

UNITED THERAPEUTICS CORP

Form 10-K405

March 20, 2002

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Securities and Exchange Commission  
Washington, DC 20549  
Form 10-K

☒ ANNUAL REPORT UNDER SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2001

OR

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

For the transition period from \_\_\_\_\_ to \_\_\_\_\_

Commission File Number 0-26301

**UNITED THERAPEUTICS CORPORATION**  
(Exact name of Registrant as specified in its charter)

Delaware	52-1984749
_____ (State or Other Jurisdiction of Incorporation or Organization)	_____ (IRS Employer Identification No.)
1110 Spring Street Silver Spring, MD	20910
_____ (Address of principal executive offices)	_____ (zip code)

Registrant's telephone number, including area code: (301) 608-9292

Securities registered under Section 12(b) of the Exchange Act:  
None.

Securities registered under Section 12(g) of the Exchange Act:  
Common Stock, par value \$.01 per share  
and associated preferred stock purchase rights  
(Title of Class)

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. ☒

The number of shares outstanding of the registrant's Common Stock, par value \$0.01 per share, as of March 13, 2002 was 20,225,200 shares. The aggregate market value of the Common Stock held by non-affiliates of the registrant, based on the average bid and asked prices on March 13, 2002 as reported by the Nasdaq National Market was approximately \$243.2 million.

DOCUMENTS INCORPORATED BY REFERENCE

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Portions of the registrant's definitive proxy statement for the registrant's 2002 annual shareholders meeting are incorporated by reference in Part III of this Form 10-K.

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**PART I**

**ITEM 1. BUSINESS**

United Therapeutics is a biotechnology company focused on chronic and life-saving therapeutics. United Therapeutics is active in three therapeutic areas cardiovascular medicine, infectious disease and oncology with four therapeutic platforms prostacyclin analogs, arginine formulations, telemedicine and iminosugars.

Most of United Therapeutics resources are focused on its analogs of the endogenous hormone prostacyclin for the treatment of pulmonary hypertension, peripheral vascular disease and metastatic cancer. United Therapeutics second principal focus is the development of iminosugar compounds for the treatment of hepatitis B and C. United Therapeutics also devotes resources to the commercialization and further development of arginine therapy, especially in coronary artery disease, and of telecardiology, principally for cardiac arrhythmia.

United Therapeutics was incorporated in June 1996 in Delaware under the name Lung Rx, Inc. The company changed its name to United Therapeutics Corporation in December 1997.

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**United Therapeutics Products**

The following table summarizes United Therapeutics' product portfolio.

<b>Product</b>	<b>Mode of Delivery</b>	<b>Indication/Market</b>	<b>Current Status</b>	<b>UT Territory</b>
CardioPAL® and PM-350	Telemedical	Arrhythmia and Angina	Commercial	Worldwide
Arginine Supplements	Medical foods	Cardiovascular Disease	Launching	Worldwide
Remodulin	Continuous Subcutaneous	Pulmonary arterial hypertension	US Approval Pending/EU Reviews Ongoing	Worldwide
Remodulin	Intermittent Subcutaneous	Critical limb ischemia	Phase II/III	Worldwide
Remodulin	Periodic Subcutaneous	Metastatic cancer	Phase I	Worldwide
Beraprost Immediate Release	Oral	Metastatic cancer	Phase I	U.S./Canada
UT231B	Oral	Hepatitis C	Preclinical	Worldwide
Iminosugar Platform	Oral	Hepatitis B	Preclinical	Worldwide
R7V Platform	Vaccine	Human immunodeficiency virus (HIV)	Preclinical	Worldwide
UT-15 Sustained Release/ Beraprost Sustained Release	Oral	Peripheral vascular disease	Preclinical	U.S./Canada
Unipeg	Inhalation/Oral	Cardiovascular	Preclinical	Worldwide
ADMA Diagnostic	Diagnostic test	Cardiovascular disease	Preclinical	Worldwide
Epicardia Auto-Trigger	Telemedical	Cardiac arrhythmia	Preclinical	Worldwide

### *Remodulin*

In December 1996 and January 1997, United Therapeutics obtained worldwide rights for all indications to Remodulin (also known as UT-15 and formerly known as Uniprost), a prostacyclin analog, from Glaxo Wellcome, Inc. and Pharmacia & Upjohn Company. In October 1999, United Therapeutics acquired all the outstanding stock of SynQuest, Inc., the manufacturer of treprostinil, the bulk active ingredient in Remodulin.

### *Pulmonary Arterial Hypertension*

United Therapeutics has focused primarily on developing Remodulin as its lead product for treating pulmonary arterial hypertension. Pulmonary arterial hypertension is a vascular disease, which affects the blood vessels between the heart and lungs known as the pulmonary blood vessels. Pulmonary arterial hypertension is characterized by the degradation of the blood-vessel wall lining, the aggregation of platelets and the disruption of smooth muscle cell function. These conditions cause blockages and affect the ability of the blood vessels to dilate and then constrict as blood flows to the lungs. The resulting elevated pulmonary blood pressure causes increasing strain on the right side of the heart as it tries to pump blood to the lungs.

Pulmonary arterial hypertension is associated with reduced production of the natural compound prostacyclin in the pulmonary blood vessels. Prostacyclin appears to dilate blood vessels where necessary, prevent platelet aggregation, and prevent proliferation of smooth muscle cells surrounding the vessels. The only currently FDA-approved prostacyclin for pulmonary arterial hypertension is Flolan®, an artificial form of prostacyclin delivered continuously by an external pump through a surgically implanted intravenous catheter. It is approved for use in certain subsets of late-stage pulmonary arterial hypertension. Remodulin is a significantly longer lived and more stable synthetic form of prostacyclin which United Therapeutics believes will provide patients with a convenient and non-intravenous life-long prostacyclin therapy.

In contrast to Flolan, Remodulin is stable at room temperature and is significantly longer lived in the human body. These attributes allow for safer and more convenient delivery of Remodulin to patients. Specifically, Remodulin is delivered by subcutaneous infusion with a pager-sized microinfusion device made by Medtronic MiniMed, Inc. Subcutaneous delivery of Remodulin also eliminates the risk of sepsis infection and related hospitalization associated with the Flolan catheter. Remodulin's extended life in the body also greatly reduces the risk of death, from an abrupt recurrence of hypertension known as rebound hypertension when treatment is interrupted. The stability of Remodulin also allows it to be prepackaged, thus eliminating the need to reconstitute the drug one or more times daily under completely sterile conditions, as is required with Flolan.

Recently, the FDA approved Tracleer, an oral treatment for patients with certain subsets of late-stage pulmonary arterial hypertension. Tracleer is the first drug in a class of drugs known as endothelin antagonists. Endothelin constricts blood vessels and is elevated in patients with pulmonary arterial hypertension. Many leading experts in pulmonary arterial hypertension believe that Tracleer or other endothelin antagonists may in the future be used in combination with Remodulin or Flolan since these drugs provide symptomatic relief in different ways and might complement each other to treat these seriously ill patients.

In March 2000, United Therapeutics completed an international, randomized, placebo-controlled, double-blind study of Remodulin involving a total of 470 patients with pulmonary arterial hypertension. Half of the patients received Remodulin subcutaneously for 12 weeks, while the other half received a placebo. The study data show that patients who received Remodulin had significant improvement in exercise capacity, pulmonary blood pressure and in the signs and symptoms of the disease. All patients in the pivotal study had the option to continue or commence Remodulin in an open-label study after completion of the 12-week study. Approximately 500 patients are now being treated with the drug, including additional patients who enrolled directly into the open-label study.

The nonclinical and manufacturing portions of the New Drug Application (NDA) for Remodulin were filed on August 14, 2000 with the U.S. Food and Drug Administration (FDA). On October 16, 2000, United Therapeutics filed the remaining sections of the NDA for Remodulin and was notified that the FDA's pre-approval inspection of United Therapeutics' manufacturing facility was successfully completed. On October 19, 2000, the FDA informed United Therapeutics that a six-month Priority Review had been granted for the NDA. The FDA's review was ultimately extended until February 2002.

On August 9, 2001, the FDA's Cardiovascular and Renal Drugs Advisory Committee voted 6 to 3 to recommend that Remodulin be approved. On February 8, 2002, the FDA determined that Remodulin was approvable for the indication of pulmonary arterial hypertension for patients with NYHA class II-IV symptoms. Final approval is conditioned on the FDA's acceptance of the product label and United Therapeutics' agreement to a post marketing Phase IV clinical study to further assess the clinical benefits of Remodulin. United Therapeutics has agreed to perform the post marketing Phase IV clinical study design and is currently discussing the content of the study protocol and product label with the FDA. Once approved, Remodulin will be the only drug that may be prescribed for all disease subsets of symptomatic pulmonary arterial hypertension. Furthermore, it will be the only pulmonary arterial hypertension treatment indicated for patients with NYHA class II (early-stage) symptoms.

In February 2001, United Therapeutics submitted a Marketing Authorization Application in France for approval of Remodulin for pulmonary arterial hypertension. In October 2001, United Therapeutics submitted a Marketing Authorization Application in Switzerland for approval of Remodulin for pulmonary arterial hypertension. Also, in December 2001, United Therapeutics submitted a New Drug Submission (NDS) in Canada for approval of Remodulin for pulmonary arterial hypertension. The NDS in Canada was accepted for filing in February 2002 and was granted priority review status. Each of these foreign reviews is pending.

#### *Peripheral Vascular Disease/Critical Limb Ischemia*

United Therapeutics is also developing Remodulin for late-stage peripheral vascular disease known as critical limb ischemia. Peripheral vascular disease is a vascular disease that affects the blood vessels in the legs. While the precise cause of peripheral vascular disease is unknown, diabetes, obesity, smoking and lack of exercise are associated with the disease. Peripheral vascular disease appears to be similar to pulmonary hypertension in that there is a reduction in natural prostacyclin in the affected blood vessels. In September 1998, United Therapeutics completed a Phase II study which assessed the safety and blood flow effects of Remodulin administered intravenously to patients with critical limb ischemia. The study demonstrated that Remodulin can be administered safely to patients with critical limb ischemia and that Remodulin substantially increased blood flow in the affected areas of the legs. United Therapeutics is planning a Phase II/III clinical study of Remodulin for critical limb ischemia to commence in 2002.

#### *Metastatic Cancer*

United Therapeutics has tested the anti-cancer capabilities of Remodulin in laboratory experiments. These in vitro studies showed that Remodulin has an anti-metastatic effect at the same dose as is given to pulmonary hypertension patients. In addition, there are many published reports of the anti-cancer effects of various analogs of the prostacyclin molecule. Much of the excitement regarding prostacyclin as an anti-cancer molecule has to do with prostacyclin's ability to block an endothelial cell receptor (called the PRAR receptor) which is believed to be needed for tumor growth. Given the potency of Remodulin, and its relative ease of use, United Therapeutics believes there may be anti-cancer potential in this lead United Therapeutics product. United Therapeutics is planning a Phase I study of Remodulin for metastatic cancer. The study is expected to commence in 2002 as no further animal studies are required.

#### *Unipeg*

In September 1999, United Therapeutics entered into an agreement with Shearwater Polymers, Inc., now a subsidiary of Inhale Therapeutics Systems, Inc. This agreement grants to United Therapeutics the exclusive right to Shearwater's know-how for the design, development, production and use of a technology known as pegylation to develop and produce sustained release Remodulin for the possible treatment of pulmonary hypertension, peripheral vascular disease, stroke, heart disease, cancer, and related diseases worldwide. During 2000, Shearwater and United Therapeutics achieved pegylation of the Remodulin molecule. It is expected that this pegylation product, known as Unipeg, would be delivered via inhalation. Unipeg is currently in the preclinical phase of development.

#### *Arginine and ADMA*

In December 2000, United Therapeutics expanded into the fields of angina and coronary artery disease when it acquired the assets and certain liabilities of Cooke Pharma, Inc., the exclusive manufacturer of the HeartBar® line of arginine products that is now operated as Unither Pharma, Inc. HeartBar is the first and only medical food to promote cardiovascular health. Medical foods are regulated by the FDA. Unither Pharma is the only company that owns the

patent rights to use HeartBar's key ingredient, arginine, for cardiovascular conditions. Although arginine is broadly sold as a nutritional supplement in pill form, there are no existing arginine products, other than HeartBar, that deliver sufficient levels of arginine to achieve a therapeutic benefit. The HeartBar, which is included in the Physicians Desk Reference, increases the relaxing effect of nitric oxide produced by blood vessels. This produces relief from the symptoms of cardiovascular disease by increasing the diameter of blood vessels and thereby increasing blood flow. Clinical studies have demonstrated the ability of the HeartBar to reduce painful symptoms of cardiovascular disease, increase exercise tolerance and improve the quality of life. One HeartBar per day delivers 6 grams of arginine. The HeartBar Sport formulation delivers 3 grams of arginine. HeartBar products are sold in seven flavors and four formulations.

Recent studies show that people with high levels of another molecule called asymmetric dimethylarginine (ADMA) may be at especially high risk of heart disease. ADMA actually blocks the conversion of arginine to nitric oxide, which is even worse on the body than the effect of not ingesting enough arginine in the first place. In December 2001, United Therapeutics acquired the exclusive worldwide rights to develop a blood test to measure a person's ADMA levels, much like a cholesterol test. As most people age, their blood pressure rises as endothelial dysfunction gradually sets in. While it is not a cure for the problems of advancing age, arginine supplementation is an excellent way to achieve dietary management of cardiovascular risk at any age. This is particularly true for those persons with genetically determined high levels of ADMA.

### ***Telemedicine Services***

Pulmonary hypertension patients require periodic monitoring of certain bodily measurements such as heart and lung function. Much of this monitoring can be achieved with less expense and inconvenience by using telemedicine devices that enable physicians to monitor patients remotely. United Therapeutics intends to provide telemedicine services for a fee to patients and physicians using and prescribing United Therapeutics' products.

In December 2000, United Therapeutics expanded into arrhythmia and ischemic monitoring by acquiring all the assets of Medicomp, Inc. and Telemedical Procedures, LLC, related telemedicine companies based in Florida that are now operated as Medicomp, Inc. Medicomp, Inc. provides cardiac holter and event monitoring analysis services remotely via telephone lines and the Internet to expert technicians at its cardiac monitoring center. These services are designed to address the needs of patients suspected of suffering from cardiac arrhythmias and other abnormalities such as ischemic events and are delivered via Medicomp's proprietary PM 350 Holter Monitor and CardioPAL® event recorder. Cardiac arrhythmias and ischemic heart disease afflict an estimated 20 million Americans, and possibly ten times that number worldwide. If left undetected and untreated, these conditions can result in heart attacks and death. Treatment of cardiac arrhythmias and ischemia with pharmaceuticals requires careful titration based upon life-long repeat cardiac monitoring.

### ***Iminosugars***

In March 2000, Unither Pharmaceuticals, Inc., a wholly owned subsidiary of United Therapeutics, entered into a license agreement with Synergy Pharmaceuticals, Inc. to obtain from Synergy the exclusive worldwide rights to certain patents relating to anti-viral compounds. These compounds are iminosugars, a class of small molecules, which may be effective as an oral therapy for hepatitis B and C infections, as well as dengue and Japanese encephalitis virus. The compounds are currently in late stages of preclinical testing. An Investigational New Drug Application (IND) is expected to be submitted for the first iminosugar compound, UT231B, in 2002. It is anticipated that a Phase I proof of concept study in patients with hepatitis C will commence in 2002.

### ***Preventis***

In 1999, United Therapeutics co-founded Preventis, Inc. to develop vaccines and anti-microbial drugs for the treatment and prevention of infectious diseases. Preventis holds a co-exclusive license from the French Health Research agency, INSERM, in a patent currently being used to develop an HIV vaccine. Preventis also has exclusive rights to patents relating to vaccine manufacture and urinary tract infections. Preventis current projects involve the development of a therapeutic HIV/AIDS vaccine and the development of a vaccine to prevent bladder and kidney infections known as urinary tract infections. Preventis' therapeutic HIV/AIDS vaccine has already demonstrated specific antibody response in preclinical animal studies. Preventis is planning to commence human trials outside of the United States in 2002. Crucial to the development of an effective HIV vaccine is a drug that targets all twelve strains of the virus. Preventis believes that it has identified a universal characteristic of HIV and is targeting that element. For this reason, Preventis is pursuing the



development of both a therapeutic and a preventive vaccine for the treatment of HIV globally. United Therapeutics owns approximately 28 percent of Preventis, Inc.

### ***Beraprost***

Beraprost is an oral form of prostacyclin that is chemically stable. Like natural prostacyclin and Remodulin, beraprost dilates blood vessels, prevents platelet aggregation and prevents proliferation of smooth muscle cells surrounding blood vessels. United Therapeutics believes that beraprost may be an important treatment for early-stage peripheral vascular disease and for early-stage pulmonary hypertension. Intermittent oral doses of immediate release beraprost do not, however, provide consistent levels of the drug in the blood necessary to treat advanced stages of pulmonary hypertension or peripheral vascular disease. In cancer, it is believed that prostacyclins block an endothelial cell receptor (PRAR receptor) which is considered necessary for tumor growth.

In September 1998, United Therapeutics obtained an exclusive license from Toray Industries, Inc. for the immediate release formulation of beraprost for the treatment of pulmonary hypertension in the United States and Canada. In March 1999, United Therapeutics obtained an additional exclusive license from Toray for the immediate release formulation of beraprost for the treatment of peripheral vascular disease in the United States and Canada. In June 2000, United Therapeutics obtained from Toray the exclusive right to develop and market beraprost in the sustained release formulation (beraprost SR) in the United States and Canada for the treatment of all vascular indications (including cardiovascular indications). In 2002, United Therapeutics expects to obtain from Toray the exclusive right to develop and market Beraprost formulations in the United States and Canada for the treatment of oncological and respiratory conditions.

United Therapeutics conducted a Phase III clinical trial program for beraprost to treat early-stage peripheral vascular disease. The results were analyzed in October 2001. Beraprost did not meet its primary endpoint of improvement in total walking distance. As a result, United Therapeutics discontinued development of the immediate release formulations of Beraprost for early stage peripheral vascular disease and pulmonary arterial hypertension. United Therapeutics hopes that the sustained release formulation will demonstrate greater efficacy. The sustained release formulation is currently in Phase I testing in Japan.

### **The Medtronic MiniMed Strategic Alliance**

Medtronic MiniMed Inc. has agreed to provide its pager-sized microinfusion pump for delivery of Remodulin continuously and subcutaneously. United Therapeutics entered into an agreement with MiniMed, Inc. (now Medtronic MiniMed) in September 1997, which was implemented in a detailed set of guidelines adopted in November 1999 and in October 2001, to collaborate in the design, development and implementation of therapies to treat pulmonary hypertension utilizing MiniMed products and Remodulin. The guidelines require United Therapeutics to purchase its Remodulin infusion pumps exclusively from Medtronic MiniMed at a discount to MiniMed list prices unless MiniMed's infusion pumps fail to receive certain government approvals. The term of the agreement commenced on September 3, 1997 and continues for seven years after the FDA grants a new drug approval for Remodulin. The agreement will be automatically extended for additional 12-month periods unless otherwise terminated. The agreement is subject to early termination in the event of a material breach or bankruptcy of either party. In the event that there are any discoveries or improvements arising out of work performed under the agreement, the parties will have joint ownership of those discoveries or improvements. United Therapeutics and MiniMed have established a Management Committee comprised of two representatives from each company to implement the agreement.

### **Priority Healthcare and Gentiva Health Services Strategic Alliances**

To provide for marketing, promotion and distribution of Remodulin in the United States, United Therapeutics entered into non-exclusive distribution agreements with Priority Healthcare Corporation and Gentiva Health Services, Inc. on February 9, 2000 and March 21, 2000, respectively. In August 2001, Gentiva announced its intention to sell its pharmacy distribution division (including Remodulin distribution) to Accredo Health, Inc. Under the distribution agreements, United Therapeutics will sell Remodulin and MiniMed products to Priority and Gentiva at a discount from an average wholesale price recommended by United Therapeutics. Priority and Gentiva will be responsible for assisting patients with obtaining reimbursement and other support services. The terms of the agreements commenced on signing and continue for two years following FDA approval of Remodulin in the case of Priority and three years following the launch of Remodulin in the case of Gentiva. The agreements will be automatically renewed thereafter for additional two-

year periods in the case of Priority and one-year periods in the case of Gentiva unless one party provides notice of termination. The agreements are subject to early termination in the event of a material breach or bankruptcy of either party or upon 180-day advance notice of termination.

### **Patents And Proprietary Rights**

United Therapeutics' success will depend in part on its ability to obtain and maintain patent protection for its products, preserve trade secrets, prevent third parties from infringing upon its proprietary rights and operate without infringing upon the proprietary rights of others, both in the United States and internationally.

#### ***Glaxo Wellcome Assignment***

In January 1997, Glaxo Wellcome Inc. assigned to United Therapeutics patents and patent applications for the use of the stable prostacyclin analog known as UT-15, now known as Remodulin, for the treatment of pulmonary hypertension and congestive heart failure. For pulmonary hypertension, the patent does not expire in the United States until October 2009 and until various dates from September 2009 to August 2013 in nine other countries. For congestive heart failure, the patent does not expire until May 2011 in the United States and from May 2011 to March 2012 in five other countries.

#### ***Shearwater Polymers, Inc. Agreement***

In September 1999, United Therapeutics entered into an agreement with Shearwater Polymers, Inc. (now a subsidiary of Inhale Therapeutic Systems, Inc.). This agreement grants to United Therapeutics the exclusive right to Shearwater's know-how for the design, development, production and use of a technology known as pegylation to develop and produce sustained release prostacyclin molecules for the possible treatment of pulmonary hypertension, peripheral vascular disease, stroke, heart disease, cancer, and related diseases worldwide, known as Unipeg.

Under United Therapeutics' agreement with Shearwater, any inventions that relate to the combination of prostacyclin and the pegylation technology, including Unipeg for the treatment of any disease or condition, will be owned solely by United Therapeutics, and any inventions relating to non-prostacyclin pegylation methods such as drug formulation or delivery will be owned solely by Shearwater. Both United Therapeutics and Shearwater have filed for U.S. patent applications relating to their respective inventions and each is responsible for prosecuting and maintaining its patent portfolio. The licensed technology has thus far resulted in one issued patent in the United States that expires in 2020 and several pending patent applications owned by United Therapeutics.

#### ***Synergy Pharmaceuticals, Inc.***

In March 2000, Unither Pharmaceuticals, Inc. (Unither), a wholly owned subsidiary of United Therapeutics, entered into a license agreement with Synergy Pharmaceuticals, Inc. (Synergy) to obtain from Synergy the exclusive worldwide rights to certain patents relating to anti-viral compounds known as iminosugars. The compounds are currently in late stages of preclinical testing, and are the subject of a combination of issued patents and pending applications in the United States and around the world. The issued patents have expiration dates ranging from 2008 to 2017. Additional inventions relating to the compounds may be owned jointly by Synergy and United Therapeutics or individually, depending on the source of the invention.

In November 2000, Unither and Synergy amended the exclusive license agreement to include the development of new analogs of the licensed compounds. As part of this amendment, Unither agreed to directly assume Synergy's role in funding ongoing research being conducted by the University of Oxford into analogs of the anti-viral compounds being developed by Unither and Synergy. United Therapeutics will receive an exclusive license from the University of Oxford to all inventions arising from such research.

#### ***Stanford University and New York Medical College Licenses***

In 2000, United Therapeutics' newly created subsidiary, Unither Pharma, Inc. (formerly Cooke Pharma, Inc.), acquired the exclusive license to patents related to amino acid based dietary supplements to enhance the level of endogenous nitric oxide in the vascular system from Stanford University and New York Medical College. The licenses

cover worldwide territories and are valid for the life of the patents (ranging from 2010 to 2018). Unither Pharma will own all rights to all new products that may be or are derived from these licenses, including Unither Pharma's HeartBar products.

#### ***Patent Term Extensions***

United Therapeutics believes that some of the patents to which it has rights may be eligible for extensions of up to five years based upon patent term restoration procedures in Europe and in the United States under the Waxman-Hatch Act. For instance, under Waxman-Hatch, the U.S. patents relating to Remodulin could be extended by up to five years, giving the product patent protection until as late as October 2014 if approval in the United States is received before expiration of the original patent term. In addition, patent extensions are available under similar laws in Europe. United Therapeutics is considering which patents it will seek to extend under Waxman-Hatch and similar laws of other jurisdictions. See Government Regulation.

#### ***Orphan Drug Status***

The FDA has approved the orphan designation for Remodulin for the treatment of pulmonary arterial hypertension, a designation that includes both primary pulmonary hypertension and advanced secondary pulmonary hypertension.

#### **Clinical Investigator Network**

United Therapeutics has established a multi-center clinical investigation network with approximately 100 leading medical centers. This network consists of pulmonologists and cardiologists from centers in North America, Europe, Australia and Israel who collectively treat a majority of patients with primary pulmonary hypertension, a substantial number of patients with secondary pulmonary hypertension as well as patients with peripheral vascular disease. These physicians understand and have extensive experience in clinical research of severe pulmonary and vascular diseases. United Therapeutics is continually expanding its clinical investigator network by adding professionals who have demonstrated success in conducting clinical research required for regulatory approval.

#### **Research & Development Expenditures**

United Therapeutics is engaged in research and development and has incurred substantial expenses for these activities. These activities generally include the cost of acquiring or inventing new technologies and products as well as their development. Research and development expenses during 2001, 2000 and 1999 totaled approximately \$32.6 million, \$70.2 million and \$30.7 million, respectively.

#### **Manufacturing and Supply**

United Therapeutics manufactures treprostinil, the bulk active ingredient in Remodulin, and has contracted with Toray Industries, Inc. to produce beraprost.

Baxter Healthcare Corporation (formerly Cook Imaging Corporation) continues to formulate Remodulin for United Therapeutics. An analytical testing laboratory, Magellan Laboratories Inc., tests the purity and stability of each batch of manufactured Remodulin for compliance with FDA standards.

HeartBar is manufactured by a contract nutritional food manufacturer in California, Nellson Nutraceuticals. Holter and event monitors are manufactured by Medicomp at its facility in Florida.

There are a limited number of companies which could replace these manufacturers and suppliers. However, a change in supplier or manufacturer could cause a delay in the manufacture, distribution and research efforts associated with the respective product.

#### **Marketing And Sales**

In accordance with the implementation of United Therapeutics' strategic alliance with Medtronic MiniMed, United

Therapeutics and Medtronic MiniMed will jointly handle aspects of distribution of the Remodulin therapy. United Therapeutics will have primary sales and marketing responsibility. United Therapeutics' marketing strategy will rely upon existing chronic care specialty pharmacy distributors to handle doctor and patient requests for Remodulin on a non-exclusive basis in the United States. To further this strategy, United Therapeutics has entered into two non-exclusive distributor agreements with Gentiva Health Services, Inc. and Priority Healthcare Corporation for the United States. See "Priority Healthcare and Gentiva Health Services Strategic Alliances" above. These specialty distributors are experienced in the sale, distribution and reimbursement of chronic therapies. Outside of the United States, United Therapeutics has entered into six exclusive distributor agreements covering Canada, Europe, Australia, South America and Israel. United Therapeutics will sell Remodulin and MiniMed products to its distributors in the United States and Canada at a discount from an average wholesale price suggested by United Therapeutics and to its international distributors at a transfer price set by United Therapeutics. The distributors will be responsible for assisting patients with obtaining reimbursement. During 2001, approximately \$1.1 million of revenues were earned from the resale of Minimed pumps and supplies to distributors.

Presently, HeartBar is marketed directly to consumers via independent distributors and the Internet.

Holter and event monitor analysis services and systems are marketed to physicians, hospitals, and managed care providers directly by Medicomp's internal sales force. During 2001, approximately \$2.8 million of revenues were earned from the sales of telemedicine services and systems.

During 2001, approximately \$801,000 of revenues was earned from the sales of chemical synthesis and manufacturing services.

### **Competition**

Many drug companies engage in research and development to commercialize products to treat cardiovascular, infectious and oncological diseases. United Therapeutics is aware of two existing treatments already approved for certain subsets of late-stage pulmonary arterial hypertension with which Remodulin will have to compete. One is Flolan, an intravenously delivered prostacyclin. The other is Tracleer, an oral endothelin antagonist, and additional endothelin antagonists are being developed. In addition, competitors may develop and commercialize additional products that compete with United Therapeutics' products and may do so more rapidly than United Therapeutics.

Many companies market or are developing products which will compete with HeartBar in the cardiovascular health market. However, only HeartBar products may claim that its active ingredient, arginine, improves cardiovascular health.

Holter and event monitor analysis services and systems are provided by many local and regional competitors and a few national competitors.

United Therapeutics competes with all of these competitors for funding, access to licenses, personnel, third-party collaborators, product development and commercialization. Almost all of these companies have substantially greater financial, marketing, sales, distribution and technical resources, and more experience in research and development, product development and marketing, clinical trials and regulatory matters, than United Therapeutics.

### **Governmental Regulation**

The research, development, testing, manufacture, promotion, marketing and distribution of drug products are extensively regulated by government authorities in the United States and other countries. Drugs are subject to rigorous regulation by the FDA in the United States and similar regulatory bodies in other countries. The steps ordinarily required before a new drug may be marketed in the United States, which are similar to steps required in most other countries, include:

Preclinical laboratory tests, preclinical studies in animals and formulation studies and the submission to the FDA of an investigational new drug application for a new drug;

Adequate and well-controlled clinical trials to establish the safety and efficacy of the drug for each indication;

The submission of a new drug application to the FDA; and

FDA review and approval of the new drug application prior to any commercial sale or shipment of the drug.

Preclinical tests include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies. The results of preclinical testing are submitted to the FDA as part of an investigational new drug application. A 30-day waiting period after the filing of each investigational new drug application is required prior to the commencement of clinical testing in humans. At any time during this 30-day period or at any time thereafter, the FDA may halt proposed or ongoing clinical trials until the FDA authorizes trials under specified terms. The investigational new drug application process may be extremely costly and substantially delay development of United Therapeutics products. Moreover, positive results of preclinical tests will not necessarily indicate positive results in clinical trials.

Clinical trials to support new drug applications are typically conducted in three sequential phases, but the phases may overlap. During Phase I, the initial introduction to the drug into healthy human subjects or patients, the drug is tested to assess metabolism, pharmacokinetics and pharmacological actions and safety, including side effects associated with increasing doses. Phase II usually involves studies in a limited patient population to:

Assess the efficacy of the drug in specific, targeted indications;

Assess dosage tolerance and optimal dosage; and

Identify possible adverse effects and safety risks.

If a compound is found to be potentially effective and to have an acceptable safety profile in Phase II evaluations, Phase III trials, also called pivotal studies, major studies or advanced clinical trials, are undertaken to further demonstrate clinical efficacy and to further test for safety within an expanded patient population at geographically dispersed clinical study sites.

After successful completion of the required clinical testing, generally a new drug application is submitted. The FDA may request additional information before accepting a new drug application for filing, in which case the application must be resubmitted with the additional information. Once the submission has been accepted for filing, the FDA has 180 days to review the application and respond to the applicant. The review process is often significantly extended by FDA requests for additional information or clarification. The FDA may refer the new drug application to an appropriate advisory committee for review, evaluation and recommendation as to whether the application should be approved, but the FDA is not bound by the recommendation of an advisory committee.

If FDA evaluations of the new drug application and the manufacturing facilities are favorable, the FDA may issue either an approval letter or an approvable letter. An approvable letter will usually contain a number of conditions that must be met in order to secure final approval of the new drug application and authorization of commercial marketing of the drug for certain indications. The FDA may refuse to approve the new drug application or issue a not approvable letter, outlining the deficiencies in the submission and often requiring additional testing or information.

The FDA may designate a product as an orphan drug if the drug is a drug intended to treat a rare disease or condition. A disease or condition is considered rare if it affects fewer than 200,000 people in the United States, or if it affects more than 200,000 people but will be sold for less money than it will cost to develop. If a sponsor obtains the first FDA marketing approval for a certain orphan drug, the sponsor will have a seven-year exclusive right to market the drug for the orphan indication.

If regulatory approval of Remodulin or any of United Therapeutics other products is granted, it will be limited to certain disease states or conditions. The manufacturers of approved products and their manufacturing facilities will be subject to continual review and periodic inspections. In addition, identification of certain side effects or the occurrence of manufacturing problems after any of its drugs are on the market could cause subsequent withdrawal of approval, reformulation of the drug, additional preclinical testing or clinical trials, and changes in labeling of the product.

The Waxman-Hatch Act provides that patent terms may be extended during the FDA regulatory review period for

the related product. This period is generally one-half the time between the effective date of an investigational new drug application and the submission date of a new drug application, plus the time between the submission date of a new drug application and the approval of that application, subject to a maximum extension of five years. Similar patent term extensions are available under European laws.

Outside the United States, United Therapeutics' ability to market its products will also be contingent upon receiving marketing authorizations from the appropriate regulatory authorities. The foreign regulatory approval process may include some or all of the risks associated with FDA approval set forth above. The requirements governing the conduct of clinical trials and marketing authorization vary widely from country to country. At present, foreign marketing authorizations are applied for at a national level, although within Europe procedures are available to companies wishing to market a product in more than one European Union (EU) member state.

Under a new regulatory system in the EU, marketing authorizations may be submitted to a centralized, a decentralized or a national level process. The centralized procedure is mandatory for the approval of biotechnology products and high technology products and available at the applicant's option for other products. The centralized procedure provides for the grant of a single marketing authorization that is valid in all EU member states. The decentralized procedure is available for all medicinal products that are not subject to the centralized procedure. The decentralized procedure provides for mutual recognition of national approval decisions, changes existing procedures for national approvals and establishes procedures for coordinated EU actions on products, suspensions and withdrawals. Under this procedure, the holder of a national marketing authorization for which mutual recognition is sought may submit an application to one or more EU member states, certify that the dossier is identical to that on which the first approval was based or explain any differences and certify that identical dossiers are being submitted to all member states for which recognition is sought. Within 90 days of receiving the application and assessment report, each EU member state must decide whether to recognize approval. The procedure encourages member states to work with applicants and other regulatory authorities to resolve disputes concerning mutual recognition. Lack of objection of a given country within 90 days automatically results in approval of the EU country. Following receipt of marketing authorization in a member state, United Therapeutics would then engage in pricing discussions and negotiations with the prescription pricing authority in that country.

United Therapeutics intends to secure European regulatory approval for the use of Remodulin for pulmonary hypertension under the decentralized procedure and filed its first Marketing Authorization Application in France in February 2001. Regulatory applications for the use of Remodulin for pulmonary hypertension in Canada and Switzerland were also filed in 2001. Review of these applications is pending.

The HeartBar is subject to FDA regulation as a medical food. The current product labeling was submitted to the FDA and future labeling changes are subject to FDA review. The HeartBar is manufactured at a cGMP facility. Telemedical products are subject to FDA regulation as medical devices. The devices manufactured and sold by Medicomp have received marketing approval from the FDA under Section 510(k) of the Food, Drug and Cosmetic Act.

## **Employees**

United Therapeutics had approximately 128 employees as of March 15, 2002. The company also maintains active independent contractor relationships with various individuals with whom it has month-to-month consulting contracts. The company believes its employee relations are excellent.

## **Revenues and Industry Segments**

The information required by Regulation S-K Items 101(b) and 101(d) related to financial information about segments and financial information about sales is contained in Note 14 of the audited consolidated financial statements, which are included in this Annual Report on Form 10-K.

## Risk Factors

This Annual Report on Form 10-K contains forward-looking statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. These statements include, among others, statements relating to the following: the anti-cancer potential of Remodulin; the timing and outcome of clinical studies and regulatory filings; the achievement and maintenance of regulatory approvals; the ability to obtain additional license rights from Toray; the ability to find alternate sources of supply and manufacturing for United Therapeutics products; the existence, capabilities and activities of competitors; the adequacy of owned or leased facilities for operations; the expectation not to pay dividends on common stock in the foreseeable future; the extent of United Therapeutics' exposure to market risk; the ability to hold debt instrument investments to maturity; the statements identified as forward-looking statements in Item 7 Management's Discussion and Analysis of Financial Condition and Results of Operations included elsewhere in this Annual Report on Form 10-K; and statements preceded by, followed by or that include the words believes, expects, anticipates, intends, estimates, may or similar expressions. These statements involve risks, uncertainties and United Therapeutics' actual results may differ materially from the results discussed in these forward-looking statements. Factors that may cause such a difference include, but are not limited to, those discussed below.

### **If United Therapeutics' Products Fail In Clinical Studies, United Therapeutics Will Be Unable To Obtain FDA Approval And Will Not Be Able To Sell Those Products.**

In order to sell its pharmaceutical products, United Therapeutics must receive regulatory approval. To obtain those approvals, United Therapeutics must conduct clinical studies demonstrating that the drug and the delivery mechanism for the drug are safe and effective. If United Therapeutics cannot obtain FDA approval for a product, that product cannot be sold and United Therapeutics' revenues will suffer. United Therapeutics completed its clinical studies of Remodulin for pulmonary arterial hypertension and filed for FDA approval and that approval is pending. Ultimate approval will be conditioned, in part, on United Therapeutics' agreement to perform a post marketing Phase IV clinical study of Remodulin and the results of such Phase IV study. United Therapeutics has completed a Phase II clinical study for Remodulin for late-stage peripheral vascular disease called critical limb ischemia. United Therapeutics expects to commence Phase I clinical trial programs to treat metastatic lung cancer with Remodulin and to treat Hepatitis C with UT231B. United Therapeutics is still completing pre-clinical studies for its other products. United Therapeutics' ongoing clinical studies might be delayed or halted for various reasons, including:

The drug is not effective, or physicians think that the drug is not effective;

Patients experience severe side effects during treatment;

Patients die during the clinical study because their disease is too advanced or because they experience medical problems that are not related to the drug being studied;

Patients do not enroll in the studies at the rate United Therapeutics expects;

Drug supplies are not sufficient to treat the patients in the studies; and

The results of preclinical testing cause delays in clinical trials.

In addition, the FDA and foreign regulatory authorities have substantial discretion in the approval process. The FDA and foreign regulatory authorities may not agree that United Therapeutics has demonstrated that its products are safe and effective.

**If United Therapeutics Cannot Maintain Regulatory Approvals For Its Products, It Cannot Sell Those Products And Its Revenues Will Suffer.**

The process of obtaining and maintaining regulatory approvals for new drugs is lengthy, expensive and uncertain. The manufacturing, distribution, advertising and marketing of these products are subject to extensive regulation. Any new product approvals United Therapeutics receives in the future could include significant restrictions on the use or marketing of the product. Product approvals, if granted, can be withdrawn for failure to comply with regulatory requirements or upon the occurrence of adverse events following commercial introduction of the products. The FDA has indicated that Remodulin is approvable for pulmonary arterial hypertension subject to United Therapeutics agreement to perform a randomized placebo-controlled clinical trial in Phase IV. Continued approval of Remodulin would, in part, be subject to the results of that trial. If approvals are withdrawn for a product, United Therapeutics cannot sell that product and its revenues will suffer. In addition, governmental authorities could seize United Therapeutics products or force United Therapeutics to recall its products. Finally, United Therapeutics and its officers and directors could be subject to civil and criminal penalties for failure to comply with these regulatory requirements.

**United Therapeutics Has A History Of Losses And May Not Be Profitable.**

United Therapeutics has lost money since its inception in 1996, and its accumulated deficit was approximately \$162.2 million at December 31, 2001. United Therapeutics expects to incur substantial additional losses, whether or not it continues to generate revenue, as it continues to develop its products. United Therapeutics expects its quarterly and annual operating results to fluctuate, depending primarily on the following factors:

Timing of regulatory approvals and commercial sales of its products;

Level of patient demand for its products;

Timing of payments to licensors and corporate partners; and

Timing of investments in new technologies.

Substantially all of United Therapeutics pharmaceutical products are in clinical studies and the related regulatory approval process, and United Therapeutics is not yet selling any of its main pharmaceutical products. United Therapeutics might not obtain regulatory approvals for its pharmaceutical products and may not be able to sell its pharmaceutical products commercially. Even if United Therapeutics sells its products, United Therapeutics may not ever be profitable and may not be able to sustain any profitability it achieves.

**Discoveries Or Developments Of New Technologies By Others May Make United Therapeutics Products Obsolete.**

Other companies may conduct research, make discoveries or introduce new products that render all or some of United Therapeutics technologies and products obsolete or not commercially viable. Researchers are continually making new discoveries that may lead to new technologies to treat the diseases United Therapeutics products are intended for. In addition, alternative approaches to treating chronic diseases, such as gene therapy, may make United Therapeutics products obsolete or noncompetitive. United Therapeutics is aware of one such new drug called Tracleer, an oral endothelin antagonist, which will compete with Remodulin and additional endothelin antagonists are being developed by others.

**United Therapeutics Products May Not Be Commercially Successful Because Physicians And Patients May Not Accept Them.**

Even if regulatory authorities approve United Therapeutics products, those products may not be commercially successful. United Therapeutics expects that most of its products, including Remodulin, will be very expensive. Patient acceptance of and demand for United Therapeutics products will depend largely on the following factors:

Acceptance by physicians and patients of United Therapeutics products as safe and effective therapies;

Reimbursement of drug and treatment costs by third-party payers;



Pricing of alternative products;

Convenience and ease of administration of United Therapeutics products; and

Prevalence and severity of side effects associated with United Therapeutics products.

**United Therapeutics May Not Be Able To Successfully Integrate The Businesses Of Companies It May Or Has Acquired.**

United Therapeutics recently acquired several businesses and may make additional acquisitions. The successful integration of the acquired businesses will require:

Definition and alignment of the management teams;

Coordination of geographically separate organizations;

Integration of product offerings;

Coordination of sales and marketing and research and development efforts;

Alignment of corporate cultures and management philosophies; and

Management focus on transitional activities.

Management may not be able to accomplish the integration of acquired businesses successfully or within planned periods. Any difficulties or material expenses encountered in the transition process could adversely affect the revenues and operating results of the businesses acquired. If United Therapeutics fails to integrate acquired businesses quickly and efficiently, it may incur unanticipated costs or be unable to successfully advance the business objectives of the acquisition.

**If Third-Party Payers Will Not Reimburse Patients For United Therapeutics Drug Products, Sales Will Suffer.**

United Therapeutics commercial success will depend in part on third-party payers agreeing to reimburse patients for the costs of United Therapeutics pharmaceutical products. Third-party payers frequently challenge the pricing of new drugs. United Therapeutics expects that its products will be very expensive. Third-party payers may not approve United Therapeutics products for reimbursement. If third-party payers do not approve a United Therapeutics product for reimbursement, sales will suffer, as patients will opt for a competing product that is approved for reimbursement.

**United Therapeutics Relies On Third Parties To Develop, Market, Distribute And Sell Its Products And Those Third Parties May Not Perform.**

United Therapeutics does not have the ability to independently conduct clinical studies, obtain regulatory approvals, market, distribute or sell most of its products and intends to rely substantially on experienced third parties to perform all of those functions. United Therapeutics may not locate acceptable contractors or enter into favorable agreements with them. If third parties do not successfully carry out their contractual duties or meet expected deadlines, United Therapeutics will be unable to get marketing approvals and will be unable to sell its products. Medtronic MiniMed Inc. is United Therapeutics exclusive partner for the subcutaneous delivery of Remodulin using the MiniMed microinfusion device in the field of pulmonary hypertension. United Therapeutics is relying on Medtronic MiniMed's experience, expertise and performance. Similarly, United Therapeutics is relying on Gentiva Health Services, Inc. and Priority Healthcare Corporation to market, distribute, and sell Remodulin in the United States once it has been approved by the FDA. If United Therapeutics partners in the United States and internationally are unsuccessful in their efforts, United Therapeutics revenues will suffer.

**United Therapeutics Has Limited Experience With Manufacturing And Depends On Third Parties, Who May Not Perform, To Synthesize And Manufacture Many Of Its Products.**

United Therapeutics itself has limited experience with manufacturing. In October 1999, United Therapeutics acquired SynQuest, Inc., a company that manufactured treprostinil, the bulk active ingredient in Remodulin, for United Therapeutics. In December 2000, SynQuest was dissolved and merged into United Therapeutics as its synthesis and manufacturing division. Prior to the acquisition of SynQuest, United Therapeutics had no experience with manufacturing. Even though United Therapeutics retained the employees and managers of SynQuest in connection with the acquisition, United Therapeutics may be unsuccessful in maintaining drug manufacturing operations and in maintaining its status as an FDA approved manufacturing site for Remodulin.

United Therapeutics relies on third parties for the manufacture of all other products other than Remodulin and its telemedicine systems. United Therapeutics is relying on Baxter Healthcare Corporation (formerly Cook Imaging Corporation) for the formulation of Remodulin. United Therapeutics relies on Magellan Laboratories Incorporated to test the purity and stability of each batch of Remodulin. United Therapeutics relies on Nellson Nutraceuticals to manufacture the HeartBar. United Therapeutics relies exclusively on Toray Industries, Inc. to manufacture beraprost. Although there are a limited number of companies that could replace each of these suppliers, management believes that other suppliers could provide similar services and materials. A change in suppliers, however, could cause a delay in distribution of Remodulin and other products, and in the conduct of clinical trials and commercial launch, which would adversely affect United Therapeutics' research and development efforts, and future sales efforts. United Therapeutics' manufacturing strategy presents the following risks:

The manufacturing processes for some of United Therapeutics' products have not been tested in quantities needed for commercial sales;

Delays in scale-up to commercial quantities could delay clinical studies, regulatory submissions and commercialization of United Therapeutics' products;

A long lead time is needed to manufacture Remodulin, and the manufacturing process is complex;

United Therapeutics and manufacturers of United Therapeutics' products are subject to the FDA's good manufacturing practices regulations and similar foreign standards, and although United Therapeutics controls compliance issues with respect to synthesis and manufacturing conducted internally, the company does not have control over compliance with these regulations by its third-party manufacturers;

If United Therapeutics has to change to another manufacturing contractor or abandon its captive manufacturing operations, FDA and comparable foreign regulators would require new testing and compliance inspections and the new manufacturer would have to be educated in the processes necessary for the production of the affected product;

Without satisfactory long-term agreements with its manufacturers, United Therapeutics will not be able to develop or commercialize its products, other than Remodulin, as planned or at all and will have to rely solely on internal manufacturing capacity;

Without substantial experience in operating a manufacturing facility, United Therapeutics may not be able to successfully manufacture Remodulin; and

United Therapeutics may not have intellectual property rights, or may have to share intellectual property rights, to many improvements in the manufacturing processes or new manufacturing processes for its products.

Any of these factors could delay clinical studies or commercialization of United Therapeutics' products, entail higher costs and result in United Therapeutics being unable to effectively sell its products.

**If The Licenses United Therapeutics Depends On Are Breached Or Terminated, United Therapeutics Would Lose Its Right To Develop And Sell The Products Covered By The Licenses.**

United Therapeutics acquires or licenses drugs which have been discovered and initially developed by others. In addition, United Therapeutics has obtained and will be required to obtain licenses to third-party technology to conduct its business, including licenses for its products and a license for the MiniMed microinfusion device. This dependence on licenses has the following risks:

United Therapeutics may not be able to obtain future licenses at a reasonable cost or at all;

If any of United Therapeutics' licenses are terminated, United Therapeutics will lose its rights to develop and market some or all of its products;

The licenses that United Therapeutics holds generally provide for termination by the licensor in the event United Therapeutics breaches the license agreement, including by failing to pay royalties and other fees on a timely basis;

In the event that Glaxo Wellcome terminates its license agreement, United Therapeutics will have no further rights to utilize their patents or trade secrets to develop and commercialize Remodulin; and

If licensors fail to maintain the intellectual property licensed to United Therapeutics as required by most of United Therapeutics' license agreements, United Therapeutics may lose its rights to develop and market some or all of its products and may be forced to incur substantial additional costs to maintain the intellectual property itself or force the licensor to do so.

**If United Therapeutics' Patent And Other Intellectual Property Protection Is Inadequate, United Therapeutics' Sales And Profits Could Suffer Or Competitors Could Force United Therapeutics' Products Completely Out Of The Market.**

The U.S. patent for the method of treating pulmonary hypertension with Remodulin expires in 2009. The U.S. patents for the beraprost composition of matter and synthesis expire in 2003 and 2010. United Therapeutics may not be able to extend these or any other patents. Competitors may develop products based on the same active ingredients as United Therapeutics' products, including Remodulin, and market those products after the patents expire, or may design around United Therapeutics' existing patents. If this happens, United Therapeutics' sales would suffer and United Therapeutics' profits could be severely impacted.

The issued beraprost patents do not cover methods of treating any disease, including pulmonary hypertension or peripheral vascular disease, using beraprost. Patents may be issued to others which prevent the manufacture or sale of United Therapeutics' products. United Therapeutics may have to license those patents and pay significant fees or royalties to the owners of the patents in order to keep marketing its products. This would cause profits on sales to suffer.

The laws of foreign jurisdictions in which United Therapeutics intends to sell its products may not protect the company's rights to the same extent as the laws of the United States.

United Therapeutics has filed a patent application in the United States for the synthesis of Remodulin, but this and other patent applications which have been or may be filed by United Therapeutics may not be issued. The scope of any patent that issues may not be sufficient to protect United Therapeutics' technology. The laws of foreign jurisdictions in which United Therapeutics intends to sell its products may not protect the company's rights to the same extent as the laws of the United States.

In addition to patent protection, United Therapeutics also relies on trade secrets, proprietary know-how and technology advances. United Therapeutics enters into confidentiality agreements with its employees and others, but these agreements may not be effective in protecting the company's proprietary information. Others may independently develop substantially equivalent proprietary information or obtain access to United Therapeutics' know-how.

Litigation, which is very expensive, may be necessary to enforce or defend United Therapeutics' patents or proprietary rights and may not end favorably for United Therapeutics. Any of United Therapeutics' licenses, patents or other intellectual property may be challenged, invalidated, canceled, infringed or circumvented and may not provide any competitive advantage to United Therapeutics.

**United Therapeutics May Not Have, Or May Have To Share Rights To, Future Inventions Arising From Its Outsourcing Agreements And May Lose Potential Profits Or Savings.**

Pursuant to United Therapeutics' agreement with Medtronic MiniMed for the subcutaneous delivery of Remodulin, any new inventions or intellectual property that arise from United Therapeutics' activities with Medtronic MiniMed will be owned jointly by United Therapeutics and Medtronic MiniMed. Under United Therapeutics' agreement with Shearwater Polymers, Inc. for pegylation, Shearwater will own any inventions that relate to a non-prostacyclin pegylation method. If United Therapeutics does not have rights to new developments or inventions that arise during the terms of these agreements, or United Therapeutics has to share the rights with others, United Therapeutics will lose the benefit of the new rights which may mean a loss of future profits or savings generated from improved technology.

**If United Therapeutics' Highly Qualified Management And Technical Personnel Leave The Company, Its Business May Suffer.**

United Therapeutics is dependent on its current management. United Therapeutics does not maintain key person life insurance. United Therapeutics' success will depend in part on retaining the services of its existing management and key personnel and attracting and retaining new highly qualified personnel. Expertise in the field of cardiovascular medicine, infectious disease and oncology is not generally available in the market, and competition for qualified management and personnel is intense.

**United Therapeutics May Not Successfully Compete With Established Drug Companies.**

United Therapeutics competes with established drug companies during product development for, among other things, funding, access to licenses, personnel and third-party collaborators. United Therapeutics will also compete with these companies following approval of its products. Almost all of these companies have substantially greater financial, marketing, sales, distribution and technical resources, and more experience in research and development, clinical trials and regulatory matters, than United Therapeutics. United Therapeutics is aware of existing treatments that will compete with its products. If United Therapeutics cannot successfully compete with new or existing products, United Therapeutics' marketing and sales will suffer and it may not ever be profitable.

**If United Therapeutics Needs Additional Financing And Cannot Obtain It, Product Development And Sales May Be Limited.**

United Therapeutics may need to spend more money than currently expected because it may need to change its product development plans or product offerings to address difficulties with clinical studies or preparing for commercial sales. United Therapeutics may not be able to obtain additional funds on commercially reasonable terms or at all. If additional funds are not available, United Therapeutics may be compelled to delay clinical studies, curtail operations or obtain funds through collaborative arrangements that may require it to relinquish rights to certain products or potential markets.

**United Therapeutics May Not Have Adequate Insurance And May Have Substantial Exposure To Payment Of Product Liability Claims.**

The testing, manufacture, marketing, and sale of human drugs involves product liability risks. Although United Therapeutics has product liability insurance, United Therapeutics may not be able to maintain this product liability insurance at an acceptable cost, if at all, and this insurance may not provide adequate coverage against potential losses. If claims or losses exceed United Therapeutics' liability insurance coverage, United Therapeutics may go out of business.

**United Therapeutics Stock Price Could Be Volatile And Could Decline.**

The market prices for securities of drug and biotechnology companies are highly volatile, and there are significant price and volume fluctuations in the market that may be unrelated to particular companies' operating performances. United Therapeutics' stock price could decline suddenly due to the following factors:

Results of clinical trials;

Timing of regulatory approvals;

Outcome of regulatory reviews;

Fluctuations in operating results;

Announcements by United Therapeutics or others of technological innovations or new products;

Failure to meet estimates or expectations of securities analysts;

Rate of product acceptance;

Developments in patent or other proprietary rights;

Public concern as to the safety of products developed by United Therapeutics or by others;

Future sales of substantial amounts of common stock by existing United Therapeutics stockholders; and

General market conditions.

**Future Sales Of Shares May Depress The Stock Price.**

If the stockholders sell a substantial number of shares of United Therapeutics' common stock in the public market, or investors become concerned that substantial sales might occur, the market price of the common stock could decrease. Such a decrease could make it difficult for United Therapeutics to raise capital by selling stock or to pay for acquisitions using stock. To the extent outstanding options or warrants are exercised or additional shares of capital stock are issued, existing stockholders may incur additional dilution.

**Existing Directors And Executive Officers Of United Therapeutics Own A Substantial Block Of Stock And Might Be Able To Direct The Outcome Of Matters Requiring Stockholder Approval.**

United Therapeutics' directors and named executive officers beneficially own approximately 22 percent of its outstanding common stock. Accordingly, these stockholders as a group might be able to direct the outcome of matters requiring approval by United Therapeutics stockholders, including the election of its directors. Such stockholder control could delay or prevent a change of control of United Therapeutics.

**Because Of The Rights Agreement And Anti-Takeover Provisions In United Therapeutics Certificate Of Incorporation And Bylaws, A Third Party May Be Discouraged From Making A Takeover Offer Which Could Be Beneficial To United Therapeutics And The Public Stockholders.**

On December 14, 2000, United Therapeutics adopted a shareholder rights plan. The effect of this rights plan and of certain provisions of United Therapeutics Amended and Restated Certificate of Incorporation and Amended and Restated By-Laws, and the anti-takeover provisions of Section 203 of the Delaware General Corporation Law, could delay or prevent a third party from acquiring United Therapeutics or replacing members of the United Therapeutics board of directors, even if the acquisition or the replacements would be beneficial to United Therapeutics stockholders. These factors could also reduce the price that certain investors might be willing to pay for shares of the common stock and result in the market price being lower than it would be without these provisions.

**If Stockholders Do Not Receive Dividends, Stockholders Must Rely On Stock Appreciation For Any Return On Their Investment In United Therapeutics.**

United Therapeutics has never declared or paid cash dividends on any of its capital stock. United Therapeutics currently intends to retain its earnings for future growth and therefore does not anticipate paying cash dividends in the future.

**EXECUTIVE OFFICERS OF THE REGISTRANT**

The following is a list, as of March 15, 2002, setting forth certain information regarding the executive officers of United Therapeutics. Each executive officer's term will end pursuant to the terms of his or her employment contract or upon his or her earlier resignation or the appointment of a successor.

<b>Name</b>	<b>Age</b>	<b>Position</b>	<b>Term Ending</b>
Martine A. Rothblatt, Ph.D., J.D., M.B.A.	47	Chairman, Chief Executive Officer and Director	2006
Roger Jeffs, Ph.D.	40	President and Chief Operating Officer	2006
David A. Walsh, Ph.D.	57	Executive Vice President and Chief Operating Officer for Production	2002
Barry B. Kanarek, M.D., Ph.D.	55	Chief Medical Officer, President and Chief Operating Officer, Unither Pharmaceuticals, Inc.,	2004
Ricardo Balda, M.S.	60	Chief Executive Officer, Medicomp, Inc. and Director	2006
Paul A. Mahon, J.D.	38	Senior Vice President, General Counsel and Corporate Secretary	2006
Fred T. Hadeed, C.P.A.	37	Chief Financial Officer	2006

*Martine A. Rothblatt, Ph.D., J.D., M.B.A.*, started United Therapeutics in 1996 and has served as Chairman and Chief Executive Officer since its inception. Dr. Rothblatt is also Chairman of the Law and Medicine Committee of the International Bar Association and President of the William Harvey Medical Research Foundation.

*Roger Jeffs, Ph.D.*, joined United Therapeutics in September of 1998 as Director of Research, Development and Medical. Dr. Jeffs was promoted to Vice President of Research, Development and Medical in July 2000 and to President and Chief Operating Officer in January 2001. Prior to 1998, Dr. Jeffs worked at Amgen, Inc. as Manager of Clinical Affairs and Associate Director of Clinical Research from 1995 to 1998, where he served as the worldwide clinical leader of the Infectious Disease Program.

*David A. Walsh, Ph.D.*, was promoted to Executive Vice President and Chief Operating Officer of Production of United Therapeutics in 2001. From 1999, Dr. Walsh had served as Vice President of Operations of SynQuest, Inc., now a division of United Therapeutics. Prior to joining SynQuest, Dr. Walsh served as Vice President of Operations of Gem Pharmaceuticals, Inc. from 1997 to 1999.

*Barry B. Kanarek, M.D., Ph.D.*, was appointed President and Chief Operating Officer of Unither Pharmaceuticals, Inc., a subsidiary of United Therapeutics, in 2000. In November 2001, he was appointed Chief Medical Officer of United Therapeutics. Prior to joining Unither Pharmaceuticals, Dr. Kanarek served as Senior Vice President of Medical and Regulatory Affairs and Chief Medical Officer of Emisphere Technology from 1998 to 2000, and Executive Vice President of Global Medical Operations and Chief Medical Officer of ClinTrials Research from 1997 to 1998. From 1990 to 1997, Dr. Kanarek served as Senior Vice President of Medical Affairs and Chief Medical Officer of GlaxoWellcome.

*Ricardo Balda, M.S.*, was appointed as the Chief Executive Officer of Medicomp, Inc. upon its acquisition by Unither Telemedicine Services Corp., a subsidiary of United Therapeutics, in December 2000. Mr. Balda also serves on the United Therapeutics Board of Directors. For the five years prior to the Medicomp acquisition, Mr. Balda served as Chairman and President of Medicomp. In 1998, Mr. Balda founded Telemedical Procedures, LLC, which was also acquired by Unither Pharmaceuticals in December 2000. Mr. Balda also serves on the Board of Advisors of the Florida Institute of Technology.

*Paul A. Mahon, J.D.*, has served as General Counsel and Assistant Corporate Secretary of United Therapeutics since its inception in 1996. In June 2001, Mr. Mahon joined United Therapeutics as a full-time employee as Senior Vice President, General Counsel, and Corporate Secretary. Prior to that, he served United Therapeutics in his capacity as

principal and managing partner of the law firm, Mahon Patusky Rothblatt & Fisher, Chartered since its formation in 1993.

*Fred T. Hadeed, C.P.A.*, has served as Chief Financial Officer of United Therapeutics since January 2000. Prior to joining United Therapeutics, Mr. Hadeed practiced public accounting from 1989 to 2000 at KPMG LLP, where he most recently served in its life sciences practice.

## **ITEM 2. PROPERTIES**

United Therapeutics currently maintains several leased and owned facilities. The company owns its corporate office in Silver Spring, Maryland. The company leases its legal and governmental affairs office in Washington, D.C. The company leases its clinical development office in Research Triangle Park, North Carolina. The company leases laboratory and office space in Chicago, Illinois where the bulk active ingredient in Remodulin is synthesized. The Chicago facility contains approximately 10,000 square feet of total space. The company's subsidiary, Unither Pharma, Inc., leases office space in Satellite Beach, Florida and office and warehouse space in Belmont, California. The company's subsidiary, Medcomp, Inc., leases manufacturing and office space in Melbourne, Florida. The Melbourne facility contains approximately 15,400 square feet of total space. United Therapeutics' subsidiary, United Therapeutics Europe Ltd., leases office space in London, England. United Therapeutics also owns a building adjacent to its corporate office in Silver Spring, Maryland. United Therapeutics believes these facilities are adequate for its current and planned operations.

The manufacturing and office space in Melbourne, Florida are used in United Therapeutics' telemedicine segment. All other properties and leased facilities are used in United Therapeutics' pharmaceutical segment.

## **ITEM 3. LEGAL PROCEEDINGS**

None.

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

No matters were submitted to a vote of security holders during the fourth quarter of the fiscal year covered by this report.



**PART II****ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY AND RELATED STOCKHOLDER MATTERS****Market for Common Equity**

United Therapeutics' common stock (and associated preferred stock purchase rights) trades on the Nasdaq Stock Market's Nasdaq National Market under the symbol UTHR. The table below sets forth the high and low closing bid prices for the common stock for the periods indicated:

		2001		2000	
		High	Low	High	Low
January 1	March 31	\$ 17.94	\$ 11.25	\$ 100.00	\$ 52.00
April 1	June 30	\$ 15.88	\$ 10.74	\$ 108.31	\$ 40.00
July 1	September 30	\$ 13.93	\$ 8.85	\$ 128.50	\$ 73.00
October 1	December 31	\$ 16.35	\$ 8.77	\$ 82.00	\$ 13.00

As of March 6, 2002, there were 98 holders of record of common stock. United Therapeutics estimates that included within the holders of record are approximately 3,700 beneficial owners of common stock. As of March 15, 2002, the closing bid price for the common stock was \$12.10.

**Dividend Policy**

United Therapeutics has never paid and does not intend to pay any dividends on the common stock in the foreseeable future but intends to retain any earnings for use in its business operations.

**Recent Sales of Unregistered Securities**

In February 2001, United Therapeutics issued 9,868 shares of its common stock to Columbia University to further research in finding the causes and cures for pulmonary hypertension.

At various times throughout 2001, United Therapeutics issued options to consultants in exchange for services. The aggregate number of options issued was 78,253. Upon exercise, each option may be converted to one share of United Therapeutics common stock in exchange for cash equal to the exercise price. All exercise prices were set at the closing price of United Therapeutics' common stock on the day preceding the grant of each of these options.

**Initial Public Offering Use of Proceeds**

United Therapeutics registered 4,500,000 shares of its common stock, par value \$.01 per share, and an additional 675,000 shares of its common stock for sale to the underwriters exclusively to cover over-allotments, on Registration Statement on Form S-1, Commission File No. 333-76409. The Securities and Exchange Commission declared United Therapeutics' registration statement effective on June 17, 1999. The net proceeds to United Therapeutics from the offering of the 5,175,000 shares, after deducting expenses was approximately \$56.4 million.

Since the completion of the initial public offering in June 1999 and the exercise of the over-allotment shares in July 1999, the net offering proceeds have been fully applied to the following uses in the following approximate amounts as of March 31, 2001: \$35.2 million for research and development, \$766,000 to purchase machinery, equipment and leasehold improvements, \$7.2 million for working capital and general corporate purposes (including compensation to employees, officers, and directors in accordance with their standard agreements), \$313,000 to purchase SynQuest, Inc., \$3.1 million to purchase a 15 percent interest in Synergy Pharmaceuticals, Inc., \$1.0 million to purchase a 59 percent interest in Northern Therapeutics, Inc., \$8.1 million to purchase Medicomp, Inc. and Telemedical Procedures, LLC, \$200,000 to purchase Cooke Pharma, Inc. and \$493,000 to repay debt. Except as indicated, all of the payments described above were direct or indirect payments to entities or persons other than directors, officers, or greater than 10% owners of any equity securities of United Therapeutics.

# ITEM 6. SELECTED FINANCIAL DATA

The following selected consolidated financial data should be read in conjunction with United Therapeutics consolidated financial statements and related notes and Management's Discussion and Analysis of Financial Condition and Results of Operations included elsewhere in this Annual Report on Form 10-K. The historical results are not necessarily indicative of results to be expected for future periods.

	Years Ended December 31,				
	2001	2000	1999	1998	1997
<b>Consolidated Statements of Operations Data:</b>					
	(In thousands, except per share data)				
Revenues	\$ 5,731	\$ 2,049	\$ 436	\$ 54	\$ 116
Operating expenses:					
Research and development	32,590	70,188	30,715	11,015	2,027
General and administrative	13,559	11,719	4,978	2,366	1,006
Sales and marketing	3,384	17			
Cost of sales	3,137	1,626	164		
Total operating expenses	52,670	83,550	35,857	13,381	3,033
Loss from operations	(46,939)	(81,501)	(35,421)	(13,327)	(2,917)
Other income (expense):					
Interest income	10,021	10,693	1,925	510	135
Interest expense	(173)	(120)	(58)	(15)	(8)
Equity loss in affiliate	(257)				
Write-down of investment		(4,790)			(111)
Other, net	60	109	50		
Total other income, net	9,651	5,892	1,917	495	16
Net loss before income tax	(37,288)	(75,609)	(33,504)	(12,832)	(2,901)
Income tax			(3)	(3)	
Net loss	<u>\$ (37,288)</u>	<u>\$ (75,609)</u>	<u>\$ (33,507)</u>	<u>\$ (12,835)</u>	<u>\$ (2,901)</u>
Net loss per common share basic and diluted (1)	<u>\$ (1.84)</u>	<u>\$ (3.93)</u>	<u>\$ (2.51)</u>	<u>\$ (1.54)</u>	<u>\$ (0.87)</u>
Weighted average number of common shares outstanding basic and diluted	<u>20,286</u>	<u>19,237</u>	<u>13,374</u>	<u>8,322</u>	<u>3,339</u>

	As of December 31,				
	2001	2000	1999	1998	1997

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## Consolidated Balance Sheet Data:

(In thousands)

Cash, cash equivalents and marketable investments	\$ 172,299	\$ 215,419	\$ 51,596	\$ 16,802	\$ 5,018
Total assets	212,121	250,645	59,943	18,747	5,074
Notes and leases payable (2)	1,938	1,907	1,841	314	
Accumulated deficit	(162,170)	(124,882)	(49,273)	(15,767)	(2,931)
Total stockholders' equity	196,399	234,738	53,566	16,676	4,617

(1) See Note 2 of Notes to Consolidated Financial Statements for a description of the computation of basic and diluted net loss per share.

(2) Includes current portion of notes and leases payable.

## **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 related notes appearing elsewhere in this annual report. The following discussion contains forward-looking statements concerning the expectation of continued losses, cash needed for clinical trials and product research and development contract obligations during 2002, the funding for such expenses, expectations concerning milestone and royalty payments in 2002, the use of net operating loss carryforwards and business tax credit carryforwards, the completion of in-process research and development products, the levels of working capital required for existing research and development and general and administrative programs, the outcome and timing of regulatory approvals, the expected levels and timing of Remodulin sales and the adequacy of United Therapeutics' resources to fund operations through 2004. These forward-looking statements reflect the plans and estimated beliefs of management as of the date of this report. Actual results could differ materially from those anticipated in the forward-looking statements. Factors that could cause or contribute to such differences include those discussed below and elsewhere in this Annual Report, particularly in Risk Factors.

### **Overview**

United Therapeutics is a biotechnology company focused on commercialization of unique therapeutic products to treat chronic and life-threatening cardiovascular, infectious and oncological diseases. United Therapeutics commenced operations in June 1996 and, since its inception, has devoted substantially all of its resources to its research and development programs. United Therapeutics' lead product is Remodulin. In February 2002, the FDA notified United Therapeutics that Remodulin was deemed approvable for the treatment of pulmonary arterial hypertension in patients with NYHA class II-IV symptoms. Final approval is conditioned on the FDA's acceptance of the product label and United Therapeutics' agreement to perform a post marketing Phase IV clinical study to further assess the clinical benefit of Remodulin. United Therapeutics has agreed to perform the post marketing Phase IV clinical study and is currently discussing the content of the study protocol and product label with the FDA. United Therapeutics has generated pharmaceutical revenues from sales of Remodulin on a government-reimbursed basis in certain European countries, arginine product sales, chemical synthesis services, the resale of certain medical supplies used for its pharmaceutical products and government grants, as well as non-pharmaceutical revenues from telemedicine products. United Therapeutics has funded its operations primarily from the proceeds of the sales of common stock.

United Therapeutics has incurred net losses each year since inception and had an accumulated deficit of \$162.2 million at December 31, 2001. United Therapeutics expects to continue to incur net losses and cannot provide assurances that, in the future, it will become profitable.

### **Financial Position**

Cash, cash equivalents and marketable investments at December 31, 2001 were \$172.3 million as compared to \$215.4 million at December 31, 2000. The decrease of approximately \$43.1 million is primarily a result of cash used in operations during the year ended December 31, 2001.

At December 31, 2001, total liabilities were approximately \$15.7 million, as compared to approximately \$15.9 million at December 31, 2000, and consisted primarily of trade payables, accrued expenses and amounts due to affiliate. At December 31, 2001, total stockholders' equity was approximately \$196.4 million, as compared to \$234.7 million at December 31, 2000.

## Results Of Operations

### *Years ended December 31, 2001 and 2000*

Revenues for the year ended December 31, 2001 were approximately \$5.7 million, as compared to approximately \$2.0 million for the year ended December 31, 2000. The increase was due primarily to sales of Remodulin and telemedicine services. Approximately \$493,000 was earned from the sale of Remodulin to foreign distributors for the use in government-reimbursed patients in certain European countries. Approximately \$1.1 million of these revenues was earned from the resale of pumps and supplies to distributors. Sales of cardiac monitoring devices and services totaled approximately \$2.8 million of these revenues. Sales of HeartBar products totaled approximately \$542,000. Approximately \$801,000 of these revenues was earned by United Therapeutics' synthesis and manufacturing division for the synthesis and manufacture of complex molecules for third parties.

Research and development expenses consist primarily of costs to acquire pharmaceutical products and product rights for development and amounts paid to contract research organizations, hospitals and laboratories for the provision of services and materials for drug development and clinical trials. Research and development expenses were \$32.6 million for the year ended December 31, 2001, as compared to approximately \$70.2 million for the year ended December 31, 2000. The decrease of approximately \$37.6 million was due primarily to the expenditure in 2000 of approximately \$19.8 million in licensing fees (consisting of \$1.0 million in cash and common stock valued at \$18.8 million) to obtain the exclusive rights to develop sustained release formulations of beraprost in the United States and Canada and expenses of approximately \$16.9 million related to the acquisition of in-process research and development (see *In-Process Research & Development*).

General and administrative expenses consist primarily of salaries, office expenses and professional fees, provisions for doubtful accounts receivable and obsolete inventory, depreciation and amortization. General and administrative expenses were \$13.6 million for the year ended December 31, 2001, as compared to \$11.7 million for the year ended December 31, 2000. This increase was primarily due to increased expenses in 2001 of approximately \$564,000 related to provisions for doubtful accounts receivable and obsolete inventory, and approximately \$1.9 million of increased depreciation and amortization of goodwill and other intangible assets resulting from the acquisitions of Medcomp, Inc., Telemedical Procedures, LLC and Cooke Pharma, Inc. in December 2000. These increases were offset by a nonrecurring grant in 2000 of stock totaling \$1.5 million.

Sales and marketing consists of the salaries, travel and other expenses necessary to market United Therapeutics' products. Sales and marketing expenses were approximately \$3.4 million for the year ended December 31, 2001, as compared to approximately \$17,000 for the year ended December 31, 2000. This increase was due primarily to expanded activities related to subsidiaries acquired in late 2000.

Cost of sales consists of the cost to manufacture or acquire products that are sold to customers. Cost of sales were approximately \$3.1 million for the year ended December 31, 2001, as compared to approximately \$1.6 million for the year ended December 31, 2000. This increase was due primarily to sales by subsidiaries acquired in late 2000.

There was no write-down of investment for the year ended December 31, 2001 as compared to \$4.8 million for the year ended December 31, 2000. The write-down in 2000 related to United Therapeutics' investment in Synergy Pharmaceuticals, Inc.

Interest income for the year ended December 31, 2001 was \$10.0 million, as compared to approximately \$10.7 million for the year ended December 31, 2000. This decrease was attributable primarily to decrease in the amount of cash available for investing due to cash used for operations.

### *Years ended December 31, 2000 and 1999*

Revenues for the year ended December 31, 2000 were approximately \$2.0 million, as compared to approximately \$436,000 for the year ended December 31, 1999. The increase was due primarily to increases in synthesis and manufacturing revenues and from sales of Remodulin pumps and supplies. Approximately \$1.1 million of these revenues was earned by United Therapeutics' synthesis and manufacturing division for the synthesis and manufacture of complex molecules for third parties. Approximately \$740,000 of these revenues was earned from the resale of pumps and supplies to distributors in connection with United Therapeutics' lead product, Remodulin.

Approximately \$150,000 of these revenues was earned under the orphan drug grant awarded by the FDA related to United Therapeutics development of Remodulin for the treatment of primary pulmonary hypertension.

Research and development expenses consist primarily of costs to acquire pharmaceutical products and product rights for development and amounts paid to contract research organizations, hospitals and laboratories for the provision of services and materials for drug development and clinical trials. Research and development expenses were \$70.2 million for the year ended December 31, 2000, as compared to \$30.7 million for the year ended December 31, 1999. The increase of approximately \$39.5 million was due primarily to the expenditure of approximately \$19.8 million in licensing fees (consisting of \$1.0 million in cash and common stock valued at \$18.8 million) in June 2000 to obtain the exclusive rights to develop sustained release formulations of beraprost in the United States and Canada, increased expenses of approximately \$7.3 million related to patient enrollment in United Therapeutics clinical trials, increased expenses of approximately \$16.9 million related to the acquisition of in-process research and development (see *In-Process Research & Development*), and increased expenses of approximately \$4.1 million related to other research. The increase was offset by the prior year expenditure of \$9.1 million in licensing fees (consisting of \$100,000 in cash and common stock valued at \$9.0 million) in 1999 to obtain the exclusive rights to develop the immediate release formulation of beraprost in the United States and Canada.

General and administrative expenses consist primarily of salaries, office expenses and professional fees. General and administrative expenses were \$11.7 million for the year ended December 31, 2000, as compared to \$5.0 million for the year ended December 31, 1999. This increase was due primarily to nonrecurring grants of approximately \$2.5 million of stock and options and increased expenses of approximately \$3.2 million related to professional fees, increased staffing and related travel to support expanded operations.

Cost of sales consists of the cost to manufacture or acquire products that are sold to customers. Cost of sales were approximately \$1.6 million for the year ended December 31, 2000, as compared to approximately \$164,000 for the year ended December 31, 1999. This increase was due primarily to increased sales of Remodulin pumps and supplies to distributors.

The write-down of investment totaled \$4.8 million during the year ended December 31, 2000 as compared to zero for the year ended December 31, 1999. The write-down in 2000 related to United Therapeutics investment in Synergy Pharmaceuticals, Inc.

Interest income for the year ended December 31, 2000 was \$10.7 million, as compared to approximately \$1.9 million for the year ended December 31, 1999. This increase was attributable primarily to an increase in the amount of cash available for investing resulting from sales of common stock since December 31, 1999, less amounts used for operations.

### ***In-Process Research & Development***

During 2000, United Therapeutics acquired the assets and assumed certain liabilities of Cooke Pharma, Inc. in a purchase transaction which resulted in a write-off of in-process research and development (IPR&D) related to in-process projects that had not yet reached technological feasibility and had no alternative future uses. The projects under development at the valuation date were expected to address the coronary and peripheral arterial disease markets as well as the market of persons that are at risk of developing some form of heart disease. It was anticipated that research and development related to these projects would be completed by 2002. However, United Therapeutics has decided to initiate studies of arginine in pulmonary hypertension prior to coronary and peripheral arterial diseases. These studies in pulmonary hypertension are expected to commence in 2002 and be completed in 2003. The delay in the coronary and peripheral arterial disease studies is not expected to have a material impact on United Therapeutics.

Also during 2000, United Therapeutics acquired the assets of Medicomp, Inc. in a purchase transaction which resulted in a write-off of IPR&D related to in-process projects that had not yet reached technological feasibility and had no alternative future uses. At the acquisition date, Medicomp was conducting design, development, engineering and testing activities associated with the completion of a number of new technological innovations that were integral to Medicomp's plan to launch a first generation automatic wireless heart monitoring system. It was anticipated that completion of these projects would range from 9 to 12 months. Completion is expected to occur in 2002. This delay is not expected to have a material impact on United Therapeutics.

## Liquidity And Capital Resources

Until June 1999, United Therapeutics financed its operations principally through various private placements of common stock. On June 17, 1999, United Therapeutics completed an initial public offering of 4.5 million shares of common stock at \$12.00 per share. Net proceeds to United Therapeutics, after deducting underwriting commissions and offering expenses, were approximately \$48.9 million. On July 16, 1999, United Therapeutics closed on the sale of 675,000 over-allotment shares to its underwriters and received net proceeds, after deducting underwriting commissions and offering expenses, of approximately \$7.5 million. On January 18, 2000, United Therapeutics closed on the sale of 2.5 million shares of common stock at \$32.00 per share in a private placement and received net proceeds, after deducting underwriting commissions and offering expenses, of approximately \$74.8 million. On July 20, 2000, United Therapeutics closed on the sale of 1.3 million shares of its common stock at \$110.00 per share in a private placement and received net proceeds, after deducting underwriting commissions and offering expenses, of approximately \$134.3 million.

United Therapeutics working capital at December 31, 2001 was \$58.2 million, as compared with \$210.6 million at December 31, 2000. This reduction is primarily due to the investment in long-term marketable investments of approximately \$116.2 million as of December 31, 2001 and cash used for operations. These long-term marketable investments consist of federally sponsored and corporate debt securities maturing in 2002 through 2006. Current liabilities at December 31, 2001 were approximately \$10.8 million, as compared with \$11.5 million at December 31, 2000. United Therapeutics debt at December 31, 2001 and 2000 was \$1.9 million and consisted of equipment leases and two mortgage notes, one secured by a certificate of deposit, and both secured by the buildings and property owned by United Therapeutics located at 1106 & 1110 Spring Street in Silver Spring, Maryland. Both mortgages are payable in monthly installments over 30 years.

Net cash used in operating activities was approximately \$38.9 million, \$31.1 million and \$23.7 million for the years ended December 31, 2001, 2000 and 1999, respectively. The increases resulted primarily from the expansion of United Therapeutics operations. For the years ended December 31, 2001, 2000 and 1999, United Therapeutics spent approximately \$687,000, \$640,000 and \$2.0 million, respectively, of cash for property, plant and equipment. Net purchases and sales of marketable investments used approximately \$134.1 million of cash in the year ended December 31, 2001, provided approximately \$19.8 million of cash in the year ended December 31, 2000, and used approximately \$21.8 million of cash in the year ended December 31, 1999. Net cash used in financing activities was approximately \$2.9 million for the year ended December 31, 2001 and was primarily used to repurchase shares of United Therapeutics common stock. The stock repurchase program expired in December 2001. Net cash provided by financing activities was approximately \$206.6 million for the year ended December 31, 2000 and was derived primarily from the private placements of common stock in January and July 2000. Net cash provided by financing activities was approximately \$59.3 million for the year ended December 31, 1999 and was primarily derived from the proceeds of the initial public offering of common stock in June 1999.

United Therapeutics has contracted with various companies and research organizations to coordinate and perform clinical trials and to provide other services related to the development of Remodulin and other products. It is anticipated that approximately \$1.4 million in cash will be used during 2002 under these agreements. These expenses will be funded from existing working capital. United Therapeutics expects to make milestone payments pursuant to existing license agreements of up to approximately \$220,000 during 2002. United Therapeutics expects to make royalty payments relating to sales of Remodulin and other products during 2002. The royalties will range from 1% to 10% of sales from these products. United Therapeutics anticipates that its existing research and development and general and administrative programs will require similar levels of working capital as has been used in recent years.

In December 2000, United Therapeutics provided guidance in respect of revenues from the expected sales of its lead drug, Remodulin, based on the prior assumption of FDA approval of Remodulin by April 16, 2001. United Therapeutics believes that its prior revenue projections will be adversely affected by the time delay in commercial launch of Remodulin, the extent of which is not known. United Therapeutics expects that existing capital resources (comprised of cash and marketable investments) will be adequate to fund its operations through 2004. United Therapeutics future capital requirements and the adequacy of its available funds will depend on many factors, including:

- Regulatory approval of Remodulin;
- Size and scope of Remodulin post marketing Phase IV clinical studies;
- Size and scope of its development efforts for existing and additional products;

Future milestone and royalty payments;  
Cost, timing and outcomes of regulatory reviews;  
Rate of technological advances;  
Status of competitive products;  
Defending and enforcing intellectual property rights;  
Development of manufacturing resources or the establishment, continuation or termination of third-party manufacturing arrangements;  
Establishment, continuation or termination of third-party clinical trial arrangements;  
Development of sales and marketing resources or the establishment, continuation or termination of third-party sales and marketing arrangements;  
Establishment of additional strategic or licensing arrangements with other companies; and  
Risks associated with acquisitions, including the ability to integrate acquired businesses.

As of December 31, 2001, United Therapeutics had available approximately \$95.9 million in net operating loss carryforwards and \$24.7 million in business tax credit carryforwards for federal income tax purposes that expire at various dates through 2020. A portion of these carryforward items is subject to certain limitations. United Therapeutics does not believe that the limitations will cause the net operating loss and general business credit carryforwards to expire unused.

### **Summary of Critical Accounting Policies**

#### *Marketable Investments*

United Therapeutics invests portions of its cash in marketable debt securities. Due to United Therapeutics' intent and ability to hold these investments until their maturities, they are reported at their amortized cost in the consolidated balance sheets. Had these investments been reported at their current fair values, United Therapeutics would have reported a net unrealized investment loss of approximately \$793,000 for the year ended December 31, 2001 and a net unrealized investment gain of approximately \$3,000 for the year ended December 31, 2000.

#### *Inventory Capitalization*

United Therapeutics capitalizes inventory costs associated with the synthesis and manufacture of Remodulin prior to regulatory approval, based on management's judgment of probable future commercialization. United Therapeutics would be required to expense previously capitalized costs related to pre-approval inventory upon a change in such judgment, due to, among other factors, a decision denying approval of the product candidate by the necessary regulatory bodies. At December 31, 2001, capitalized inventory related to Remodulin totaled \$3.4 million.

#### *Stock Options*

United Therapeutics applies the principles of APB No. 25 in accounting for its stock options issued to its employees. Had it applied the principles of SFAS No. 123 for its employee options, its net loss for the years ended December 31, 2001, 2000 and 1999 would have increased by \$13.0 million, \$42.5 million and \$1.3 million, respectively.

#### *Investments in Affiliates*

The equity method of accounting is used to account for most investments in United Therapeutics' affiliates. The equity method of accounting generally requires United Therapeutics to report its share of the affiliates' net losses or profits in its financial statements, but does not require that assets, liabilities, revenues and expenses of the affiliates be consolidated with United Therapeutics' financial statements. The equity method of accounting is being applied generally due to the lack of control over these affiliates and the levels of ownership held by United Therapeutics.

#### *Options Issued in Exchange for License*

In connection with the license from Toray Industries for the sustained release formulation of beraprost, United Therapeutics agreed to grant 500,000 options to Toray upon Toray's transfer of clinical trial material for use in clinical trials in the U.S. These options will not be priced until the clinical trial material milestone has been met by Toray. Before Toray can produce the clinical trial material, it will need to complete formulation, preclinical testing



and early clinical studies. Due to the uncertainties in drug development, it is not yet known if Toray will provide the appropriate clinical trial material. Therefore, in accordance with EITF Issue No. 96-18, Accounting for Equity Instruments that are Issued to Other than Employees, these options are measured at their lowest aggregate fair value at each interim reporting date, which amount has been zero. As a result, no expense related to these options has been recorded in the consolidated financial statements.

#### **Recent Accounting Pronouncements**

In July 2001, the Financial Accounting Standards Board (the FASB) issued SFAS No. 141, *Business Combinations* (SFAS 141), and SFAS No. 142, *Goodwill And Other Intangible Assets* (SFAS 142). SFAS 141 addresses the accounting for acquisitions of businesses and is effective for acquisitions occurring on or after July 1, 2001. SFAS 142 addresses the method of identifying and measuring goodwill and other intangible assets acquired in a business combination, eliminates further amortization of goodwill, and requires periodic evaluations of impairment of goodwill balances. SFAS 142 is effective for the Company's fiscal year beginning January 1, 2002. The Company amortized \$1.1 million and \$495,000 of goodwill during the years ended December 31, 2001 and 2000, respectively. Unamortized goodwill at January 1, 2002, the date of adoption, was approximately \$7.5 million. All other unamortized intangible assets totaled \$7.9 million at January 1, 2002.

In October 2001, the FASB issued SFAS No. 144, *Accounting for Impairment or Disposal of Long-Lived Assets* (SFAS 144). The provisions of SFAS 144 require the use of a consistent accounting model for long-lived assets to be disposed of by sale, whether previously held and used or newly acquired and extend the presentation of discontinued operations to include more disposal transactions. SFAS 144 is effective for the Company's fiscal year beginning January 1, 2002.

The Company has not yet completed its assessment of the impact of the adoption of these new standards.

#### **Recent Developments**

On February 8, 2002, the FDA notified United Therapeutics that its lead product Remodulin was deemed approvable for the indication of pulmonary arterial hypertension for patients with NYHA class II-IV symptoms. Final FDA approval is subject to the FDA's agreement on the product label and United Therapeutics' agreement to perform a post marketing Phase IV clinical study to further assess Remodulin's clinical benefits in pulmonary arterial hypertension. United Therapeutics has agreed to perform the post marketing Phase IV clinical study and is currently discussing the content of the study protocol and the product label with the FDA.

#### **ITEM 7A: QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK**

United Therapeutics does not believe that it has material exposure to market risk. However, a substantial portion of United Therapeutics assets are investment grade debt instruments such as securities of federal agencies which carry the direct or implied guarantee of the U.S. government and corporate debt securities. The market value of these investments fluctuates with changes in current market interest rates. In general, as rates increase, the market value of a debt instrument would be expected to decrease. The opposite is also true. To minimize such market risk, United Therapeutics has in the past and, to the extent possible, will continue in the future to hold such debt instruments to maturity at which time these instruments will be redeemed at their stated or face value (which approximates their original cost). Due to the short average duration (approximately 2 years) and the intent of holding these investments to maturity, United Therapeutics does not believe that it has material exposure to market risk. Marketable investments at December 31, 2001 were \$147.9 million and the weighted average effective interest rate was approximately 5.2 percent.

**ITEM 8: FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA**

**UNITED THERAPEUTICS CORPORATION**

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**Independent Auditors' Report**

The Board of Directors  
United Therapeutics Corporation:

We have audited the accompanying consolidated balance sheets of United Therapeutics Corporation and subsidiaries (the Company) as of December 31, 2001 and 2000, and the related consolidated statements of operations, stockholders' equity, and cash flows for each of the years in the three-year period ended December 31, 2001. These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated financial statements based on our audits.

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

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of United Therapeutics Corporation and subsidiaries as of December 31, 2001 and 2000, and the results of their operations and their cash flows for each of the years in the three-year period ended December 31, 2001, in conformity with accounting principles generally accepted in the United States of America.

KPMG LLP

McLean, Virginia  
February 22, 2002

## UNITED THERAPEUTICS CORPORATION

## Consolidated Balance Sheets

	December 31,	
	2001	2000
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 24,372,675	\$ 200,935,244
Marketable investments (note 9)	31,676,959	14,483,637
Accounts receivable, net of allowance of \$197,742 and \$98,281 for 2001 and 2000, respectively	1,451,536	1,534,362
Interest receivable	2,772,147	
Prepaid expenses	916,641	1,077,608
Inventories (note 2)	6,024,574	2,896,469
Other current assets	1,788,149	1,192,784
Total current assets	69,002,681	222,120,104
Property, plant, and equipment, net (note 2)	6,403,414	5,939,036
Certificate of deposit	605,135	571,445
Goodwill and other intangible assets, net (notes 2 and 11)	15,365,275	17,549,224
Marketable investments (note 9)	116,249,015	
Investments in affiliates (note 11)	4,341,835	4,348,693
Other	154,016	116,482
Total assets	\$ 212,121,371	\$ 250,644,984
<b>Liabilities and Stockholders' Equity</b>		
Current liabilities:		
Accounts payable	\$ 6,348,952	\$ 5,273,445
Accounts payable to affiliate (note 3)	318,156	678,897
Accrued expenses (note 13)	3,453,626	4,522,550
Due to affiliate (note 11)	500,000	946,497
Current portion of notes and leases payable (note 8)	101,794	70,803
Other current liabilities	75,339	
Total current liabilities	10,797,867	11,492,192
Notes and leases payable, excluding current portion (note 8)	1,836,406	1,835,960
Due to affiliate (note 11)	3,079,111	2,385,229
Other liabilities	8,863	193,821
Total liabilities	15,722,247	15,907,202
Commitments and contingencies (notes 5 and 10)		
Stockholders' equity (note 6):		
Preferred stock, par value \$.01, 10,000,000 shares authorized at December 31, 2001 and 2000, no shares issued		
Series A junior participating preferred stock, par value \$.01, 100,000 authorized at December 31, 2001 and 2000, no shares issued		

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Common stock, par value \$.01, 100,000,000 shares authorized at December 31, 2001 and 2000, 20,751,820 and 20,740,086 shares issued at December 31, 2001 and 2000, respectively, 20,225,220 and 20,434,086 shares outstanding at December 31, 2001 and 2000, respectively	207,519	207,401
Additional paid-in capital	365,235,398	363,484,585
Accumulated deficit	(162,169,637)	(124,881,888)
Treasury stock at cost, 526,600 and 306,000 shares at December 31, 2001 and 2000, respectively	(6,874,156)	(4,072,316)
	<u>196,399,124</u>	<u>234,737,782</u>
Total stockholders' equity	196,399,124	234,737,782
	<u>\$ 212,121,371</u>	<u>\$ 250,644,984</u>
Total liabilities and stockholders' equity	\$ 212,121,371	\$ 250,644,984

See accompanying notes to consolidated financial statements.

**UNITED THERAPEUTICS CORPORATION**

**Consolidated Statements of Operations**

	Years Ended December 31,		
	2001	2000	1999
Revenues:			
Sales			