

# Medicines for Life® 2004 Annual Report



# Corporate Profile



The medical artwork on the cover is a thousand-word picture of what United Therapeutics is all about. We are a cardiovascular company. We have begun the necessary spade-work to one day also offer medicines that combat cancer and infectious diseases. For now, though, our revenue-generating products are all in the field of cardiovascular medicine.

Our lead product and largest revenue earner is Remodulin® for the treatment of pulmonary arterial hypertension. This life-threatening disease results from the pulmonary arteries becoming dysfunctional, causing right heart failure if not adequately treated. In 2002, Remodulin was approved for subcutaneous administration in the United States, Canada and Israel, and in France in March 2005, opening the way for mutual recognition of that approval in other countries of the European Union. In November 2004, the United States Food and Drug Administration approved the intravenous use of Remodulin for those not able to tolerate subcutaneous infusion. Other international approvals are pending.

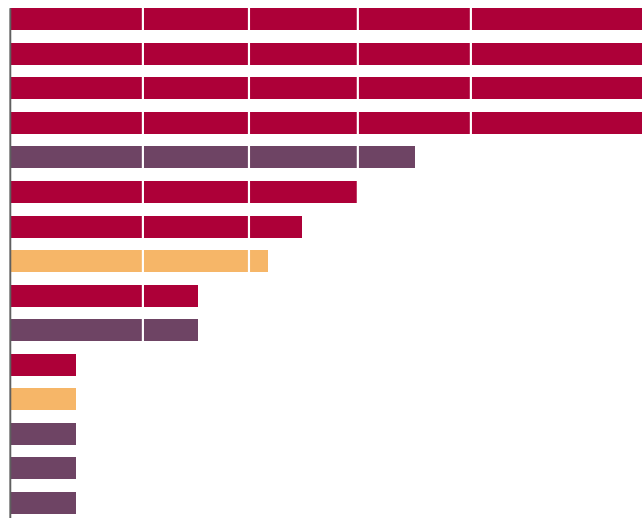
Telecardiology services for patients with an array of possible cardiac arrhythmias are our next largest revenue earner. Our CardioPAL® family of event monitors is the most technologically advanced portable heart monitor in the industry. Our newest heart monitor, the CardioPAL SAVI, was recently approved by the Food and Drug Administration as the first ambulatory device to detect the p-wave, a diminutive but critical portion of the electrocardiogram (ECG) that represents atrial activity. Our EpiCordia service provides cardiologists with a printed ECG report on their patients anywhere in the United States as quickly as one hour after the patient connects our device to a telephone receiver. Indeed, our cardiac monitoring technology is so reliable and advanced that it was selected for use onboard the International Space Station.

A third revenue earner for us in the field of cardiovascular health is our arginine supplementation business. Arginine is one of the twenty amino acids necessary for life. In our bodies, enzymes convert arginine into nitric oxide. This conversion is crucial for maintaining circulatory function along our 100,000 kilometers of blood vessels and capillaries. United Therapeutics is the exclusive licensee of several Stanford University patents covering the use of arginine for the promotion of vascular function.

## Product Pipeline

- Subcutaneous Remodulin® for PAH
- Intravenous Remodulin® for PAH
- Telemedical Services
- Arginine Formulations
- OvaRex® for Ovarian Cancer
- Remodulin for CLI
- Inhaled Treprostinil for PAH (TRIUMPH)
- UT-231B for Hepatitis C
- Oral UT-15C SR for PAH
- BrevaRex® for Multiple Myeloma
- Beraprost® SR for PVD
- Glycobiology Antiviral Agent Lead for Infectious Disease
- OncoRex® for Various Cancers
- ProstaRex® for Prostate Cancer
- GivaRex® for Gastrointestinal Cancer

Preclinical    Phase I    Phase II    Phase III    Commercialized



- List of Abbreviations
- PAH = pulmonary arterial hypertension
  - CLI = critical limb ischemia
  - PVD = peripheral vascular disease
  - Cardiovascular
  - Oncology
  - Infectious Disease



Cardiovascular medicine is a good place for United Therapeutics to be. There are two reasons why we believe we can provide more benefits in this therapeutic area than in any other market segment. First, our products are strong leaders in this market. Most doctors who treat significant numbers of pulmonary hypertension patients are now prescribing Remodulin. Our telecardiology devices are the smartest, smallest products in the industry. The strength of our arginine intellectual property portfolio was demonstrated in 2003 when the United States Patent and Trademark office issued a patent to us that solidified our existing coverage. More people succumb to cardiovascular disease than to any other illness in America, as well as in Europe, China, and India.

While building our company's business value in the cardiovascular field, we are also laying important foundations for future franchises in oncology and infectious diseases. We are undertaking the largest ever placebo-controlled pivotal trials of a potential medicine for preventing the recurrence of ovarian cancer. In addition, this medicine is part of a family of similar therapies to which United Therapeutics owns the rights and which are designed to combat prostate, breast, lung, pancreatic, gastrointestinal and multiple myeloma cancers.

In the field of infectious disease, we are targeting hepatitis C and other diseases with unique glycochemistry antiviral agents discovered by the field's founder, Professor Raymond Dwek of Oxford University. While this work is at an early stage, with proof-of-concept testing in patients underway, it holds immense promise. The diseases being targeted afflict over a billion people worldwide, and the compounds are part of an entire new class of pharmacological agents.

United Therapeutics has been singularly successful at developing therapies with a comparatively low cash burn rate as compared to other public biotechnology companies. We accomplish this by working efficiently and by outsourcing our pre-clinical research efforts to major academic centers whenever feasible. Another major factor in our success has been our control over manufacturing, with a company-owned facility that produces our lead product. We are also efficient in the sales and marketing arena by virtue of partnerships with half a dozen drug distribution and detailing firms. These partnerships are complemented by in-house commercialization professionals and our commitment to providing doctors and patients with accurate information and ongoing research related to our products.

The heart and lungs are remarkable organs. Perhaps more than any other word, "balance" describes what they do. Their excellence at balancing blood flow and gas exchange is far more marvelous than any machine man has yet devised. As a company, we too aspire to balance. Our balanced approach to cardiovascular medicine includes a pharmaceutical (Remodulin), a diagnostic (telecardiology) and a nutraceutical (arginine). Our cardiovascular drug development strategy is balanced with a commercialized use (PAH), as well as novel uses and new routes of administration. And our overall company strategy is balanced among mature programs (cardiovascular), pivotal development (oncology), and early-stage pipeline activities (infectious disease).

In addition to balance, the heart also symbolizes vitality and caring. At United Therapeutics, we find tremendous inspiration for our work and view our products as being "new beginnings" for patients and doctors, with quality of life as our utmost therapeutic goal.



## Senior Management

(Pictured left to right)

**David Walsh, Ph.D.**  
Executive Vice President and  
Chief Operating Officer, Production

**Yu-Lun Lin**  
President and Chief Executive Officer,  
Unither Pharma

**Roger Jeffs, Ph.D.**  
President and Chief Operating Officer

**Shola Oyewole**  
Chief Information Officer

**Martine Rothblatt, Ph.D.**  
Chairman and Chief Executive Officer

**Paul Mahon**  
Executive Vice President,  
Strategic Planning and General Counsel

**Fred Hadeed**  
Executive Vice President,  
Business Development and  
Chief Financial Officer

**Dan Balda, M.D.**  
President and Chief Operating Officer,  
Medicomp

**Peter Gonze**  
Chief Operating Officer,  
Unither Pharmaceuticals

# To Our Shareholders

2004 was the best year yet in United Therapeutics' history. We attained over \$70 million in revenues, achieved profitability, and helped more patients than ever before.

Soon after United Therapeutics was formed, we began to augment our pulmonary hypertension mission by acquiring the rights to other technologies for chronic, life-threatening conditions. In this way we would leverage the expertise we gained with Remodulin into new therapeutic areas, while heightening the upside potential for our shareholders and reducing the risk inherent in a one-drug business. 2004 was also a great year for this strategy of focused diversity. Our potential medicine for ovarian cancer, OvaRex, is over half enrolled in its Phase 3 trials, while our glycobiology platform continues to generate new molecules for our clinical consideration.

United Therapeutics' strategy of focused diversity can be summarized with the following key points:

- One Mission – chronic therapy for life-threatening conditions
- Three Market Segments – cardiovascular, cancer, and infectious diseases
- Five Technology Platforms – prostacyclin analogs, arginine formulations, telemedicine, immunotherapeutic antibodies, and glycobiology
- Fifteen Products and Product Candidates – from intravenous Remodulin to ProstaRex for prostate cancer

This focused diversity strategy enables us to concentrate our staff resources and capital in areas that are our core competencies, such as clinical development of pharmaceuticals for chronic, life-threatening conditions.

2004 was also a very positive year for United Therapeutics in terms of financial performance. We achieved profitability on \$73 million in revenues. We ended the year with virtually no debt and over \$139 million in cash and investments.

The ability of United Therapeutics to accomplish such an outstanding year is due to the extraordinary efforts of its senior management, including:

- Roger Jeffs, President and Chief Operating Officer, who heads our Clinical Development Group in Research Triangle Park, NC
- David Walsh, Executive Vice President and Chief Operating Officer, Production, who heads our Pharmaceutical Production Group in Chicago, IL
- Fred Hadeed, Executive Vice President, Business Development and Chief Financial Officer, who heads our Corporate and Financial Group in Silver Spring, MD

- Paul Mahon, Executive Vice President, Strategic Planning and General Counsel, who heads our Legal and Governmental Affairs Group in Washington, DC

- Dan Balda, M.D., President and Chief Operating Officer of our Medicomp subsidiary, who heads our Telemedicine Group in Melbourne, FL

- Peter Gonze, Chief Operating Officer of our Unither Pharmaceuticals subsidiary, who heads our Oncology Group in Wellesley Hills, MA

The efforts of our senior managers are seamlessly sewn together using state-of-the-art networking technology managed by Shola Oyewole, our Chief Information Officer. Ultimately, we are all working to support our company's various sales and marketing efforts, especially those of our lead product, which are led worldwide by Robert

Roscigno, Senior Vice President of Commercial Development, and from our UK office, by Carl Sterritt, Vice President of European Commercial Development.

While 2004 was a great year for United Therapeutics, as we look toward 2005-2006 we feel that the best is yet to come. We still have major challenges ahead of us, such as growing Remodulin sales in pulmonary arterial hypertension, successfully completing a Phase IV post-approval study of Remodulin in pulmonary arterial hypertension, further development of Remodulin in new territories and new uses, and proof of safety and efficacy in our oncological and infectious disease

programs. Of paramount importance is demonstrating our ability to grow the company's profitability. However, we are making steady progress towards all of these goals.

The robust United Therapeutics pipeline, if successfully developed, has enough compounds and product candidates to push revenues and earnings ever higher for many years to come. It is to the realization of this potential to which all of us at United Therapeutics are steadfastly committed.

We are honored to work with our best efforts for our shareholders, the medical community and the patients who rely upon our therapies.

Sincerely,



Martine Rothblatt, Ph.D.  
Chairman and CEO

**"WE ATTAINED  
OVER \$70 MILLION  
IN REVENUES,  
ACHIEVED  
PROFITABILITY,  
AND HELPED  
MORE PATIENTS  
THAN EVER BEFORE."**

# Scientific Advisory Board



Professor Baruch S. Blumberg, Ph.D.,  
NOBEL LAUREATE

We are proud of our Scientific Advisory Board. Our founding Chairman until his death in November 2004 was Sir John Vane, a Nobel Laureate who co-discovered the molecule prostacyclin, upon which much of our business is based. The knowledge of our Scientific Advisory Board members is of immense value to us as we explore the use of prostacyclin-like molecules (such as Remodulin) in cardiovascular conditions.

As we extended our business into infectious diseases, we strengthened our Board with Nobel Laureate Baruch S. Blumberg, Ph.D., who succeeded Sir John Vane as Chairman, and 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, UT-231B). 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.

It is also important to have individuals on a Scientific Advisory Board who have operational responsibility and vast expertise 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, Victor J. Dzau, M.D., President and CEO, Duke University Medical Center & Health System, and the Hon. Louis W. Sullivan, M.D., founding President and now President Emeritus of Morehouse School of Medicine and former Secretary of the United States Department of Health and Human Services.

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.

**"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."**



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



Professor  
Victor J. Dzau, M.D.



Urban Ramstedt, Ph.D.



Louis W. Sullivan, M.D.



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



Sir John Vane, D.Sc. F.R.S.  
March 29, 1927 - November 20, 2004

## Dear Shareholders,

By now, many of you may have learned of the passing of the Chairman of our Scientific Advisory Board, Sir John Vane. While obituaries are covering his more public accomplishments, such as those referenced in his Nobel Prize, I thought you might like to know how essential he was to the success of United Therapeutics. When our company was formed in 1996, we had no intellectual property. The company was a bet on the prospect that Glaxo Wellcome (now GlaxoSmithKline, and then Burroughs-Wellcome) would license to us its prostacyclin-like molecule we now call Remodulin (then called 15AU81). Glaxo was not eager to do this. They had to be persuaded, cajoled and urged. As I sometimes say, big drug companies are like the famous advertisement for the Roach Motel – intellectual property comes in, but does not go out. Shortly after our company was formed, Sir John Vane agreed to join us as Chairman of a yet-to-be-constituted Scientific Advisory Board. This was a great coup for the nascent company because, when he was previously head of research at Wellcome, he had received the Nobel Prize for discovering prostacyclin, and he oversaw the efforts that led to the creation of medicinal versions of the natural prostacyclin molecule – including the prostacyclin-like medicine we call Remodulin today. He agreed to join us because he felt that we had a good chance of enabling many more people to benefit from his discoveries as compared to having the intellectual property collect dust on the shelves of Glaxo Wellcome. He also appreciated the entrepreneurial spirit of United Therapeutics and was proud to be associated with the company. The executives at Glaxo were amazed when they heard that the famous Sir John Vane had joined our tiny company's Scientific Advisory Board. This went a long way in persuading them to license to us what is now called Remodulin. With Sir John ultimately in charge of the company's science and pharmacological development, they felt that the drug they licensed to us would be responsibly developed via clinical trials. History proved them right. I last spoke with Sir John a few weeks before his death. He was thrilled with our intravenous route of delivery, excited about the prospect of an implantable pump to dispense Remodulin and hopeful that our oral prostacyclin program would succeed. Sir John was a person who always went out of his way to help other scientists and drug developers succeed with their careers. He loved to put people in touch with other people who could help them. He was a great networker. He was also a bon vivant. The success of United Therapeutics was one of his fondest accomplishments. All of us made him proud. May the spirit of Sir John continue to dwell within all of us, inspiring us to help others, to think creatively and to enjoy life.

Martine Rothblatt, Ph.D.



The theme of United Therapeutics is “Medicines for Life” because all of our therapeutics address life-threatening illnesses.



# Multiple Market Segments

## Remodulin®, a prostacyclin analog

United Therapeutics has focused primarily on developing Remodulin as our lead product for treating pulmonary arterial hypertension, a life-threatening vascular disease that affects the blood vessels between the heart and lungs. 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. It is estimated that there are between 50,000 and 100,000 individuals with pulmonary arterial hypertension worldwide.

Pulmonary arterial hypertension is associated with reduced production of the natural hormone prostacyclin in the pulmonary blood vessels. As an analog of natural prostacyclin, Remodulin appears to dilate blood vessels where necessary, prevent platelet aggregation, and prevent proliferation of smooth muscle cells surrounding the vessels.



## OvaRex®, an immunotherapeutic monoclonal antibody

Ovarian cancer is the fifth most frequent cause of cancer death in women and the leading cause of gynecologic cancer death in the United States. It is typically diagnosed when it has already progressed to an advanced stage. There is a high rate of initial response to front-line therapy (surgery and chemotherapy), generally leading to a period of remission known as “watchful waiting”. Unfortunately, however, most women will eventually experience a recurrence of their cancer.

There are no approved therapies to follow front-line treatment that might delay or prevent the relapse of ovarian cancer. Our goal is to use OvaRex, a monoclonal antibody, to help the body mount an immune response against the tumor and its associated surface proteins known as CA125, helping the body directly fight the cancer during the pivotal “watchful waiting” period. Our Phase III clinical trials are enrolling at more than 60 medical centers throughout the United States and are designed to demonstrate clinical benefit by extending the time to disease relapse.

## Iminosugars, glycobiology antiviral agents

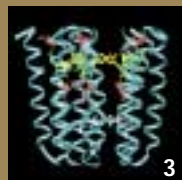
Sugars are fundamental to human biochemistry: glucose is our energy molecule, ribose holds our DNA together, and other sugars are crucial building blocks in our cellular membranes, enzymes, and organelles. United Therapeutics has exclusive rights to therapeutic iminosugars, a class of small molecules that act like sugars but are created synthetically. In laboratory tests, our iminosugars were found to be effective at reversing the symptoms of infection by flaviviruses which cause hepatitis B and C, dengue fever, and Japanese encephalitis.



1



2



3



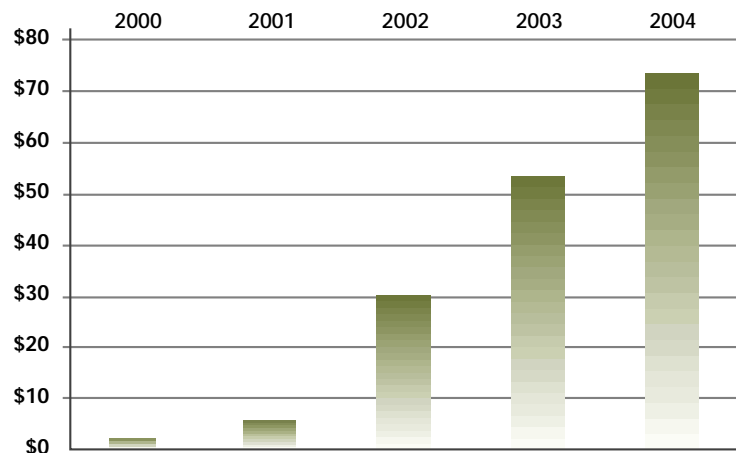
4

1. HCV p7 pentamer (side view). red: serine, yellow: histidine, green: threonine; 2. HCV p7 pentamer (view from top); 3. Same as number 1 with the United Therapeutics glycobiology compound docked (side view); 4. Same as number 3 with the United Therapeutics glycobiology compound docked (view from top)

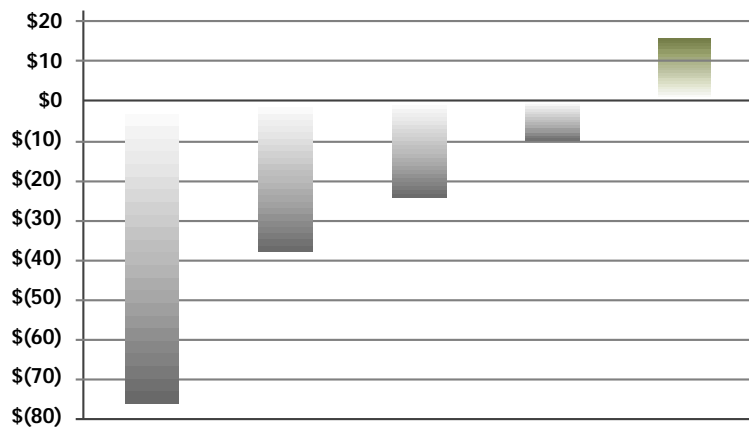
HCV = Hepatitis C virus

# Selected Financial Highlights

**Revenue Growth**  
(in millions)

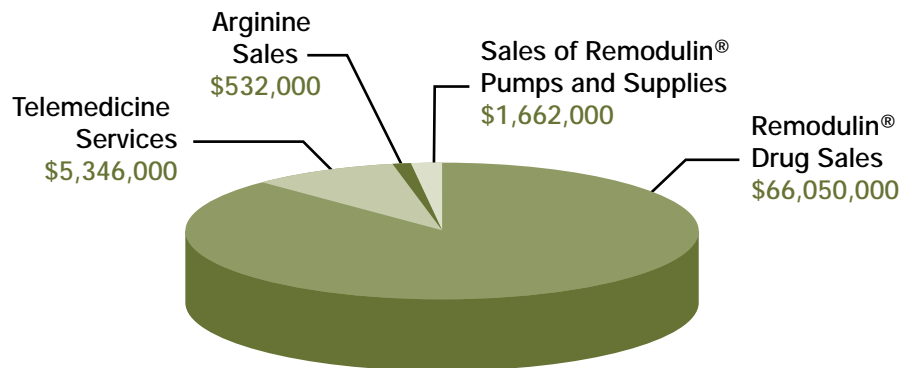


**Net Income (Losses)**  
(in millions)



**Revenues and Net Income** – United Therapeutics' revenues grew 38% to \$73.6 million in 2004 and achieved its first ever annual profit totaling \$15.5 million for the year. These results were achieved mainly due to increased demand for Remodulin®, United Therapeutics' flagship product. Remodulin was first launched in the United States in 2002 following its FDA approval. Remodulin is now also approved in France, Canada, Israel, Switzerland and Australia.

## 2004 Revenue Sources Total \$73.6 million



**Cash and Investments** – United Therapeutics had cash, cash equivalents and marketable investments totaling \$139.1 million and virtually no long-term debt as of December 31, 2004.

# Corporate Information

## Management

Dan Balda, M.D.  
President and Chief Operating Officer  
Medicomp, Inc.

Peter C. Gonze  
Chief Operating Officer  
Unither Pharmaceuticals, Inc.

Fred T. Hadeed  
Executive Vice President,  
Business Development and  
Chief Financial Officer

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

Yu-Lun Lin  
President and Chief Executive Officer  
Unither Pharma, Inc.

Paul A. Mahon, J.D.  
Executive Vice President,  
Strategic Planning and General Counsel

Shola Oyewole, MSc., M.C.S.E.+1  
Chief Information Officer

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

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

## Board of Directors

Christopher Causey, M.B.A.  
Principal  
Causey Consortium

Professor Raymond A. Dwek, F.R.S.  
Professor of Biochemistry  
Director of the Glycobiology Institute  
Chairman of the Department of Biochemistry  
University of Oxford

R. Paul Gray  
Managing Partner,  
Core Concepts, LLC

Roger Jeffs, Ph.D.\*

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

Christopher Patuskus, J.D., M.G.A.  
Executive Director, Chief Operating Officer,  
Member of the Faculty  
Fels Institute of Government  
University of Pennsylvania

Martine Rothblatt, Ph.D, J.D., M.B.A.\*

Hon. Louis W. Sullivan, M.D.  
Founding President and  
President Emeritus of  
Morehouse School of Medicine  
Former Secretary of United States  
Department of Health and Human Services

\* United Therapeutics' Management

## Scientific Advisory Board

Sir John Vane, D.Sc., F.R.S. (1927-2004)  
1982 Nobel Laureate in Physiology  
or Medicine

Professor Baruch S. Blumberg, Ph.D.  
Chairman of the Scientific Advisory Board  
1976 Nobel Laureate in Physiology  
or Medicine  
Fox Chase Distinguished Scientist,  
Fox Chase Cancer Center

Professor Raymond A. Dwek, F.R.S.  
Professor of Biochemistry  
Director of the Glycobiology Institute  
Chairman of the Department of Biochemistry  
University of Oxford

Professor Victor J. Dzau, M.D.  
President and CEO,  
Duke University Medical Center  
& Health System

Urban Ramstedt, Ph.D.  
Head of Tumor Immunology  
Genitrix

Hon. Louis W. Sullivan, M.D.  
Founding President and President Emeritus  
Morehouse School of Medicine  
Former Secretary of United States  
Department of Health and Human Services

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

## Investor Relations

Andrew Fisher, J.D.  
Deputy General Counsel and Vice President,  
Investor Relations

## Transfer Agent and Registrar

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Shareholder Relations Department  
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(800) 524-4458  
(610) 382-7833 (outside the United States)  
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Stock Transfer Website: www.stockbny.com

## Attorneys

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## Auditors

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Fax. (919) 485-8352

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Wellesley Hills, Massachusetts 02481  
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Fax. (781) 235-7241

## Common Stock

Listed on Nasdaq National  
Market symbol "UTHR"

## Annual Meeting

June 29, 2005

## Internet Access

www.unither.com



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