
2019 Annual Reportfolio
United Therapeutics Corporation
UNITED THERAPEUTICS ANNUAL REPORT
UTHR REPORTFOLIO
2019
Performance
Insightful Clinical Trials
Romantic
Helicopters for Everybody
Understatements
OPERATING INSTRUCTIONS


United Therapeutics
UNITED THERAPEUTICS ANNUAL REPORT
UTHR REPORTFOLIO
2019

2019 Annual Reportfolio

United Therapeutics Corporation

OPERATING INSTRUCTIONS

2019

United Therapeutics Annual Reportfolio

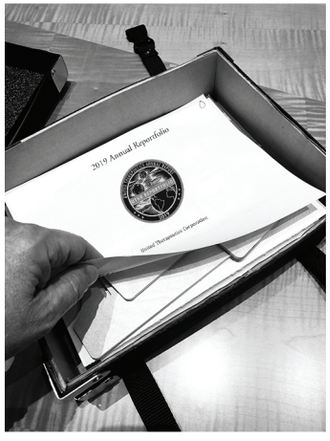
Catalog # BDR529

Open red mailing box to reveal
intriguing black case

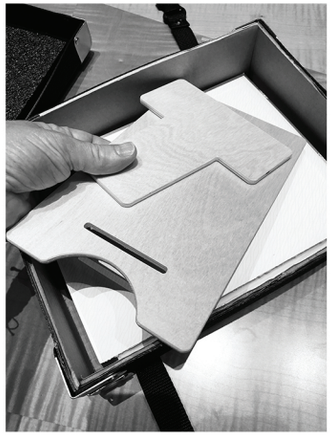
Pinch sides of belt clip
on strap...

And pull
Repeat on both straps

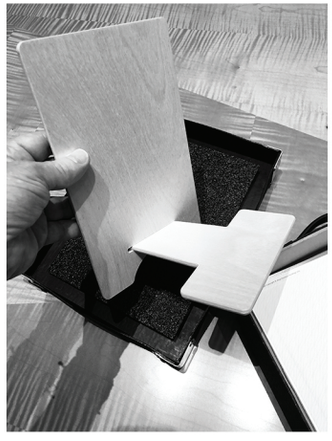
OPEN CASE!



WELCOME!
Remove title page
Study

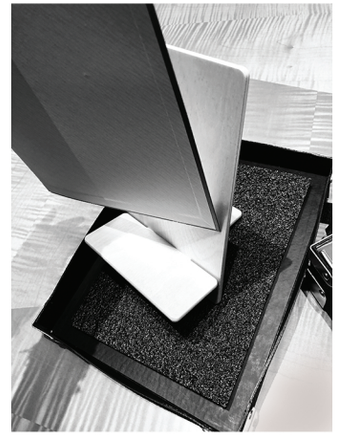


What's this?
A two-piece stand!



Simply insert "T" piece
into backing

Remove
gray backing board



Place
gray backing board
on stand

Remove
each fine art print

Place on stand and reflect
on the beauty of fine art

Enjoy
all 11 fine art prInts in your
office, vehicle, or home

SPECIAL BONUS!
The exciting 2019 United Therapeutics
story on all reverse sides!

NOTES

"When you start walking the best path will appear. I am not really sure of the way from A to Z, but when I began walking the rest of the alphabet appeared."

We currently market and sell four therapies for pulmonary arterial hypertension and one drug for a rare pediatric cancer. Our net revenues from these therapies in 2019 totaled approximately **$1.45 billion.**

Three of these medicines, **Remodulin**, **Tyvaso**, and **Orenitram**, contain the active ingredient treprostinil, and we saw combined net revenue growth for these three products in 2019 despite the onset of generic competition for Remodulin in March 2019.

We plan to continue to grow revenue from our treprostinil-based products through label expansions, new indications, new formulations, and the introduction of new delivery devices.

We are also working on a number of entirely new therapies to treat pulmonary hypertension and other rare diseases that we hope to launch over the next several years.

Longer term, we have set the ambitious goal of solving the acute national shortage of transplantable organs through our innovative organ manufacturing programs.

REMODULIN® (treprostinil) Injection

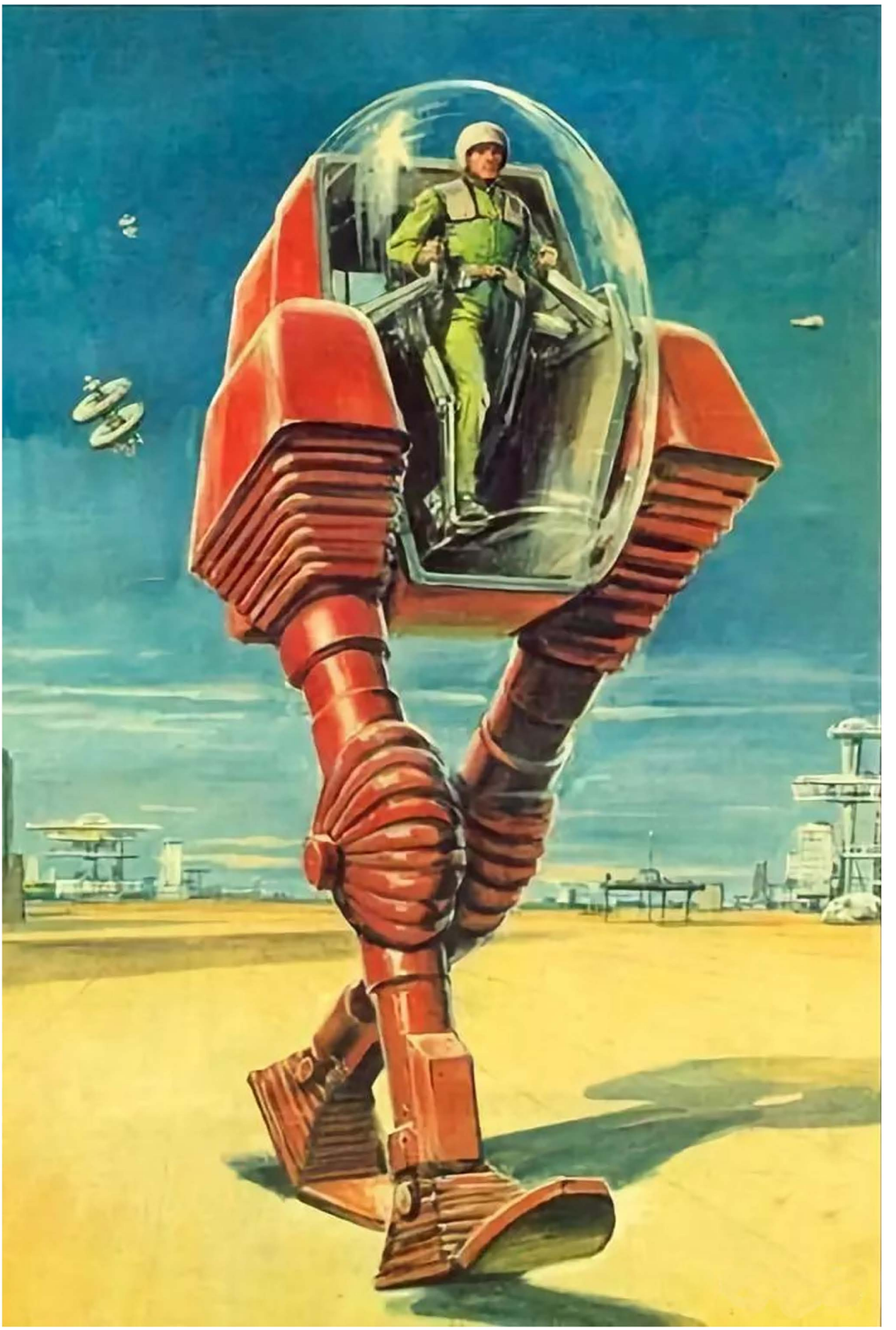
TYVASO® (treprostinil) INHALATION SOLUTION

orenitram® treprostinil EXTENDED-RELEASE TABLETS

adcirca® tadalafil tablets 20mg

Unituxin® (dinutuximab) Injection

Artwork: Walter Molino, *The Pedipulator*, La Domenica del Corriere (Italy), 1966



"This is why we keep two years finished inventory plus three years active pharmaceutical ingredient plus three years working capital"

Our historically strong profitability has generated strong cash flow resulting in an extremely healthy balance sheet.

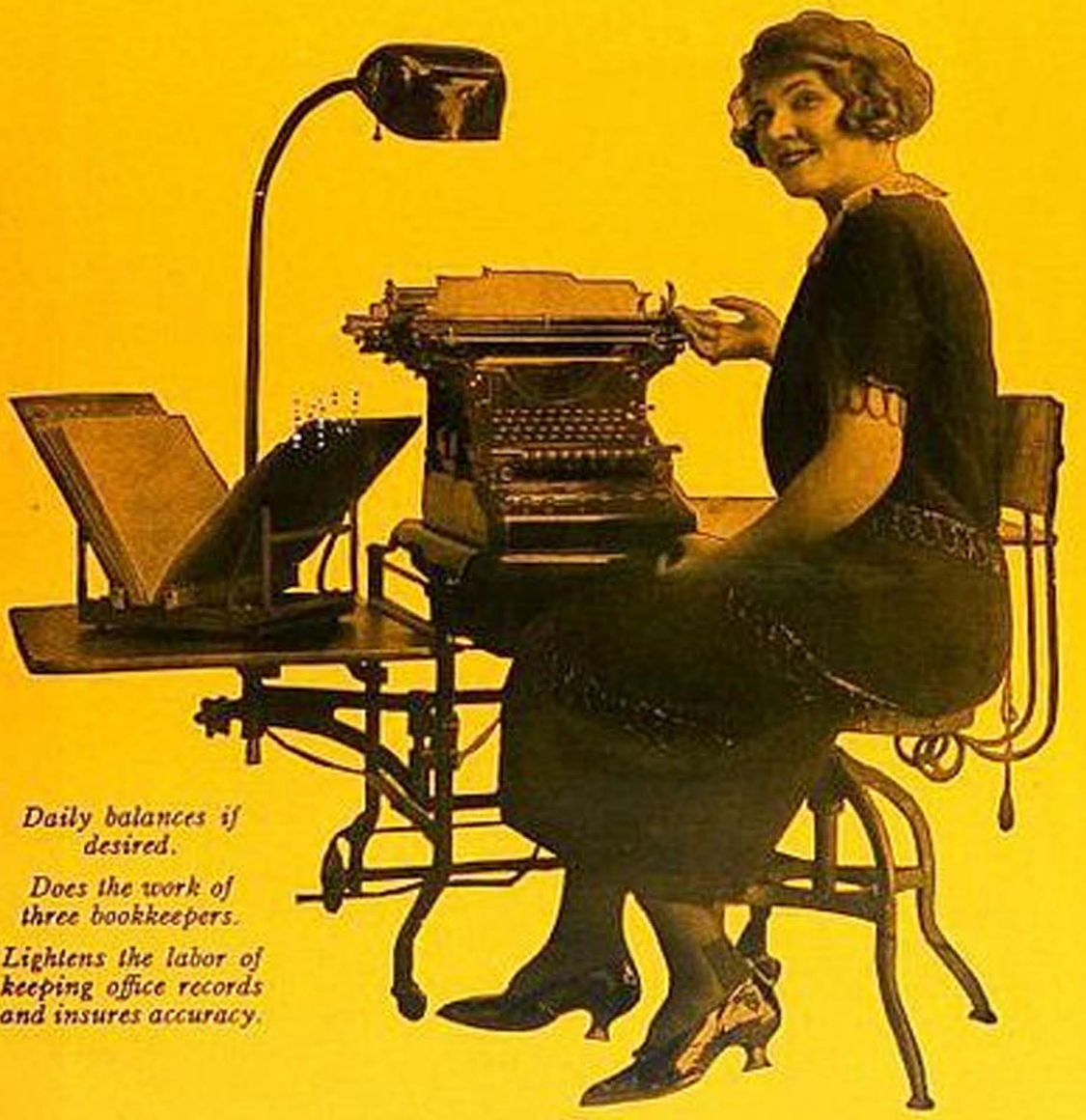
At December 31, 2019, we had cash, cash equivalents and marketable securities totaling **$2.3 billion**, with $850 million outstanding indebtedness, up from $1.86 billion at the end of 2018.

On March 23, 2020, Jefferies Equity Research screened over 1,000 companies, and highlighted United Therapeutics among a list of just six with a "***Fortress Balance Sheet***" that are best positioned to weather the Covid-19 storm.

Artwork: *Underwood Bookkeeper Machine*, advertisement, 1921

This is the

UNDERWOOD BOOKKEEPING MACHINE



Daily balances if desired.

Does the work of three bookkeepers.

Lightens the labor of keeping office records and insures accuracy.

It straightens out your office tangles and does your work *your* way

THE UNDERWOOD TYPEWRITER COMPANY, Inc.

UNDERWOOD BUILDING NEW YORK CITY

"Persistence is omnipotence, if you don't give up you will succeed"

In 2019, we achieved:

- The **highest number** of new patient starts on our treprostinil therapies, highlighted by the **highest level** of new Remodulin starts in ten years and the **highest number** of new Orenitram and Tyvaso starts in nearly four years. This resulted in an **all-time high number** of active patients on a treprostinil medicine at the end of 2019, for the **second year in a row**. We are reaching **more patients** with our treprostinil therapies than ever before in our history.
- **$1.45 billion in revenues**, which exceeded analyst consensus estimates in the face of generic competition
- The FDA **approved** our label expansion for Orenitram reflecting the successful results of our *FREEDOM-EV* study and **granted initial clearance** for the patient-fill version of our Remunity system for the delivery of Remodulin
- Orenitram revenue **rose 10%** compared to 2018 with the *FREEDOM-EV* label expansion
- Revenue per employee of **$1.6 million** compared to the NASDAQ Biotechnology Index median of $0.2 million
- The acquisition of the rights to **ralinepag**, a next-generation, oral pulmonary arterial hypertension therapy in Phase III clinical trials

Further, in early 2020 we received positive results of our pivotal ***INCREASE*** study of Tyvaso in a new indication which met its primary and all secondary endpoints. We also received FDA approval of the **pharmacy-filled version of the Remunity system** for the delivery of Remodulin. We expect these two key accomplishments to support long-term revenue growth.

Artwork: Alex Schomburg, *Cosmatomic Flyer*, Science Fiction Plus, 1953. Courtesy of the Estate of Alex Schomburg.


ALEX
SCHOMBURG
XR

"Go big, or go home"

United Therapeutics is a most creative company.

Consider some of the incredible things that we make. We commandeer the DNA of cells to make Unituxin, an infusion that increases by 50% the odds of children with certain types of neuroblastoma being able to leave their cancer behind. We also creatively figured out how to make a potential medicine out of tiny droplets or "vesicles" of cellular material, called exosomes. And we make a variety of medicine delivery devices such as inhalers and pumps, including some that are so accurate in their dosing it is measured in nanograms (billionths of a gram).

We are also creative in figuring out how to prove things that have never been proven before. We recently established that Tyvaso, which is approved by the FDA for the treatment of pulmonary arterial hypertension, is able to help improve health markers for a subset of pulmonary hypertension patients with a type of pulmonary fibrosis. We are the only company to have successfully achieved this proof, although several have tried. Even more remarkably, we proved that Orenitram is able to delay disease progression of patients with pulmonary arterial hypertension on top of background therapy and lead to improvement across key clinical parameters. This was the first time this has ever been shown for an oral prostanoid therapy. We frame our hypotheses to produce innovative clinical trial designs. Our mantra is "go big, or go home!"

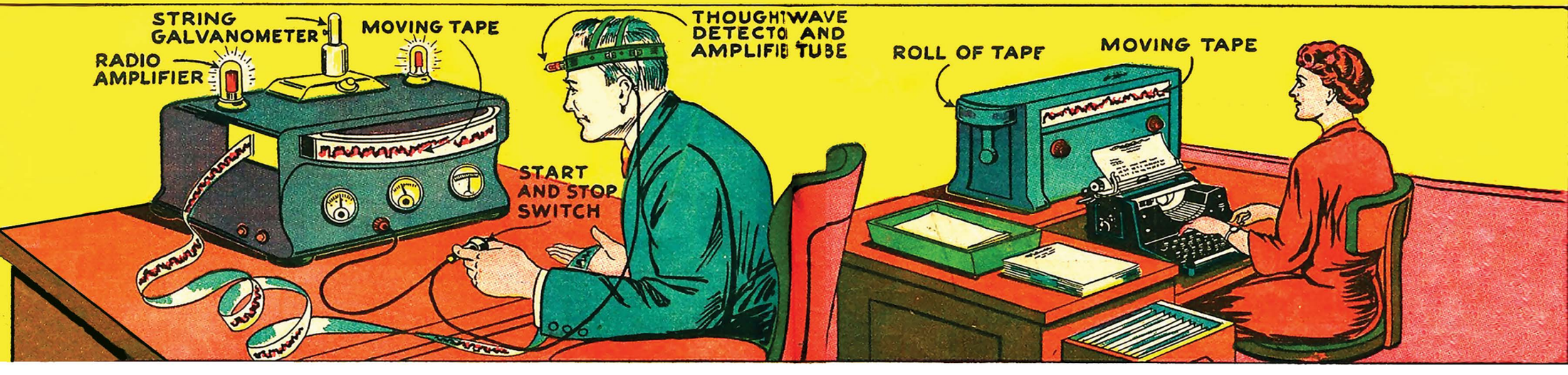
But perhaps most exciting of all is that we are now working to save patients' lives in ways that people have never seen before. This kind of creativity involves manufacturing replacement organs for failing hearts, lungs, kidneys, and livers. Already we have saved over 130 patients' lives by taking human donor lungs that no surgeon in the USA wanted to transplant – they were in that bad condition – and within 24 hours using our technology and skills we made them transplantable. Every organ saved is potentially a life saved. We have numerous innovative approaches in pre-clinical development toward our goal of creating immunosuppressant-free transplants.

I believe everyone at United Therapeutics is proud to work at a company where creativity is cherished. This is a company where "think differently" is encouraged and "outside of the box" is welcomed. We do not do the easy things at United Therapeutics, for those do not require creativity. We thrive on the daring challenges, the revolutions in medicine. We empower each other to see what others have seen, be guided by the data, but to think of solutions that no one imagined before. And then to make them, prove them, and deploy them to the betterment of human health as rapidly as possible.

Martine A. Rothblatt, Ph.D., Chairman and CEO

Artwork: Hugo Gernsback/editor, *The Thought Writer*, Super World Comics, 1940

THE THOUGHT WRITER



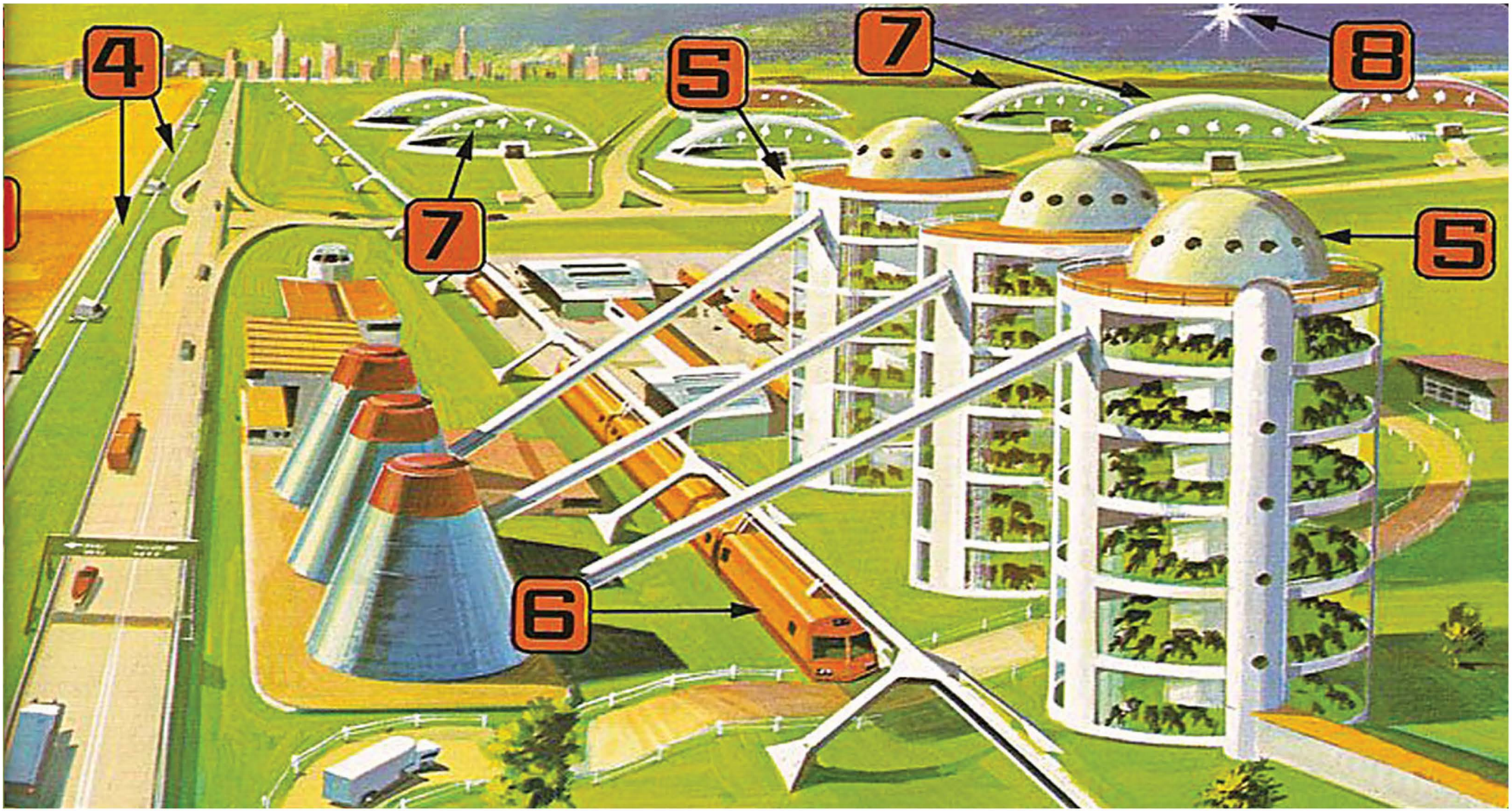
"Do The Right Thing"

Our work doesn't stop with addressing unmet medical needs of life-threatening conditions. Our company was founded under the principal of "do the right thing". It is a core aspect of our culture that has been translated into various policies and programs across United Therapeutics. As a forward-thinking company, we prioritize environmental stewardship, human capital management, ethics and social impact, with the strong belief that our values will drive not only long-term shareholder value, but also provide hope for the future.

For example, we believe we are the first public biotechnology company to have a site net zero office building the size of our new Unisphere facility, to create a public benefit subsidiary to target a clear public benefit mission alongside our emphasis on shareholder value, and to have a company-wide minimum living wage for all employees of approximately $75,000 per year (cash salary and bonus, not including company-wide equity compensation).

We also seek to operate in a way that is environmentally sustainable, as we believe that reducing the community's carbon footprint benefits us all. Through our focus on constructing site net zero buildings, we are taking a leadership role in driving the use of sustainable technologies forward.

Artwork: Kenneth William Garland, *Superfarm*, *Year 2020*, Robots – World of the Future, 1979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"Approve, then improve. Never stop improving the solution."

In 2019 we achieved **two key FDA approvals**, advanced **eight phase III programs**, progressed **two early-stage development programs**, and moved **two new therapy candidates into early-stage development**. Our therapy development teams have been incredibly productive.

For our approved therapy **Orenitram**, the FDA approved a label expansion in October reflecting the successful results of our Phase III *FREEDOM-EV* study and we relaunched Orenitram to a potential population of 45,000 patients in the U.S. The results of *FREEDOM-EV* showed that Orenitram, when taken with an oral pulmonary hypertension background therapy, decreased the risk of a clinical worsening event versus placebo by 25%, driven by a 61% decrease in the risk of disease progression, when compared to placebo (p=0.0002). Orenitram's label now notes that it delays disease progression because it reduces morbidity and mortality. We believe this success will drive growth in revenues, with Orenitram being prescribed earlier in the patient's history of their disease. We have also advanced **OreniPro**, an oral prodrug version of Orenitram, to the next stage of development as our next pipeline improvement in order to provide increased tolerability and convenience through a once-daily dosing regimen.

For our approved therapy **Remodulin**, we are conducting phase I studies to develop a prodrug of treprostinil called **RemoPro**, which is intended to reduce site pain currently associated with subcutaneous delivery of treprostinil. We expect to launch our **Implantable System for Remodulin** in 2021, which we are developing with Medtronic and which, among other benefits, reduces the risk of infection associated with intravenous treprostinil.

For our approved therapy **Tyvaso**, we are developing a dry powder formulation of treprostinil called **Treprostinil Technosphere** under a license from MannKind Corporation for its inhaler, which was approved by the FDA in 2014 to deliver an inhaled form of insulin. We believe this small, pocket-sized inhaler that does not need electricity will have significant convenience advantages over current inhaled prostacyclin alternatives which rely on the use of lengthy breathing sessions with nebulizers that need to be plugged in.

Approve then improve.

Artwork: John R. Armstrong, 1940

"Identify the corridors of indifference and run like hell down them"

We are studying our therapies in new corridors of indifference by investigating the treatment of pulmonary hypertension associated with lung disease, where the underlying lung disease is complicated by co-existing pulmonary hypertension.

We were pleased to receive positive results in early 2020 of our phase III ***INCREASE*** study of our approved therapy **Tyvaso** in a new indication for the treatment of pulmonary hypertension associated with **interstitial lung disease**. The ***INCREASE*** study met its primary endpoint and all secondary endpoints. We believe these successful study results will enable us to obtain FDA approval of a label expansion to extend **Tyvaso** to help this new population of 30,000 patients in the U.S. alone with no approved treatment options.

We are also conducting a parallel phase III study of **Tyvaso** called ***PERFECT*** for the treatment of pulmonary hypertension associated with **chronic obstructive pulmonary disease**, a new population of 100,000 patients in the U.S. alone with no approved treatment options. The successful ***INCREASE*** results give us confidence in the ***PERFECT*** study, which were designed by the same researchers.

Artwork: Courtesy of Ralph Steadman

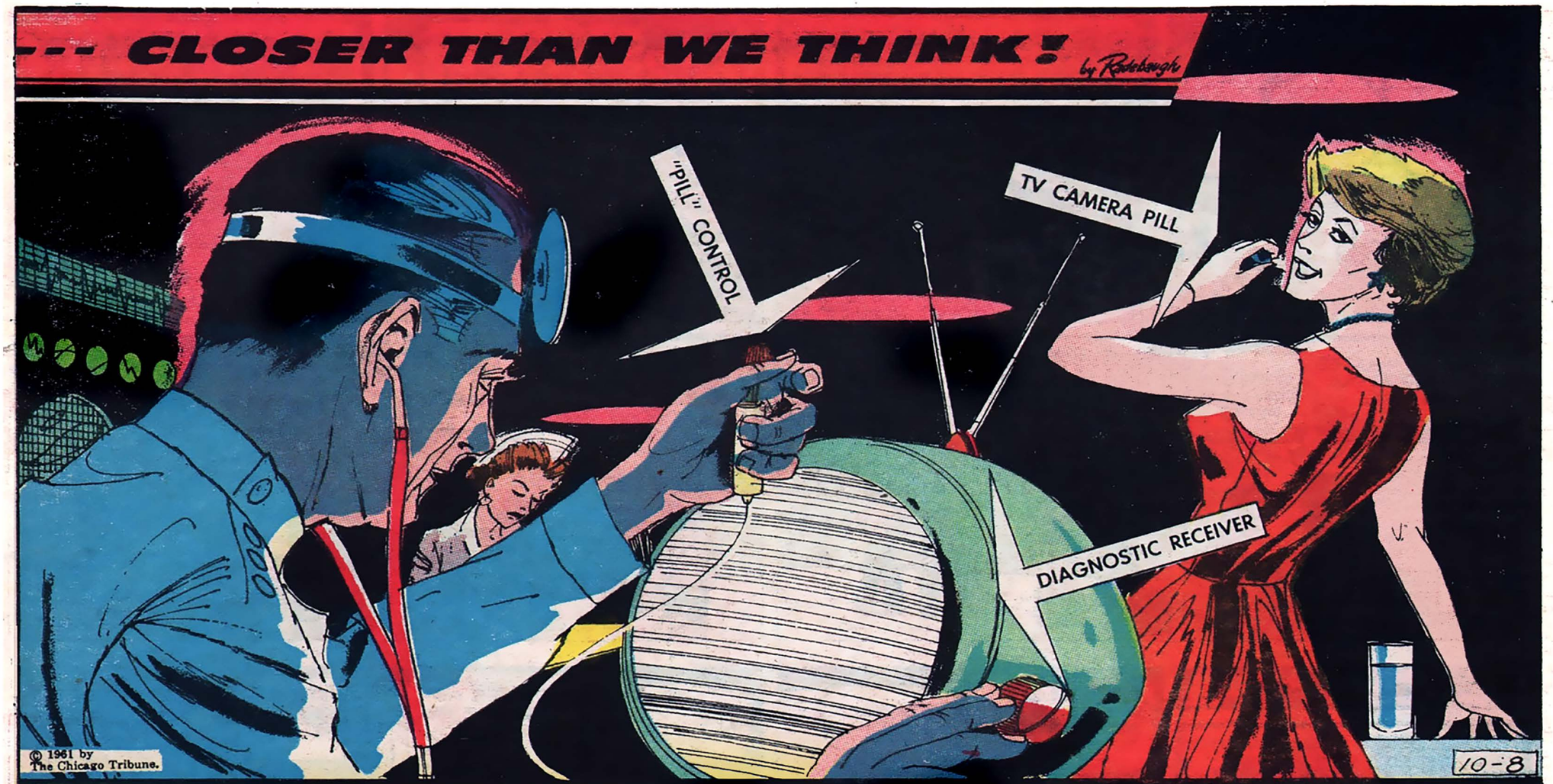
"I'm a person who likes to hear why something can't be done, and I'll whittle down every one of the 'can'ts' one at a time"

The current pump that is used to subcutaneously deliver our approved therapy **Remodulin** is fairly bulky. We want to do better for our patients.

Since 2014 we have been developing a much more elegant and simplified pump. Working with the prominent inventor and engineer Dean Kamen and his firm DEKA, we have made tremendous progress toward this goal with the **Remunity** system for the delivery of **Remodulin**. It incorporates innovative technology which has not previously been used in these pumps, including acoustic volume sensing technology which directs sound waves to establish very precise dosing. It does not require a motor drive, is very small, attractive, intuitive, and interfaces wirelessly with control devices.

In 2019 the FDA granted initial clearance for the patient-fill version of the **Remunity** system and in early 2020 we also received FDA clearance of the pharmacy-filled version of the **Remunity** system. DEKA is hard at work producing **Remunity** pumps.

Artwork: Arthur Radebaugh, *Closer than we think: Innerscope TV Pills*, 1961



INNERSCOPE TV PILLS

Before long, doctors will be saying, "Just swallow this little pill. I want to take a look at the way your digestive system is working."

Pills that are actually sub-miniature FM television transmitters will faithfully relay to your doctor's screen for visual study what they see inside your body. The doctor may take pictures of his television screen from time to time for closer scanning of the report from the innerscope pill.

The pill will be so small (about an eighth of an inch or so in length) that it will be able to go through a human system without being digested, thanks to the wonderful strides made in the field of miniaturization.

XR

"Most of my successes occurred after most people advised me to give up. There is always another way."

While we believe that treprostinil will be one of the standards of care in pulmonary hypertension for some time to come, we are also working on programs beyond treprostinil that we think could have an outsized impact on patients with pulmonary hypertension and other lung diseases. Here are some of them:

- **Ralinepag.** We are developing ralinepag, a next-generation, oral, selective, and potent prostacyclin receptor agonist, in global phase III studies for pulmonary arterial hypertension. If successful, we think ralinepag could improve patient outcomes with a more convenient dosing route and schedule than other therapies.

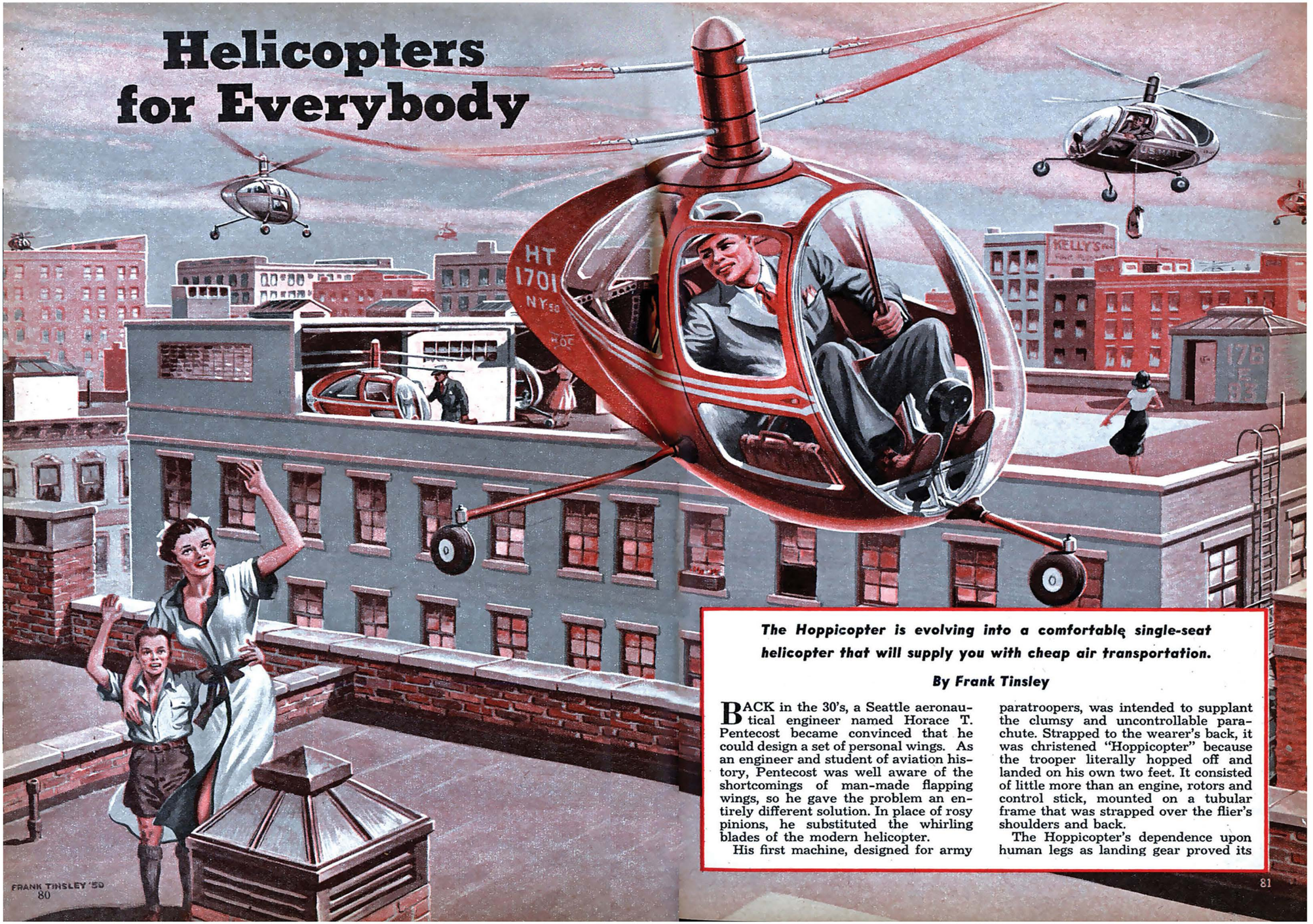
- **Aurora-GT.** We are conducting a phase II/III study (called SAPPHIRE) to explore the use of gene therapy for disease modification in pulmonary arterial hypertension. This therapy is intended to rebuild the blood vessels in the lungs that are destroyed by the disease.

- **Unexisome.** We are pioneering the use of extracellular vesicles called exosomes in a phase I clinical trial of this novel biologic for the treatment of bronchopulmonary dysplasia.

- **Organ Transplantation.** While potentially revolutionary in their own right, we think these and other development programs are stepping stones for what we believe is the ultimate therapy for patients with pulmonary hypertension and many other life-threatening diseases: organ transplantation. We are heavily engaged in early-stage research and development of a number of organ transplantation-related technologies, including ex-vivo lung perfusion, xenotransplantation, regenerative medicine, biomechanical lungs, and organ printing, among others – seeking to address the acute shortage of donated lungs, kidneys, hearts, and livers available for transplantation. With advances in technology, we believe that creating an unlimited supply of tolerable manufactured organs is now principally an engineering challenge, and we are dedicated to finding engineering solutions.

Artwork: Frank Tinsley, *Helicopters for Everybody*, Mechanix Illustrated, 1951

Helicopters for Everybody



The Hoppicopter is evolving into a comfortable single-seat helicopter that will supply you with cheap air transportation.

By Frank Tinsley

BACK in the 30's, a Seattle aeronautical engineer named Horace T. Pentecost became convinced that he could design a set of personal wings. As an engineer and student of aviation history, Pentecost was well aware of the shortcomings of man-made flapping wings, so he gave the problem an entirely different solution. In place of rosy pinions, he substituted the whirling blades of the modern helicopter.

His first machine, designed for army paratroopers, was intended to supplant the clumsy and uncontrollable parachute. Strapped to the wearer's back, it was christened "Hoppicopter" because the trooper literally hopped off and landed on his own two feet. It consisted of little more than an engine, rotors and control stick, mounted on a tubular frame that was strapped over the flier's shoulders and back.

The Hoppicopter's dependence upon human legs as landing gear proved its

"This is a place for rockers, outside-of-boxers, creators, work-laters, and mission focused, happy, exuberant can-doers. This helps us keep the culture more than anything."

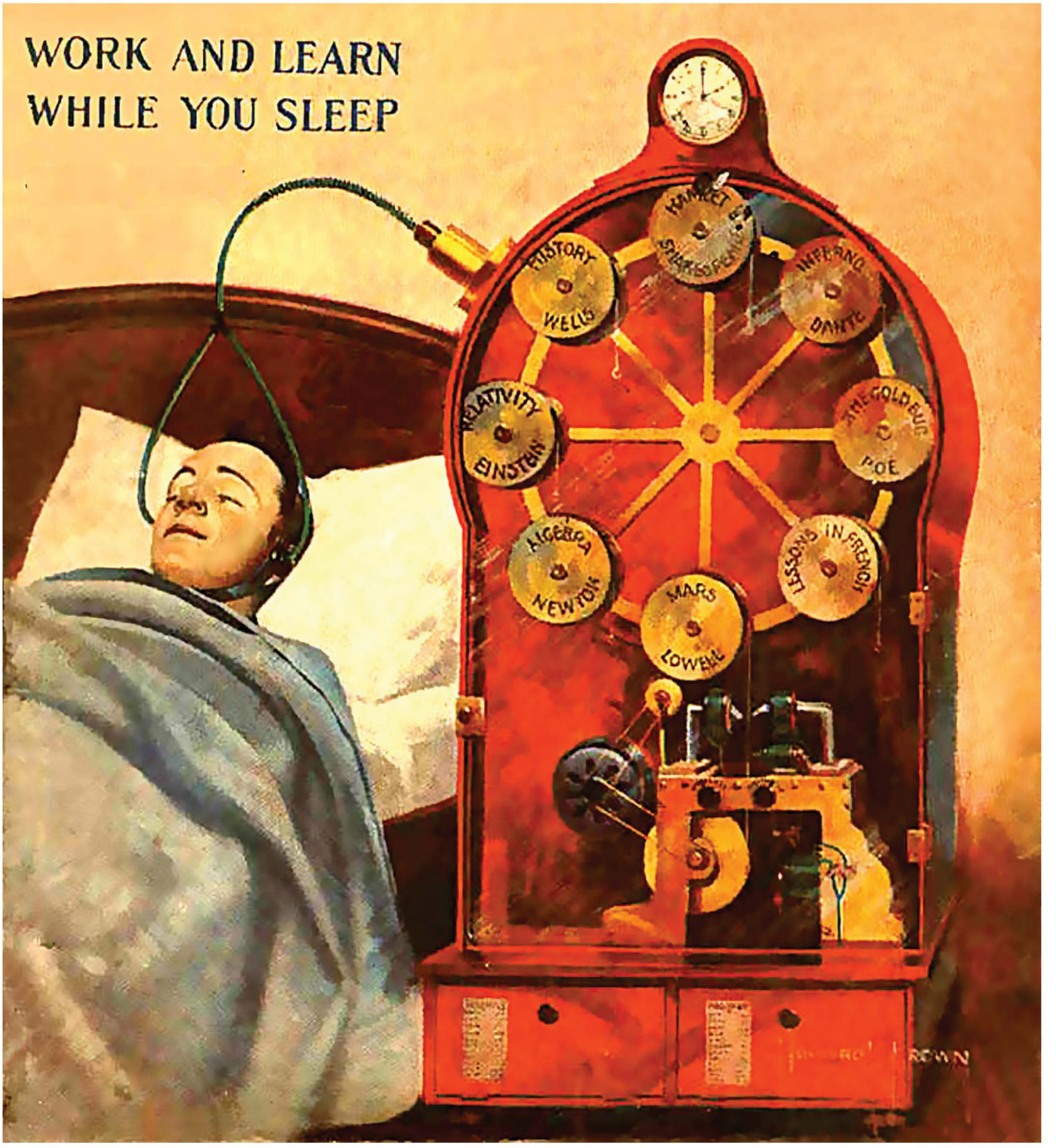
We are proud of our Unitherian employees, and ever grateful to them. Without their hard work and ingenuity, none of our successes would be possible, and none of our goals would be achievable. We believe in work-life integration and personal development, and that has led us to adopt a company-wide minimum living wage, on-site subsidized day care, and a number of health and wellness programs.

We strive to hire the best and brightest people who are passionately committed to our goals. We provide our employees with the opportunity to work on innovative, revolutionary projects, with the autonomy and freedom to operate in a manner they believe is best to complete any project, and with inspiring surroundings with state of the art facilities in which to think, work, and problem solve.

We are intentional in our effort to maintain our small, entrepreneurial culture. We believe this differentiated approach instills a greater sense of ownership, meaning, and commitment in our employees, motivating them to work as hard as possible to achieve our ambitious goals.

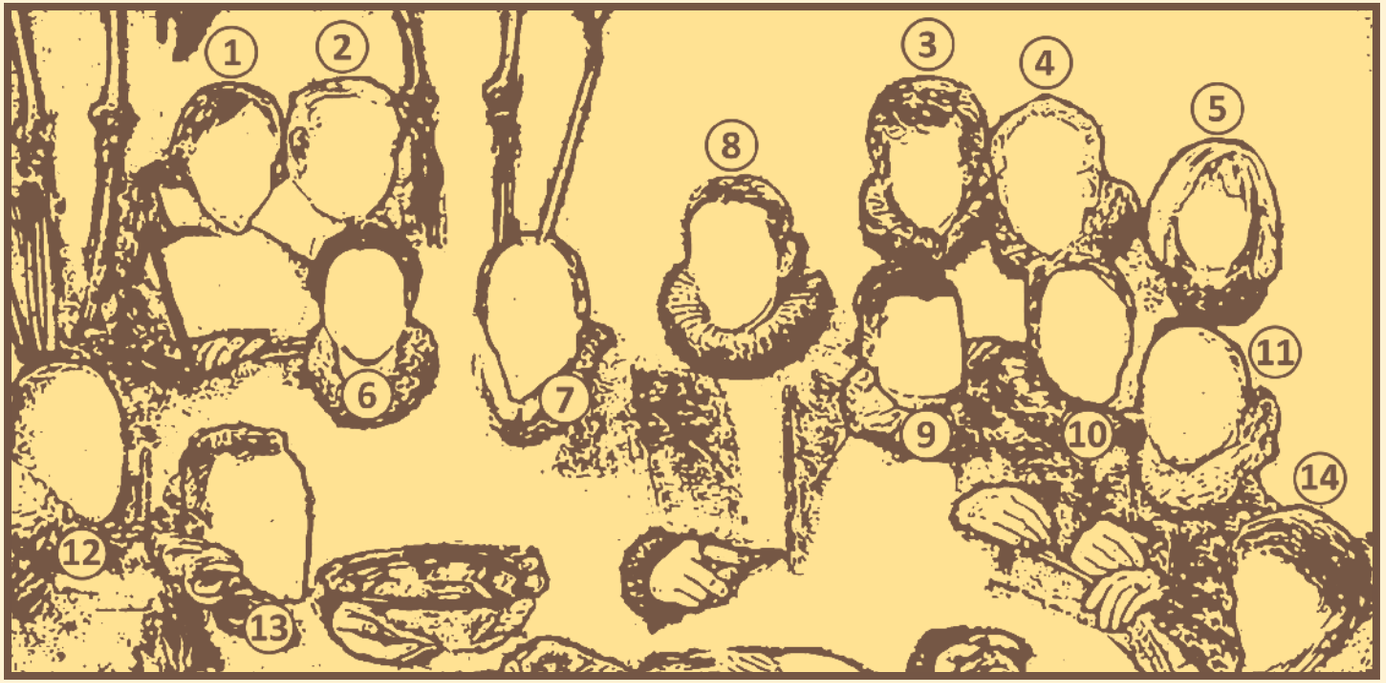
Our voluntary turnover is well below that of our industry peers. In 2019 our voluntary turnover was 6.3%, compared to the median turnover of 12.0% for the biotech industry.

Artwork: Howard U. Brown, *Work and Learn While You Sleep*, Science and Invention, 1921


WORK AND LEARN
WHILE YOU SLEEP
HISTORY
WELLS
HAMLET
SHAKESPEARE
INFERNO
DANTE
RELATIVITY
EINSTEIN
THE GOLD BUG
POE
ALGEBRA
NEWTON
LESSONS IN FRENCH
MARS
LOWELL

Board of Directors

"We go, not ego"



1. **Ray Kurzweil**
2. **Tommy Thompson, JD**
3. **Rich Giltner**
4. **Raymond Dwek, CBE, FRS**
5. **Judy Olian, PhD**
6. **Nilda Mesa, JD**
7. **Michael Benkowitz**
   President and COO
8. **Martine Rothblatt, PhD, JD**
   Chairman and CEO
9. **James Edgemond,**
   CFO and Treasurer
10. **Chris Patusky, JD, MGA**
11. **Louis Sullivan, MD**
12. **Chris Causey, MBA**
13. **Paul Mahon, JD**
    EVP, General Counsel, and Corporate Secretary
14. **Katherine Klein, PhD**

Artwork: Inspired by Michiel Jansz van Mierevelt (1566-1641), *Anatomy lesson of Dr. Willem van der Meer*, 1617