alchemgen in addition to the revenues from the January 2002 five−year strategic alliance with Allergan. The 2003 licensing revenue was comprised of the amortization of the upfront licensing fee from Allergan coupled with recognition of the value of cash and stock received from Oxford Biomedica as revenue.

Research and Development Expenses. At December 31, 2004, accumulated direct project expenses for Panzem®, our lead drug candidate, totaled $27,851,000. Reflected in our 2004 R&D expenses totaling $10,523,000 are direct project expenses for Panzem® of $3,708,000 and $2,135,000 related to our 2ME2 analog program

Also reflected in our 2004 R&D expenses are project costs of $341,000 related to the Endostatin and Angiostatin compounds, programs that have been discontinued and will not be funded in the future. Pursuant to the February 2004 Alchemgen licensing agreement, we are no longer responsible for the further development of these two compounds. The balance of our R&D expenditures includes facilities costs and other departmental overhead, and expenditures related to the advancement of our pre−clinical pipeline.

Research and Development expenses for 2003 totaled $14,252,000, including direct project costs for Panzem®, Endostatin and Angiostatin of $6,328,000, $1,107,000 and $808,000, respectively. The higher costs recorded for Panzem® reflect reformulation activities including material acquisition, animal testing and sample analysis. The significant decrease in overall research and development spending in 2004 and 2003 reflect the Company's shift in focus to small molecules and the resulting dramatic decrease in costs associated with Endostatin and Angiostatin. Research and Development expenses were $31,308,000 in 2002. The 2002 amount includes project costs for Panzem®, Endostatin and Angiostatin of $3,150,000, $8,949,000 and $4,839,000, respectively.

The expenditures that will be necessary to execute our business plan are subject to numerous uncertainties, which may adversely affect our liquidity and capital resources. As of December 31, 2004, our proprietary product candidate, Panzem®, is in Phase I and Phase II clinical trials. Completion of clinical trials may take several years or more, but the length of time generally varies substantially according to the type, complexity, novelty and intended use of a product candidate.

We estimate that clinical trials of the type we generally conduct are typically completed over the following timelines:

CLINICAL PHASE	ESTIMATED COMPLETION PERIOD
Phase I	1 Year
Phase II	1−2 Years
Phase III	2−4 Years

The duration and the cost of clinical trials may vary significantly over the life of a project as a result of differences arising during the clinical trial protocol, including, among others, the following:

- the number of patients that ultimately participate in the trial;
- the duration of patient follow−up that seems appropriate in view of the results;
- the number of clinical sites included in the trials; and
- the length of time required to enroll suitable patient subjects.

We test our potential product candidates in numerous pre−clinical studies to identify indications for which they may be product candidates. We may conduct multiple clinical trials to cover a variety of indications for each product candidate. As we obtain results from trials, we may

elect to discontinue clinical trials for certain product candidates or for certain indications in order to focus our resources on more promising product candidates or indications.

Our proprietary product candidates also have not yet achieved FDA regulatory approval, which is required before we can market them as therapeutic products. In order to proceed to subsequent clinical trial stages and to ultimately achieve regulatory approval, the FDA must conclude that our clinical data establish safety and efficacy. Historically, the results from pre−clinical testing and early clinical trials have often not been predictive of results obtained in later clinical trials. A number of new drugs and biologics have shown promising results in clinical trials, but subsequently failed to establish sufficient safety and efficacy data to obtain necessary regulatory approvals.

An important element of our business strategy is to pursue the research and development of a range of product candidates for a variety of oncology and non−oncology indications. This allows us to diversify the risks associated with our research and development expenditures. As a result, we intend to pursue development of our existing product candidates internally or through development partnerships, as well as through the acquisition and subsequent development of promising candidates. The goal is to align our future capital requirements with multiple product candidates and to increase the likelihood that our future financial success is not substantially dependent on any one product candidate. To the extent we are unable to maintain a broad range of product candidates, our dependence on the success of one or a few product candidates would increase.

Furthermore, our business strategy includes the option of entering into collaborative arrangements with third parties to complete the development and commercialization of our products. In the event that third parties take over the clinical trial process for one of our product candidates, the estimated completion date would largely be under the control of that third party rather than us. We cannot forecast with any degree of certainty which proprietary products or indications, if any, will be subject to future collaborative arrangements, in whole or in part, and how such arrangements would affect our capital requirements.

As a result of the uncertainties discussed above, among others, we are unable to estimate the duration and completion costs of our research and development projects. Our inability to complete our research and development projects in a timely manner or our failure to enter into collaborative agreements, when appropriate, could significantly increase our capital requirements and could adversely impact our liquidity. These uncertainties could force us to seek additional, external sources of financing from time to time in order to continue with our business strategy. Our inability to raise additional capital, or to do so on terms reasonably acceptable to us, would jeopardize the future success of our business.

Research and development expenses consist primarily of compensation and other expenses related to research and development personnel, research collaborations, costs associated with internal and contract pre−clinical testing and clinical trials of our product candidates, including the costs of manufacturing the product candidates, and facilities expenses. Our 2004 research and development expenses reflect continuing preclinical costs and the cost of a Phase I clinical trial to test various dosing approaches for reformulated Panzem®. The 2004 amount also includes increased costs associated with further development of various drug candidates, including analogs of 2ME2. These expenses, however, were offset by decreased expenditures for Endostatin and Angiostatin versus the corresponding 2003 and 2002 periods. Overall research and development expenses decreased to approximately $10,523,000 in 2004 from $14,252,000 in 2003 and from $31,308,000 in 2002. The significant decreases in overall research and development spending in 2004 and 2003 reflect the Company’s shift in focus to small molecules, including Panzem®, and the resulting dramatic decrease in costs associated with Endostatin and Angiostatin. The decrease in R&D expenses reflected in 2004 and 2003 was specifically impacted by the following:

- Outside Services – We utilize outsourcing to conduct our product development activities. Larger−scale small molecule synthesis, in vivo testing and data analysis are examples of the services that we outsource. We expended $1,741,000 in 2004, $2,357,000 in 2003 and $1,080,000 in 2002 on these activities. The higher 2003 expenses reflect our focus on reformulating Panzem® while our 2004 efforts have been directed towards optimizing Panzem®NCD and selecting a lead 2ME2 analog candidate. The 2002 outside service costs relate primarily to our thalidomide analog, ENMD 0995 which was sold to Celgene in 2002.

- Collaborative Research Agreements— We made payments to our collaborators of $622,000, $170,000 and $3,426,000 in years 2004, 2003 and 2002, respectively. Sponsored research payments to academic collaborators include payments to Children's Hospital of $300,000 in 2004, $75,000 in 2003, and $1,000,000 in 2002. Our 2004 collaborative efforts are primarily directed towards further exploration of Panzem® mechanism−of−action (MOA), in−vivo testing of therapeutic combination studies, and non−oncology applications. In 2002 the majority of our collaborative efforts were focused on Angiostatin and Endostatin.

- Clinical Trial Costs— Clinical costs decreased from $1,432,000 in 2003 to $1,008,000 in 2004. The decrease reflects less overall clinical activity as we secured reformulated Panzem® liquid clinical material for use in clinical trials that began in January 2005. We continue to maintain the ongoing trials using the solid dosage format including the supply of clinical material under our Collaborative Research and Development Agreement (CRADA) with the NCI. The 2004 decrease also reflects that we are no longer responsible for supporting the Endostatin and Angiostatin trials as a result of the February 2004 licensing agreement with Alchemgen. Clinical costs decreased from $3,085,000 in 2002 to $1,432,000 in 2003. The 2003 decrease reflects the shift in focus to small molecules and the resulting changes in the clinical programs for Endostatin and Angiostatin. As of December 31, 2003, we had ongoing clinical trials for all three drug candidates although we did not initiate any new clinical trials in 2003 as a result of our Panzem® reformulation efforts. In 2002 we initiated a phase I clinical trial for a fourth drug candidate ENMD 0995, a thalidomide analog. Rights to this program were transferred to Celgene as part of the December 31, 2002 transaction. Costs of Company−sponsored clinical trials include clinical investigator site fees, monitoring costs and data management costs. Contracted regulatory support costs primarily represent costs associated with IND preparation and maintenance. These costs were $21,000, $62,000 and $682,000 in 2004, 2003 and 2002, respectively. The decreases in 2003 and 2004 result from significantly less clinical activity. The 2002 costs reflect the preparation and filing of an IND for the Thalidomide analog program which was sold to Celgene in 2002.

- Contract Manufacturing Costs— The costs of manufacturing the material used in clinical trials for our product candidates is reflected in contract manufacturing. These costs include bulk manufacturing, encapsulation and fill finish services and product release costs. Contract manufacturing costs decreased significantly in 2004 to $1,392,000. The 2004 costs reflect expenditures for the preparation of Panzem®NCD for preclinical and clinical use and encapsulation runs for the tablet form to support our phase II and NCI clinical trials. Product manufacturing costs were $3,012,000 and $8,717,000 in 2003 and 2002, respectively. The 2003 costs include the acquisition of 105kg of bulk material and multiple encapsulation runs for the tablet form of Panzem®. Additionally, these amounts included $6,000 in 2003 and $7,946,000 in 2002 relating to the manufacture of Angiostatin and Endostatin.

- Personnel Costs— The 2004 personnel costs were approximately $3,000,000. Personnel costs were $3,151,000 in 2003 down from $7,830,000 in 2002. The 2002 amount includes $700,000 in severance obligations resulting from the refocus of our scientific efforts in 2002 and the elimination of some research and development programs and the associated staff reductions.

Also reflected in our 2004 research and development expenses are patent costs of $492,000 and facility and related expenses of $1,551,000. In 2003, these expenses totaled $916,000 and $1,736,000, respectively, and in 2002, these expenses totaled $1,574,000 and $1,912,000, respectively. The 2003 decrease in patent costs results from the Company's shift in focus to small molecules, which resulted in the elimination of some programs including the associated patent costs. The 2004 decrease reflects the transfer of responsibility for Endostatin and Angiostatin patent costs.

General and Administrative Expenses. General and administrative expenses include compensation and other expenses related to finance, business development and administrative personnel, professional services and facilities.

General and administrative expenses decreased to approximately $6,571,000 in 2004 from $7,023,000 in 2003 and $13,932,000 in 2002.

The 2004 decrease results primarily from reduced personnel costs and lower severance obligations related to top management changes than that recorded in 2003. These decreases were in part offset by an increase in accounting fees related to compliance with the Sarbanes−Oxley Act of 2002. The dramatic 2003 decrease reflects the Company's late 2002 shift in focus and the resulting staff reductions. Also contributing to the decrease was the absence of legal fees associated with the Abbott and Celgene litigations, and charges incurred in 2002 of $1,995,000 related to the potential repurchase of our common stock from Bristol−Myers Squibb and the related guaranteed minimum purchase price. The Abbott and Celgene litigations were settled and the terms of the Bristol−Myers Squibb repurchase agreement were renegotiated in 2002.

Interest expense. The Company had no interest−bearing debt during 2004 and 2003. The 2002 amount results primarily from the accrual of interest relating to MaxCyte's issuance of convertible promissory notes.

Investment income. Investment income increased by 52% in 2004 to $313,000 as a result of higher yields on interest bearing cash accounts and investments. Investment income was $206,000 in 2003, a decrease of 35% from $318,000 in 2002.

Dividends on Series A convertible preferred stock. The Consolidated Statements of Operations for the years ended December 31, 2004 and December 31, 2003 reflect dividends of $1,005,000 relating to Series A Convertible Preferred Stock held by Celgene pursuant to a Securities Purchase Agreement dated December 31, 2002. The holders of Series A Preferred Stock will accumulate dividends at a rate of 6% and will participate in dividends declared and paid on the common stock, if any. All accumulated dividends must be paid before any dividends may be declared or paid on the Common Stock. The Company has no plans to pay any dividends in the foreseeable future.

Gain on sale of asset. The Consolidated Statement of Operations for the year ended December 31, 2002 reflects a gain of $2,940,000 resulting from a purchase agreement by and between Celgene and the Company. Celgene purchased our right, title and interest in a licensing agreement with Children's Hospital and certain other property described as the thalidomide analog program. The gain on the transaction is reflected net of transaction fees and other costs, including cash payments and warrants issued to Children's Hospital.

Gain on the discharge of liabilities. The Consolidated Statement of Operations for the year ended December 31, 2002 also reflects a gain of $2,175,000 resulting from the renegotiation and settlement of $8,086,000 of the Company's current liabilities. The terms of the settlement agreements, reached with five creditors, including Bristol−Myers Squibb, required the use of cash, stock and warrants to satisfy the renegotiated obligations.

Gain on sale of securities. The Consolidated Statement of Operations for the year ended December 31, 2004 reflects a gain of $520,000 resulting from the sale of certain securities of an independent private biotechnology company. The securities were acquired in 1996 through 1999 and accounted for using the equity method. The cost of these securities was written off in prior periods and we had no residual cost basis in the securities when sold. As such, we have recorded a gain on the sale equal to the sale proceeds.

Gain on sale of royalty interest. The Consolidated Statement of Operations for the year ended December 31, 2004 reflects a gain of $3,000,000 which represents a one−time purchase price adjustment pursuant to a purchase agreement dated August 6, 2001 by and between Bioventure Investments kft ("Bioventure") and the Company. The adjustment was triggered by $800,000,000 in cumulative Thalidomide sales through December 31, 2004.

LIQUIDITY AND CAPITAL RESOURCES

To date, we have been engaged primarily in research and development activities. As a result, we have incurred and expect to continue to incur operating losses for 2005 and the foreseeable future before we commercialize any products. In addition, under the terms of the license agreement for 2ME2, we must be diligent in bringing potential products to market and may be required to make future milestone payments of up to $850,000. If we fail to comply with the milestones or fail to make any required sponsored research or milestone payment, we could face the termination of the relevant sponsored research or license agreements.

At December 31, 2004, we had cash and short−term investments of approximately $34,539,516 with working capital of approximately $34,979,936, reflecting a financing transaction that resulted in net proceeds of approximately $13,300,000, completed in December 2004.

We invest our capital resources with the primary objective of capital preservation. As a result of trends in interest rates in 2004, we have invested in some securities with maturity dates of more than 90 days to enhance our investment yields. As such, some of our invested balances are classified as short−term investments rather than cash equivalents in our consolidated financial statements at December 31, 2004.

To accomplish our business plans, we will be required to continue to conduct substantial development activities for some or all of our proposed products. Under our current operating plans, results of operations are expected to reflect a net loss of approximately $20,000,000 in 2005. We expect that the majority of our 2005 revenues will be from royalties on the sale of Thalomid®. Pursuant to the satisfaction of certain provisions of a purchase agreement dated June 14, 2001 by and between Bioventure Investments kft ("Bioventure") and the Company, beginning in 2005 we are entitled to share in the royalty payments received by Royalty Pharma Finance Trust, successor to Bioventure, on annual Thalomid® sales above a certain threshold. Based on the licensing agreement royalty formula, this annual royalty sharing point equates to Thalomid® annual sales of approximately $235 million. Pursuant to public guidance provided by Celgene for Thalomid® sales in 2005, we expect to record royalty sharing revenues in excess of $4.0 million in 2005. Under our licensing agreement with Oxford Biomedica, PLC and Oxford Biomedica (UK) Limited Oxford, we are entitled to receive payments upon the achievement of certain milestones. We do not control the drug development efforts of Oxford and have no control over when or whether such milestones will be reached. We do not believe that we will receive any developmental milestone payments under these agreements in 2005.

Based on our assessment of our current capital resources coupled with anticipated inflows, in the absence of additional financing, we believe that we will have adequate resources to fund planned operations into 2006. Our estimate may change, however, based on our decisions with respect to future clinical trials related to Panzem®, the timing of receipt of milestone payments, developments in our business including the acquisition of additional intellectual property, other investments in new or complimentary technology, and our success in executing our current business plan.

To address our long−term capital needs, we intend to continue to pursue strategic relationships that would provide resources for the further development of our product candidates. There can be no assurance, however, that these discussions will result in relationships or additional funding. In addition, we may continue to seek capital through the public or private sale of securities, if market conditions are favorable for doing so. If we are successful in raising additional funds through the issuance of equity securities, stockholders will likely experience substantial dilution, or the equity securities may have rights, preferences or privileges senior to those of the holders of our common stock. If we raise funds through the issuance of debt securities, those securities would have rights, preferences and privileges senior to those of our common stock. There can be no assurance that we will be successful in seeking additional capital.

INFLATION AND INTEREST RATE CHANGES

Management does not believe that our working capital needs are sensitive to inflation and changes in interest rates.

CONTRACTUAL OBLIGATIONS

The table below sets forth our contractual obligations at December 31, 2004.

CONTRACTUAL OBLIGATIONS	**PAYMENTS DUE BY PERIOD**				
	Total	**Less than 1 year**	**1−3 years**	**3 − 5 years**	**More than 5 years**
Operating Leases Obligations	$4,099,000	$ 952,000	$1,954,000	$1,193,000	$ −
Purchase Obligations					
Clinical Trial Contracts	696,000	696,000	−	−	−
Collaborative Research Contracts	534,000	534,000	−	−	−
Contract Manufacturing	198,000	198,000	−	−	−
Outside Service Contracts	688,000	688,000	−	−	−
Total Contractual Obligations	$6,215,000	$ 3,068,000	$1,954,000	$1,193,000	$ −

ITEM 7(a) QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

The primary objective of our investment activities is to preserve our capital until it is required to fund operations while at the same time maximizing the income we receive from our investments without incurring investment market volatility risk. Our investment income is sensitive to the general level of U.S. interest rates. In this regard, changes in the U.S. interest rates affect the interest earned on our cash and cash equivalents. Due to the short term nature of our cash and cash equivalent holdings, a 10% movement in market interest rates would not materially impact on the total fair market value of our portfolio as of December 31, 2004.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

The response to this item is submitted in a separate section of this report. See Index to Consolidated Financial Statements on Page F−1.

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

None.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

Under the supervision and with the participation of the Company's President and Chief Executive Officer and its Chief Financial Officer (its principal executive officer and principal financial officer), management has reviewed and evaluated the effectiveness of the design and operation of the Company's disclosure controls and procedures. Based on that evaluation, the President and Chief Executive Officer and the Chief Financial Officer have concluded that these disclosure controls and procedures are effective as of December 31, 2004.

Management's Report on Internal Control Over Financial Reporting

The management of EntreMed, Inc. is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rules 13a−15(f) and 15d−15(f) under the Securities Exchange Act of 1934, as amended). EntreMed's internal control over financial reporting was designed to provide reasonable assurance to EntreMed's management and board of directors regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. All internal controls over financial reporting, no matter how well designed, have inherent limitations. As a result of these inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Therefore, even those internal controls determined to be effective can provide only reasonable assurance with respect to reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles.

EntreMed's management assessed the effectiveness of EntreMed's internal control over financial reporting as of December 31, 2004 based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in *Interal Control – Integrated Framework.* Management's assessment included an evaluation of the design of EntreMed's internal control over financial reporting and testing of the operational effectiveness of EntreMed's internal control over financial reporting. Based on this assessment, EntreMed's management concluded that, as of December 31, 2004, EntreMed's internal control over financial reporting was effective.

Ernst & Young LLP, an independent registered public accounting firm, has issued an attestation report on management's assessment of EntreMed's internal control over financial reporting. The report of "Ernst & Young LLP is contained in Item 8 of this Annual Report on Form 10−K.

Changes in Internal Control Over Financial Reporting

There were no changes in the Company's internal control over financial reporting during the quarter ended December 31, 2004 that have materially affected, or are reasonably likely to materially affect, the internal control over financial reporting.

PART III

ITEM 10−14. INCORPORATED BY REFERENCE FROM THE COMPANY'S PROXY STATEMENTS

Except as set forth below, the information called for by Item 10: Directors and Executive Officers of the Registrant; Item 11: Executive Compensation; Item 12: Security Ownership of Certain Beneficial Owners and Management; Item 13: Certain Relationships and Related Transactions; and Item 14, Principal Accounting Fees and Services will be included in and is incorporated by reference from the registrant's definitive proxy statement to be filed pursuant to Regulation 14A of the Securities Exchange Act of 1934 within 120 days after the close of its fiscal year.

PART IV

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES

(a) 1. FINANCIAL STATEMENTS − See index to Consolidated Financial Statements.

2. Schedules

All financial statement schedules are omitted because they are not applicable, not required under the instructions or all the information required is set forth in the financial statements or notes thereto.

3. Exhibits

3.1	Amended and Restated Certificate of Incorporation of EntreMed, Inc. (incorporated by reference from our Form 10−K for the year ended December 31, 2002 previously filed with the Securities and Exchange Commission)
3.2 (1)	By−laws of EntreMed, Inc.
4.1	Certificate of Designations of the Series A Convertible Preferred Stock (incorporated by reference to Exhibit 99.4 of our Form 8−K dated December 31, 2002, and filed with the Commission on January 15, 2003)
4.2	Warrant to Purchase Common Stock, dated January 13, 2003, issued by EntreMed, Inc. in favor of Celgene Corporation (incorporated by reference to Exhibit 99.5 of our Form 8−K dated December 31, 2002, and filed with the Commission on January 15, 2003)
10.1 (1)	1992 Stock Incentive Plan*
10.2 (1)	Amended and Restated 1996 Stock Option Plan*
10.3 (1)	Form of Stock Option Agreement*
10.4 (2)	License Agreement between Children's Hospital Medical Center Corporation and EntreMed, Inc.

	signed December 20, 1996 regarding Estrogenic Compounds as Anti−Mitotic Agents
10.5 (3)	Amendment to the 1996 Stock Option Plan*
10.6 (4)	License Agreement between Celgene Corporation and EntreMed, Inc. signed December 9, 1998 regarding thalidomide intellectual property
10.7 (4)	Lease Agreement between EntreMed, Inc. and Red Gate III Limited Partnership, dated June 10, 1998
10.8 (5)	1999 Long−Term Incentive Plan*
10.9 (6)	EntreMed, Inc. 2001 Long−Term Incentive Plan*
10. 10.1 (7)	Purchase Agreement between Bioventure Investments kft and EntreMed, Inc., dated June 15, 2001+
10.10.2 (7)	Amendment 1 to Purchase Agreement between Bioventure Investments kft and EntreMed, Inc., dated July 13, 2001
10.10.3 (7)	Amendment 2 to Purchase Agreement between Bioventure Investments kft and EntreMed, Inc., dated July 30, 2001
10.10.4 (7)	Amendment 3 to Purchase Agreement between Bioventure Investments kft and EntreMed, Inc., dated August 3, 2001
10.11 (8)	Board Service Agreement, dated February 5, 2003, between Michael M. Tarnow and EntreMed, Inc. *
10.12 (9)	Asset Purchase Agreement by and Between Celgene Corporation and EntreMed, Inc., dated as of December 31, 2002
10.13 (9)	Securities Purchase Agreement by and among EntreMed, Inc., and Celgene Corporation, dated as of December 31, 2002
10.14 (9)	Investor and Registration Rights Agreement by and between EntreMed, Inc. and Celgene Corporation, dated as of December 31, 2002
10.15 (10)	Private Placement of Common Stock and Warrants to Certain Institutional Investors, dated as of November 3, 2003
10.16 (11)	Employment Agreement between EntreMed and Neil J. Campbell effective January 1, 2004*
10.17 (12)	Employment Agreement between EntreMed and James S. Burns effective June 15, 2004*
10.18 (13)	Employment Agreement between EntreMed and Dane Saglio effective July 1, 2004*
10.19 (14)	Employment Agreement between EntreMed and Carolyn F. Sidor, M.D. effective December 1, 2004*
10.20 (15)	Private Placement of Common Stock and Warrants to Certain Institutional Investors, dated as of December 23, 2004
10.21 (16)	EntreMed, Inc. 2001 Long Term Incentive Plan Non−Qualified Stock Option Grant Agreement (Director)*
10.22 (16)	EntreMed, Inc. 2001 Long Term Incentive Plan Non−Qualified Stock Option Grant Agreement (Non−Director Employee)*
10.23 (17)	Form of Letter Agreement between EntreMed and James S. Burns*
10.24 (17)	Form of Restricted Stock Award*
23.1	Consent of Independent Registered Public Accounting Firm

31.1	Rule 13a−14(a) Certification by President and CEO
31.2	Rule 13a−14(a) Certification by Chief Financial Officer
32.1	Rule 13a−14(b) Certification of President and CEO
32.2	Rule 13a−14(b) Certification of Chief Financial Officer
*	Compensatory Plan, Contract or Arrangement.
+	Certain portions of this exhibit have been omitted based upon a request for confidential treatment. The omitted portions have been filed with the Commission pursuant to our application for confidential treatment.
(1)	Incorporated by reference from our Registration Statement on Form S−1 (File No. 333−3536) declared effective by the Securities and Exchange Commission on June 11, 1996.
(2)	Incorporated by reference from our Form 10−K for the year ended December 31, 1996 previously filed with the Securities and Exchange Commission.
(3)	Incorporated by reference from our Form 10−K for the year ended December 31, 1997 previously filed with the Securities and Exchange Commission.
(4)	Incorporated by reference from our Form 10−K for the year ended December 31, 1998 previously filed with the Securities and Exchange Commission.
(5)	Incorporated by reference from our Form 10−Q for the quarter ended June 30, 1999 previously filed with the Securities and Exchange Commission.
(6)	Incorporated by reference from our Form 8−K filed with the Securities and Exchange Commission on August 21, 2001.
(7)	Incorporated by reference from our Form 10−Q for the quarter ended June 30, 2001 previously filed with the Securities and Exchange Commission.
(8)	Incorporated by reference from our Form 10−K/A for the year ended December 31, 2002 previously filed with the Securities and Exchange Commission.
(9)	Incorporated by reference from our Form 8−K dated December 31, 2002 filed with the Securities and Exchange Commission on January 15, 2003
(10)	Incorporated by reference from our Form 8−K filed with the Securities and Exchange Commission on November 4, 2003
(11)	Incorporated by reference from our Form 10−Q for the quarter ended March 31, 2004 previously filed with the Securities and Exchange Commission.
(12)	Incorporated by reference from our Form 10−Q for the quarter ended June 30, 2004 previously filed with the Securities and Exchange Commission.
(13)	Incorporated by reference from our Form 10−Q for the quarter ended September 30, 2004 previously filed with the Securities and Exchange Commission.

(14) Incorporated by reference from our Form 8−K filed with the Securities and Exchange Commission on December 6, 2004

(15) Incorporated by reference from our Form 8−K filed with the Securities and Exchange Commission on December 29, 2004

(16) Incorporated by reference from our Form 8−K filed with the Securities and Exchange Commission on February 23, 2005

(17) Incorporated by reference from our Form 8−K filed with the Securities and Exchange Commission on March 11, 2005

SIGNATURES

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

ENTREMED, INC.

By: /s/ James S. Burns.
James S. Burns
President and Chief Executive Officer
March 14, 2005

Pursuant to the requirements of the Securities Act of 1934, this report has been signed below by the following persons in the capacities and on the dates indicated.

SIGNATURE	TITLE	DATE
/s/ Michael M. Tarnow Michael M. Tarnow	Chairman of the Board	March 14, 2005
/s/ James S. Burns James S. Burns	President and Chief Executive Officer	March 14, 2005
/s/ Dane R. Saglio Dane R. Saglio	Chief Financial Officer (Principal Financial and Accounting Officer)	March 14, 2005
/s/ Donald S. Brooks Donald S. Brooks	Director	March 14, 2005
/s/ Dwight L. Bush Dwight L. Bush	Director	March 16, 2005
/s/ Jennie C. Hunter−Cevera Jennie C. Hunter−Cevera	Director	March 14, 2005
/s/ Mark C. M. Randall Mark C. M. Randall	Director	March 14, 2005
/s/ Ronald Cape Ronald Cape	Director	March 14, 2005
/s/ Peter S. Knight Peter S. Knight	Director	March 14, 2005

The following consolidated financial statements of EntreMed, Inc. are included in Item 8:

Report of Ernst & Young LLP, Independent Registered Public Accounting Firm,
on the Audited Consolidated Financial Statements

Board of Directors
EntreMed, Inc.

We have audited the accompanying consolidated balance sheets of EntreMed, Inc. as of December 31, 2004 and 2003, and the related consolidated statements of operations, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2004. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the 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 financial statements referred to above present fairly, in all material respects, the consolidated financial position of EntreMed, Inc. at December 31, 2004 and 2003, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2004, in conformity with United States generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the effectiveness of EntreMed, Inc.'s internal control over financial reporting as of December 31, 2004, based on criteria established in Internal Control – Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated March 14, 2005 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP
McLean, Virginia
March 14, 2005

Report of Ernst & Young LLP, Independent Registered Public Accounting Firm,
Regarding Internal Control over Financial Reporting

Board of Directors
EntreMed, Inc.

We have audited management's assessment, included in the accompanying Management's Report on Internal Control Over Financial Reporting, that EntreMed maintained effective internal control over financial reporting as of December 31, 2004, based on criteria established in Internal Control – Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (the COSO criteria). EntreMed's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting. Our responsibility is to express an opinion on management's assessment and an opinion on the effectiveness of the Company's internal control over financial reporting based on our audit.

We conducted our audit in accordance with standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, evaluating management's assessment, testing and evaluating the design and operating effectiveness of internal control, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

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

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

In our opinion, management's assessment that EntreMed maintained effective internal control over financial reporting as of December 31, 2004, is fairly stated, in all material respects, based on the COSO criteria. Also, in our opinion, EntreMed maintained, in all material respects, effective internal control over financial reporting as of December 31, 2004, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets of EntreMed as of December 31, 2004 and 2003, and the related consolidated statements of operations, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2004 and our report dated March 14, 2005 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP
McLean, Virginia
March 14, 2005

EntreMed, Inc.
Consolidated Balance Sheets

	DECEMBER 31, 2004	2003
ASSETS		
Current assets:		
Cash and cash equivalents	$ 20,425,495	$ 34,811,847
Short−term investments	14,114,021	2,129,583
Accounts receivable	3,250,783	428,979
Interest receivable	85,089	262,192
Prepaid expenses and other	367,222	528,190
Total current assets	38,242,610	38,160,791
Property and equipment, net	1,150,087	1,991,516
Other assets	11,305	1,457
Total assets	$ 39,404,002	$ 40,153,764
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 1,550,413	$ 3,799,304
Payable to related parties	200,321	153,213
Accrued liabilities	1,416,444	706,961
Current portion of deferred revenue	95,496	95,495
Total current liabilities	3,262,674	4,754,973
Deferred revenue, less current portion	95,496	192,993
Deferred rent	324,106	329,815
Minority interest	16,972	17,100
Stockholders' equity:		
Convertible preferred stock, $1.00 par and $1.50 liquidation value: 5,000,000 shares authorized and 3,350,000 shares issued and outstanding at December 31, 2004 and 2003	3,350,000	3,350,000
Common stock, $.01 par value: 90,000,000 shares authorized, 43,628,173 and 37,848,011 shares issued and outstanding at December 31, 2004 and 2003, respectively	436,282	378,480
Additional paid−in capital	285,387,288	271,977,321
Treasury stock, at cost: 874,999 shares held at December 31, 2004 and 2003	(8,034,244)	(8,034,244)
Accumulated deficit	(245,434,572)	(232,812,674)
Total stockholders' equity	35,704,754	34,858,883
Total liabilities and stockholders' equity	$ 39,404,002	$ 40,153,764

See accompanying notes.

EntreMed, Inc.
Consolidated Statements of Operations

	YEAR ENDED DECEMBER 31, 2004	2003	2002
Revenues:			
Collaborative research and development	$ —	$ 667,796	$ 835,493
Licensing	495,496	310,496	115,496
Grants	—	508,243	131,681
Royalties	5,918	2,705	38,790
Other	12,581	86,306	55,030
	513,995	1,575,546	1,176,490
Costs and expenses:			
Research and development	10,523,252	14,252,196	31,308,427
General and administrative	6,570,664	7,022,986	13,932,133
	17,093,916	21,275,182	45,240,560
Interest expense	—	—	(390,941)
Investment income	313,940	205,580	317,910
Gain on sale of assets	124,083	—	2,940,184
Gain on sale of securities (Note 3)	520,000	—	—
Gain on discharge of liabilities	—	—	2,174,765
Gain on sale of royalty interest (Note 5)	3,000,000	—	—
Net loss	(12,621,898)	(19,494,056)	(39,022,152)
Dividends on Series A convertible preferred stock	(1,005,000)	(1,005,000)	—
Net loss attributable to common shareholders	$(13,626,898)	$(20,499,056)	$(39,022,152)
Net loss per share (basic and diluted)	$ (0.37)	$ (0.68)	$ (1.78)
Weighted average number of shares outstanding (basic and diluted)	37,170,544	29,943,161	21,892,520

See accompanying notes.

ENTREMED, INC.

CONSOLIDATED STATEMENT OF STOCKHOLDERS' EQUITY
Periods Ended December 31, 2004, 2003 and 2002

	Preferred Stock		Common Stock		Treasury	Additional Paid−in	Deferred Stock	Accumulated	
	Shares	Amount	Shares	Amount	Stock	Capital	Compensation	Deficit	Total
Balance at December 31,2001	—	$ —	21,193,997	$217,773	$(7,666,746)	$205,013,706	$(73,369)	$(174,296,466)	$ 23,194,898
Issuance of common stock for options and warrants exercised	—	—	8,500	85	—	9,180	—	—	9,265
Sale of common stock at $6.86 per share	—	—	728,863	7,289	—	4,992,711	—	—	5,000,000
Sale of preferred stock at $5 per share convertible to 5 shares of common stock	3,350,000	3,350,000	—	—	—	11,055,000	—	—	14,405,000
Issuance of common stock and warrants pursuant to debt settlement agreements	—	—	1,314,334	16,060	(367,498)	1,999,100	—	—	1,647,662
Recognition of non cash stock compensation	—	—	25,000	250	—	83,101	—	—	83,351
Deferred compensation − option grants							11,523		11,523
Fair value of warrants issued	—	—	—	—	—	5,164,099	—	—	5,164,099
Net loss	—	—	—	—	—	—	—	(39,022,152)	(39,022,152)
Balance at December 31, 2002	3,350,000	$3,350,000	23,270,694	$241,457	$(8,034,244)	$228,316,897	$(61,846)	$(213,318,618)	$ 10,493,646
Issuance of common stock for options and warrants exercised	—	—	172,575	1,725	—	189,092	—	—	190,817
Sale of common stock at $2.50 per share	—	—	4,100,000	41,000	—	7,125,344	—	—	7,166,344
Sale of common stock at $3.00 per share	—	—	3,000,000	30,000	—	8,016,609	—	—	8,046,609
Sale of common stock at $4.25 per share	—	—	5,250,000	52,500	—	18,020,631	—	—	18,073,131
Issuance of common stock and warrants pursuant to debt settlement agreements	—	—	1,147,872	11,479	—	1,102,521	—	—	1,114,000
Recognition of non cash stock compensation	—	—	31,871	319	—	174,681		—	175,000
Fair value of warrants issued	—	—	—	—	—	4,452,117	—	—	4,452,117
Change in basis in MaxCyte	—	—	—	—	—	4,579,429	61,846		4,641,275
Net loss	—	—	—	—	—	—		(19,494,056)	(19,494,056)

Balance at December 31, 2003	3,350,000	$3,350,000	36,973,012	$378,480	$(8,034,244)	$271,977,321	$ —	$(232,812,674)	$ 34,858,883
Issuance of common stock for options and warrants exercised	—	—	208,946	2,090	—	5,677	—	—	7,767
Sale of common stock at $2.55 per share	—	—	5,490,198	54,902	—	10,781,472	—	—	10,836,374
Recognition of non cash stock compensation	—	—	81,018	810	—	174,189	—	—	174,999
Fair value of warrants issued	—	—	—	—	—	2,448,629	—	—	2,448,629
Net loss	—	—	—	—	—	—	—	(12,621,898)	(12,621,898)
Balance at December 31, 2004	3,350,000	$3,350,000	42,753,174	$436,282	$(8,034,244)	$285,387,288	$ —	$(245,434,572)	$ 35,704,754

See accompanying notes.

EntreMed, Inc.
Consolidated Statements of Cash Flows

	YEAR ENDED DECEMBER 31,		
	2004	2003	2002
CASH FLOWS FROM OPERATING ACTIVITIES			
Net loss	$(12,621,898)	$(19,494,056)	$(39,022,152)
Adjustments to reconcile net loss to net cash used by operating activities:			
Depreciation and amortization	773,775	930,772	1,508,559
Loss on disposal of equipment	—	9,679	83,635
Gain on discharge of liabilities	—	—	(2,174,766)
Gain on sale of assets	(124,083)	—	(2,940,184)
Gain on sale of securities	(520,000)	—	—
Gain on sale of royalty interest	(3,000,000)	—	—
Recognition of non−cash stock compensation	174,999	175,000	94,874
Non−cash interest expenses	—	—	331,950
Common stock repurchase liability	—	—	1,995,007
Minority interest	(127)	(124)	(229)
Changes in operating assets and liabilities:			
Accounts receivable	178,196	(209,693)	(132,134)
Interest receivable	177,103	—	56,943
Prepaid expenses and other	151,120	(247,939)	130,167
Accounts payable	(2,248,891)	(4,683,579)	(5,784,568)
Payable to related parties	47,108	153,213	—
Accrued liabilities	709,483	(1,119,462)	(158,891)
Contingent grant	—	—	80,000
Deferred rent	(5,709)	329,815	—
Deferred revenue	(97,496)	(93,496)	397,297
Net cash used in operating activities	(16,406,420)	(24,249,870)	(45,534,492)
CASH FLOWS FROM INVESTING ACTIVITIES			
Proceeds from sale of property and equipment, net	355,275	—	—
Proceeds from sale of asset, net	—	—	2,940,184
Proceeds from sale of securities	520,000	—	—
Reduction in ownership of MaxCyte's cash	—	(418,108)	—
Purchases of short term investments	(11,984,438)	(2,391,680)	
Purchases of furniture and equipment	(163,539)	(32,715)	(558,187)
Net cash provided by (used in) investing activities	(11,272,702)	(2,842,503)	2,381,997
CASH FLOWS FROM FINANCING ACTIVITIES			
Net proceeds from sale of common stock	13,292,770	33,476,901	5,009,265
Net proceeds from sale of warrants	—	4,452,117	5,164,099
Net proceeds from sale of preferred stock	—	—	14,405,000
Proceeds from issuance of note payable	—	—	91,843
Payment of principal on note payable	—	(91,843)	(1,005,727)
Proceeds from issuance of long−term debt	—	—	2,168,760
Net cash provided by financing activities	13,292,770	37,837,175	25,833,240
Net increase (decrease) in cash and cash equivalents	(14,386,352)	10,744,802	(17,319,255)
Cash and cash equivalents at beginning of year	34,811,847	24,067,045	41,386,300
Cash and cash equivalents at end of year	$ 20,425,495	$ 34,811,847	$ 24,067,045
SUPPLEMENTAL DISCLOSURE OF CASH FLOW INFORMATION			
Interest paid	$ —	$ 2,451	$ 58,992

1. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

DESCRIPTION OF BUSINESS AND BASIS OF PRESENTATION

EntreMed, Inc. ("EntreMed" or the "Company") is a clinical−stage biopharmaceutical company developing therapeutics primarily for the treatment of cancer. Panzem®, the Company's lead drug candidate, is currently in clinical trials for cancer, as well as preclinical development for indications outside of oncology. The Company's research and development programs are designed to identify new chemical entities by understanding the interrelationships of cell cycle regulation, inflammation, coagulation and angiogenesis – processes vital to the treatment of multiple diseases, including cancer. These programs have led to the identification of new therapeutic targets such as inhibition of the tissue factor pathway and the proteinase−activated receptor−2 (PAR−2). Based on these targets, EntreMed scientists are designing additional drug candidates for in−house development or partnering opportunities. EntreMed's clinical and commercial focus is oncology, but its strategy is to form strategic alliances, licensing relationships and partnerships with other companies to develop compounds in non−oncology therapeutic areas.

The accompanying consolidated financial statements include the accounts of our controlled subsidiary, Cytokine Sciences, Inc. The consolidated financial statements as of December 31, 2002 also included the accounts of MaxCyte, Inc., a clinical stage biotechnology company aimed at commercializing cell loading technology. Effective the first quarter of 2003 the Company no longer controlled or funded and no longer consolidated MaxCyte and as a result, the Company's 2003 financial statements reflect MaxCyte using the equity method. Due to MaxCyte's cumulative losses, EntreMed's financial statements reflect no basis in it's investment in MaxCyte. And, as such, no income or loss resulting from MaxCyte's operations are reflected in EntreMed's financial statements for the current reporting period. All intercompany balances and transactions have been eliminated in consolidation.

To date, we have been engaged primarily in research and development activities. As a result we have incurred operating losses through 2004 and expect to continue to incur operating losses for 2005 and the foreseeable future before we commercialize any products. To accomplish our business plans, we will be required to continue to conduct substantial development activities for all of our proposed products. We intend to continue to pursue strategic relationships to provide resources for the further development of our product candidates. There can be no assurance, however, that these discussions will result in relationships or additional funding. In addition, we will continue to seek capital through the public or private sale of securities. There can be no assurance that we will be successful in seeking such additional capital.

SEGMENT INFORMATION

The Company currently operates in one business segment, which is the development of therapeutics primarily for the treatment of cancer. The Company is managed and operated as one business. A single management team that reports to the Company's President and Chief Executive Officer comprehensively manages the entire business. The Company does not operate separate lines of business with respect to its products or product candidates. Accordingly, the Company does not have separately reportable segments as defined by FASB Statement No. 131, *Disclosures about Segments of an Enterprise and Related Information.*

RESEARCH AND DEVELOPMENT

Research and development expenses consist primarily of compensation and other expenses related to research and development personnel, research collaborations, costs associated with pre−clinical testing and clinical trials of our product candidates, including the costs of manufacturing the product candidates, and facilities expenses. Research and development costs are expensed as incurred, including costs incurred in filing, defending and maintaining patents.

PROPERTY AND EQUIPMENT

Furniture and equipment and leasehold improvements are stated at cost and are depreciated over their estimated useful lives of 5 to 10 years. Depreciation is determined on a straight−line basis. Depreciation expense was $773,775, $930,772 and $1,508,559 in 2004, 2003 and 2002, respectively. Property and equipment consists of the following:

	DECEMBER 31	
	2004	2003
Furniture and equipment	$ 5,575,772	$ 6,515,694
Leasehold improvements	1,284,991	1,284,991
	6,860,763	7,800,685
Less: accumulated depreciation	(5,710,676)	(5,809,169)
	$ 1,150,087	$ 1,991,516

CASH AND CASH EQUIVALENTS

Cash and cash equivalents include cash and highly liquid investments with original maturities of less than 90 days. Substantially all of the Company's cash equivalents are held in short−term money market accounts of banks and brokerage houses.

SHORT−TERM INVESTMENTS

Short−term investments consist primarily of corporate debt securities, all of which mature within one year. The Company has classified these investments as available for sale. Such securities are carried at aggregate cost which approximates market. The cost of securities sold is calculated using the specific identification method. Unrealized gains and losses on these securities, if any, are reported as accumulated other comprehensive income (loss), which is a separate component of stockholders' equity. There were no unrealized gains or losses as of December 31, 2004 and 2003. Realized gains and losses and declines in value judged to be other than temporary on securities available for sale, if any, are included in operations. Short−term investments are principally uninsured and subject to normal credit risk. (See Note 3 for Gain on Sale of Securities).

ACCOUNTS RECEIVABLE

Accounts receivable is stated net of allowances for doubtful accounts. Allowances for doubtful accounts are determined on a specific item basis. Management reviews the credit worthiness of individual customers and past payment history to determine the allowance for doubtful accounts.

INCOME TAXES

Income taxes have been provided using the liability method in accordance with Statement of Financial Accounting Standards No. 109, *Accounting for Income Taxes*.

REVENUE RECOGNITION

The Company recognizes revenue in accordance with the provisions of Staff Accounting Bulletin No. 104, Revenue Recognition, whereby revenue is not recognized until it is realized or realizable and earned. Revenue is recognized when all of the following criteria are met: persuasive evidence of an arrangement exists, delivery has occurred or services have been rendered, the price to the buyer is fixed and determinable and collectibility is reasonably assured.

Collaborative Research and Development Revenue − The Company receives revenues for performance under commercial research and development contracts. These contracts require that the Company provide services directed toward specific objectives and include developmental milestones and deliverables. These revenues are recognized at the time that research and development activities are performed.

Royalty Revenue − Royalties from licenses are based on third−party sales and recorded as earned in accordance with contract terms, when third−party results are reliably measured and collectibility is reasonably assured.

Grant Revenue − The Company received a government grant in 2002 for the development of potential malaria vaccines. In 2003 we received a government grant to financially support our Phase II Endostatin clinical trial in patients with neuroendocrine tumors. Grants are funded in specific amounts based on funding requests submitted to the grantor. Grant revenues are recognized and realized at the time that research and development activities are performed.

Licensing Revenue – The Company recognizes licensing revenues resulting from a strategic alliance with Allergan to develop and commercialize small molecule angiogenic inhibitors for treatment and prevention of diseases and conditions of the eye. The initial fees were deferred and amortized to revenue over the license term as the Company has an ongoing obligation under the license. In the fourth quarter of 2003, the Company recorded revenue for the fair value of the initial net cash and shares of common stock received under a licensing agreement with Oxford Biomedica, PLC and Oxford Biomedica (UK) Limited. The agreement provides Oxford exclusive worldwide rights to use endostatin and angiostatin genes in the development of locally delivered gene therapy for ophthalmologic applications. We have no continuing obligations under this agreement and as a result the revenue was recognized upon receipt. The Company also recognizes licensing revenue from a February 2004 licensing agreement with Alchemgen. Under this agreement Alchemgen was granted commercialization rights to Endostatin and Angiostatin in Asia. The Company’s obligations under this agreement were completed in 2004 and as such the initial licensing fee was fully amortized in 2004.

NET LOSS PER SHARE

Net loss per share (basic and diluted) was computed by dividing net loss by the weighted average number of shares of common stock outstanding. Common stock equivalents, including Preferred Series A common stock equivalents, totaling 27,781,813 were anti−dilutive and, therefore, were not included in the computation of weighted average shares used in computing diluted loss per share.

COMPREHENSIVE LOSS

Under Financial Accounting Standard No. 130 (“SFAS 130”), Reporting Comprehensive Income, the Company is required to display comprehensive loss and its components as part of the consolidated financial statements. Comprehensive loss is comprised of the net loss and other comprehensive income (loss), which includes certain changes in equity that are excluded from net loss. Comprehensive loss for the Company was the same as net loss for all years presented.

STOCK−BASED COMPENSATION

The Company recognizes expense for stock−based compensation arrangements in accordance with the provisions of Accounting Principles Board Opinion No. 25, Accounting for Stock Issued to Employees, and related Interpretations. Accordingly, compensation cost is recognized for the excess of the estimated fair value of the stock at the grant date over the exercise price, if any. The Company accounts for equity instruments issued to non−employees in accordance with EITF 96−18, *Accounting for Equity Instruments that are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods, or Services.*

Disclosures regarding alternative fair values of measurement and recognition methods prescribed by Statement of Accounting Standards No. 148, *Accounting for Stock−Based Compensation−Transition and Disclosure* and Statement of Financial Accounting Standards No. 123, *Accounting for Stock−Based Compensation* (SFAS No. 123) are presented in Note 9 and in the table below. The following table illustrates the effect on net loss if the Company had applied the fair value recognition provisions of SFAS No. 123, to stock−based compensation:

	Year ended December 31		
	2004	2003	2002
Actual net loss	$(12,621,898)	$(19,494,056)	$(39,022,152)
Add: Stock−based employee compensation included in reported net loss	—	—	—
Deduct: Stock−based employee compensation expense if SFAS No. 123 had been applied to all awards	(4,511,639)	(8,902,175)	(14,088,860)
Proforma net loss	$(17,133,537)	$(28,396,231)	$(53,111,012)
Dividend on Series A convertible preferred stock	$ (1,005,000)	$ (1,005,000)	—
Proforma net loss per share available to common shareholders	$(18,138,537)	$(29,401,231)	$(53,111,012)
Basic and diluted – as reported	$ (0.37)	$ (0.68)	$ (1.78)
Basic and diluted – pro forma	$ (0.49)	$ (0.98)	$ (2.43)

The effect of applying SFAS No. 123 on a pro forma net loss as stated above is not necessarily representative of the effect on reported net loss for future years due to, among other things, the vesting period of the stock options and the fair value of additional options to be granted in future years.

Significant assumptions used in the Black−Scholes option pricing model are as follows:

	Year ended December 31,		
	2004	2003	2002
Risk free rate	3.73%	4.0%	4.0%
Expected life	5 yrs	6 yrs	6 yrs
Volatility	1.20	1.20	1.15
Expected dividend yield	—	—	—

FINANCIAL INSTRUMENTS AND CONCENTRATIONS OF RISK

Financial instruments that potentially subject the Company to concentrations of credit risk consist principally of cash and cash equivalents, short−term investments, accounts receivable, accounts payable and accrued expenses. The Company maintains its cash and cash equivalents in bank deposit accounts, which, at times, may exceed federally insured amounts. The Company believes it is not exposed to any significant credit risk on cash and cash equivalents or short−term investments. The carrying amount of current assets and liabilities approximates their fair values due to their short−term maturities.

RECENT ACCOUNTING STANDARDS

In October 2004, the FASB concluded that SFAS No. 123 (revised 2004), “Share−Based Payment” (“SFAS 123R”), which would require all companies to measure compensation cost for all share−based payments (including employee stock options) at fair value, would be effective for interim or annual periods beginning after June 15, 2005. SFAS 123R provides two tentative adoption methods. The first method is a modified prospective transition method whereby a company would recognize share−based employee costs from the beginning of the fiscal period in which the recognition provisions are first applied as if the fair−value−based accounting method had been used to account for all employee awards granted, modified, or settled after the effective date and to any awards that were not fully vested as of the effective date. Measurement and attribution of compensation cost for awards that are unvested as of the effective date of SFAS 123R would be based on the same estimate of the grant−date fair value and the same attribution method used previously under SFAS 123. The second adoption method is a modified retrospective transition method whereby a company would recognize employee compensation cost for periods presented prior to the adoption of SFAS 123R in accordance with the original provisions of SFAS 123; that is, an entity would recognize employee compensation costs in the amounts reported in the pro forma disclosures provided in accordance with SFAS 123. A company would not be permitted to make any changes to those amounts upon adoption of SFAS 123R unless those changes represent a correction of an error. For periods after the date of adoption of SFAS 123R, the modified prospective transition method described above would be applied. The Company currently expects to adopt SFAS 123R in the quarter ended September 30, 2005, using the modified prospective method, although the Company continues to review its options for adoption under this new pronouncement. The adoption of Statement 123R is expected to have a material impact on the Company’s financial position, results of operations and cash flows. The Company currently anticipates recording non−cash compensation expense of approximately $500,000 in each of the third and fourth quarters of 2005, respectively.

USE OF ESTIMATES

The preparation of consolidated financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results may differ from those estimates, and such differences may be material to the financial statements.

2. CHANGE IN BASIS OF MAXCYTE

In November 2002, the Boards of Directors of both EntreMed and MaxCyte adopted a plan to recapitalize MaxCyte. As a result of the recapitalization, the Company no longer controls and no longer consolidates MaxCyte effective the first quarter of 2003; EntreMed then owned 45% of MaxCyte. Effective January 1, 2003, the investment in MaxCyte is accounted for using the equity method. The reduction of EntreMed’s ownership in MaxCyte resulted in a change in EntreMed’s basis in MaxCyte. The change from fully consolidating MaxCyte to reflecting the investment in MaxCyte on the equity method resulted in a $4.6 million credit to additional paid−in capital. In February 2004, MaxCyte closed a series B financing which resulted in the dilution of our equity ownership in MaxCyte to approximately 10%. Subsequent to this dilution, our investment in MaxCyte was accounted for under the cost method; although our basis in this investment is $0 at December 31, 2004 and 2003.

3. SALE OF SECURITIES

In September 2004, the Company sold certain securities of an independent private biotechnology company. The securities were acquired in 1996 through 1999 and accounted for using the equity method. Consistent with this approach, the cost of these securities was written down to $0 in prior periods and the Company had no residual cost basis in the securities when sold. As such, the Company recorded a gain on the sale equal to the sale proceeds of $520,000.

4. SPONSORED RESEARCH PROGRAM AGREEMENTS

Prior to 2003, the Company entered into several agreements to sponsor external research programs. The Company’s primary external research program agreement was entered into with the Children’s Hospital, in Boston, Massachusetts, an entity affiliated with Harvard Medical School (“Children’s Hospital, Boston”).

Under this sponsored research agreement, the Company agreed to pay Children’s Hospital, Boston to continue the research on the role of angiogenesis in pathological conditions. In accordance with the terms of this sponsored research agreement, the Company agreed to pay $1,500,000 each year to Children’s Hospital, Boston. As of December 31, 2003, all amounts were paid and there was no remaining commitment.

In November 2003, the Company reached an agreement to extend one of the sponsored research agreements with Children's Hospital, Boston. Under the extended agreement the Company will pay $300,000 each year for the period of November 1, 2003 through November 1, 2005. Payments under the agreement are made quarterly in advance and are expensed as paid. In 2004, the Company made four quarterly payments of $75,000 each.

5. LICENSE AGREEMENTS

On January 18, 2002 the Company entered into a five−year strategic alliance with Allergan, an ophthalmic research and development and pharmaceutical company, to develop and commercialize small molecule angiogenic inhibitors for treatment and prevention of diseases and conditions of the eye (the "Agreement"). Panzem® is the first small molecule to be licensed and developed under this Agreement. Allergan and EntreMed plan to co−develop Panzem® to treat age−related macular degeneration (ARMD), a leading cause of blindness that is the result of bleeding from ruptured new blood vessels that form under the retina. The Company is entitled to receive royalties on any revenues resulting from this arrangement and specified milestone payments upon the completion of initiation of defined development stages and regulatory approvals.

Concurrent with the Agreement, a stock purchase agreement was executed whereby Allergan purchased 728,863 shares of EntreMed common stock and received a detachable warrant to purchase an additional 109,329 shares of EntreMed common stock. The Company received $5.0 million as consideration for the investment. The stock price was based on the average closing price of EntreMed's common stock for the three days ended January 17, 2002, which was $6.86 per share of common stock. The warrants have a five−year contractual life and an exercise price of $12.15 per share of common stock. In addition the Company received a non−refundable up−front payment of $1.0 million. Due to the fact that the license agreement and the stock purchase agreement were negotiated and entered into concurrently, the Company determined that it was appropriate to allocate the consideration received of $6.0 million between the securities that were sold and the license arrangement. Approximately $5.0 million was allocated to the common stock, $323,000 to the detachable warrants, $477,000 was recorded as deferred revenue and $200,000 related to a the Company's royalty obligation to CMCC. Deferred revenue is being recognized as revenue on a straight−line basis over the term of the arrangement.

On December 31, 2002, the Company entered into a series of agreements and transactions with Celgene and Children's Medical Center Corporation ("CMCC") including an Exclusive License Agreement among Celgene, CMCC and EntreMed (the "License Agreement"), Asset Purchase Agreement by and between Celgene and EntreMed (the "Asset Purchase Agreement") and a Securities Purchase Agreement between EntreMed and Celgene (the "Securities Purchase Agreement").

The net effect of the agreements was the sale to Celgene of the Company's assets, properties and rights related to Thalidomide Analogs, the transfer to Celgene and elimination of the Company's rights and obligations under its Analog licensing agreements with Children's Medical Center Corporation (CMCC), the settlement of all litigations between the Company and Celgene, the issuance of 3,350,000 shares of Series A Convertible Preferred Stock and a warrant to purchase 7,000,000 shares of common stock of the Company to Celgene, the issuance of 900,000 warrants to CMCC and the payment of $26.75 million to the Company by Celgene.

In summary, EntreMed received $26,750,000 from Celgene for the series of agreements and transactions signed on December 31, 2002. The proceeds have been allocated as follows, based on the estimated fair value of the instruments.

Convertible Preferred Stock	$14,405,000
Warrants issued to Celgene	4,200,000
Warrants issued to CMCC	540,000
Royalties paid to CMCC	3,000,000
Transaction fees	1,665,000
Gain on sale of asset	2,940,000
	$26,750,000

On September 8, 2003 the Company entered into a licensing agreement with Oxford Biomedica, PLC and Oxford Biomedica (UK) Limited. Under the terms of the agreement, Oxford BioMedica receives exclusive worldwide rights to use EntreMed's endostatin and angiostatin genes in the development of locally delivered gene therapy for ophthalmologic applications. Oxford BioMedica plans to utilize EntreMed's genes in its proprietary therapeutic RetinoStat™ program for the treatment of age−related macular degeneration and diabetic retinopathy. In return, EntreMed received an initial cash payment of $125,000 and 301,748 shares of Oxford BioMedica common stock valued at $129,000. Additionally, EntreMed may collect up to $10 million on the achievement of regulatory and clinical milestones. The Company may receive royalties on future worldwide sales of products resulting from the agreement. EntreMed retains rights to gene therapy applications outside of localized delivery to the eye. EntreMed also retains the rights to the endostatin and angiostatin proteins and is actively pursuing alternative commercialization of these two clinical drug candidates.

In February 2004, the Company transferred rights for its protein−based drug candidate programs, endostatin and angiostatin, in an agreement with Children's Medical Center Corporation in Boston (CMCC) and Alchemgen Therapeutics, Inc. ("Alchemgen") Under the agreement, CMCC and Alchemgen are continuing the development of endostatin and angiostatin and bear all expenses associated with the programs, including costs that the Company may incur in transferring these compounds. In exchange, the Company receives upfront and future cash and royalty payments. Under the terms of the three−party agreement, the Houston−based, privately−held company Alchemgen received exclusive rights to market endostatin and angiostatin in Asia. CMCC holds the license for the rest of the world therefore the Company has no future milestone payment obligations. The Company would receive 20% of all future proceeds (e.g. upfront, milestone and royalty payments) resulting from any subsequent CMCC license outside of Asia; however, there can be no assurance that the Company will receive future additional payments under this arrangement.

Pursuant to a purchase agreement dated June 14, 2001 by and between Bioventure Investments kft ("Bioventure") and the Company, as amended July 13, 2001, July 30, 2001 and August 3, 2001 (the "Purchase Agreement"), Bioventure purchased as of August 6, 2001 all of the Company's right, title and interest to the net royalty payments payable by Celgene Corporation ("Celgene") to the Company under the agreement dated as of December 9, 1998 by and between the Company and Celgene (the "Celgene Sublicense"). As a result of this transaction the Company recorded a $22.6 million gain.

A provision of the Bioventure purchase agreement provided the potential for an adjustment in the purchase price if cumulative sales of Thalomid® exceeded $800 million by December 31, 2004. Based on Thalomid® sales reported publicly by Celgene, the Company concluded that cumulative Thalomid® sales had reached this milestone by December 31, 2004. As such, the Company recorded a gain on the sale of our royalty rights and a corresponding receivable of $3.0 million. The Company received payment of this amount in March 2005. In addition to triggering this one−time adjustment in the purchase price, exceeding the $800 million cumulative sales amount also triggers a royalty sharing provision. Beginning the year after cumulative sales reach $800 million, EntreMed is entitled to share in the royalty payments received by Royalty Pharma Finance Trust, successor to Bioventure, on annual Thalomid® sales above a certain threshold. There can be no assurance that the Company will receive material royalties under the royalty sharing provision in the future.

6. RELATED PARTY TRANSACTIONS

The Company receives legal services from a law firm with which one of the Company's officers is associated. The amounts reflected as research and development in the table below primarily represent patent work. The amounts reflected as general and administrative represent legal and financial advisory services including the costs associated with three litigations settled in 2002. In addition to legal services, the Company also received financial advisory services from Ferghana Partners, Inc., a provider of corporate financial advice to firms in the Life Sciences field. The Company's chairman also serves as non−executive chairman of Ferghana Partners, Inc. The Company's chairman and CEO both hold a de minimis ownership interest in Ferghana Partners, Inc. Pursuant to a series of business transactions the Company paid $100,000 and $3,205,000 in fees to Ferghana Partners, Inc. in 2004 and 2003, respectively. The fees were recorded as offsets against gross equity transaction proceeds and as such are not reflected as expenses in the current period. Expenses from related parties are included in the following accounts within the consolidated financial statements, $200,321 of which are included in accounts payable at December 31, 2004:

	2004	2003	2002
Research and development	$ 628,000	$ 916,000	$1,747,000
General and administrative	387,000	276,000	2,092,000
Additional paid in capital	100,000	3,205,000	—
	$1,115,000	$4,397,000	$3,839,000

7. INCOME TAXES

The Company has net operating loss carryforwards for income tax purposes of approximately $249,988,000 at December 31, 2004 ($237,841,000 at December 31, 2003) that expire in years 2006 through 2024. The Company also has research and development tax credit carryforwards of approximately $10,889,000 as of December 31, 2004 that expire in years 2007 through 2024. These net operating loss carryforwards include approximately $19,800,000, related to exercises of stock options for which the income tax benefit, if realized, would increase additional paid−in capital. The utilization of the net operating loss and research and development carryforwards may be limited in future years due to changes in ownership of the Company pursuant to Internal Revenue Code Section 382. For financial reporting purposes, a valuation allowance has been recognized to reduce the net deferred tax assets to zero due to uncertainties with respect to the Company's ability to generate taxable income in the future sufficient to realize the benefit of deferred income tax assets.

Deferred income taxes reflect the net effect of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant components of the Company's deferred income tax assets and liabilities as of December 31, 2003 and 2002 are as follows:

	DECEMBER 31,	
	2004	2003
Deferred income tax assets (liabilities):		
Net operating loss carryforwards	$ 94,995,000	$ 90,380,000
Research and development credit carryforward	10,889,000	11,272,000
Deferred revenues	88,000	110,000
Equity investment	69,000	69,000
Other	721,000	661,000
Depreciation	263,000	126,000
Valuation allowance for deferred income tax assets	(107,025,000)	(102,618,000)
Net deferred income tax assets	$ —	$ —

A reconciliation of the provision for income taxes to the federal statutory rate is as follows:

	2004	2003	2002
Tax benefit at statutory rate	$(4,291,000)	$(7,034,000)	$(14,725,000)
State taxes	(505,000)	(826,000)	(1,728,000)
Tax credits	383,000	(853,000)	(2,712,000)
Permanent differences	6,000	9,000	35,000
Valuation allowance	4,407,000	8,704,000	19,130,000
	$ —	$ —	$ —

8. STOCKHOLDERS' EQUITY

In January 2002, the Company entered into a five−year strategic alliance with Allergan, a leader in ophthalmic research and development and pharmaceutical products, to develop and commercialize small molecule angiogenic inhibitors for treatment and prevention of diseases and conditions of the eye. Panzem® is the first small molecule to be licensed, developed and marketed under this agreement. Under the terms of the agreement, Allergan also purchased 728,863 shares of common stock and 109,329 warrants for $5,000,000.

In December 2002, the Company reached agreements with five creditors, including BMS, to settle $8,086,000 in current liabilities. The Company issued consideration of $5,911,000 in cash, stock and warrants to satisfy the renegotiated obligations, resulting in a $2,175,000 gain in discharge of liabilities. 1,314,000 shares of common stock, net of 291,666 repurchased from BMS, and warrants to purchase 675,000 shares of common stock were issued in December 2002 and 1,147,872 shares of common stock were issued in January 2003.

The Company issued 3,350,000 shares of Series A Preferred Stock to Celgene (See Note 5). The Series A Preferred Stock is convertible, at the option of Celgene, at any time, into common stock at an initial per share conversion price of $5.00 (1 share of preferred converts into 5 shares of common). The conversion price is subject to change for certain dilutive events, as defined. At any time after December 31, 2004, the Company may cause the Series A Preferred Stock to convert automatically provided all of the following conditions are met:

(i) As of the conversion date, the common stock is traded and was traded during the 60 trading days preceding the conversion date, on a national securities exchange;

(ii) The average per share closing price of the common stock is greater than $5.00 over a 60−trading day period ending on the conversion date, and

(iii) A registration statement with respect to resale of the common stock issuable in the conversion to the holders of the Series A Preferred Stock has been filed with the SEC, such registration statement is effective and the Company has agreed to maintain the effectiveness of the registration statement for at least 180 consecutive days beginning with the conversion date.

The Series A Preferred Stock accrues and accumulates dividends at a rate of 6% and will participate in dividends declared and paid on the common stock, if any. At December 31, 2004, cumulative unpaid preferred stock dividends totaled $2,010,000 or $.60 per share. All unpaid preferred stock dividends must be paid before any dividends may be declared or paid on the Common Stock, and will be added to the liquidation preference of the Series A Preferred Stock payable upon the liquidation, dissolution or winding up of the Company.

The liquidation preference is equal to the greater of:

(i) Two times the original per share purchase price plus accrued and unpaid dividends or

(ii) The amount per share that would be payable to a holder of shares of the Series A Preferred Stock had all of the shares been converted to common stock immediately prior to a liquidation event.

The liquidation preference of the series A Preferred Stock on a converted basis at December 31, 2004 totaled approximately $54,000,000. This value is calculated based on the closing share price of the Company's common stock on December 31, 2004. There can be no assurance what impact the conversion of the Series A Preferred to common stock would have on the trading value of the Company's common stock.

Holders of the Series A Preferred Stock generally vote together with the holders of common stock, with each share of Series A Preferred Stock representing the number of votes equal to that number of shares of common stock into which it is then convertible.

In April 2003, the Company completed a private placement of 4,100,000 shares of its common stock and warrants to purchase a total of 1,025,000 shares of common stock at an exercise price of $3.375, resulting in gross proceeds, prior to the deduction of fees and commissions of approximately $10.25 million (net proceeds of $9 million).

In May 2003, the Company completed a private placement of 3,000,000 shares of its common stock resulting in gross proceeds, prior to the deduction of fees and commissions of $9 million (net proceeds of $8.1 million).

In November 2003, the Company completed a private placement of 5,250,000 shares of its common stock and warrants to purchase a total of 787,500 shares of common stock at an exercise price of $5.00, resulting in gross proceeds, prior to the deduction of fees and commissions of approximately $22.3 million (net proceeds of $20.7 million).

In conjunction with the three 2003 transactions described above, we issued to Ferghana Securities, Inc., warrants to purchase 123,500 shares of our common stock at exercise prices ranging from $2.75 to $4.67 for services as financial advisors. The fair value of the warrants issued to Ferghana Securities, Inc. in 2003 ranged from $1.72 to $3.08.

In December 2004, the Company completed a private placement of 5,490,198 shares of its common stock and warrants to purchase a total of 1,098,040 shares of common stock at an exercise price of $3.67, resulting in gross proceeds, prior to the deduction of fees and commissions of approximately $14.0 million (net proceeds of $13.3 million).

9. STOCK COMPENSATION

The Company has adopted incentive and nonqualified stock option plans whereby 9,983,333 shares of the Company's common stock were reserved for grants to various executive, scientific and administrative personnel of the Company as well as outside directors and consultants, of which 913,277 shares remain available for grant as of December 31, 2004. These options vest over periods varying from immediately to four years and generally expire 10 years from the date of grant.

The Company recorded non−cash compensation charges of $175,000 in 2004 and 2003 related to the issuance of restricted stock to members of our Board of Directors. Each Non−employee director receives as an annual retainer a fee of $25,000 that is payable in restricted stock.

The Black−Scholes option valuation model was developed for use in estimating the fair value of traded options which have no vesting restrictions and are fully transferable. In addition, option valuation models require the input of highly subjective assumptions including the expected stock price volatility. Because the Company's employee stock options have characteristics significantly different from those of traded options, and because changes in the subjective input assumptions can materially affect the fair value estimate, in management's opinion, the existing models do not necessarily provide a reliable single measure of the fair value of its employee stock options.

For purposes of pro forma disclosures, the estimated fair values of the options and warrants are amortized to expense over the vesting period. The estimated weighted average fair value per option granted in 2004, 2003 and 2002 was $2.00, $2.43 and $1.77, respectively.

A summary of the Company's stock options granted to employees and directors and related information for the years ended December 31 follows:

	Number of Options	Weighted Average Exercise Price
Outstanding at January 1, 2002	5,733,702	$ 14.86
Exercised	(8,500)	$ 1.09
Granted	1,316,551	$ 2.07
Canceled	(432,488)	$ 18,84
Outstanding at December 31, 2002	6,609,265	$ 12.04
Exercised	(172,575)	$ 1.42
Granted	1,487,505	$ 2.75
Canceled	(416,918)	$ 11.32
Outstanding at December 31, 2003	7,507,277	$ 10.48
Exercised	(7,125)	$ 1.09
Granted	1,176,728	$ 2.39
Canceled	(308,902)	$ 6.29
Outstanding at December 31, 2004	8,367,978	$ 9.50
Exercisable at December 31, 2004	7,066,020	$ 10.77

The following summarizes information about stock options granted to employees and directors outstanding at December 31, 2004:

	Options Outstanding			Options Exercisable	
Range of Exercise Prices	Number Outstanding at 12/31/04	Weighted Average Remaining Contractual Life in Years	Weighted Average Exercise Price	Number Exercisable at 12/31/04	Weighted Average Exercise Price
$ 0.00−$ 9.35	4,972,432	7.2	$ 4.05	3,673,099	$ 4.57
$ 9.36−$18.70	2,335,659	3.9	$ 13.70	2,335,659	$ 13.70
$18.71−$28.05	760,711	4.3	$ 23.67	758,086	$ 23.68
$28.06−$37.40	277,053	5.2	$ 29.56	277,053	$ 29.56
$37.41−$46.75	1,962	5.1	$ 42.12	1,962	$ 42.12
$46.76−$56.10	19,299	5.4	$ 52.53	19,299	$ 52.53
$56.11−$65.45	862	5.2	$ 58.31	862	$ 58.31
	8,367,978	6.0	$ 9.50	7,066,020	$ 10.77

Warrants granted generally expire after 5 years from the date of grant. Stock warrant activity to non−employees is as follows:

	Number of Shares	Weighted Average Exercise Price
Outstanding at January 1, 2002	1,405,631	$ 27.20
Granted	8,705,949	$ 1.55
Outstanding at December 31, 2002	10,111,580	$ 4.13
Granted	1,936,001	$ 4.06
Outstanding at December 31, 2003	12,047,581	$ 4.12
Granted	1,098,040	$ 3.67
Exercised	(337,500)	$ .94
Expired	(566,071)	$ 32.55
Outstanding at December 31, 2004	12,242,050	$ 2.85
Exercisable at December 31, 2004	12,242,050	$ 2.85

10. COMMITMENTS AND CONTINGENCIES

Commitments

The Company entered into two license agreements with Children's Hospital, Boston for the exclusive, worldwide, royalty−bearing licenses to make, use and sell Endostatin and 2−methoxyestradiol ("2ME2"), both inhibitors of angiogenesis. In February 2004, the Company transferred rights to Endostatin in an agreement with Children's Medical Center Corporation and Alchemgen Therapeutics. Therefore, the Company has no future milestone payment obligations related to endostatin. In consideration for retaining the 2ME2 rights, the Company must pay a royalty on any sublicensing fees, as defined in the agreement, to Children's Hospital, Boston. The agreement obligates the Company to pay up to $1,000,000 "upon the attainment of certain milestones." As of December 31, 2004, the Company has paid $150,000 under this agreement for the milestones that have been achieved to date.

The Company leases its primary facilities through February 2009. The lease agreement provides for escalation of the lease payments over the term of the lease; however, rent expense is recognized under the straight−line method. Additionally, the Company leases office equipment under operating leases. The future minimum payments under its facilities and equipment leases as of December 31, 2004 are as follows:

2005	934,616
2006	962,654
2007	991,534
2008	1,021,280
2009	171,644
Thereafter	—
Total minimum payments	$4,081,728

Rental expense for the years ended December 31, 2004, 2003 and 2002 was $926,000, $1,296,000, and $1,031,000, respectively.

Contingencies

EntreMed is subject in the normal course of business to various legal proceedings in which claims for monetary or other damages may be asserted. Management does not believe such legal proceedings, unless otherwise disclosed herein, are material.

11. EMPLOYEE RETIREMENT PLAN

The Company sponsors the EntreMed, Inc. 401(k) and Trust. The plan covers substantially all employees and enables participants to contribute a portion of salary and wages on a tax−deferred basis. Contributions to the plan by the Company are discretionary. Contributions by the Company totaled $87,000, $89,000 and $230,000 in 2004, 2003 and 2002, respectively.

12. QUARTERLY FINANCIAL INFORMATION (UNAUDITED)

Summarized unaudited quarterly financial information for the years ended December 31, 2004 and 2003 is as follows:

	QUARTER ENDED			
	MARCH 31,	JUNE 30,	SEPTEMBER 30,	DECEMBER 31,
2004				
Revenues	$ 97,967	$ 139,380	$ 142,738	$ 133,910
Research and development costs	3,056,970	2,484,426	2,553,494	2,428,362
General and administrative expenses	2,092,939	1,963,410	1,337,922	1,176,393
Investment income	84,594	60,733	75,495	93,118
Gain on sale−royalty interest	−	−	−	3,000,000
Gain on sale of securities	−	−	520,000	−
Gain on sale of assets	−	−	6,335	117,748
Net loss	(4,967,348)	(4,247,723)	(3,146,848)	(259,979)
Dividends on Series A convertible preferred stock	(251,250)	(251,250)	(251,250)	(251,250)
Net loss attributable to common shareholders	(5,218,598)	(4,498,973)	(3,398,098)	(511,229)
Net loss per share (basic and diluted)	$ (0.14)	$ (0.12)	$ (0.09)	$ (0.02)
2003				
Revenues	$ 513,547	$ 285,988	$ 258,478	$ 517,533
Research and development costs	2,630,606	3,918,915	3,151,002	4,551,673
General and administrative expenses	1,627,204	1,674,517	1,748,055	1,973,210
Investment income	53,647	48,546	43,485	59,902
Net loss	(3,690,616)	(5,258,898)	(4,597,094)	(5,947,448)
Dividends on Series A convertible preferred stock	(251,250)	(251,250)	(251,250)	(251,250)
Net loss attributable to common shareholders	(3,941,866)	(5,510,148)	(4,848,344)	(6,198,698)
Net loss per share (basic and diluted)	$ (0.16)	$ (0.19)	$ (0.15)	$ (0.18)

EXHIBIT 23.1

CONSENT OF ERNST & YOUNG LLP, INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference of our reports dated March 14, 2005, with respect to the consolidated financial statements of EntreMed Inc., EntreMed Inc.'s assessment of the effectiveness of internal control over financial reporting, and the effectiveness of internal control over financial reporting of EntreMed Inc., included in this Annual Report (Form 10−K) for the year ended December 31, 2004, the following registration statements:

1. Registration Statement Number 333−26057 on Form S−8
2. Registration Statement Number 333−67063 on Form S−8
3. Registration Statement Number 333−41218 on Form S−8
4. Registration Statement Number 333−68048 on Form S−8
5. Registration Statement Number 333−101617 on Form S−8
6. Registration Statement Number 333−80193 on Form S−3
7. Registration Statement Number 333−84907 on Form S−3
8. Registration Statement Number 333−94665 on Form S−3
9. Registration Statement Number 333−76824 on Form S−3
10. Registration Statement Number 333−104380 on Form S−3
11. Registration Statement Number 333−110604 on Form S−3
12. Registration Statement Number 333−26057 on Form S−3
13. Registration Statement Number 333−87940 on Form S−3

/s/ Ernst & Young LLP

McLean, Virginia
March 14, 2005

Exhibit 31.1

CERTIFICATION OF PRESIDENT AND CHIEF EXECUTIVE OFFICER

I, James S. Burns, certify that:

1. I have reviewed this annual report on Form 10−K of EntreMed, Inc.:

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a−15(e) and 15d−15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a−15(f) and 15d−15(f)) for the registrant and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 14, 2005

/s/ James S. Burns
James S. Burns
President and Chief Executive Officer

Exhibit 31.2

CERTIFICATION OF CHIEF FINANCIAL OFFICER

I, Dane R. Saglio, certify that:

1. I have reviewed this annual report on Form 10−K of EntreMed, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a−15(e) and 15d−15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a−15(f) and 15d−15(f)) for the registrant and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 14, 2005

/s/ Dane R. Saglio
Dane R. Saglio
Chief Financial Officer

Exhibit 32.1

CERTIFICATION BY CHIEF EXECUTIVE OFFICER
PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES−OXLEY ACT OF 2002

In connection with the Annual Report of EntreMed, Inc. (the "Company") on Form 10−K as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, James S. Burns, as Chief Executive Officer of the Company, hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes−Oxley Act of 2002, to the best of my knowledge, that:

(1) The Report fully complies with the requirements of section 13(a) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company for the dates and periods covered by the Report.

This certificate is being made for the exclusive purpose of compliance by the Chief Executive Officer of the Company (or equivalent) with the requirements of Section 906 of the Sarbanes−Oxley Act of 2002, and may not be used by any person or for any reason other than as specifically required by law.

/s/ James S. Burns
James S. Burns
President and CEO

March 14, 2005

Exhibit 32.2

CERTIFICATION BY CHIEF FINANCIAL OFFICER
PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES−OXLEY ACT OF 2002

In connection with the Annual Report of EntreMed, Inc. (the "Company") on Form 10−K as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Dane R. Saglio, as Chief Financial Officer of the Company, hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes−Oxley Act of 2002, to the best of my knowledge, that:

(1) The Report fully complies with the requirements of section 13(a) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company for the dates and periods covered by the Report.

This certificate is being made for the exclusive purpose of compliance by the Chief Financial Officer of the Company with the requirements of Section 906 of the Sarbanes−Oxley Act of 2002, and may not be used by any person or for any reason other than as specifically required by law.

March 14, 2005

/s/ Dane R. Saglio
Dane R. Saglio
Chief Financial Officer

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