# **UTHR 2005**

# MEDICINES FOR E

United Therapeutics Corporation Annual Report

# United Therapeutics is a biotechnology company

focused on the development and commercialization of innovative therapeutic products for patients with chronic and life-threatening cardiovascular, cancer and infectious diseases.

Pipeline of Re	v e	n u e	Sc	o u r	c e s	
	Pre-clinical	Phase I	Phase II	Phase III	Commercial	
Subcutaneous Remodulin® for PAH						
Intravenous Remodulin for PAH						
Telemedical Services and Systems						
Arginine Supplements and Licenses						
OvaRex® for Ovarian Cancer						
Inhaled Treprostinil for PAH (TRIUMPH)						
UT-15C Sustained Release for PAH and PVD						
BrevaRex® for Pancreatic Cancer						
Beraprost® SR			PAH = Pulmonary Arterial Hypertension PVD = Peripheral Vascular Disease			
Glycobiology Leads for Infectious Disease						
Monoclonal Antibody Leads		Ρi	pelin	e Le	gend	

Cardiovascular

Oncology Infectious

# United Therapeutics Corporate Profile





United Therapeutics is a cardiovascular company that is also developing medicines to 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, a stable synthetic form of prostacyclin, an important molecule produced by the body that has powerful effects on blood-vessel health and function. Remodulin has been approved in the United States. most of Europe, Canada, Israel and other countries for the subcutaneous (through the skin) treatment of pulmonary arterial hypertension (PAH), a life-threatening condition characterized by elevated blood pressures between the heart and lungs. Remodulin is also approved for intravenous use in the United States, Canada and Israel, with marketing authorization applications currently under review in other countries.

Telecardiology services approved for health care reimbursement for patients with an array of possible cardiac arrhythmias are our next largest revenue earner. We have developed sophisticated telecardiology technology that quickly provides cardiologists with reports on their patients from anywhere in the United States, including devices that can automatically capture valuable information on





patients' heart rate, rhythm, morphology and abnormalities, including silent arrhythmias.

Cardiovascular medicine is a good place for United Therapeutics to be. It is the largest health care market with more people succumbing to cardiovascular disease than to any other disease in the United States and throughout the world.

Our cardiovascular products are strong leaders in their markets. Today, most doctors who treat large numbers of pulmonary hypertension patients are prescribing either subcutaneous or intravenous Remodulin.

While building our company's business value in the cardiovascular field, we are also laying important foundations for future franchises in the treatment of cancer and infectious diseases. We are conducting a pivotal trial of OvaRex, a monoclonal antibody for preventing the recurrence of ovarian cancer. OvaRex is part of a family of similar therapies to which we own the rights and which are designed to combat other cancers.

In the field of infectious disease, we are targeting hepatitis C and other diseases with unique iminosugar compounds discovered by the field's founder, Professor Raymond Dwek of





Oxford University. While this work remains at an early stage and has experienced setbacks, it holds immense promise. The diseases being targeted by our glycobiology agents afflict over a billion people worldwide.

United Therapeutics has been singularly successful at developing therapies in as expeditious a manner as possible at low cost. We accomplish this by working efficiently and by outsourcing our pre-clinical research efforts to maior 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 our internal sales team, partnerships with half a dozen drug distribution and detailing firms, and our commitment to providing doctors and patients with accurate information and ongoing research related to our products.

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.

- 1 -

# **UT** Senior

Raju Penmasta, Ph.D. Vice President, Research and Process Development

**Peter Gonze** Chief Operating Officer, Unither Pharmaceuticals Liang Guo, Ph.D. -Vice President, Production

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

Shola Oyewole Chief Information Officer

Paul Mahon Executive Vice President, Strategic Planning and General Counsel Roger Jeffs, Ph.D. President and Chief Operating Officer Martine Rothblatt, Ph.D. Chairman and Chief Executive Officer

# Management



# Many Disciplines Contribute to United Therapeutics' Growth

Many senior managers are responsible for our largest current and prospective products and operations. In the front row, from left-to-right, are our executive officers: Paul Mahon (Executive Vice President, Strategic Planning and General Counsel): Roger leffs. Ph.D. (President and Chief Operating Officer); and Martine Rothblatt, Ph.D. (Chairman and Chief Executive Officer). At the far right is Fred Hadeed (Executive Vice President. **Business Development and Chief Financial** Officer). These officers are responsible for making the legal, clinical, financial, commercialization and strategic decisions for our business.

From left-to-right, David Walsh, Ph.D.; Shola Oyewole; Peter Gonze; Raju Penmasta, Ph.D.; Liang Guo, Ph.D.; and Alyssa Friedrich are key senior managers with the following responsibilities:

Shola Oyewole is responsible for coordinating the flow of information among our ten offices in seven states and three countries. Smooth inter-office communication is essential to our company's dynamism. Peter Gonze is responsible for our OvaRex program, now more than half-way through its pivotal trial for the treatment of ovarian cancer.

Dave Walsh, Ph.D.; Liang Guo, Ph.D.; and Raju Penmasta, Ph.D.; are responsible for production and research of our dominant source of revenue: Remodulin. Our reliable production of Remodulin is a fundamental basis for our success.

Alyssa Friedrich is responsible for the recruitment and maintenance of our rapidly growing staff. Continual expansion of our highly professional employee base, especially in the area of sales and marketing, is key to our maturation into major а biotechnology company.

Many additional individuals occupy key senior and executive management roles at United Therapeutics, and dozens of employees provide crucial support in a wide variety of positions. The senior managers presented here represent a vital crosssection of our team.

Alyssa Friedrich Vice President, Human Resources and Community Relations Fred Hadeed Executive Vice President, Business Development an Chief Financial Officer

# A Successful Year

2005 was United Therapeutics' best year ever. It was a year that produced highly significant clinical trial results, more than \$116 million in revenues, and our first year of four profitable quarters. To use a metaphor, we are firing on all thrusters.

I believe the reason we are doing so well is because of our tight adherence to our management-byobjective philosophy. Our senior management team has developed, and our Board has validated, the following five strategic milestone objectives:

1: Develop and manufacture the best possible medicines from our intellectual property platforms in prostacyclin analogs, monoclonal antibodies and iminosugars;

2: Conduct the most insightful clinical trials possible of our medicines as evidenced by high rankings in medical consensus statements and publication in leading medical journals;

**3:** Communicate accurately and effectively our clinical information to prescribers;

**4:** Demonstrate earnings per share (EPS) growth in the top quintile of our peer group; and

**5:** Accomplish all of the above with the highest level of ethical conduct.

Financial success in biotechnology is founded upon superior medicines. Hence, the first of our five milestone objectives is to develop the best possible medicines from our intellectual property platforms. These efforts include Remodulin from our prostacyclin analog platform, OvaRex from our monoclonal antibody platform, and several early stage candidates from our iminosugar platform. We are now offering or developing Remodulin for subcutaneous. intravenous, inhaled and oral delivery. Each means of delivery appears to have its own advantages for various patient populations and expands Remodulin's potential.

Our lead cancer product, OvaRex, is now completing its pivotal patient enrollment. The next step in the protocol is to assess whether patients on OvaRex have a statistically greater duration of ovarian cancer remission than those patients who are taking a placebo. If so, we will begin to prepare a regulatory approval application for the FDA's consideration.

Nothing spurs pharmaceutical sales more than excellent clinical trial results. Hence, our second milestone objective is to conduct the most insightful possible clinical trials. We believe the OvaRex trial will be considered highly insightful, as is likely to be the



case with new intravenous Remodulin trials we just finished last year. We are also conducting a trailblazing study that compares the combination of an inhaled form of treprostinil with the leading oral treatment for pulmonary hypertension, Tracleer®, as compared to Tracleer alone with inhaled placebo.

Our first and second strategic objectives will also come into play during 2006. The results of our combination clinical trial of inhaled treprostinil with Tracleer are being eagerly awaited by the pulmonary hypertension field. Meanwhile, the results of our recently completed clinical studies are being submitted to several of the world's leading medical journals, in accordance with our third strategic objective. In addition, we are laying crucial foundation stones for future recognition of the excellence of our medicines with our oral Remodulin studies, our OvaRex studies and our iminosugar work.

In the area of EPS growth, the top quintile of our peer group tends to grow their revenues and profits at very high annualized rates, and hence this is the fourth objective we set for ourselves. This objective helps to provide us with the discipline to manage spending to those activities that have a high chance of producing a significant pay-off. Thanks in large part to the excellent accounting controls maintained by our finance group led by our Chief Financial Officer, Fred Hadeed, I am pleased to say that our financial performance is currently well within the top quintile of our peer group.

To achieve EPS growth strong sales are, of course, essential. Yet, in the highly regulated pharmaceutical industry we must be extremely vigilant to ensure that our sales team communicates only such messages as are compliant with regulations. To this end we have hired an outstanding North American and European sales force of highly seasoned professionals. We also keep clinical development, regulatory affairs and commercialization under a single senior executive, our President and Chief Operating Officer, Dr. Roger Jeffs, to help ensure both the accuracy and the effectiveness of our marketing messages.

"Saving lives is important, Making money is important, But nothing is more important than doing everything the right way and the honest way."

Finally, nothing is more important at United Therapeutics than carrying out all of our activities with impeccable medical, professional and corporate ethics. Every year I repeat to our gathered senior managers the following company mantra: "Saving lives is important, Making money is important, But nothing is more important than doing everything the right way and the honest way."

I'm pleased to share with everyone that United Therapeutics enjoys an excellent reputation for high ethics and professionalism. Our clean slate is certainly in good part due to the superb legal leadership we receive from our General Counsel, Paul Mahon.

As we enter 2006, we intend to use our five strategic objectives to continue building critical momentum toward our ultimate destiny as a model biotechnology company. For example, even when revenues rise, our spending controls do not permit our planned spending to rise faster than revenues. In the domain of marketing, we are planning to synchronize our first large-scale advertising campaign with the availability of a broadened label for our lead product, Remodulin. The new label is based upon the FDA's acceptance of our recently reported highly statistically significant clinical trial results demonstrating the medicine's safety and efficacy.

United Therapeutics is a muchappreciated company. We try to do right by the patients who pray for our clinical trial results, the doctors who expect great medicines from us, the employees who spend much of their lives in our facilities, and the shareholders who invest in our success. We hope that our five strategic objectives capture the spirit of all that we need to be doing to continue earning everyone's respect and admiration.

Onward and Upward,

Martine Rathblatt

Martine Rothblatt, Ph.D. Chairman and CEO

# DRAMATIC RESCUE OF OVAREX TUMOR BANK FROM HURRICANE KATRINA

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

Wellesley Hills, MA: Last August, the world watched in anticipation nervous as Hurricane Katrina approached the shores of the Gulf Coast and New Orleans, then was horrified as the scenes of destruction came into national view. Once again, we are reminded of the force of nature and how it can affect millions of people. The true impact of the storm was only realized in the aftermath, and then it seemed that everyone could only watch helplessly as flood waters rose swallowing New Orleans in massive floods. Amid the devastation, many acts of courage and heroism went unnoticed.

Not only did the tragedy of Katrina impact the region, it threatened to wash away the tumor banks which were located at the Tulane University Health Sciences Center. These banks are large, specially designed freezers that store patient samples for further research.

The tumor banks included samples from over 40 patients that are part of the OvaRex research project under the direction of Tvler Curiel, MD. MPH. Professor, and Section Chief of and Hematology Medical Oncology and Henderson Chair in Medicine at Tulane University School of Medicine and his associate Weiping Zou, M.D., Ph.D., Associate Professor of



Only days after hurricane Katrina flooded New Orleans, Dr. Tyler Curiel boards a private plane to return to save important research samples.

Medicine and Associate Professor of Cell and Molecular Biology. The tumor samples had been provided by patients participating in an OvaRex Phase 2 study that is evaluating immune responses when OvaRex is dosed either in conjunction with chemotherapy or a week followchemotherapy. ina This research is designed to help identify new approaches to treat ovarian cancer. The tumor samples banked at the Tulane facility are integral to the research program. The loss of these samples would have terminated the research and might have been just another tragic footnote had it not been for the efforts of Dr. Curiel and his associates.

The following is an excerpt from an article written by Amy Dockser Marcus which appeared in the *Wall Street Journal*. It provides some insight into the extraordinary actions of Dr. Curiel and his efforts to save a critically important research project:

n August 30, one day after Hurricane Katrina hit New Orleans, floodwaters started rising inside the Tulane University Health Sciences Center, and researchers were told the emergency power generators world fail in 90 minutes.

To save the cells, Dr. Curiel and Michael Brumlik, a cancer researcher and assistant professor at Tulane, decided to move the freezers storing them to the medical



reached in and pulled out a rack containing boxes of vials.... Quickly, they put the material, and as many other vials that could fit, into the coolers packed with dry ice. Back in Dallas, UT Southwestern and Baylor University Medical Center arranged freezer space where the researchers could store their material until they re-established their cancer labs.

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Engulfed in flood waters, Tulane University Health Sciences Center became an island, accessible only by boat or helicopter.

building next door, where generators were still working. The freezers were huge, weighing "as much as three or four refrigerators," said Dr. Curiel. The two started pushing the first one down the hall, trying to get it into the elevator before the emergency power in their building went out. It was dark in the hallway, with the temperature above 100°. They worked by flashlight.

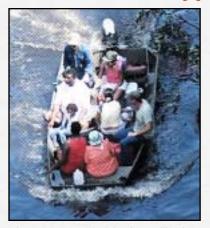
They got the first freezer to the other medical building and out of the elevator, but it was too big to fit through the door into the hall. They started carrying vials by hand, stuffing them into any available freezer in other labs. They walked down five flights of stairs to get out of the building, then up seven more flights to their own lab over and over in order to retrieve hundreds of boxes containing vials.

A few hours later, the generators failed in the other building too. Now they had to get as many vials as possible back to their own building, where there were three liquidnitrogen tanks that they hoped could stay frozen two weeks without power. There wasn't enough room to save all of their projects, and over the next day, they had to quickly decide what to discard and what to put in the tanks. They never got to finish. On Thursday, armed guards told them to get out or they would be forcibly removed. They left everything behind and took a canoe over to Charity Hospital to help out the doctors there. On Saturday they were evacuated to Dallas.

As soon as he was out of New Orleans, Dr. Curiel sent emails to friends and colleagues, trying to find a way to go back. Executives at two companies, Trident Aviation Services and Phazar Corp., agreed to help. The University of Texas Southwestern Medical Center at Dallas donated 800 pounds of dry ice; Fisher Scientific International supplied insulated containers. The researchers bought axes to break down doors and stocked up on dry rations and bottled water. Trident flew Dr. Curiel and Dr. Brumlik in its corporate jet back to New Orleans, then arranged for a helicopter that landed on the roof of the hospital two blocks away. When the researchers finally managed to get to the medical school, guards told them they only had four hours.

Working in the dark, they went back to the three liquid nitrogen tanks. Shining their flashlights on the tanks, they popped the top on the first one. A big puff of white vapor hit them in the face. Dr. Curiel Late last fall all of the tumor samples that are part of the OvaRex research program were located and carefully packed up and transported by members of Dr. Curiel's staff. Today, the OvaRex research work continues in a temporary research lab in the New Orleans area. This important work will elucidate potential new therapeutic treatment options for women with ovarian cancer.

We are indebted to the patients who agreed to participate in this study and who donated their tumor samples, and to the heroic efforts of Dr. Curiel and his associates. It is through these efforts we all hope to make advances in the treatment of ovarian cancer.



Photos courtesy of Michael Brumlik, Ph.D.

# We take United in our name very seriously.



# Spread over ten offices in seven states and three countries, our 210 employees

are united in pursuing our corporate strategic milestone objectives to achieve our mission for our patients, our shareholders and all of our other stakeholders, and to do so with the highest level of ethical conduct. Our scientists and research partners around the world are united in efforts to develop and manufacture the best possible medicines from our intellectual property platforms. Our clinical investigators and the academic centers we work with worldwide are united in successfully overcoming the challenges of developing and conducting the most insightful possible clinical trials of our medicines.

Our sales and marketing personnel and our distributors around the world are united in communicating accurately and effectively our clinical information to prescribers and bringing our products to the patients who need them. We are also pleased to be nearing completion of our new state-of-the-art laboratory facility adjacent to our corporate headquarters in Silver Spring, Maryland, pictured above, which will support both our prostacyclin and monoclonal antibody programs.

# 

We are a technology company and everything we do is built upon the creative insights and technologies necessary to discover, formulate, devise manufacturing processes, manufacture and improve our medicines.

# Remodulin®, a prostacyclin analog

United Therapeutics has focused primarily developing on 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 in the United States alone.

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







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)

the body directly fight the cancer during the pivotal "watchful waiting" period. Our Phase III clinical trials are enrolling at approximately 60 medical centers throughout the United States and are designed to demonstrate clinical benefit by lengthening the period of remission.

## 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 bv flavoviruses which cause hepatitis B and C, dengue fever, and Japanese encephalitis. The challenge now is to replicate that success in humans.

There are innumerable challenges to overcome as we work to develop and manufacture the best possible medicines from our intellectual property platforms in prostacyclin analogs, monoclonal antibodies and iminosugars. But we are pleased with our progress in developing our three technology platforms.

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# **Remodulin**Pioneering New Routes of Delivery Through Drug Discovery

United Therapeutics has focused much of its research and development activity on expanding the ways which our lead product, in Remodulin, may be delivered to patients. By offering a variety of of administration routes for Remodulin, physicians will be able to select the best way to deliver the drug to meet the particular needs of each pulmonary arterial hypertension (PAH) patient. In addition, we believe that less invasive routes of administration may make Remodulin an appropriate therapy to treat a number of other diseases. Our clinical work to achieve four different routes of administration for Remodulin demonstrates our commitment to develop the best possible medicines we can from the intellectual property we have, and to conduct the most insightful possible clinical trials of these medicines.

# SUBCUTANEOUS REMODULIN

Remodulin first gained commercial approval in the Untied States in May 2002 as a subcutaneous therapy for patients with pulmonary arterial hypertension. A therapy is administered subcutaneously when it is delivered through the skin. This accelerated approval was granted on the condition that we perform an additional efficacy study as a postapproval commitment.

As a subcutaneous therapy, Remodulin is indicated to improve the symptoms associated with exercise in PAH patients with New York Heart Association (NYHA) Class II, III or IV symptoms. Subcutaneous Remodulin is continuously delivered through a mobile pager-sized pump that requires refills every 72 hours and no ice packs since Remodulin is stable at room temperature. Subcutaneous delivery avoids the systemic infection risk associated with an indwelling intravenous catheter.

Unfortunately, pain and reaction at the site of infusion is a common occurrence which can limit the ability of some patients to remain on the therapy. Our research into pain management remains ongoing. Additionally, in 2005 we were able to complete a controlled study demonstrating that PAH patients previously managed with an approved intravenous therapy called Flolan® could be transitioned to subcutaneous Remodulin. This study was submitted to the FDA and we announced in March 2006 that the FDA concluded that we satisfied our post-approval study commitment.

## **INTRAVENOUS REMODULIN**

In November 2004, we achieved an expanded FDA approval to permit intravenous delivery of Remodulin to those PAH patients who are not able to tolerate subcutaneous delivery. A therapy is administered intravenously when it is delivered directly into a patient's veins.

Clinical data generated during 2005 and subsequently presented at major scientific meetings demonstrated both that intravenous Remodulin could provide long-term benefits to PAH patients who were new to prostacyclin therapy and that patients could be transitioned from the other approved intravenous therapy Flolan without detriment. Additionally, studies demonstrated that rapid transition from Flolan to Remodulin was possible, without the need to carefully titrate the two drugs independently. While these open-label trial results were encouraging, we wanted to demonstrate more conclusively the benefits of intravenous Remodulin in a placebocontrolled trial.

To this end, TRUST-1, a 12-week multicenter randomized double-blind placebo-controlled trial of the safety and efficacy of intravenous Remodulin, was the first-ever placebo controlled study of intravenous therapy in PAH patients and showed that intravenous Remodulin provided a clinically and statistically significant improvement when used as first line therapy. Specifically, intravenous Remodulin produced an 83-meter median improvement in six-minute walk distance compared to placebo in NYHA Class III/IV patients with PAH.

With this controlled result in hand, we also endeavored in 2005 to 'miniaturize' the pump platform that is used for intravenous delivery of Remodulin. Conventional and prevailing wisdom was that higher flow rates were required to maintain the indwelling lines used for intravenous delivery. In 2005, we challenged that dogma and demonstrated that patients could receive Remodulin at much lower flow rates using smaller



pumps. Now, patients are able to use pager-sized pumps for intravenous as well as subcutaneous delivery of Remodulin, an important advance for patients.

### **INHALED TREPROSTINIL**

Since 2004, a wholly owned subsidiary of United Therapeutics, Lung Rx, Inc., has been developing a new form of treprostinil that can be delivered by inhalation, which permits the drug to be administered directly to the lungs and dosed to therapeutic levels with potentially less risk of systemic side effects. Inhaled treprostinil is an investigational drug, meaning that it is in clinical studies and has not yet been approved for commercial use. A key goal of the TRIUMPH (TReprostinil Sodium Inhalation Used in the Management of Pulmonary Arterial Hypertension) program is to develop a portable therapy in which a new form of treprostinil would be inhaled for about a minute just four times per day. Such a therapy might be used to treat PAH patients early in the course

of the disease. Initially the TRIUMPH program is focusing on using an ultra-sonic nebulizer to deliver medication to patients in four daily doses, with the next goal to administer the product with a handheld, pocket-sized metered dose inhaler.

The medical leadership of the TRI-UMPH program comes from two well known centers of excellence: Prof. Werner Seeger of the University of Giessen, Germany and Dr. Lewis Rubin from the University of California, San Diego. Between these two centers more than 200 patients with various forms of PAH have been dosed in acute settings under cardiac catheterization. The data collected so far suggests that dosing PAH patients with an inhaled form of treprostinil appears to be safe, that each dose can be administered very quickly, and that the time course of effect supports chronic dosing of patients with four daily doses. Much of the work conducted at Giessen and San Diego has been presented at major scientific congresses including the 2005 European Society of Cardiology and American Heart Association meetings. Currently, the Lung Rx team is focused on the successful completion of its first multinational, double blind placebo controlled study of the efficacy and tolerability of inhaled treprostinil in patients with severe PAH – the TRIUMPH-1 study.

# **ORAL TREPROSTINIL**

The next, and perhaps final search for the most convenient and effective formulation of treprostinil is our investigational sustained-release oral treprostinil program. In 2005, we were able to both develop a new formulation of treprostinil that was orally bioavailable as well as formulate a controlled-release tablet that provided sustained release of the drug over approximately 12-13 hours following a single dose. This formulation work suggests that a twice-a-day tablet form of treprostinil is viable. With the formulation work complete, we are now beginning Phase 2/3 studies in patients with PAH in 2006. 



# Financial Results

At United Therapeutics, health is our business. And in order to help our patients improve their health, we must ourselves be healthy.

We believe that the way to achieve and remain in great corporate health is to do our best to adhere to our five strategic milestone objectives.

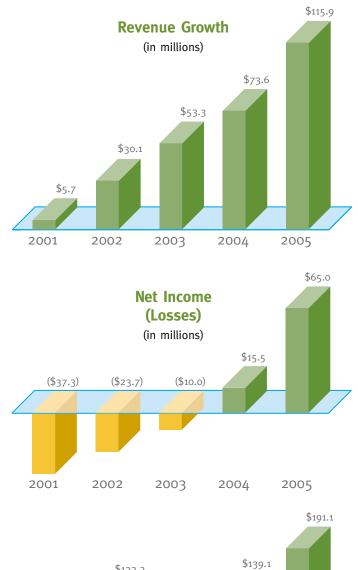
That's what we did in 2005 and the healthy financial results show the result. There is strength in these numbers.

### **Revenues and Net Income**

United Therapeutics' revenue grew 58% to \$115.9 million in 2005 and achieved \$65.0 million in net income, including a tax benefit of \$17.5 million, for the year. Remodulin is now approved in approximately thirty countries.

# **Cash and Investments**

United Therapeutics had cash, cash equivalents and marketable investments totaling \$191.1 million and virtually no long-term debt as of December 31, 2005.





# United Therapeutics

### Management

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

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

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

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

> **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.\*

Ray Kurzweil Founder, Chairman, and Chief Executive Officer Medical Learning Company, Inc. & Kurzweil Technologies, Inc.

Christopher Patusky, 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

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 Senior Vice President, **Investor Relations** 

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Auditors Ernst & Young LLP 8484 Westpark Drive McLean, Virginia 22102 Tel. (703) 747-1000 Fax. (703) 747-0100

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> Unither **Pharmaceuticals**

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> United Therapeutics

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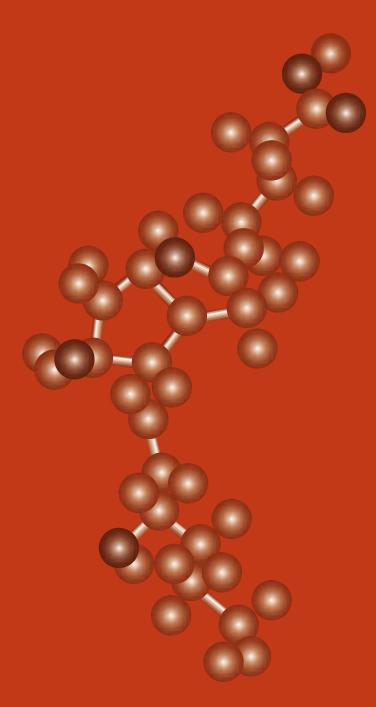


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