



C O R P O R A T I O N

2001 United Therapeutics Corporation Annual Report

**Medicines
for Life®**

Corporate Profile

United Therapeutics is focused on combating chronic and life-threatening cardiovascular, infectious, and oncological diseases with unique therapeutic products. There are several key steps involved in carrying out this mission:

- We inlicense exclusive rights to promising new medical therapies from pharmaceutical companies or universities that are unable or unwilling to put the projects through clinical development. We are quite selective about which medical therapies we inlicense, as we want to ensure for our shareholders a good probability for success in proving the therapy medically effective and commercially successful.
- Our clinical development team, headquartered in Research Triangle Park, North Carolina, takes charge of designing and carrying out clinical trials to prove the safety and efficacy of the inlicensed therapy. If the clinical trials are successful, then our clinical development team handles the complex task of applying for regulatory approval of the product in the U.S. and overseas.
- Our manufacturing team, headquartered in Chicago, Illinois, takes responsibility for ensuring that an adequate supply of the new product is manufactured according to strict government standards. In addition, this team ensures that an adequate supply of the new medicine is stored safely in more than one location.
- Our sales and marketing team, headquartered in Silver Spring, Maryland, negotiates distribution and pharmaceutical educational efforts with contract sales organizations.

Upon regulatory approval of a new therapy, we prepare to launch the product under business arrangements that provide United Therapeutics with the largest share of the revenue generated by the therapy.

Product Pipeline – 11 Products in Development

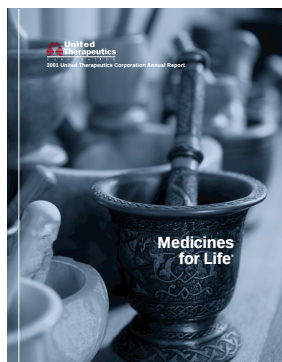
Product	Market	US and EU Size (people/patients)	2002 Status
Arginine Supplements	Arginine Deficiency	20 Million	Launching
Continuous Remodulin SubQ	Pulmonary Arterial Hypertension	50 Thousand	US Approval Pending/EU Reviews Ongoing
Intermittent Remodulin SubQ	Critical Limb Ischemia	1 Million	Phase 2/3
Periodic Remodulin SubQ	Metastatic Cancer	2 Million	Phase 1
Beraprost Immediate Release	Metastatic Cancer	1 Million	Phase 1
UT 231B	Hepatitis C	13 Million	Phase 1
Iminosugar Platform	Hepatitis B	3 Million	Preclinical
R7V Platform	HIV Vaccine	2 Million	Preclinical
UT 15 Sustained Release/ Beraprost Sustained Release	Peripheral Vascular Disease	8 Million	Preclinical
ADMA Diagnostic Test	Cardiovascular Disease	120 Million	Preclinical
Epicardia Auto-Trigger	Cardiac Arrhythmia	2 Million	Preclinical

We are currently nearing completion of this process for the therapy we call Remodulin™, which is a life-long treatment for pulmonary arterial hypertension, a devastating cardiovascular condition. We are near the middle of this process for the development of this same therapy for another devastating cardiovascular condition – critical limb ischemia. In the field of oncology, we have begun the process of designing clinical studies to test the efficacy of another of our products, Beraprost, for the prevention of metastatic lung cancer. We are near the beginning of the process for the development of our iminosugar molecules for hepatitis C, hepatitis B, and dengue.

In addition to these activities, subsidiaries and affiliates of United Therapeutics are engaged in fighting chronic and life-threatening cardiovascular, infectious, and oncological diseases:

- Our Unither Pharma, Inc. subsidiary has begun marketing an arginine supplementation product in the U.S. based on our exclusive rights, via patents owned by Stanford University and New York Medical College, to manufacture and sell HeartBar® to promote cardiovascular health. In addition, Unither Pharma is pursuing regulatory approval for the product overseas and is conducting a global clinical study of the product's efficacy in early-stage pulmonary arterial hypertension.
- Our Medicomp, Inc. subsidiary is a leader in cardiac digital holter monitoring based on its proprietary chip-based algorithms that detect cardiac arrhythmias. Medicomp is also expanding its activities to include telemedical cardiac event monitoring using new automatically triggered and wireless devices that hold promise for ultimate mass-market appeal among the “worried well.”
- Our Preventis, Inc. affiliate is preparing to conduct early human trials of a promising HIV therapeutic vaccine based on exclusively licensed patent rights to the R7V antibody discovered at the Institute Pasteur by the co-discoverer of HIV.
- Our Northern Therapeutics affiliate is progressing on a form of gene therapy that uses the patient's own cells, rather than a potentially dangerous viral vector, and holds special promise for treating diseases of the lung.

United Therapeutics has a broad-based program of research, development and commercialization in medical therapeutics. In the coming years, as these products and technologies demonstrate their utility, United Therapeutics expects to be well-positioned to reap substantial rewards from its pioneering investments.



The Cover:

The mortar and pestle has been used by apothecaries, pharmacists, and researchers alike in search of cures in every era, and is a timeless symbol of our search for an end to all disease. Featured on the cover is a 19th century mortar and pestle from Syria. Courtesy of the collection of Sir John Vane.

To Our Shareholders



FRONT ROW: Ricardo Balda, Chief Executive Officer, Medicomp, Inc.; Martine Rothblatt, Ph.D., J.D., M.B.A., Chairman & Chief Executive Officer; Roger Jeffs, Ph.D., President & Chief Operating Officer; **BACK ROW:** David Walsh, Ph.D., Executive Vice President & Chief Operating Officer for Production; Paul Mahon, J.D., Senior Vice President & General Counsel; Barry Kanarek, M.D., Ph.D., Chief Medical Officer, President & Chief Operating Officer, Unither Pharma, Inc.; Fred Hadeed, C.P.A., Chief Financial Officer

2001 was a tough year for United Therapeutics as well as for all America. For us it was a year of persevering and future-building rather than thriving.

We hoped to obtain regulatory approval of our lead drug, Remodulin, for the treatment of pulmonary arterial hypertension, but settled for a favorable recommendation for approval from an FDA Advisory Committee. We expected that the recommendation would be quickly converted into an approvable letter, but settled for a delay into 2002. Despite these delays, hundreds of patients continue to benefit from using Remodulin in our long-term open-label studies. These and other studies are now making their way into peer-reviewed medical literature.

Interest continues to grow in using Remodulin for additional medical conditions, including critical limb ischemia (which results in over 200,000 leg amputations annually) as well as for the prevention of

metastatic lung, breast, and colon cancer. The National Cancer Institute, for example, is now funding clinical studies on the use of prostacyclin analogs for the prevention of cancer in high-risk patients, such as heavy smokers. Meanwhile, the *American Journal of Respiratory Cell and Molecular Biology* published an article showing several different ways in which Remodulin was the most potent of all analogs of prostacyclin with published data. Our robust Remodulin platform is firmly in place, and we are committed to extending its therapeutic benefits to growing patient populations.

We received a major disappointment in 2001 when our lead oral drug, Beraprost, failed to show efficacy in the treatment of peripheral vascular disease. Nevertheless, we picked ourselves up, dusted ourselves off, and refocused our resources on our next lead compound, a molecule called UT231B that shows great potential in preclinical studies for treating hepatitis C.

UT231B was created by a team led by Professor Raymond Dwek, head of the Biochemistry Department at the University of Oxford, and Professor Robert Moriarty, our own Chief Molecular Design Officer. During the latter half of 2001, we cleared most preclinical toxicology hurdles and produced an adequate supply of UT231B in our Chicago manufacturing facility. In addition, because we own the intellectual property rights to a whole platform of compounds called iminosugars from which UT231B is just one of many possible options, we have continued designing and improving additional iminosugar molecules within this extensive platform. These additional molecules have been designed to combat hepatitis B as well as hepatitis C.

An estimated 12% of the world population may be infected with hepatitis C, including more than 4 million Americans and 9 million Europeans. Hepatitis B infection rates are even higher worldwide, although they are lower in the U.S. and Europe, but still in the millions. As with Remodulin for cardiovascular disease and metastatic cancer, we persevered in 2001 to build a strong platform for the future with our anti-infective disease drugs.

We have continued building our company's infrastructure in other important areas as well. During 2001, we consolidated our acquisition of Unither Pharma, Inc., the company with exclusive patent rights to sell the amino acid arginine for cardiovascular conditions, including the HeartBar and HeartAid products. These rights are protected by patents issued to New York Medical College and Stanford University as a result of the pioneering research of Stanford's Director of Vascular Medicine, Professor John Cooke, M.D.

Just as peer-reviewed publications began to document the relationship between arginine deficiency and heart disease, we acquired the exclusive rights to develop a test (like the cholesterol level test) to identify people at risk of heart disease. A growing number of doctors believe this test, called an ADMA test, will be a better predictor of heart disease than cholesterol tests. Fortunately, people with high ADMA levels can reduce their risks by taking supplemental arginine, which our Unither Pharma subsidiary now makes available in four formulations and seven flavors.

Our telemedicine subsidiary, Medicomp, made rapid progress during 2001 in developing a device that will automatically detect an irregular heartbeat in an outpatient and send that person's instantaneous ECG patterns over the Internet to a cardiac technician. This technology can revolutionize cardiac telemonitoring and also pave the way for a paradigm expansion into regular use by millions of worried-well senior citizens. Meanwhile, Medicomp continued to provide reimbursed telediagnostic service to hundreds of clinics and hospitals throughout the country.

As we enter 2002, we have two flagship molecules, Remodulin and UT231B, well-positioned to enter the cardiovascular marketplace and anti-infectives clinical development, respectively. In addition, the anti-metastatic potential of Remodulin will also be studied intensively, as will be more easy-to-use sustained-release formulations of this versatile molecule. To fund these efforts, the company enters the year with over \$170 million of cash and liquid investments.

With expected regulatory approval from the FDA for Remodulin, 2002 will be a pivotal year for United Therapeutics. We learned from the setbacks of 2001 and used the extra time to strengthen our operational launch preparations. We are committed to making our first operational launch a precursor to major expansions into new indications with new compounds in the coming years.

We at United Therapeutics see the potential of the compounds in our hands and we believe that we have the capability to be a major provider of therapeutics in cardiovascular medicine, infectious disease, and oncology. This is our goal.

Onwards to a great 2002,



Martine Rothblatt
Chairman and CEO



Professor Raymond A. Dwek, F.R.S.

Director, University of Oxford Glycobiology Institute, Chairman of the Department of Biochemistry

"United Therapeutics' idealistic approach to providing drug therapy, particularly in the areas where there are unmet medical needs, sets high standards for the pharmaceutical industry. It also serves as an inspiration for researchers seeking cures for such disease."



Professor Victor J. Dzau, M.D.

Chairman of the Department of Medicine of Brigham & Women's Hospital, Harvard Medical School

"I look forward to working with dedicated scientists of the company and members of its distinguished scientific board to develop novel and innovative therapies to treat cardiovascular diseases."



Professor Robyn J. Barst, M.D.

Professor of Pediatrics, Columbia University College of Physicians & Surgeons; Director, Pulmonary Hypertension Center, New York Presbyterian Hospital

"Remodulin, an analog of prostacyclin, was developed by the United Therapeutics Corporation as a subcutaneous treatment for patients with pulmonary arterial hypertension. Flolan, the intravenous form of prostacyclin, requires continuous intravenous administration. The development program for Remodulin represents the largest placebo-controlled program ever conducted in patients with pulmonary hypertension. The administration of subcutaneous Remodulin in patients with pulmonary hypertension results in consistent and clinically meaningful improvements in a variety of measures that reflect the impaired clinical status of these patients. These measures include exercise capacity as well as overall assessments of quality of life. The improvement in these efficacy parameters is comparable to that seen with other drugs, such as Flolan, that have been shown to be effective in the treatment of pulmonary hypertension. In addition, the ability to administer Remodulin by the subcutaneous route improves the overall benefit to risk profile for patients with pulmonary arterial hypertension who need chronic treatment with a prostacyclin analog. Furthermore, in short-term studies, the efficacy of Remodulin administered intravenously was comparable to its effects when administered subcutaneously. Adding Remodulin to the armamentarium in treating patients with pulmonary arterial hypertension is a significant advancement in the treatment options for these patients."



Professor Salvador Moncada, M.D., Ph.D., D.Sc.

The Wolfson Institute for Biomedical Research University College London; Vice Chairman of the Scientific Advisory Board

"The use of prostacyclin and its analogues in pulmonary arterial hypertension is something that we owe to United Therapeutics and has proven to be of great benefit to sufferers of this life-threatening condition."



Professor John Eric Deanfield, M.B., BChir, F.R.C.P.

Senior Lecturer, St. Bartholomew's Hospital, London

"United Therapeutics is now focusing on prevention strategies for cardiovascular disease. This approach will translate to huge clinical benefits for the next generation of patients."



Urban Ramstedt, Ph.D.

Head of Immunology, Zycos Inc.

"UTHR represents a company willing to think outside the box, constantly searching for new opportunities in their field, but always built on a foundation of good science. It is a pleasure to interact with the company's dynamic and very competent group of people, headed by Martine Rothblatt. I have been impressed with the company's strong commitment to help patients and their rapid way of moving products into the clinic as well as their process of getting the job done."



Sir Magdi Yacoub, M.D., F.A.C.S.

England's National Heart & Lung Institute

"United Therapeutics is a very progressive company involved in developing new effective therapies. I am interested in their cutting edge biomedical research which I support"





Sir John Vane, D.Sc., F.R.S.

1982 Nobel Laureate in Physiology or Medicine, Chairman of the Scientific Advisory Board

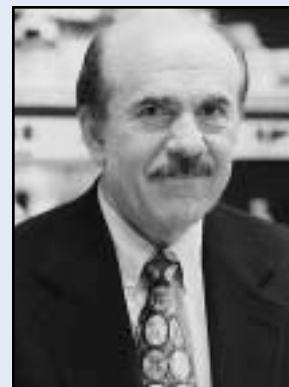
"We discovered prostacyclin in 1976 and I am delighted that United Therapeutics is developing its therapeutic and life-saving potential"



Professor Baruch S. Blumberg, Ph.D.

1976 Nobel Laureate in Physiology or Medicine, Fox Chase Distinguished Scientist, Fox Chase Cancer Center

"Therapeutic agents that are discovered in the research laboratory require special facilities to bring them to a level where they can be prescribed by physicians and used by patients. Agents for hepatitis viruses as well as other viruses are, currently, not as effective as we hope they will be in the future. United Therapeutics is highly skilled in developing the products of research and sensitive to the scientific style of the academic researcher. We are enthusiastic that a collaboration can hasten the introduction of medications that will ease the burden of those suffering from hepatitis virus infections"



Louis J. Ignarro, Ph.D.

Professor, Molecular and Medical Pharmacology, Jerome J. Belzer, M.D. Distinguished Professor of Pharmacology, UCLA; 1998 Nobel Laureate in Physiology or Medicine

"I am excited about working with talented and innovative scientists of the company toward the common goal of developing novel therapeutic strategies to prevent and treat cardiovascular disease."

Scientific Advisory Board

We are proud of our Scientific Advisory Board. It is chaired by Sir John Vane, a Nobel Laureate who, along with fellow Board member Professor Salvador Moncada, M.D., Ph.D., D.Sc., co-discovered the molecule prostacyclin, upon which much of our business is based. The knowledge of these men is of immense value to us as we explore the use of prostacyclin-like molecules (such as Remodulin) in cardiovascular and oncological conditions. The Scientific Advisory Board member who helps us pilot the use of variants of the prostacyclin molecule in the field of pulmonary hypertension is a globally recognized expert in this condition, clinician-scientist Robyn J. Barst, M.D.

As we extended our business into infectious diseases, we strengthened our Board with Nobel Laureate Baruch S. Blumberg, Ph.D., who discovered the hepatitis B virus and created the hepatitis B vaccine, an innovation that has saved millions of lives. Professor Blumberg works closely with another of our Board members, Raymond A. Dwek, F.R.S., who discovered our iminosugar-based anti-infective platform of molecules (such as our lead drug candidate for treating hepatitis C, UT231B). Professor Dwek is also able to share with us some of the brilliance that permeates University of Oxford's Biochemistry Department, which he chairs, and its Glycobiology Institute, which he founded. The anti-infectives expertise of Professors Blumberg and Dwek is further complemented on the UT Scientific Advisory Board by Dr. Urban Ramstedt, Head of Immunology at Zycos Inc., and an expert on retroviruses, particularly HIV and hepatitis C.

Most recently, United Therapeutics made a bold move into the nutraceutical field by acquiring the exclusive worldwide rights to use the amino acid L-arginine for cardiovascular purposes. This therapy was patented by New York Medical College and Stanford University and developed into a commercial product by the Director of Stanford's Department of Vascular Medicine, Professor John Cooke, M.D., Ph.D. Arginine works by increasing the body's production of nitric oxide and hence we welcomed onto our Scientific Advisory Board one of the 1998 Nobel Laureates recognized for discovering the therapeutic role of nitric oxide, Louis J. Ignarro, Ph.D. Also helping us to pioneer the nutraceutical use of nitric oxide for cardiovascular health is Professor John Eric Deanfield, M.B., BChir, F.R.C.P. of St. Bartholomew's Hospital in London, and Professor Salvador Moncada, M.D., Ph.D., D.Sc., mentioned above in connection with his discovery of prostacyclin. While he was head of Burroughs Wellcome Labs, Professor Moncada also discovered that nitric oxide relaxes blood vessels.

Finally, it is important to have on one's Scientific Advisory Board individuals who have operational responsibility for overseeing the appropriateness of how scientific breakthroughs are translated into clinical protocols, and how medical discoveries are integrated into clinical practice. For us, we are honored to have as these individuals Sir Magdi Yacoub, M.D., F.A.C.S., one of the world's foremost transplant surgeons and cardiopulmonary scientists, and Victor J. Dzau, M.D., Chairman of Medicine at Harvard University's Brigham & Women's Hospital.

The Scientific Advisory Board at United Therapeutics plays an important role. Fortunately for us, the caliber of the scientists on our Board are second to none in our missions of developing prostacyclin-like molecules and arginine supplementation for cardiovascular medicine and proving the usefulness of iminosugar compounds for safely treating serious infectious disease. As we accelerate our efforts to test the ability of prostacyclin therapy to halt the metastasis of cancer, we look forward to adding further oncological expertise to our Scientific Advisory Board.

United Therapeutics' Products

Prostacyclin is an Amazing Molecule

Prostacyclin is one of the most ubiquitous hormones in the human body. Prostacyclin is produced throughout the body, via an interaction between the endothelial cells that line blood vessel walls and the platelets that float through the blood vessels. Prostacyclin also has an effect throughout the body, principally upon smooth muscle cells that surround blood vessels but also on other endothelial cells and platelets.

As one might expect, any molecule as ubiquitous in the body as prostacyclin would have a number of important roles to play in maintaining a person's physical health. Studies have shown this expectation has to be true:

- Prostacyclin extends the survival rate of people suffering from primary pulmonary hypertension (PPH).
- Prostacyclin acutely opens blocked blood vessels in the legs of people with critical limb ischemia (CLI).
- Longer-acting versions of the prostacyclin molecule, such as United Therapeutics' Remodulin, improve the exercise ability and symptoms of people diagnosed with pulmonary arterial hypertension (PAH).
- Longer-acting versions of the prostacyclin molecule have demonstrated anti-cancer effects in animal models that may be applicable to metastatic lung, breast, and colon cancer.

The way the body produces prostacyclin is geared to its rapid use and reproduction. A typical prostacyclin molecule produced in the body lasts only about 30 seconds before being put to use and degraded. This is not surprising since many molecules produced in the body last for only a short time and are thus produced at very high rates. Molecules of the crucial energy source adenosine triphosphate (ATP), for example, are made, used, and re-made about every five seconds inside our cells – each of which has 80 million or so of such molecules at any time. Consequently, there are only three ways prostacyclin can be put to therapeutic use by doctors:

- Infuse a replica of the prostacyclin molecule continuously into the blood stream.
- Deliver a longer-acting variant of the prostacyclin molecule through the skin, via inhalation, or by frequently taken pills.
- Offer to patients a sustained-release version of the prostacyclin molecule that gradually dissolves over a period of many hours.

Most patients diagnosed with PAH today take prostacyclin via the continuous, intravenous infusion approach. This therapy is called Flolan and is keeping over 2,000 patients alive at a cost of about \$50,000 per year. Unfortunately, this therapy exposes patients to high risks, including a chance each year of developing a sepsis infection and an omnipresent risk of rebound hypertension from dislodged or blocked catheters. The therapy is also extremely inconvenient because the patient must have a catheter sewn into his or her chest, keep the prostacyclin cold with a portable ice pack, carry around an intravenous infusion pump, and reconstitute the drug each day.

United Therapeutics' Remodulin is the next generation in prostacyclin therapy. This longer-acting analog, or variant, of prostacyclin, lasts over 100 times longer than the natural molecule. As a result, Remodulin can be delivered subcutaneously (through the skin), completely eliminating the risks of sepsis, greatly reducing the risk of rebound hypertension, and substantially improving the therapy's convenience to patients. On the other hand, many patients do complain of pain at the point on the skin

where the drug is delivered. However, hundreds of patients have already found this side effect to be well worth the advantages of not having to deal with an intravenous therapy. Consequently, even before regulatory approval of Remodulin, there is one patient using Remodulin in clinical studies for every five patients using Flolan.

Assuming FDA approval, there is good reason to expect that the number of patients using Remodulin will substantially increase. Doctors already have successfully transitioned patients from Flolan to Remodulin. These case studies are now being reported and published at scientific conferences and in a leading peer-reviewed medical journal.

Scientists supported by United Therapeutics' research grants have conducted laboratory tests comparing Remodulin with all other generally used analogs of prostacyclin. These tests show Remodulin to be significantly more potent and to have greater intrinsic activity than the other analogs. In addition, United Therapeutics has produced a sustained-release version of Remodulin, using the innovative "pegylation" technology that has revolutionized alpha interferon therapy. This sustained-release version of Remodulin, which we call Unipeg, appears in preclinical studies to be effective. As we bring sustained release versions of Remodulin into the clinic, we will be embarking on the third possible way to offer prostacyclin therapy: through easy-to-use, once- or twice-a-day administration.

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 dozens of 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 PPAR receptor), which is believed to be needed for tumor growth. Given the potency of Remodulin, and its relative ease-of-use, we believe there is anti-cancer potential in this lead United Therapeutics product.

Patent protection for Remodulin is strong. The patent for Remodulin for the treatment of pulmonary hypertension expires in 2009, and United Therapeutics plans to seek an extension of up to five years under the provisions of the Waxman-Hatch patent term extension act. United Therapeutics also has patents pending for its synthesis of Remodulin which, when issued, will provide an additional layer of patent protection for the drug. United Therapeutics also holds an issued patent for Remodulin for the treatment of peripheral vascular disease and a pending patent for the treatment of cancer. Finally, United Therapeutics holds several issued and pending patents for the composition and use of sustained release formulations of Remodulin for various indications, including pulmonary hypertension, peripheral vascular disease, congestive heart failure, and cancer.

Another product in our prostacyclin portfolio is the oral prostacyclin analog called Beraprost. This drug was licensed to us in both immediate-release and sustained-release formulations by the Japanese chemical company Toray Industries, Inc. The immediate-release formulation is approved in Japan for the treatment of peripheral arterial occlusive disease and primary pulmonary hypertension. While our clinical studies of Beraprost for those indications were disappointing in the U.S., we are quite hopeful that the sustained-release formulation of Beraprost will demonstrate greater efficacy. In addition, based on the growing excitement over the use of prostacyclin analogs as anti-metastatic agents, we expect to receive an exclusive license to also develop Beraprost for oncological conditions.

In summary, from pulmonary hypertension to critical limb ischemia to lung, breast, and colon cancer, prostacyclin appears to be one of the most promising natural hormones under development as a pharmaceutical therapy. We at United Therapeutics are highly energized by our worldwide exclusive rights to the most potent and long lasting of the prostacyclin analogs in use today, Remodulin. We are using this energy, and our resources, to make Remodulin available to patients as rapidly as the clinical development and regulatory approval processes allow.

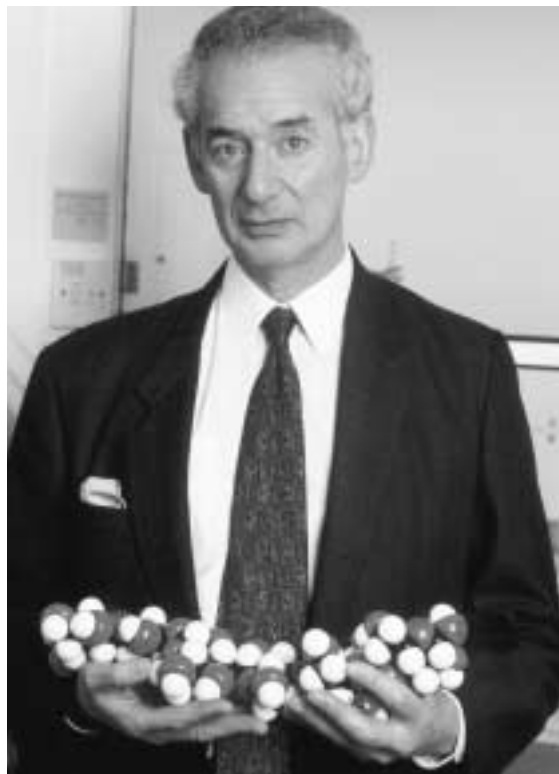
"I have had the pleasure of working with the scientists and staff of United Therapeutics since the formation of the company. The dedication and experience of the development and clinical studies team has allowed the rapid development of modalities to improve the lives of our patients with pulmonary arterial hypertension."

Dr. Robert C. Bourge,
Professor of Medicine, Division
of Cardiovascular Disease,
University of Alabama at
Birmingham

Iminosugars Interfere with Viruses

Sugars are fundamental to human biochemistry: glucose is our energy molecule, ribose holds our DNA together, and other sugars are crucial building blocks in our cellular membranes, enzymes, and organelles. One of the members of our Scientific Advisory Board, University of Oxford Glycobiology Institute Founder and also Chairman of the Biochemistry Department, Professor Raymond A. Dwek, F.R.S., is one of the foremost experts on iminosugars, a class of small molecules that act like sugars but are created synthetically. In particular, Professor Dwek discovered a way to use iminosugars so that they have impressive therapeutic benefits.

The first therapeutic iminosugars used by Professor Dwek were called alpha-glucosidase inhibitors. This kind of molecule was found to be quite effective in treating Gaucher's Disease and other glycolipid storage disorders and was licensed exclusively to the U.K. company Oxford Glycosciences via Searle/Monsanto.



Professor Dwek holding a model of an iminosugar molecule.

More recently, Professor Dwek and his colleagues have discovered a new set of therapeutic iminosugars that in laboratory tests were found to be effective at reversing the symptoms of infection by flavoviruses. There are four well-known diseases caused by flavoviruses: hepatitis B, hepatitis C, dengue, and Japanese encephalitis. The exclusive worldwide rights to use these therapeutic iminosugars were licensed to United Therapeutics. We are now actively engaged in:

- Producing clinical trial quantities of our lead iminosugar, UT231B, as well as arranging for the production of yet larger quantities.
- Ensuring the safety of UT231B via required preclinical tests.
- Preparing to file an Investigational New Drug application with the FDA to commence human proof-of-concept studies in patients with hepatitis C.
- Continuing research and development efforts to produce additional iminosugars with favorable safety and efficacy profiles.

Our iminosugars have a novel mechanism of action against viruses that is different from conventional antiviral therapies. Our iminosugars are able to slip through cellular membranes and take up residence in the endoplasmic reticulum, where many viruses are assembled. Many of the glycoproteins, and possibly the proteins, in the viruses interact with iminosugars, such as UT231B. In the specific case of hepatitis C, our data suggest that UT231B alters the assembly of the viruses and thereby prevents them from being able to continue infecting and replicating other cells.

Recent published reports estimate that as many as 12% of the world population may be infected with hepatitis C and 20% with hepatitis B. In addition, the plague of dengue fever has been spreading rapidly. We believe our iminosugar product line offers tremendous potential for combating these major worldwide health threats.

Arginine Is Patented for the Treatment of Cardiovascular Disease

Amino acids have evolved over billions of years. However, only in recent years did man discover that the amino acid arginine is essential to forestalling cardiovascular disease. The discoverer of this therapeutic breakthrough was John Cooke, M.D., Ph.D., Director of Vascular Medicine at Stanford University. United Therapeutics now owns the exclusive worldwide rights to Dr. Cooke's patented discoveries.

Almost every kind of food we eat contains arginine, but red meat has the highest level. Consequently, meat-eaters consume about six grams of arginine per day, while vegetarians take in only about three grams per day. Studies show that an average-weight person gets a therapeutic effect from consuming about 6-9 grams of arginine per day. Therefore, especially in an age of decreasing meat consumption, patients at risk of cardiovascular disease may benefit from arginine supplementation.

In earlier centuries, when average life expectancy was around 40 years, the risk of cardiovascular disease was not the biggest concern. In those days, infectious diseases took most people's lives. Nowadays, heart disease and stroke are the number one and number three killers not only in the United States and Europe but also in China, Japan, and India. Arginine supplementation may be a very useful tool in combating these killers because our diets cannot reasonably provide us with enough arginine to forestall the gradual deterioration of the endothelial wall lining that surrounds all of our blood vessels.

The body converts arginine into nitric oxide, which is the molecule that instructs the endothelial wall lining of our blood vessels to dilate when pulsed with blood. When the endothelial wall linings of our blood vessels become dysfunctional, by not dilating enough, then high blood pressure and atherosclerosis occur. These symptoms, in turn, signal sharply elevated risks of heart disease and stroke.

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.

In the developed regions of North America and Europe, people age 60 and over will total some 200 million. This population segment is particularly likely to benefit from arginine supplementation. United Therapeutics now makes arginine supplementation products available in seven different flavors and four different formulations. In addition, if ADMA tests augment the approximately 30 million cholesterol level tests given annually, then royalty revenues to United Therapeutics from this diagnostic alone should be substantial.



"In my experience, recommending Heart Bar has helped to stop heart disease in my patients."

Joe Prendergast, M.D.
Diabetes Specialist





"United Therapeutics is a company that combines innovative out-of-the-box creativity with rigorous science. For this reason, I'm excited to work with Martine Rothblatt and her dedicated team of scientists."

Raymond Kurzweil



Telemedicine

The fourth United Therapeutics platform features a remarkable device called the Epicardia® monitor. This telecardiology device incorporates a proprietary, patented digital algorithm called "Diogenes™". The Diogenes algorithm enables the monitor to detect whether a patient wearing the device is experiencing any potentially life-threatening cardiac arrhythmias. If so, the information will be transmitted via telephone lines and the Internet to expert technicians at our cardiac monitoring center. After the technicians have assessed the information, we promptly inform the patient's doctor of what we have learned via the Diogenes algorithm.

Our telemedicine technology is so advanced, and convenient to use, that it was selected for installation on the International Space Station for cardiac monitoring of the astronauts. We previously established an excellent record for quality as the cardiac monitor for the Mir Space Station and potentially saved the life of Cosmonaut Commander Tsibliev by detecting an arrhythmia. Our record in space is matched on earth, with the Epicardia system now in use by over 50 hospitals and hundreds of physicians.

Our engineering team is making rapid advances in our Epicardia monitoring system. Our next-generation devices will automatically detect arrhythmias without the need for any buttons to be pressed by the patient. In addition, we are adding wireless communications capability to the monitors, advancing the Diogenes algorithm to detect a greater variety of cardiac problems, and improving the patient processing throughput efficiency of our cardiac monitoring center.



"By utilizing Medicomp's state-of-the-art outsourcing technology, the Ohio Kaiser region has been able to improve patient care while maximizing personnel and financial resources."

**Vikki Valente, Manager
Cardiology/Pulmonology
Services
Kaiser Permanente
Ohio Region**

In the coming years, telemedicine may become a natural part of many seniors' lives, with medical problems being detected and diagnosed before they are even aware of them. Our cardiac monitors are on a development path to becoming so intelligent, lightweight and convenient that they could be worn by millions of people on a daily basis. Since earlier treatment is almost always better than later treatment, we hope our telemedicine capability will play an important role in saving many seniors' lives.

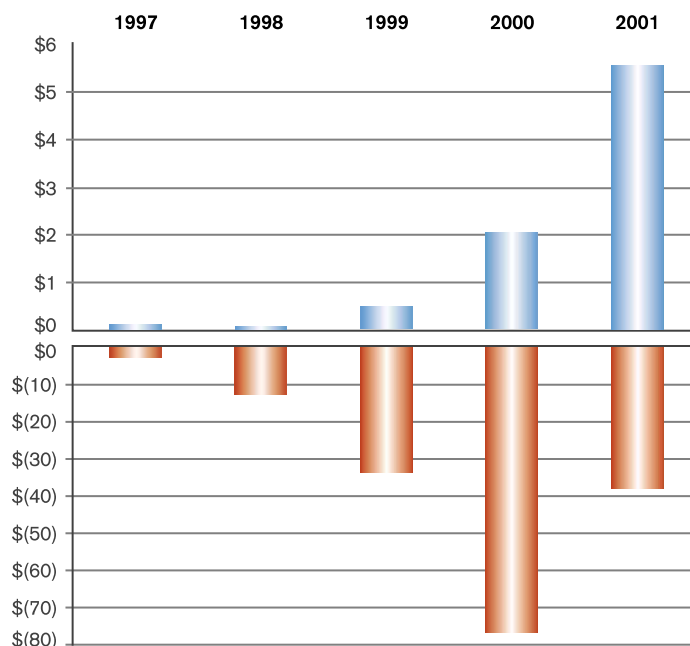
Selected Financial Highlights

Revenue Growth

(in millions)

Net Losses

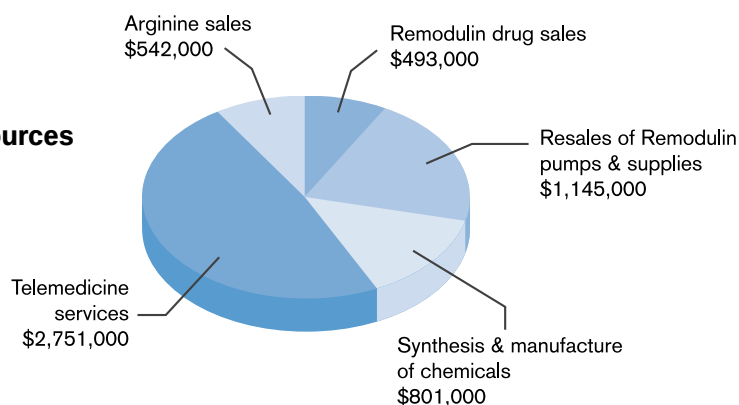
(in millions)



United Therapeutics' revenues grew from \$116,000 in 1997 to over \$5.7 million in 2001. Revenues in 2001 more than doubled from the prior year due to revenues from acquired subsidiaries and sales of Remodulin prior to approval for use with government-reimbursed patients in Europe. Annual net losses in these years have also grown due to the ramp-up of clinical trials, acquisitions, and one-time charges. In 2001, spending leveled compared to prior years and there were no major non-recurring charges.

2001 Revenue Sources

Total \$5.7 million



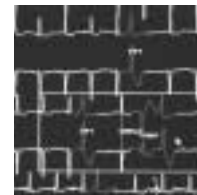
Cash and Investments – United Therapeutics had cash and marketable investments totaling approximately \$172.9 million at December 31, 2001.

Company Summary

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

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

The theme of United Therapeutics is "Medicines for Life" because all of its therapeutics are geared toward life-threatening conditions. This focus enables the company to concentrate on some of the highest-value applications of biotechnology. The company's mission is carried out using corporate partners for product sales and academic affiliates for research, and the company generally retains all rights to the products it develops. This strategy streamlines company overhead and enables United Therapeutics' employees to concentrate on clinical trials, regulatory approvals, and business development.



Corporate Information

Senior Executives and Board Members

Martine Rothblatt, Ph.D., J.D., M.B.A.*
Chairman & Chief Executive Officer

Roger Jeffs, Ph.D.
President & Chief Operating Officer

David Walsh, Ph.D.
Executive Vice President &
Chief Operating Officer for Production

Barry Kanarek, M.D., Ph.D.
Chief Medical Officer,
President & Chief Operating Officer
Unither Pharma, Inc.

Fred Hadeed, C.P.A.
Chief Financial Officer

Paul Mahon, J.D.
Senior Vice President &
General Counsel

Ricardo Balda*
Chief Executive Officer
Medicomp, Inc.

* = Also a Board Member

Outside Board Members

David Gooray, M.D.
Cardiologist

Henry Beecher Hicks, III, M.B.A.
Principal
Katalyst L.L.C.

Raymond Kurzweil
Founder, Chairman &
Chief Executive Officer
Medical Learning Company, Inc.

Michael C. Miles, M.B.A.
Co-founder
McManus & Miles

Noah A. Samara, J.D., M.B.D.
Chairman & Chief Executive Officer
WorldSpace Corporation

Scientific Advisory Board United Therapeutics

Sir John Vane, D.Sc., F.R.S.
1982 Nobel Laureate in
Physiology or Medicine
Chairman of the
Scientific Advisory Board

Professor Salvador Moncada
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Vice Chairman of the
Scientific Advisory Board

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Director, Pulmonary
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New York Presbyterian Hospital

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1976 Nobel Laureate in
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Fox Chase Distinguished Scientist
Fox Chase Cancer Center

**Professor John Eric Deanfield, M.B.,
Bchir, F.R.C.P.**
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Glycobiology Institute,
Chairman of the
Department of Biochemistry

Professor Victor J. Dzau, M.D.
Chairman of the Department of
Medicine of Brigham & Women's
Hospital, Harvard Medical School

Louis J. Ignarro, Ph.D.
Professor, Molecular and
Medical Pharmacology,
Jerome J. Belzer, M.D.
Distinguished Professor of
Pharmacology, UCLA
1998 Nobel Laureate in
Physiology or Medicine

Urban Ramstedt, Ph.D.
Head, Immunology
Zycos Inc.

**Professor Sir Magdi Yacoub, M.D.,
F.A.C.S.**
England's National Heart
& Lung Institute

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Common Stock

Listed on Nasdaq National
Market symbol "UTHR"

Included in iShares NASDAQ
Biotechnology Index Fund (NBI)
Member of Russell 2000 Index

Annual Meeting

June 26, 2002

Website

www.unither.com



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