UTHR 2020

MULTIPLE SHOTS ON GOAL

We have always followed multiple pathways to unlocking our goals. Disappointment is inevitable and the only way to increase our odds of success is to always place multiple, sound, well-reasoned, well-executed, shots on goal.

The combination of our strategic plans, steady revenue streams, conservative budgeting, and a powerhouse of creative Unitherians helped us deliver a 72% stock price increase during 2020.

UTHR 2020: MULTIPLE SHOTS ON GOAL

A STRATEGY MANUAL

BY

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Illustrations by Aylin S. Erkan, aylinsop.com
Design by Glenn Dellon, dellondesign.com
Printing by Mt. Royal Printing and Communications, mtroyalprinting.com

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RULES

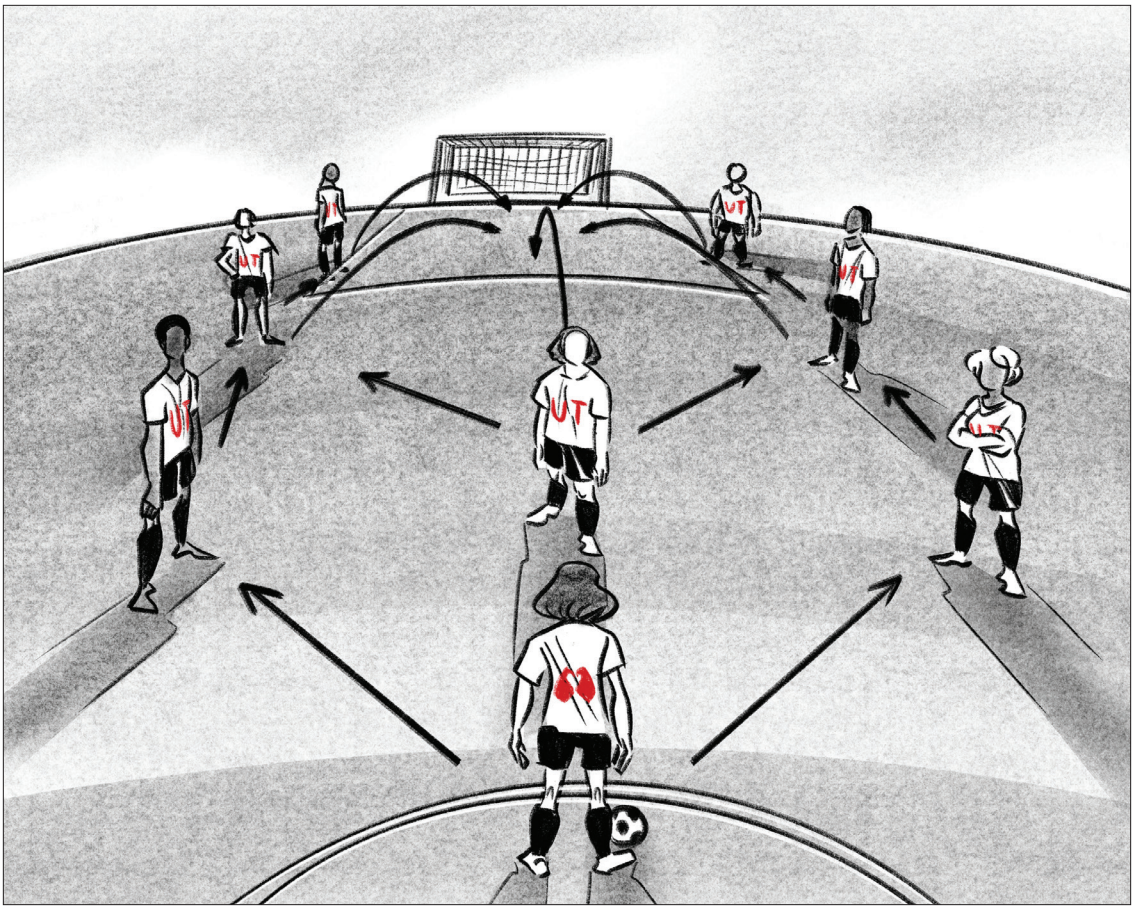
COACH ROTHBLATT ON *MULTIPLE SHOTS ON GOAL*

WINNING FORMULA: MULTIPLE SHOTS ON GOAL

Dear players, owners, fans, and all stakeholders:

At United Therapeutics **we believe in a diversity of approaches** to developing new therapeutics. The reason for this is that creating new therapeutics is an inherently risky endeavor. In our industry, only a small portion of preclinical projects make it to phase 1 studies, and only a small portion of phase 1 projects make it to phase 2 or 3. Even phase 3 studies have just about a three out of four chance of being approved by the FDA. **The only way to beat these kind of odds is to make multiple shots on goal.**

As an example of **our emphasis on technological diversity,** we are developing a new less painful method of delivering our Remodulin medicine subcutaneously while at the same time we are developing an implanted Remodulin pump to completely eliminate any pain associated with its delivery. Another example of our technological diversity is that we are developing a once-daily formulation of our Orenitram pill, while at the same time we are developing a once-daily pill called Ralinepag, which aims to achieve the same purpose but through different biochemistry. Also very interesting is that we are working to increase the supply of transplantable organs by using both genetically modified kidneys from pigs and by using 3D bioprinting technology to create new transplantable kidneys from a patient's own cells. **We refer to our strategy of technological diversity as always having *multiple shots on goal.***



THE MORE SHOTS, THE MORE SCORES

Our business diversity strategy has served us well. For example, while we have four different FDA-approved therapies for pulmonary hypertension, each of these therapies has **reduced our business risk** by enabling us to help different populations of patients. Just as life itself demonstrates tremendous diversity in Nature's quest to find solutions for every niche, so does United Therapeutics rely upon **business and technology diversity to find helpful solutions for as many patients as we can.**

Onward!

Martine Rothblatt

Martine A. Rothblatt, PhD
Chairperson and Chief Executive Officer

ALWAYS KEEP YOUR EYES ON THE GOAL

APPROVE THEN IMPROVE. NEVER STOP IMPROVING THE SOLUTION.

SCORE AND THEN SCORE AGAIN. NEVER STOP SCORING.

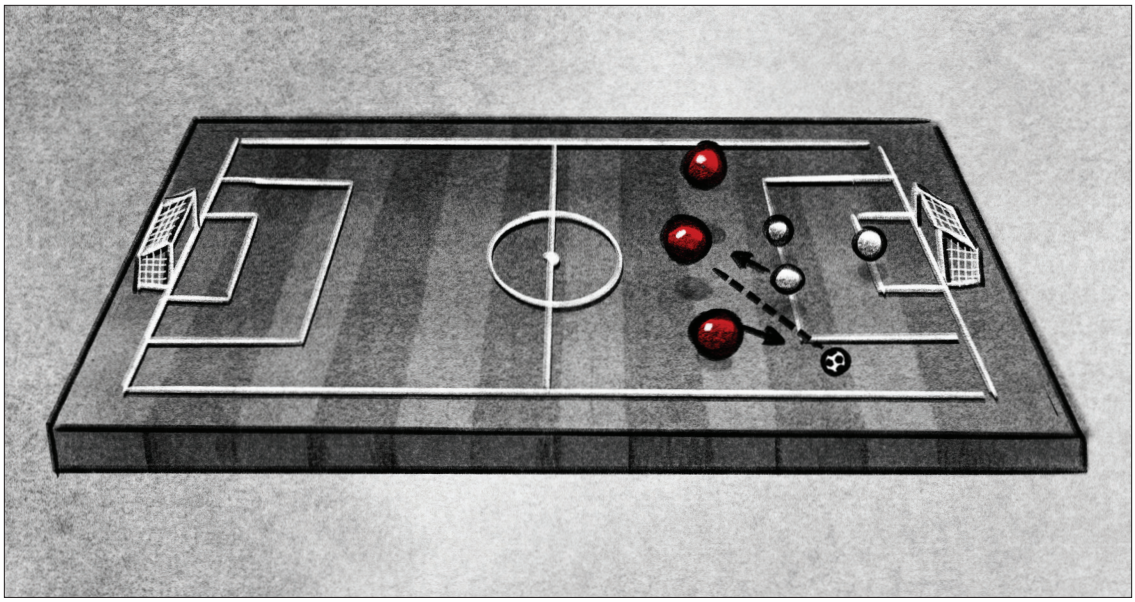
We market four therapies for pulmonary arterial hypertension, three of them based on our trepostinil molecule, and one therapy for a rare pediatric cancer.

When we receive an approval for a therapy, we challenge ourselves to continue to improve that therapy and broaden the universe of patients it can benefit. Our goal is to be as useful to as many patients as possible. Accordingly, we are actively working to improve our treprostinil molecule and each of its delivery systems to enhance convenience, safety, and patient outcomes. We expect to grow the use of our treprostinil-based therapies through label expansions, new formulations, and the introduction of new delivery devices. And we are also actively studying additional indications where treprostinil may be able to address unmet medical needs.

We call this strategy ***"Approve, Then Improve"*** and also ***"Innovate, Grow, Expand".***

Our game plan for ***Approve, Then Improve*** has been successful for our patients and for United Therapeutics.

Here is how we have ***Approved, Then Improved*** each of our three treprostinil-based therapies:



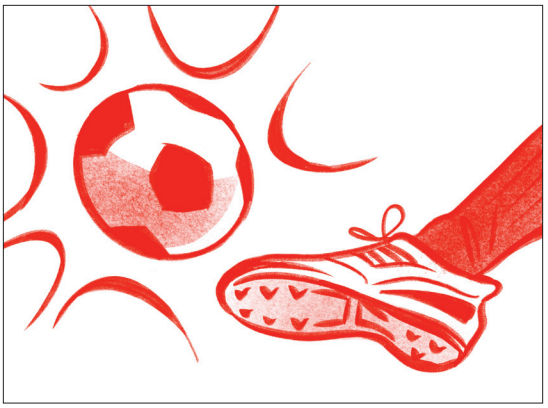
FOLLOW THE GAME PLAN

REMODULIN was *approved* by the FDA in 2002 as the *first subcutaneous* therapy for the treatment of pulmonary arterial hypertension.

▪ Because of injection site pain associated with *subcutaneous* delivery of Remodulin, we ran the trials necessary to obtain *FDA approval* in 2004 to expand the label for Remodulin to include *intravenous* delivery.

▪ Because of the inconvenience and interference with lifestyle choices associated with of *subcutaneous* pumps, we ran the clinical studies necessary to obtain *FDA approval* in 2020 to expand the label for Remodulin to include a *next-generation subcutaneous pump* called Remunity which we developed with DEKA Research & Development Corp. Remunity is small, lightweight, and durable with disposable pre-filled cartridges. We launched Remunity to our patients in February 2021.

▪ Because of injection site pain and interference with lifestyle choices associated with *subcutaneous* delivery of Remodulin, we are developing a prodrug version of Remodulin called RemoPro, currently in phase 1 clinical studies, that is *intended to reduce site pain.*



▪ Because of the heightened risk of bloodstream infections, inconvenience, and interference with lifestyle choices of *intravenous* pumps, we ran the clinical studies necessary to obtain *FDA approval* in 2018 to expand the label for Remodulin to include the *first implantable pump* for pulmonary arterial hypertension we developed with Medtronic called the Implantable System for Remodulin. We are ready to launch the Implantable System for Remodulin if and when Medtronic satisfies certain post-approval requirements with the FDA.

TYVASO was *approved* by the FDA in 2009 as an *inhaled* therapy for the treatment of pulmonary arterial hypertension via a nebulizer.

▪ Because of patient convenience advantages, we developed and ran the clinical studies necessary to request FDA approval of a *dry powder formulation* of Tyvaso we developed with MannKind Corporation called Tyvaso DPI, which is used with MannKind's device called Dreamboat, already approved by the FDA for inhaled insulin delivery. Tyvaso DPI offers a much smaller, pocket-sized inhaler that does not need electricity. We filed for FDA approval of Tyvaso DPI in April 2021.

▪ Because we believed that Tyvaso might be able to help patients with *pulmonary hypertension associated with interstitial lung disease (PH-ILD)*, a condition affecting over 30,000 patients in the U.S. with no previously-approved therapies, we ran the *INCREASE* phase 3 clinical study of Tyvaso in this new indication. In 2020, we announced the successful results of this study for Tyvaso in PH-ILD – the primary endpoint and all secondary endpoints were met – as reported in *The New England Journal of Medicine*. In March 2021 the *FDA approved* the addition of PH-ILD to the Tyvaso label.

▪ Because we believe that Tyvaso might be able to help patients with *pulmonary hypertension associated with chronic obstructive pulmonary disease (PH-COPD),* a condition affecting over 100,000 patients in the U.S. with no approved therapies, we are running the *PERFECT* phase 3 clinical study of Tyvaso in this new indication.

▪ Because we believe that Tyvaso might be able to help patients with *idiopathic pulmonary fibrosis (IPF),* we are conducting the *TETON* phase 3 clinical study of Tyvaso in this new indication, based on data from the *INCREASE* study. For the first time, we are moving into a phase 3 study in which fibrosis rather than pulmonary hypertension is patients' primary condition.

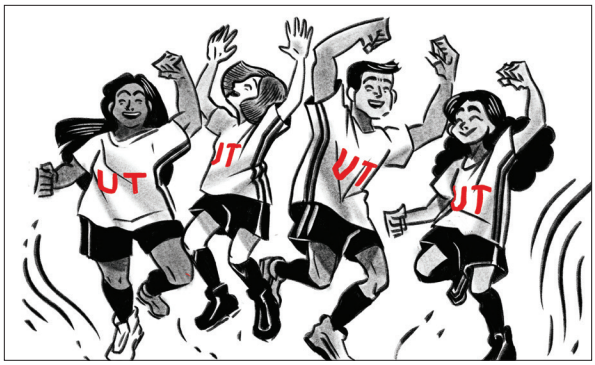
ORENITRAM was *approved* by the FDA in 2013 as an *oral* therapy for the treatment of pulmonary arterial hypertension.

▪ Because we believed that Orenitram was helping patients with *pulmonary arterial hypertension* beyond what its FDA-approved label described, we ran the *FREEDOM-EV* phase 3 clinical study of Orenitram. In 2019 the *FDA approved* the expansion of the Orenitram label and Orenitram is now indicated to *delay disease progression and improve exercise capacity.*

▪ Because we believe that we can provide increased tolerability and convenience for Orenitram through *a once-daily dosing regimen,* we are developing an oral prodrug formulation of Orenitram we call OreniPro, currently in phase 1 clinical studies.

MOVE WITH A SENSE OF URGENCY

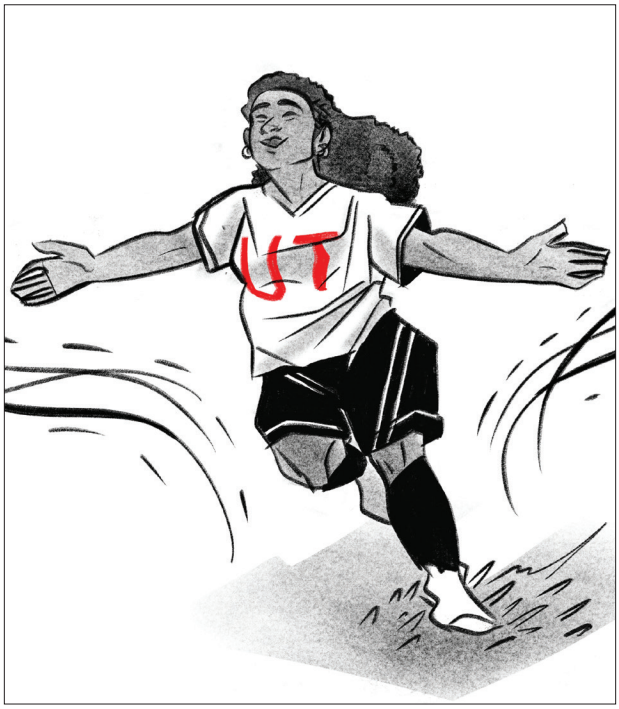
2020 PERFORMANCE



CELEBRATE SUCCESS

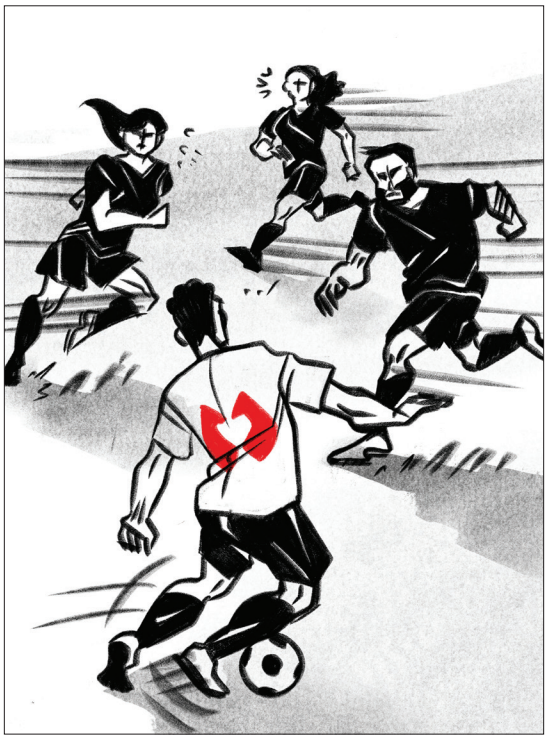
In 2020, we:

- Achieved a record number of patients in the U.S. treated with our treprostinil-based therapies
- Achieved strong operating results from our four pulmonary arterial hypertension therapies and our pediatric cancer treatment, yielding revenues of approximately $1.5 billion
- Achieved profit margins among the strongest in the biotechnology industry
- Achieved strong revenue performance despite covid-19, including U.S. treprostinil-based revenues reaching an all-time high, Orenitram revenues up 30% compared to 2019, and Tyvaso revenues growing by 16% compared to 2019
- Achieved industry-leading profitability, with a 35% profit margin and GAAP diluted earnings per share of $11.54
- Achieved industry-leading productivity, with $1.6 million in 2020 revenue per employee
- Achieved positive INCREASE study results in February 2020 supporting FDA approval of the Tyvaso label extension to treat PH-ILD in March 2021, meeting the primary endpoint and every secondary endpoint
- Achieved FDA approval of the pharmacy-filled Remunity Pump in February 2020
- Achieved progress on clinical studies supporting Tyvaso DPI leading to an April 2021 NDA submission with the FDA
- Achieved progress on our phase 3 Ralinepag clinical study despite the covid-19 pandemic
- Achieved a strong balance sheet poised for security and future investment, with $3 billion in cash and investments at December 31, 2020
- Wall Street clearly recognized our performance, as our stock price grew by 72% in 2020, compared to return from the Nasdaq Biotechnology Index of only 26%.



AFTER A GOAL CELEBRATE, BUT MOVE ON, WORK TO BE DONE TO WIN

IDENTIFY THE CORRIDORS OF INDIFFERENCE AND RUN LIKE HELL DOWN THEM



SEEK AREAS OF OPPORTUNITY

Our guiding mantra is to find areas where patients are unserved – patients with life-threatening unmet medical needs – and develop therapies to serve them. But we must also innovate and move quickly as our success encourages tag-alongs, copycats, and opportunists.

Here are some examples:

We did this in 2002, when the FDA approved Remodulin, the *first subcutaneous therapy* to treat pulmonary arterial hypertension.

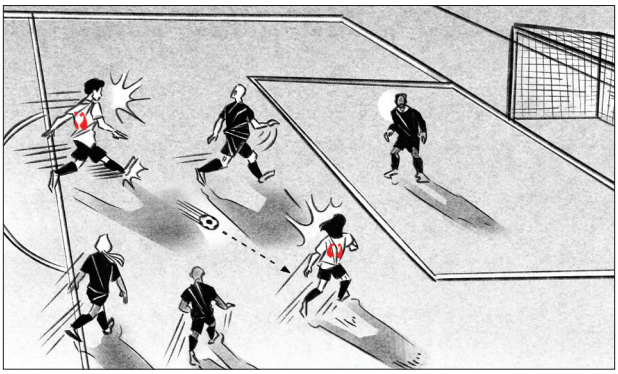
We did this in 2013, when the FDA approved Orenitram, the *first oral prostacyclin therapy to treat pulmonary arterial hypertension.*

We did this in 2015, when the FDA approved Unituxin, the *first antibody therapy* to treat high-risk neuroblastoma, among the highest mortality rates for pediatric cancers, and an ultra-orphan disease with less than 1,000 patients in the U.S.

We did this in 2017 as we began enrolling our registration stage *SAPPHIRE* clinical study of the *first gene therapy* for the treatment of pulmonary arterial hypertension, intended to rebuild the blood vessels in the lungs that are destroyed by pulmonary arterial hypertension.

We did this in 2018, when the FDA approved our Implantable System for Remodulin, the *first implantable pump* to treat pulmonary arterial hypertension we developed with Medtronic. We are ready to launch the Implantable System for Remodulin if and when Medtronic satisfies certain post-approval requirements with the FDA.

We did this beginning in 2018, when we developed our *PERFECT* phase 3 clinical study of Tyvaso to treat patients with pulmonary hypertension associated with chronic obstructive pulmonary disease (PH-COPD), a condition affecting over 100,000 patients in the U.S. *with no approved therapies.*

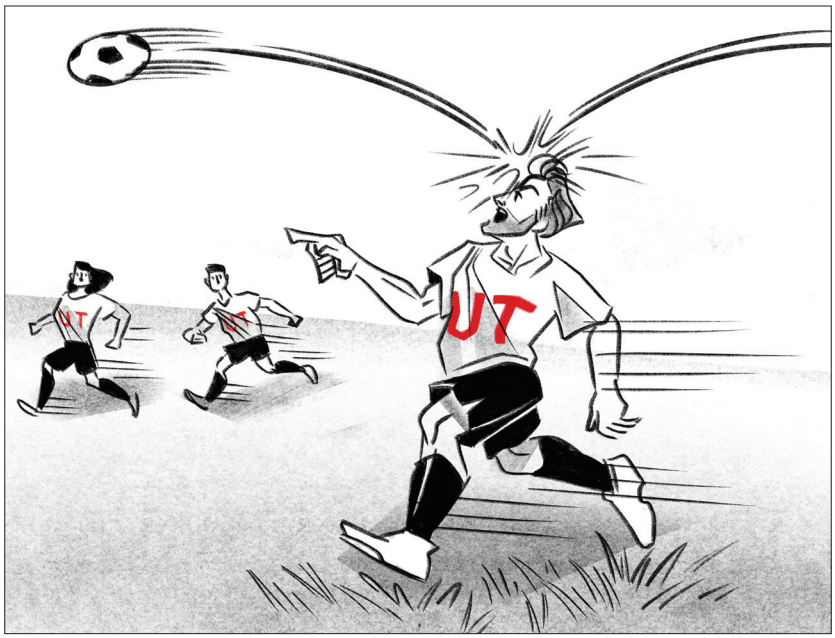


SHOOT WHERE THEY AREN'T

We did this in 2021, when the FDA approved the addition of pulmonary hypertension associated with interstitial lung disease (PH-ILD) to the Tyvaso label, the *first FDA approval of any therapy to treat PH-ILD* – after the primary endpoint and each secondary endpoint were met in its pivotal clinical study – as reported in *The New England Journal of Medicine*. There are 30,000 PH-ILD patients in the U.S. *with no approved therapy except Tyvaso.*

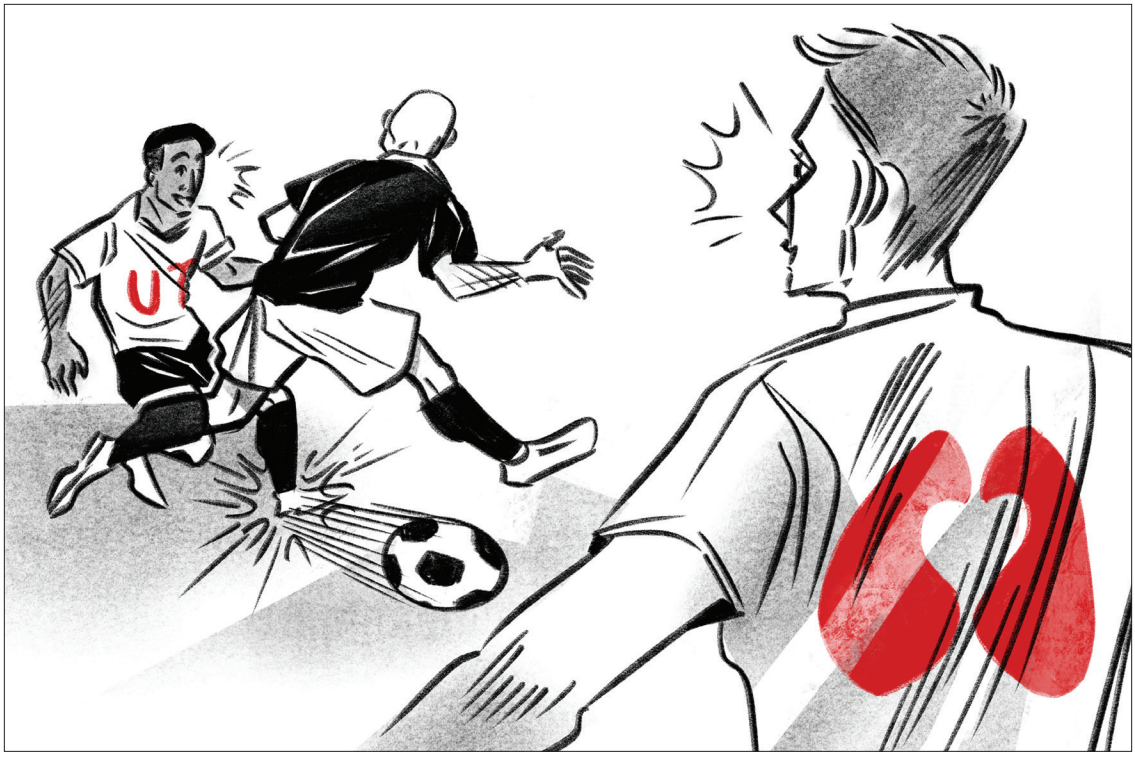
We did this beginning in 2020, as we developed our *TETON* phase 3 clinical study of Tyvaso in idiopathic pulmonary fibrosis (IPF), a condition affecting over 100,000 patients in the U.S. *with limited treatment options,* after our INCREASE phase 3 clinical study provided evidence of a potentially disease-modifying effect on patients with pulmonary fibrosis.

We are doing this with our four approaches to creating transplantable, tolerable, manufactured organs to address the shortage of kidneys, hearts, and lungs, probably *one of the largest unmet medical needs in the U.S.*

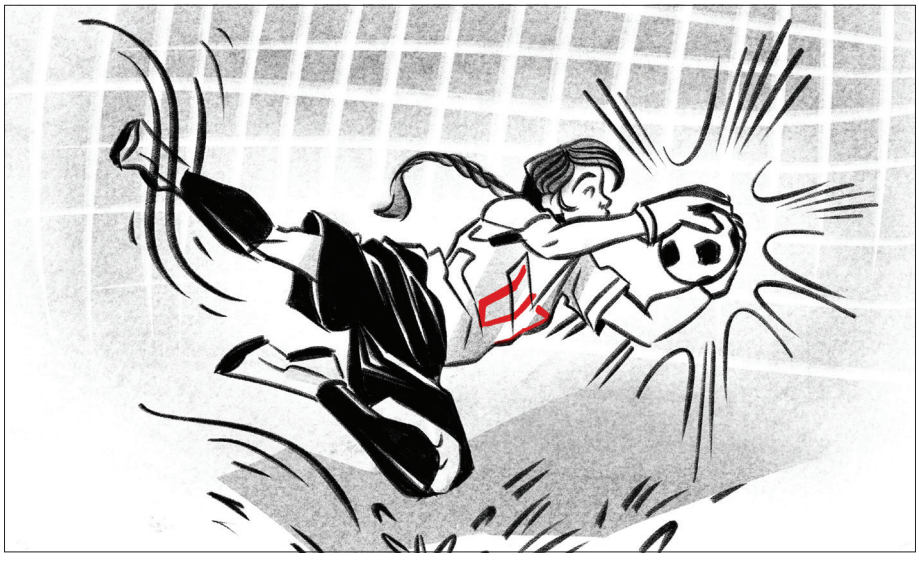


PLAY THE BALL WHERE YOU WANT IT TO BE, NOT WHERE IT IS

PERSEVERANCE IS OMNIPOTENCE.
IF YOU DON'T GIVE UP, YOU WILL SUCCEED.



WHEN BLOCKED, ALWAYS LOOK FOR OTHER OPTIONS



THINK ON YOUR FEET, AND WHEN NECESSARY, TRY ANOTHER ANGLE

OUR BUDGET ALGORITHMS ARE DESIGNED TO PROVIDE INDUSTRY-LEADING PROFITABILITY

We have delivered profit margins among the strongest in the biotechnology industry because we spend far less than we make.

We do this through a strict budget algorithm under which we plan United Therapeutics' total cash budget in a current year based on 50% of prior year revenues.

Our budget algorithm forces us to continuously evaluate programs and investments across our company to make sure we are putting the highest and best uses forward, trimming costs we can trim, and focusing on priority and efficiency. We are committed to adhering to this rigorous formula and we have the financial discipline to do so, ensuring the most strategic deployment of financial capital and resources.

All Unitherians know that there is only one way to get additional budget dollars for our existing and planned programs: we need to grow our revenues.

Simple.

DISCIPLINED PURSUIT OF GOALS

OUR FIVE STRATEGIC OBJECTIVES

We have *Five Strategic Objectives* that drive everything we do.

IT TAKES MANY SKILLS TO WIN

OBJECTIVE #1:
Develop the Best Medicines Possible From Our Intellectual Property

DON'T FORGET TO USE YOUR HEAD

OBJECTIVE #2:
Conduct the Most Insightful Clinical Trials of Our Medicines

CAREFULLY SELECT YOUR SHOT

OBJECTIVE #3:
Achieve Superior Communication and Awareness of Our Therapies Among Physicians

BE VOCAL

OBJECTIVE #4:
Grow The Financial Parameter of Our Business to be in the Top Quintile of Our Peers

PUT POINTS ON THE BOARD

OBJECTIVE #5:
Achieve our Goals by Doing the Right Thing and Using the Highest Ethical Standards

ALWAYS KNOW THE RULES AND REGULATIONS OF THE GAME

CREATING TRANSPLANTABLE, TOLERABLE MANUNFACTURED ORGANS

GO BIG OR GO HOME

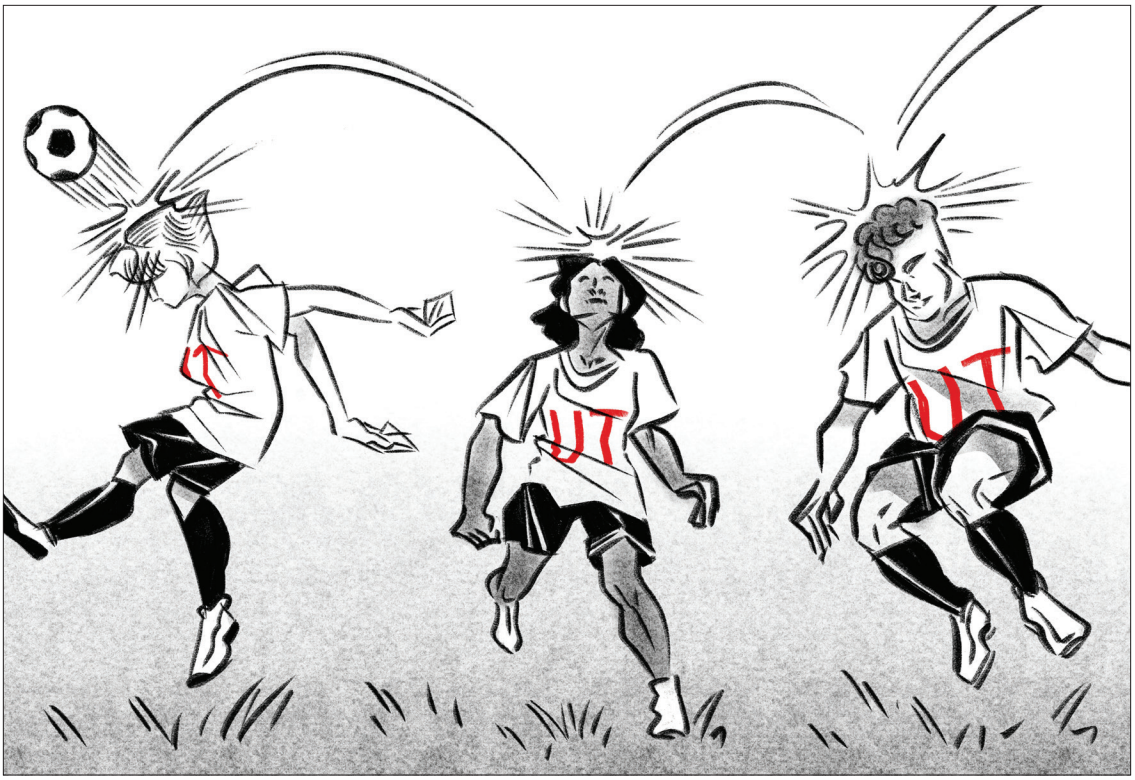
We believe that the ultimate solution for our patients and for patients with many other life-threatening diseases is a cure through transplantation.

Each year, approximately one million people in the U.S. have end-stage organ disease and may need a heart, kidney, or lung transplant. Unfortunately, the number of usable, donated organs available for transplantation has not grown significantly over the past half century, while the need has soared. Our long-term goals are aimed at addressing this shortage. With advances in technology, we believe that creating tolerable manufactured organs is now principally an engineering challenge, and we are dedicated to finding engineering solutions. We are heavily engaged in the early-stage research and development of a number of organ transplantation-related technologies including regenerative medicine, organ bio-printing, xenotransplantation, and ex-vivo lung perfusion.

We have made tremendous progress toward our ambitious goal. At our North Carolina campus you can see an actual lung breathing in and out in an ex-vivo lung perfusion machine, a lung which we have made from scratch. To address the over 100,000 patients on dialysis waiting for a kidney transplant, and the over 300,000 patients who will need a kidney transplant but are not yet on dialysis, we are developing what we call our 10-gene pig to produce a modified porcine kidney which is intended to present no greater obstacles to the human immune system than a transplant from an unrelated other human donor. We are also working on making autologous manufactured organs, so that organ recipients would not need to take immunosuppressants.

It will be a capstone of United Therapeutics' trajectory and commitment to patients for our manufactured organs to help supply the demand.

IN UNITHERIANS WE TRUST



TEAMWORK KEEPS THE BALL MOVING TOWARD THE GOAL

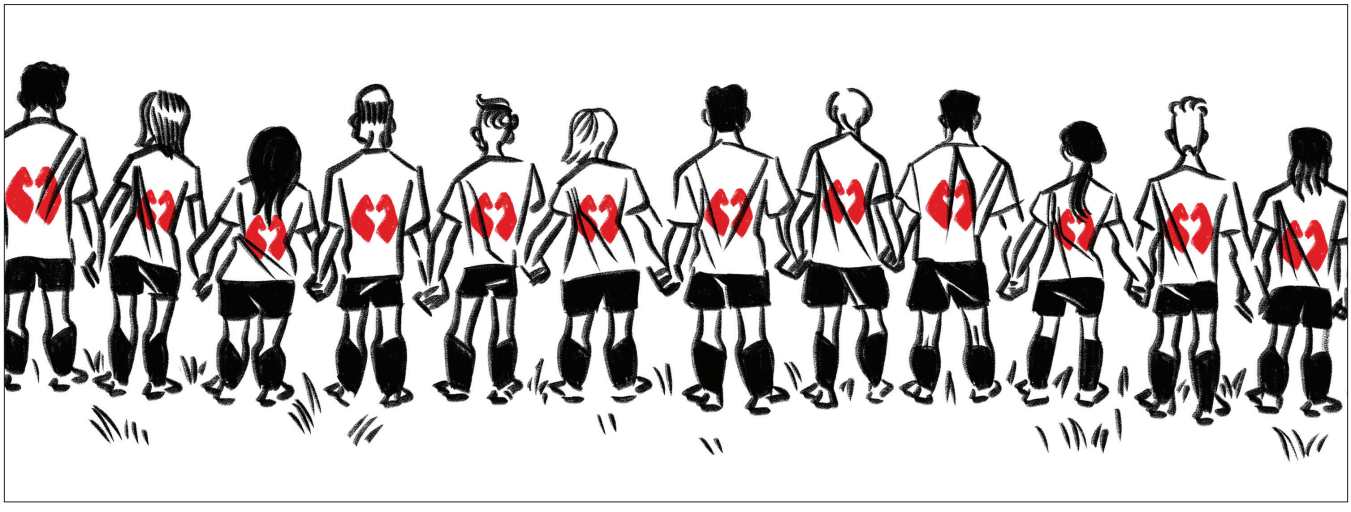
Since our founding 25 years ago, we have worked to set ourselves apart as a caring, daring, and happily different team that enables Unitherians to give their best and get our best. We believe love and loyalty are better motivators than fear and threats. We believe that an inclusive, and even irreverent, culture makes clear to Unitherians that we want their creativity and value their differences that produce it.

We focus on the value of a diverse team, both in creativity and our leadership. Our twelve-member Board of includes five women, three directors who self-identify as under-represented minorities, and one who self identifies as a member of the LGBTQ+ community. Our management team is similarly diverse: 47% female and 29% identify as racial or ethnic minorities. We have also created new structures and company-wide training to support our commitment to diversity, equity, and inclusion, including establishing an Inclusion Advisory Group and a DE&I Executive Council, two working groups comprised of Unitherians whose purpose is to provide input, education, and oversight for our ongoing DE&I initiatives.

ALWAYS BE OPEN TO ASSIST A TEAMMATE

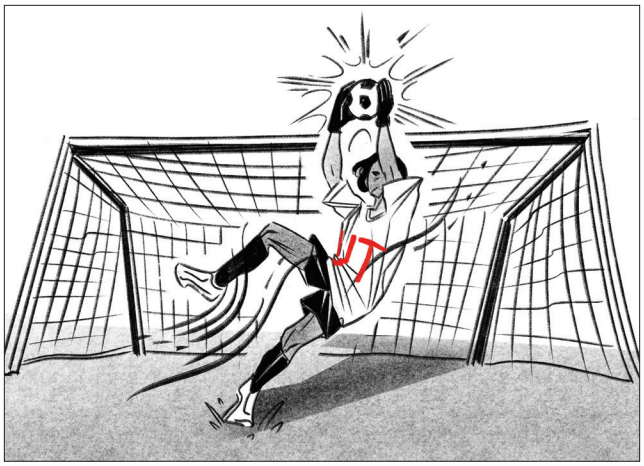
We adhere to a minimum $75,000 “living wage” including salary and bonus eligibility, enabling every employee to become a shareholder, and providing an array of market-leading health, savings, education, work-life integration, family, and other benefits to treat Unitherians holistically and turn jobs into careers. Our benefit programs are designed to demonstrate how much we value Unitherians, and to enable them all to participate in our financial success.

Not only did we not lay off, furlough, or reduce the pay of any Unitherians as a result of the COVID-19 pandemic – despite initially having to stop enrollment of our clinical trials and put other projects on hold – we gave every employee multiple additional bonuses in 2020 to help them face the sometimes major challenges that new work protocols and family changes created.



WE GOAL, NOT EGO

PROTECT THIS HOUSE



OUR DEFENSE IS AS IMPORTANT AS OUR OFFENSE

Like many companies, we felt the impact of the covid-19 pandemic. It delayed the launch of our Remunity Pump for Remodulin until February 2021. Enrollment of our clinical trials was temporarily paused as hospitals shut down. We felt pressure on our revenues, as it became difficult for patients to start advanced therapies, and our staff was limited to virtual interactions with healthcare providers. Our product development teams, however, quickly found ways to adapt clinical trial protocols and expand clinical site activation efforts, and we worked hard to make sure patients had uninterrupted access to our therapies. Our solid balance sheet and conservative budgeting algorithm mitigated these impacts, and we made no pandemic-related reductions in staffing, employee compensation, or research and development programs. Many Unitherians were forced to quickly adjust to a new work-from-home environment, while others continued to work in-person to keep our manufacturing and research and development efforts on track. We are very proud of the work of our Unitherians, and grateful for their efforts during these challenging times.

Our risk management strategy focuses on maintaining a two-year supply of inventory and a three-year supply of active pharmaceutical ingredients for our treprostinil therapies; in-house manufacturing, storage, logistics, and distribution capabilities; and multiple contracts with contract manufacturing organizations to supplement and back-up our existing manufacturing capabilities.

PROTECT OUR GOALS

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LISTEN TO YOUR COACHES

PROTECT YOUR GOALS

NOTES

SEE YOU NEXT SEASON!