### United Therapeutics Corporation Annual Report



# Corporate Profile

United Therapeutics Corporation is a biotechnology company focused on the development and commercialization of unique products to address the unmet medical needs of patients with chronic and life-threatening cardiovascular and infectious diseases and cancer.

> At United Therapeutics, we derive tremendous inspiration and satisfaction from our work. Quality of life for our patients is our utmost therapeutic goal. Currently, our revenue-generating products are all in the field of cardiovascular medicine. While building United Therapeutics' business value in the cardiovascular field, we are also laying important foundations for future franchises in the treatment of infectious diseases and cancer.

*Remodulin, a prostacyclin analog* Our lead product and primary revenue earner is Remodulin, a stable synthetic analog of prostacyclin, a molecule produced by the body that has powerful effects on blood-vessel health and function. Remodulin is currently approved for subcutaneous and intravenous delivery. We have also successfully completed our registration trial of an inhaled version of treprostinil, the active ingredient in Remodulin, and we are in the process of completing trials of a tablet version of treprostinil.

Our goal is to constantly improve upon and find new ways to administer treprostinil, providing patients and physicians with more and better therapeutic options. We have focused primarily on developing Remodulin for treating pulmonary arterial hypertension, a life-threatening disease that affects the blood vessels in the lungs.

Pulmonary arterial hypertension is associated with reduced production of prostacyclin in the pulmonary blood vessels and is characterized by degradation of the blood vessel wall lining, aggregation of platelets and disruption of smooth muscle cell function. These conditions cause blockages and affect the ability of blood vessels to dilate as blood flows through the lungs. The resulting elevated pulmonary blood pressure strains the right side of the heart as it tries to pump blood to the lungs. We are also in the early stages of studying our formulations of treprostinil in other diseases, such as peripheral vascular disease, pulmonary fibrosis, and organ transplantation.

### 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

## 2007 Product Pipeline

Pre-Clinical Phase I Phase II Phase III Commercial Subcutaneous Remodulin® for PAH Intravenous Remodulin for PAH CardioPAL® SAVI and Decipher<sup>™</sup> Cardiac Event Monitors..... Inhaled Treprostinil for PAH..... Oral Treprostinil for PAH Intravenous Remodulin for Improved Transplant Outcome..... Beraprost-MR for PAH 3F8 MAb for Neuroblastoma Oral Treprostinil for PVD **CardioPAL SAVI Wireless** Cardiac Event Monitors Miglustat for Hepatitis C..... Inhaled Treprostinil for IPF Inhaled Treprostinil with AERx Essence® for PAH. 8H9 MAb for Metastatic Brain Cancer Glycobiology Antiviral Agents

organelles. United Therapeutics has the exclusive rights to a class of therapeutic iminosugars discovered by the field's founder, Professor Raymond Dwek of the University of Oxford. These small molecule synthetic sugars target hepatitis C, HIV AIDS, and other infectious diseases with a novel mechanism of action: they are able to enter through cellular membranes and alter the assembly of viruses preventing them from replicating in host cells. While this work remains at an early stage, it holds immense promise. The diseases targeted by our glycobiology agents afflict over a billion people worldwide.

### Monoclonal Antibodies, cancer therapies We are developing two

monoclonal antibodies which we licensed from Memorial Sloan-

Kettering Cancer Center for the treatment of neuroblastoma and metastatic brain cancer. Mainly affecting children, neuroblastoma is a rare cancer of the sympathetic nervous system. It is the most common extracranial solid cancer in children and the most common cancer in infants. One antibody, 3F8, is a murine monoclonal antibody that has specificity for GD2 (disialoganglioside), an antigen that is abundantly expressed on the surface of neuroblastoma cancer cells. As such, GD2 is an ideal target for antibody directed immunotherapy. The 3F8 antibody has been used to treat over 400 patients to date.

The other murine monoclonal antibody, 8H9, is highly reactive in a range of human solid tumors, including brain tumors. We are initially developing 8H9 for the = Cardiovascular
= Infectious Diseases
= Cancer

treatment of metastatic brain cancer, which develops in the brain from the spread of cancers from other tissues in the body. Metastatic brain cancers are ten times more common than cancers that originate in the brain, and prognosis is very poor. In the United States, more than 100,000 cases of metastatic brain cancer are diagnosed each year.

Cover Art: "Leaf" Mary Rodd Furbee www.mfurbee.com



PAH = pulmonary arterial hypertension PVD = peripheral vascular disease IPF = idiopathic pulmonary fibrosis



# Shareholder Letter

United Therapeutics has continued to make great progress in its climb up biotechnology's mountain of success. We are now U.S. biotechnology's revenue growth leader with six consecutive years of greater than 30% gains. We are also ranked fourth overall in terms of market capitalization per employee, and seventh overall in terms of revenue per employee. These are astounding achievements for a company founded just over ten years ago.

2007 also marked another year of significant accomplishments in advancing our pipeline of new therapeutics. We announced positive results for our TRIUMPH clinical trial, a pivotal trial of inhaled treprostinil in pulmonary hypertension patients optimized on oral therapies. We also reached the halfway mark for enrollment of our oral treprostinil trials for pulmonary hypertension, called FREEDOM-C and FREEDOM-M. It is rare for a biotechnology company to advance its pipeline so much in a single year.

We are thrilled to continue building a culture of excellence, teamwork and camaraderie within the Unither Family of Companies. It is our culture of "doing the right thing" that is the key ingredient to our success. As we continue to grow in 2008, we commit ourselves to maintaining our company culture for the benefit of our patients, physicians and many others who have a vital stake in our success.

Martine Rathhlatt

\$210.9



United Therapeutics Revenue since 2003 (in millions)

# Shareholder Letter

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Martine Rathblatt

# United Therapeutics Senior Management

We have great respect for medical science and medical education. It is only through the brilliant and creative efforts of scientists and clinicians that our work is possible. This is why, with permission from the Philadelphia Museum of Art, we were inspired by Thomas Eakins' painting, *The Agnew Clinic* (1889), to portray our own scientists and management team in this year's annual report. Thomas Eakins (1844–1916) was a painter, photographer, sculptor, and fine arts educator. He was one of the greatest American painters of his time, an innovative teacher, and an uncompromising realist.

Eakins was commissioned by the University of Pennsylvania Medical Class of 1889 to paint a portrait of Dr. David Hayes Agnew to commemorate his exemplary career as a physician and teacher at The University of Pennsylvania. Dr. Agnew was acclaimed as "the most experienced surgeon, the clearest writer and teacher, the most venerated and beloved man", a tribute that Eakins carved on the finished work's frame. Author of the three-volume *Treatise on the Principles and Practice of Surgery*, Dr. Agnew became an expert in gunshot wounds during the Civil War. When President Garfield was shot by an assassin in 1881, Dr. Agnew acted as the chief surgeon. Students revered him.

What was originally proposed as a three-quarters portrait of the retiring professor quickly became an enormous 6 x 11 ft. painting – the largest of Eakins' career – depicting an operating theater with Dr. Agnew assuming the role of both surgeon and educator. To research the painting, Eakins regularly visited the medical school to watch Dr. Agnew in action, completing the painting in three months. At the presentation of the painting, Dr. Agnew was overwhelmed by his students' applause and admiration. *The Agnew Clinic* was first widely seen at the World's Columbian Exhibition in Chicago in 1893. It is considered to be one of the two most important American paintings on the subject of medicine.

We take the "United" in our name very seriously. Although located in eight offices in five states and three countries, our 310 employees are united in pursuing our corporate strategic objectives to achieve our mission for all of our stakeholders, and to do so with the highest level of ethical conduct. Many individuals occupy key senior and executive management roles at United Therapeutics, and many more employees provide crucial support in a wide variety of positions. The managers included on these pages represent a critical cross-section of those responsible for making the clinical, financial, commercial, strategic and legal decisions for our business.



Philadelphia Museum of Art: Courtesy of the University of Pennsylvania Art Collection, Philadelphia, Pennsylvania

## Senior Management Legend

- 1 Martine Rothblatt, PhD Chairman & Chief Executive Officer
- 2 Roger Jeffs, PhD President & Chief Operating Officer
- 3 John Ferrari Chief Financial Officer & Treasurer
- 4 Paul Mahon Executive Vice President, Strategic Planning & General Counsel
- 5 Eugene Sullivan, MD FCCP *Chief Medical Officer*
- 6 Melissa Silverman Assistant Vice President of Finance
- 7 Andrew Fisher Senior Vice President, Investor Relations & Deputy General Counsel
- 8 James Levin, DVM Senior Vice President, Biologics Production, United Therapeutics Corporation; Chief Manufacturing Officer, Lung Rx, Inc.
- 9 Alyssa Friedrich Vice President, Human Resources & Community Relations
- 10 David Zaccardelli, PharmD Senior Vice President, Pharmaceutical Development
- 11 Shola Oyewole *Chief Information Officer*
- 12 Raju Penmasta, PhD Vice President, Research & Development
- 13 David Walsh, PhD Executive Vice President, Operations
- 14 Dean Bunce Senior Vice President, Regulatory Affairs
- 15 Robert Grover, MBBS FRCA European Medical Director & Chief Safety Officer, United Therapeutics Europe, Ltd.
  16 Alex Sapir
  - Vice President, Marketing & Sales

- 17 Daniel Balda, MD President & Chief Operating Officer, Medicomp, Inc.
- 18 Larry Somerville Senior Vice President, Sales & Marketing, Lung Rx, Inc.
- 19 Jay Watson, PharmD Assistant Vice President, Commercial Development
- 20 Ken Phares, PhD Senior Director, Pharmaceutical Development
- 21 Theodore Staub Head of Research & Development, Lung Rx, Inc.
- 22 David Mottola, PhD Vice President, Product Development
- 23 Liang Guo, PhD Senior Vice President, Production
- 24 Anthony Adson Jr. Director, Quality Control
- 25 Sam Mancuso Director, Quality Assurance
- 26 Karl Gotzkowsky, PharmD Director, Product Development
- 27 Joy Cieszynski Director, Clinical Operations
- 28 Avi Halpert Construction & Facility Manager
- 29 Yu-Lun Lin Director, Business Development & Commercial Informatics
- 30 Michael Wade, PhD Vice President, Product Development
- 31 Carl Arneson Director, Biostatistics & Data Management
- 32 Ravi Mehra, PhD, CQA Senior Director, Quality Assurance/Quality Control









# Remodulin

## Advancing New Routes of Delivery Through Innovative Approaches

We focus much of our research and development activity on expanding the ways in which our lead product, Remodulin, may be delivered to patients. By offering a variety of routes of administration for Remodulin, physicians may select the optimal therapy for each pulmonary arterial hypertension (PAH) patient's needs. In addition, we believe that other routes of administration may make



Unfortunately, pain and reaction at the infusion site is a common occurrence that may limit the ability of some patients to remain on subcutaneous therapy. Our research into pain management remail We are firmly committed utoerdeveloping at the previously managed fin an approved intravenous therapy called Floran could be transit great to subfutaneous Remodilin in approved intravenous therapy called Floran could be transit great to be transit g

Clinical data presented at major scientific meetings demonstrated that intravenous Remodulin could provide long-term benefits to PAH patients who were new to prostacyclin therapy, and that patients could be transitioned from Flolan without detriment. Additionally, studies demonstrated that rapid transition from Flolan to intravenous Remodulin was possible, without the need to carefully titrate the two drugs independently. Finally, a 12-week multicenter, randomized double blind, placebo controlled trial of the safety and efficacy of intravenous Remoduling the first-over placebo controlled study of intravenous therapy in PAH patients — showed that intravenous Remoduling provided a clinically and statistically significant improvement Remoduling (treprostinil sodium) Injection

We have also continued to advance miniaturization of the pump platform that is used for intravenous delivery of Remodulin. Now, patients are able to use pager-sized pumps for intravenous as well as subcutaneous delivery of Remodulin, an important advance in the treatment of PAH.

# Remodulin

## Advancing New Routes of Delivery Through Innovative Approaches

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### Subcutaneous Remodulin

Remodulin first gained commercial approval in the United States in May 2002 as a subcutaneous therapy for patients with PAH. A therapy is administered subcutaneously when it is delivered through the skin.

As a subcutaneous therapy, Remodulin is indicated to improve 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 is refilled every 72 hours. No ice packs are required 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 infusion site is a common occurrence that may limit the ability of some patients to remain on subcutaneous therapy. Our research into pain management remains ongoing. We subsequently completed a controlled study demonstrating that PAH patients previously managed with an approved intravenous therapy called Flolan<sup>®</sup> could be transitioned to subcutaneous Remodulin.

#### Intravenous Remodulin

In November 2004, the FDA expanded our 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 presented at major scientific meetings demonstrated that intravenous Remodulin could provide long-term benefits to PAH patients who were new to prostacyclin therapy, and that patients could be transitioned from Flolan without detriment. Additionally, studies demonstrated that rapid transition from Flolan to intravenous Remodulin was possible, without the need to carefully titrate the two drugs independently. Finally, a 12-week multicenter, randomized double-blind, placebo controlled trial of the safety and efficacy of intravenous Remodulin — the first-ever placebo controlled study of intravenous therapy in PAH patients — showed that intravenous Remodulin provided a clinically and statistically significant improvement when used as front-line therapy.

We have also continued to advance miniaturization of the pump platform that is used for intravenous delivery of Remodulin. Now, patients are able to use pager-sized pumps for intravenous as well as subcutaneous delivery of Remodulin, an important advance in the treatment of PAH.



# Inhaled Treprostinil

Inhaled treprostinil is a new form of treprostinil in development that can be delivered by inhalation directly to the lungs 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. We released the results of our clinical trial program for inhaled treprostinil, called TRIUMPH (TReprostinil Sodium Inhalation Used in the Management of Pulmonary Arterial Hypertension). November 2007. A key goal of the TRIUMPH program was to develop a portable therapy to develop the treprostinil that could be inhaled for about one minute just four night be used to treat PAH patients earlier in the course of their disease. I haled the treprostinin is focused on using an ultra-sonic nebulizer to deliver doses. We have a subsequent goal to administer inhaled treprostinin.

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Oral Treprostinil The next, and perhaps he is our investigational sustained formulation of treprostinil that prove following a single dose, suggesting that tw

With the formulation work complete, we are currently cebo controlled clinical trials of oral treprostinil in patients with 12 Mercesson of the cebo M-C, is a 16-week study of up to 300 patients currently on background therapy PAH. The second trial, FREEDOM-M, is a 12-week study of up to 150 patients who are not on any background therapy. These trials are being conducted in approximately 50 centers throughout the world.

## Treprostinil Development Timeline





FDA Accepts IND for Intravenous Remodulin



FDA Approva of Intravenou Remodulin TRIUMPH Inhaled Treprostinil Enrollment Begir



Oral Treprostini FREEDOM Tria Enrollment Begir



Unblinding of RIUMPH Inhaled Treprostinil Trial

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The TRIUMPH program was led by two well-known physicians and their respective centers of excellence: Professor Werner Seeger from 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 completed the TRIUMPH study. On November 1, 2007, we announced that the TRIUMPH study robustly met its primary endpoint, an increase in exercise capacity measured by a six-minute walk test, and that inhaled treprostinil was generally well-tolerated by patients in the trial. We are now focusing our energies on completing the necessary regulatory filings so that patients may have access to inhaled treprostinil as a prescribed route of delivery.

### 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. We have developed a new tablet formulation of treprostinil that provides sustained release of the drug over approximately 10-12 hours following a single dose, suggesting that twice-a-day dosing may be viable.

With the formulation work complete, we are currently enrolling two multi-national placebo controlled clinical trials of oral treprostinil in patients with PAH. One trial, FREEDOM-C, is a 16-week study of up to 300 patients currently on background therapy of approved oral therapies for PAH. The second trial, FREEDOM-M, is a 12-week study of up to 150 patients who are not on any background therapy. These trials are being conducted in approximately 50 centers throughout the world.

## Treprostinil Development Timeline



FDA Approval of Subcutaneous Remodulin



FDA Accepts IND for Intravenous Remodulin



FDA Approval of Intravenous Remodulin



TRIUMPH Inhaled Treprostinil Trial Enrollment Begins



**Oral Treprostinil** 

FREEDOM Trial

**Enrollment Begins** 

10/07

Unblinding of TRIUMPH Inhaled Treprostinil Trial

# Selected 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 achieve our strategic corporate objectives. That is what we did in 2007 with healthy financial results. There is strength in these numbers.

### Revenue and Net Income

United Therapeutics' revenue grew 32% to \$210.9 million in 2007 and achieved \$19.9 million in net income.

### Cash and Investments

United Therapeutics had unrestricted cash, cash equivalents and marketable investments totaling \$299.3 million as of December 31, 2007.

## About the Artist

The artworks reproduced throughout this annual report are abstract paintings and digital art selected from the Artery Project by Mary Rodd Furbee. The artist died from pulmonary hypertension in 2004.

For more information about Mary Rodd Furbee and her artwork, please visit: www.mfurbee.com





### Comparison of the Five Year Cumulative Total Return



#### Stock Price Performance

The following graph and table set forth United Therapeutics' total cumulative stockholder return over the past five years as compared to the cumulative returns of the NASDAQ US Stock Market Index and the NASDAQ Pharmaceutical Stocks Index. Total stockholder return assumes \$100.00 invested at the beginning of the period in United Therapeutics common stock, the stocks represented in the NASDAQ US Stock Market Index and the stocks represented in the NASDAQ Pharmaceutical Stocks Index, respectively.

United Therapeutics Corporation	12/31/02 \$100.00 \$100.00	12/31/03 \$137.43 \$149.52	12/31/04 \$270.36 \$162.72	12/31/05 \$413.89 \$166.18	12/31/06 \$325.57 \$182.57	12/31/07 \$584.73 \$197.98	United Therapeutics C Nasdaq US Stock Ma
NASDAQ US Stock Market Index	\$100.00	\$149.52	\$162.72	\$166.18	\$182.57	\$197.98	▲ Nasdaq DS Stock Ma
NASDAQ Pharmaceutical Stocks Index	\$100.00	\$146.59	\$156.13	\$171.93	\$168.29	\$176.97	

# **Corporate Information**

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

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

John Ferrari Chief Financial Officer and Treasurer

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 Glycobiology Director of the Glycobiology Institute University of Oxford President, Institute of Biology

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. Director, Office of Real Estate, Maryland Department of Transportation

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

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

\* 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 Glycobiology Director of the Glycobiology Institute University of Oxford President, Institute of Biology

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

Urban Ramstedt, Ph.D. Senior Director, Immunobiology Elusys Therapeutics, Inc. 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 H. Yacoub, F.R.S. Professor of Cardiothoracic Surgery National Heart and Lung Institute Imperial College London

> INVESTOR RELATIONS Andrew Fisher, J.D. Senior Vice President, Investor Relations & Deputy General Counsel

#### TRANSFER AGENT AND REGISTRAR

BNY Mellon Shareowner Services 480 Washington Boulevard Jersey City, New Jersey 07310 (800) 522-6645 From outside the U.S. and Canada: (201) 680-6578 TDD: (800) 231-5469 http://www.bnymellon.com/shareowner/isd

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## Advancing discounts in a 1981

Lung Rx, Inc. 1104 Spring Street Silver Spring, MD 20910 Phone: (240) 821-1759 Fax: (301) 608-1139 www.lungrx.com



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Unither Virology, LLC 1110 Spring Street Silver Spring, Maryland 20910 Tel. (301) 608-9292 Fax. (301) 608-9291



Unither Neurosciences, Inc. 82 Pearl Street Burlington, VT 05402 Tel. (802) 651-0147 Fax. (802) 651-1057

#### Unither Neurosciences

COMMON STOCK Listed on Nasdaq National Market symbol "UTHR"

ANNUAL MEETING April 29, 2008

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