PIVOT CENTER

2022 ANNUAL REPORT

THE UNIVERSITY OF UTAH®

Vision

Be a global leader in innovation management that creates value for the University of Utah, its stakeholders, and society.

Spirit of Innovation

Taylor R. Randall
President
University of Utah

As the state's flagship university, the University of Utah is committed to generating discoveries that change lives, and the PIVOT Center plays an essential role in helping us deliver on this commitment to Utah.

Our goal to secure $1 billion in funded research over the next ten years will accelerate the commercialization of university research technology. The U's proximity to the state's growing innovation economy and its robust biotech, financial, and information technology sectors, gives PIVOT the unique opportunity to help university innovators form lasting partnerships with business and government leaders and help us reach that goal.

My hope is that, with PIVOT's support, the University of Utah will lead the way in developing dynamic innovation hubs throughout the state. These hubs will foster groundbreaking research and technology commercialization that address the challenges we face today and create a prosperous future for rising generations of Utahns.

PIVOT's work in bringing stakeholders together is a vital component of the university's efforts to harness the entrepreneurial spirt of innovation needed to positively make a difference in the lives of all Utahns and advance our quality of life. I commend the PIVOT Center's continued efforts and look forward to our partnerships and progress as we strive to make the University of Utah a top ten public university with unsurpassed societal impact.

10 year goal to secure $1B in funded research

Innovating the Innovators

Keith Marmer
Chief Innovation & Economic Engagement Officer, University of Utah

For many of us, this past year has been a constant unwinding and redirecting from the effects of the COVID-19 pandemic. Old routines have been modernized, and we are all adapting to an ever-evolving new normal. Office and work time is settling into a hybrid work schedule, giving us autonomy and allowing us to balance our lives and work in an unprecedented manner. As you will read in the pages that follow, innovation management at the U is innovating itself: while we are doing many of the traditional things like starting companies and filing patents, we're also coming at it in new ways.

In years past, this letter has reflected on programs we've launched at the U to support innovation to achieve impact. While I will stay true to form in this respect, there is also something different this year. The scope of our impact is unlike ever before. You'll read about innovative researchers, entrepreneurs and companies and the challenges they overcame to bring impactful products and services to the world. Our adventures in innovation reach beyond campus as we challenged ourselves to expand our tagline "catalyst for innovation" to include every University of Utah student and alumnus.

Partnering with Lassonde Institute and Alumni Relations, for example, the Lassonde for Life program was launched to provide entrepreneurial and startup support for every alum of the U. If you've ever studied at the U, we have a program to assist your innovative efforts. Collectively, we now reach more than 300,000 individuals. We're also working with Lassonde Institute to support entrepreneurs in the Master of Business Creation program. These are just two new ways we're expanding the reach of our economic development mandate.

Another traditional element of this report is metrics. As you read about this past year's metrics, I'm proud to say the U ranked among the top-10 public universities for issued patents and revenue generation. As a leading public university, the University of Utah continues to build on our long history of innovation by these and other measures.

top10

The U ranked among the top-10 public universities for issued patents and revenue generation.

Creativity and Resilience at the U

U of U Health began treating patients infected with SARS-CoV-2 in March 2020. The mysterious respiratory disease seemed like a distant threat to Utahns at the time. However, leaders from across the U had been preparing for the pandemic's inevitable arrival. Before a single case was confirmed in the United States, campus leaders met regularly with infectious disease experts and the Utah Department of Health to strategize and build COVID-19 safety protocols.

By early spring, the virus disrupted all aspects of normal campus life, and everyone's top priority became safety. University of Utah leadership implemented a variety of protocols to continue educating students while preventing spread of the disease. Staff, students and faculty dealt with canceled conferences, recruitment events and other gatherings, while in-person events meant to foster collaboration, exchange ideas and create community suddenly moved online. U of U Health implemented a limited visitor policy, leaving many to support and grieve their loved ones from behind panes of glass.

When the COVID-19 task force determined that all nonessential personnel should work from home, project timelines were initially delayed as home work spaces became established. During the peak of the pandemic, 65% of the U's non-faculty and non-health personnel were working in some hybrid capacity. Today, 53% of workers still follow a hybrid model, demonstrating just one of the lasting impacts of pandemic workplace adaptations.

Amid the challenges, U community members used their creativity and resilience to address the pandemic from a health, research and entrepreneurial angle. The U's 3i Initiative, together with the Vice President for Research Office, created impactful seed grants for COVID-19-related research. University faculty also procured record amounts of external funding. In fiscal year 2021, researchers were awarded $641 million in total funding; they then beat that record with $686 million in fiscal year 2022. There was a significant uptick in COVID-19-applicable disclosures, with many existing applications being repurposed toward COVID-19. For example, sensor technology invented at the U, originally used to detect the Zika virus, was quickly adapted to detect SARS-CoV-2.

People worked around the clock to convert some of the U's world-class scientific facilities into sites that could both administer COVID-19 tests and analyze them onsite. The U's Health Science Center Sequencing Core tweaked its usual work of sequencing genetic material for research to detect the genetic material of the SARS-CoV-2 virus. ARUP Laboratories became one of the country's go-to places to process COVID-19 samples. Together with U of U Health, they developed a method for testing antibodies to determine whether people had been previously infected.

Despite this tumultuous period, U community members relied on the attributes that make them stellar innovators. They rose to the challenge with persistence, creativity and thinking outside of the box.

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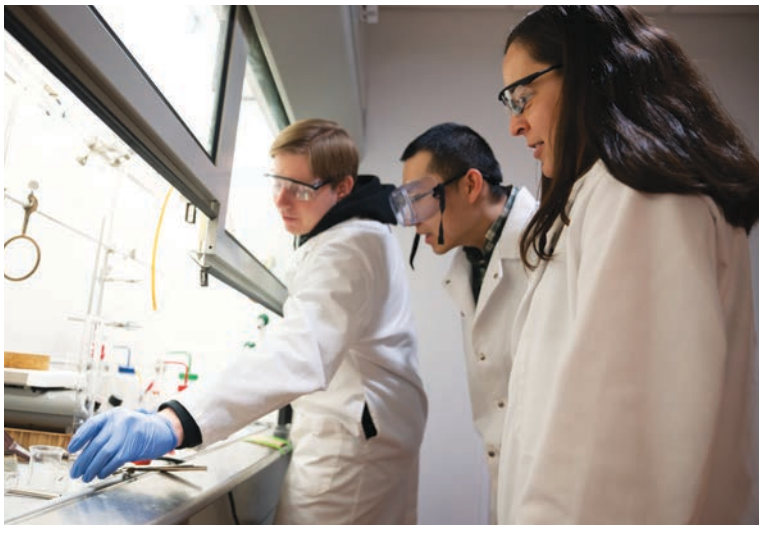

Improving Lives Through Innovation

From the first beat of the artificial heart to the first finger wiggles of the robotic prosthesis known as the LUKE Arm, the University of Utah has long been a home to innovative technologies and products that advance knowledge and improve lives. More than 330 startups have spun out of the U in industries like biotech, medical devices, software, manufacturing and engineering.

The accolades back up the university's reputation as an innovation powerhouse, as the U was recently ranked second among large research universities for "innovation productivity impact." It was also recognized by the Association of University Research Parks in 2020 as the Outstanding Research Park of the year.

Innovation and entrepreneurship are crucial to a thriving economy, which means the U is a major contributor to the state's economic health. The university is one of the state's largest and most important economic assets. According to the Kem C. Gardner Policy Institute, the U directly or indirectly supports more than 83,000 jobs and contributed an estimated $7 billion to Utah's GDP in 2021.

University of Utah President Taylor Randall wants to see that impact grow. "I believe as the state's flagship university, we have an obligation to serve the people of Utah and have a positive impact on all 3.3 million Utahns," Randall said. He named innovation as one of his three presidential priorities, with initiatives aimed at creating innovation districts and labs and refreshing the U's research and commercialization leadership strategy.

Randall's plan focuses on boosting research, speeding the transfer of technology to the marketplace and facilitating partnerships between stakeholders. This plan will require obtaining even more research funding than the unprecedented $686 million of 2022. Randall has challenged the institution to secure and sustain $1 billion of research funding annually within seven years.

The next step after boosting funding is bringing our research to market more quickly. "I call this picking up our 'clock speed' by increasing the velocity of our engagement to speed up transfer," Randall said. His plan is to invest $100 million in innovation programs that increase the translation of basic research into

commercially useful output. Therapeutics, orthopedics, clean energy, financial and regulatory technology, and social policy innovation are just a few examples of research areas that address society's urgent issues and will likely translate into commercially viable enterprises.

The Partners for Innovation, Ventures, Outreach & Technology (PIVOT) Center is key to these efforts. The PIVOT Center leads the U's strategy and operation for technology commercialization, corporate engagement, and economic development. The center supports research projects through their entire lifecycle, from the lab bench to the wider world. Through the PIVOT Center, revenue from patents and licensing agreements has skyrocketed to a historic high of $21.5 million in 2021.

The U is focused on developing strategic collaborations that allow new ideas to blossom. Public-private partnerships remove barriers to innovation and pave commercialization pathways for marketable products and technologies. Altitude Lab, a life sciences incubator founded by U spinout company Recursion and the PIVOT Center, provides inventors with the lab space they need to work toward the next biotech breakthrough. The Orthopedic Innovation Center accelerator ensures that faculty, fellows, residents, students and external collaborators have access to resources to move early orthopedic-related medical device concepts, ideas and discoveries through the product development and commercialization process.

Randall said higher education is evolving from a focus on academics into an era of entrepreneurship. "We are now poised to leverage our talent and resources to usher in this era at the U," he said. "Innovation and entrepreneurship are where we take the learning and knowledge enterprise beyond campus to improve lives and change the world."

The Tetraski, developed at the U, uses electric actuators to provide turning and speed variability using a joystick or breath control, giving the skier a high degree of performance and independence.

By the Numbers

As a leading public research university, the University of Utah continues to build on our long history of innovation by these and other measures.

Licensing Revenue

$21.8M

122 Patents issued

203
Invention Disclosures

18
Licenses

307
Patents Filed

5
Startups

Partners for Innovation, Ventures, Outreach & Technology

Since 1965, the University of Utah and the state of Utah have established a global reputation for leadership in technology commercialization. On behalf of the U, PIVOT Center serves as a catalyst for the regional innovation economy by ensuring faculty research and inventions move off campus and into the hands of consumers.

PIVOT prioritizes connecting stakeholders

From disclosure and intellectual property protection to funding, licensing and forming startups, PIVOT guides and connects stakeholders along each step of the commercialization process. By facilitating the process, PIVOT Center positions the U and Utah to uniquely take advantage of the U's burgeoning innovation.

Partnering for more impactful regional research

Research at the university-level is often collaborative, and few things better demonstrate the power of collaboration than the relationship between the University of Utah and the Idaho National Laboratory. In the last decade, the two groups have worked together to research nuclear energy, power grid security, and high-performance computing.

In February 2022, the U and INL further strengthened their partnership by signing the Strategic Understanding for Premier Education and Research, or SUPER agreement. The five-year SUPER agreement allows the organizations to collaborate more easily on projects and builds on the past decade of research.

"INL has many areas of interest that are well-aligned with our work at the U. It'll be a very natural and productive relationship," said University of Utah College of Engineering Dean Richard R. Brown. Before making a trip to INL in Idaho Falls in October 2021, Brown learned that 22 faculty members in his college had current projects with INL and 91 faculty members were interested in working with INL. Collaborative projects have ranged from a medical isotope project that could improve cancer treatments to a wireless technology to help first responders and law enforcement agencies communicate.

One faculty member in particular stood out for his continued partnership with INL. Behrouz Farhang, an electrical and computer engineering professor, has collaborated with Hussein Moradi at INL for 10 years, and together they have had 25 joint publications. INL even opened an office in the U's Research Park to enhance the partnership after INL wanted to hire some of Farhang's PhD students who preferred living in Salt Lake City. "That's a long and very productive collaborative effort," Brown said.

The Idaho National Laboratory focuses on nuclear energy research and development and performs research in the Department of Energy's strategic goal areas: energy, national security, science and the environment.

"As a national laboratory supporting national priorities, we see significant value in regional partnerships to advance innovative science and technology," said INL Laboratory Director John Wagner. "Partnerships with regional institutions like the University of Utah expand our reach and elevate our impact."

The SUPER agreement not only expands research collaboration for faculty, it opens the door for more U students to receive hands-on experience exploring critical nuclear, cybersecurity and clean energy projects. These students will be more prepared as they leave the university and move on to careers in the surrounding community. The College of Engineering awarded 1,287 degrees in 2022 and more than 85% of engineering graduates take jobs in Utah, according to Dean Brown.

The SUPER agreement opens doors for U students.

"It's our goal to see more Utah students getting the education they need to take these high-paying jobs and contribute to the Utah economy" Brown said.

University of Utah Chief Corporate Engagement Officer Patti Ross pointed out that this partnership has already generated positive outcomes for not just the university or INL, but also in "ongoing internship and employment opportunities for students across a broad range of disciplines."

"The University of Utah is delighted to have formalized the mutually beneficial partnership with Idaho National Labs," Ross said. "The partnership has also generated significant interest from corporate partners seeking to address similar challenges in cybersecurity, secure communications, manufacturing and other high-tech areas shared by INL and the University of Utah."

85 percent of engineering graduates take jobs in Utah

Allison Payne

Allison Payne says she is "trying to make some small dent in helping people with **breast cancer**" with her work at the University of Utah. Payne, who joined the university as a professor in the radiology and imaging sciences department in 2011, and her team have designed a breast-specific system for treating breast cancer that completed a first-in-human trial in France with another enrolling at the Huntsman Cancer Institute. The system, a focused ultrasound technology, allows clinicians to conduct an ultrasound inside an MRI and noninvasively manipulate tissues in the body.

"We're trying to bring advanced, patient-specific imaging for the treatment of breast cancer to give women more options for how they're treated," Payne said. Hopefully, this new treatment will result in not just another option for patients and clinicians but also a better cosmetic outcome that leaves patients with intact breasts if desired.

The process of developing the technology hasn't been without difficulty. Payne's team had to expand their mindsets early on to ensure their product was prepared with all the necessary features, so the device has "the tools and the ability to be able to capture this potential market when the science is backing it up," Payne said.

When the team took the product to France, Payne realized they "had designed it without considering how the clinicians would interact with the device," and she should have involved the clinicians earlier on in the process to make sure the product answered the right questions.

"I can chuck a bunch of data at you, but what do you need to process this to make it a useful clinical tool?" Payne said. Payne and her team were then able to pivot and revamp the product to focus on the clinicians' specific needs. "When you're inventing something totally new and you're giving it to people who haven't used it before, there's going to be a feedback loop that's going on."

As research continues, Payne hopes this technology will be able to change the treatment options for all breast cancer patients. In the forefront of her mind, she's trying to address health disparities by asking, "Can I pivot this technology to something that's really appropriate for a low resource setting?"

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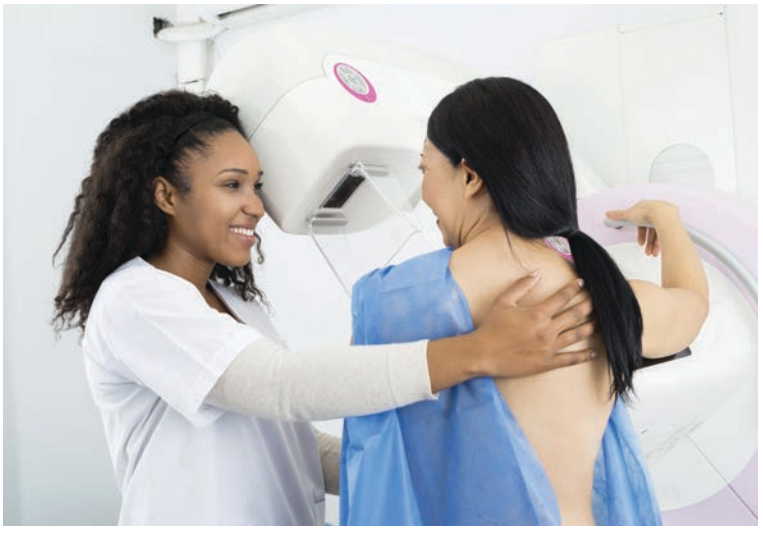


Preventing vision problems one drop at a time

iVeena has been developing eye drops for noninvasive treatment options.

Keratoconus, a rare condition, develops when the cornea of the eye thins and bulges, distorting its usual dome into a cone shape. The structural irregularity typically appears in childhood or adolescence and worsens with age, causing blurred vision and light sensitivity. If the condition becomes severe, patients may need a corneal transplant. However, currently, the only treatment for keratoconus is a surgical procedure.

iVeena, a Salt Lake City company, has been developing eye drops for the noninvasive treatment of vision problems, including keratoconus. In August, the company licensed its experimental keratoconus treatment, an eye drop called IVMED-80, to Glaukos Corporation, a pharmaceutical and technology company focused on ophthalmic disorders.

iVeena's IVMED-80 aims to achieve similar results to the existing surgical procedure, cross-linking collagen fibers and strengthening the cornea by activating an enzyme in the eye. Its developers hope the eye drops, which build on technology originally developed at the U of U, will slow the progression of keratoconus in patients, possibly preventing the need for surgery. In 2020, iVeena reported that in a Phase 1/2a clinical trial, IVMED-80 was well tolerated by patients and a 16-week course of treatment was associated with corneal flattening.

iVeena Vice President of Product Development Michael Burr said Glaukos is a fitting partner to further IVMED-80's development as a potential new option for patients with the disorder. The corporation's cross-linking technology is currently the only FDA-approved treatment for keratoconus. "Glaukos is the world leader in treatment of this rare condition, and so they know the space really well," Burr said. "They understand our technology and its potential future value and benefit."

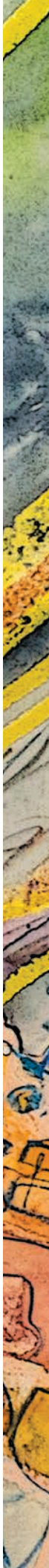
Under a licensing deal negotiated with the aid of the PIVOT Center, Glaukos has made an upfront payment of $10 million to iVeena for exclusive rights to continue IVMED-80's development as a potential therapeutic. iVeena will receive additional payments, as well as potential sales royalties, as developmental and commercial milestones are met.

Burr said the licensing fee gives iVeena the capital it needs to continue developing an intervention for a much more common eye condition, myopia—better known as nearsightedness. Like keratoconus, myopia arises when eye tissue adopts an abnormal shape. In this case, the eye is elongated along its front-to-back axis, creating an oval shape that changes the way light is focused in the eye.

Myopia is becoming increasingly prevalent around the world, and the condition doesn't just cause the sort of blurry vision that can be readily corrected with glasses or contacts. More severe forms, known as high myopia, are thought to increase the risk of developing more serious vision problems, such as glaucoma, cataracts, or retinal detachment later in life. According to a 2016 study published by the American Academy of Ophthalmology, nearly half of the world's population may be myopic by 2050. "It's a very large unmet medical need to prevent progression of these myopias," Burr said.

To address the problem, iVeena is developing an eye drop called IVMED-85, which aims to strengthen both the cornea and the sclera of the eye through a collagen cross-linking strategy similar to that deployed by IVMED-80. This, they hope, will slow or prevent the progression of myopia in children.

With preclinical studies yielding encouraging results, the company met with Food and Drug Administration staff in 2022 for a pre-investigational new drug meeting. It anticipates beginning clinical trials of IVMED-85 in 2023.



Lassonde for Life

Helping U alumni start and grow businesses

Lassonde for Life, provided by the Lassonde Entrepreneur Institute in partnership with the PIVOT Center and the Office of Alumni Relations, supports U alumni from every department and major who want to start or grow a business.

University of Utah alumni can participate in the program for free at any time and from anywhere in the world. The mostly online program is expected to keep alumni engaged and attract new students who want to obtain more than a degree from their university experience.

Members of the Lassonde for Life program receive many benefits and opportunities. In addition to workshops on topics like market research and prototyping, they get access to helpful content, mentors, networking opportunities, and more.

The PIVOT Center plays a vital role in the program by consulting, offering office hours and providing the same resources to Lassonde for Life members that it gives its licensees and startups. That means members have access to PIVOT's connections and expertise in invention management, patent prosecution, licensing, startup formation and support, equity management and early-stage funding.

The Lassonde for Life partnership also means that U alumni looking to use the expertise and experiences they gained after graduation to give back to the university can use the PIVOT Center's resources to facilitate these efforts. Whether they are looking to offer internships or mentorship opportunities to students or to be a networking resource for the U community, PIVOT's role at the university makes these connections easier, benefiting more than just the participating alumni but also students, faculty, and U startups.

Lassonde for Life is expected to further the University of Utah's long history of entrepreneurship and innovation. All across campus, many faculty, staff, and students are creating products, inventing new technologies, and launching companies. Now, alumni can be more engaged than ever and help grow this tradition.

Alumni can now be more engaged than ever and help grow the U's tradition of entrepreneurship.

Justin English

Do you know what Parkinson's, schizophrenia, MS, gastrointestinal disorders, kidney and liver diseases and bone dysmorphias all have in common? According to University of Utah biochemistry professor Justin English, they are "all strongly driven by **dysregulation of G-protein coupled receptors**."

These small receptors play a vital role in human health. On a cellular level, they detect what's going on outside a cell and tell it how to respond accordingly. This means they assist in a human's sense of smell and taste as well as mood and immune system regulation. Roughly 40% of all prescriptions filled in the United States target G-protein coupled receptors because of this relationship. That's where English and his lab enter the picture. "Our goal is to both understand how they work and control their function pharmaceutically, so we can improve patient health."

English has found that his research often involves slowing down rather than changing course completely. By slowing down, "you can make strong foundations for answering scientific questions or delivering on technologies that you think are the most impactful that you can generate."

This "recollecting" ensures that English and his lab are able to continue forward on their projects by focusing on process and developing methodology and quality control. "When we pivot, we're speeding along toward a particular project goal but then hit roadblocks where things aren't progressing the way that we anticipate and we really need to switch gears to understand where it is that we're coming up short."

In the two years English has been at the U, he and his lab have made significant strides toward their goals. Along with the lab's research into G-protein coupled receptors and directed evolution, they have collaborated with industry partners like Eli Lilly and started a company with the help of the PIVOT Center. With PIVOT, English is working to develop IP around applications in the startup. All this work helps English and his team progress toward their goal to develop new ways of treating patients with unmet needs or largely untreatable diseases.

40%

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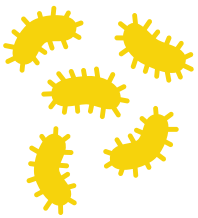
From an idea to a life-saving prototype

Light Line Medical started as an idea for a U competition and is now on its way to FDA clearance.



24
issued patents
and
18 pending
patents

Over 2.8 million antimicrobial-resistant infections happen yearly in the U.S., resulting in over 35,000 deaths, according to CDC estimates. In 2017, as part of a university competition to solve an unmet medical need, a group of University of Utah undergraduates set out to invent a product that would hopefully prevent catheter-associated infections that are increasingly difficult to treat because of the growing prevalence of those antibiotic-resistant pathogens.

Light Line Medical, the resulting startup of that original group of undergraduates, designed a system that cut out the use of antibiotics by using visible light to safely disinfect the inside and outside of multiple types of catheters, starting first with a dialysis product and later moving to urinary, respiratory and vascular products.

Light Line's PhotoDisinfection™ technology uses a reusable light engine and an innovative, disposable fiber optic cable that attach to off-the-shelf catheters, and then emits light down the cable into the catheters. Researchers found that using visible light rather than UV light—which degrades catheter material and is unsafe for human tissue—successfully killed pathogens, disinfected the catheter, and prevented infections while doing no harm to the patient or the catheter.

"Our technology has proven in study after study to kill more than the 99.99% pathogen kill rate required by FDA," said CEO Vicki Farrar. "With this success rate we will significantly decrease the number of infections treated, reducing the use of antibiotics, and preventing pain, suffering, and in many cases, death."

Light Line Medical made "significant progress on all fronts" in 2022, according to Farrar. The company entered into a collaboration agreement with Mayo Clinic that validates the potential impact of its product and also grants access to world-class investigators and their patients. On top of the Mayo Clinic agreement, Light Line Medical filed and obtained many patents, bringing its total to 24 issued and 18 pending patents, and raised another $1.9 million.

While Light Line achieved many milestones in 2022, the company also felt the impact of the lingering pandemic and successfully pivoted to meet its goals. Along with many other companies across the U.S., Light Line faced the challenge of hiring the right people during intense labor shortages. Its team grew to include Dr. Robert Hitchcock, a University of Utah microbiology professor and Light Line's chief technology officer. It also retained three former Fresenius Medical engineers and senior executives to assist with the dialysis product.

With the addition of these new team members, Light Line employees refined the product design in 2022 to improve manufacturability, product safety and performance as they prepare to submit the design for FDA approval.

"Our 2023 goal is crystal clear: we will submit our first 510(k) for FDA clearance on the Peritoneal Dialysis PhotoDisinfection System™," Farrar said. "That means doing ALL the work required for the FDA submission, including producing our first production units for the required verification and validation testing."

In the last five years, Light Line Medical has gone from an undergraduate research project to a budding company with a product that upon launch will impact the lives and health of people across the globe in part due to the help of the University of Utah and the PIVOT Center.

Farrar added, "In addition to providing the culture of innovative thinking that inspired the undergraduate students to identify the opportunity, the University of Utah and the PIVOT Center have provided the resources and mentorship needed to take our technology from an idea to a prototype."

The Master of Business Creation program

Providing resources that reduce the risk of starting a company and give founders a jump-start toward achieving a profitable enterprise

The University of Utah's Master of Business Creation (MBC) program assists founders as they grow their companies through innovative, application-focused curriculum and access to mentoring, grants, and scholarships.

The unique program combines the best parts of a business accelerator and a graduate business-degree program to help entrepreneurs advance their startup companies. Founders receive personalized, in-depth support and resources while also taking classes on related topics from renowned faculty at the top-ranked David Eccles School of Business. The program is available both online and in person.

"Our goal is to provide the same quality learning across both programs," said Taft Price, a co-director of the MBC program and a professor in the Department of Entrepreneurship & Strategy. "By offering our content both in person and online, we will meet the needs and schedules of a wider variety of founders than ever before."

MBC founders enter the program—provided in partnership with the Lassonde Entrepreneur Institute and the Department of Entrepreneurship & Strategy—with a viable startup, and once the program begins, it's full steam ahead on working to improve their businesses. They spend their time cultivating their ideas while accessing classes, people and resources that will help them develop their concept and make it successful.

The program supports a variety of business types and ideas. For example, the 2022-23 cohort of founders has launched 22 companies ranging from the production of bioactive proteins created in South Africa to a product-design company focused on the needs of people with disabilities.

Founders in the MBC program gain access to resources that support their startups, including working space, exclusive access to experts and funding, and more. The PIVOT Center offers its expertise as the IP center at the U to file trademarks for MBC founders. With PIVOT's assistance, students learn how to protect IP and receive a trademark upon completion of the program. These resources reduce the risk of starting a company and give founders a jump-start toward achieving a profitable enterprise.

Founders spend their time cultivating their ideas while accessing classes, people and resources that will help them develop their concept.

22

companies launched by 2022-23 cohort

Robin Shaw

Heart disease is the major cause of death in the United States, yet there are very few new treatments or therapies for failing hearts. Robin Shaw said that as a cardiologist, "it's embarrassing how few therapies exist" in light of the high health toll associated with failing hearts. In his work, he's made heart failure the core of his research and, more specifically, cardiac muscle biology and understanding what happens when muscle becomes diseased.

"Essentially we are learning about the mechanisms of heart failure and arrythmias and developing therapies to treat both," said Shaw, a professor of medicine who joined the University of Utah in 2019 and now directs the Nora Eccles Harrison Cardiovascular Research and Training Institute (CVRTI). As his and other CVRTI labs delve into the details behind heart failure, he said they "let basic investigation of fundamental biology lead us to discovery and then development of clinical therapies."

But letting science lead the way is easier said than done, according to Shaw. In his career, that means having to pivot when he gets an unexpected answer from his research. "Since the activity of the lab is based on testing mechanistic hypotheses, when we don't get the answer we're expecting, we accept we have to look in another direction. The value of rigorous science is that we get definitive answers: yes or no."

Before joining the U, Shaw and TingTing Hong, who is now a University of Utah professor as well, discovered a molecule they expected would make essential and classic membrane domains in a heart muscle cell. They spent years researching and asking if the expected behavior of the molecule was the reality. "The answer was a definitive no: the molecule existed yet did not do what we thought it did, and so we struck out."

Or so they thought. When they went back over the data, they discovered that rather than making large structures in the heart muscle cells, the molecule made small, essential microdomains that collect critical proteins that determine how well the heart can contract and relax. The molecule they were studying is lost in heart failure, and they learned that by replacing it with gene therapy, failing hearts will regain their organization and function. That original "definitive no" caused Shaw and his team to pivot, and they instead found something much more important. "We now have what we believe is a very promising gene therapy for heart failure which originated from a failed experiment," he said.

Shaw hopes this new therapy will combat the lack of treatment options for patients with failing hearts. Based on pre-clinical studies, the developing therapy "can restore failing hearts to normal function, and we will save lives."

> **"Essentially we are learning about the mechanisms of heart failure and arrythmias and developing therapies to treat both."**

TingTing Hong

As TingTing Hong says, "the career of a researcher is up and down." Hong, an associate professor of pharmacology and toxicology at the University of Utah, studies the structural organization of cardiomyocyte, or heart muscle cells, and how these structures impact **heart function**. Hong compares her career and research to catching waves. "Sometimes we encounter difficulties, but we always see how the data lead us to the next step," she said.

In her research, Hong and her lab identified a microdomain organized by a membrane binding protein that helps the heart contract and relax. This microdomain and protein are impaired during heart failure, resulting in worsened cardiac contraction and relaxation. They are now working to target this microdomain using gene therapy to introduce outside genes and proteins to improve cardiac function.

"We always see how the data lead us to the next step."

Early in her research journey, Hong said, they didn't expect to be able to use the protein for therapeutics. "We first found this protein was associated with ways heart failure is reduced and is responsible for the structural change," she said. "At the time we were just like 'Oh, let's give it a try' and didn't realize it can actually work."

In addition to pivoting based on new discoveries, Hong and her team found some of their initial beliefs about the protein turned out to be the complete opposite after further research. For example, they thought the blood levels of the cardiac protein would be higher in heart attack patients than in normal patients, but their studies later proved that it's higher in the blood of normal patients and drops in blood from patients with heart failure. "In the beginning we thought it's a release from damaged muscle cells, but now we see it's an equilibrated continuous release process," she said. "We changed in a totally different direction."

Hong hopes her research will offer a new therapeutic option for heart failure patients. "If we can just bring back this protein by gene therapy or potentially new methods of delivery, then we can rescue their heart function. That will really improve both survival and the life quality of patients with heart failure."

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Stopping blood flow to start healing

Fluidx Medical Technology is working on an innovative solution to improve on products and provide better patient care.

Doctors often need to stop blood flow to a particular area when treating patients, such as cutting off blood supply to cancerous or benign tumors, repairing blood vessel malformations, treating uterine fibroids, or as an alternative to surgery for polycystic kidney disease. While there are many existing methods to stop the flow – like coils, microparticles, beads and liquids – none of them are perfect.

For example, coils might not provide reliable long-term blockage, and microparticles can be hard to control. University of Utah spinout company Fluidx Medical Technology is working on an innovative solution to improve on these earlier products and provide better patient care. This year the company hit a major milestone in completing a clinical trial in New Zealand.

The first-in-human trial demonstrated the safety of Fluidx's GPX Embolic Device as well as early indicators of performance across a range of medical scenarios. Now, the company is planning a multi-center trial in the United States and working with the FDA to gather the necessary data to satisfy the agency's regulatory requirements. "We have a really unique and better material that offers some nice advantages for the physicians and patients as well," said Libble Ginster, Fluidx Medical Technology CEO.

The innovative GPX Embolic Device uses a specially formulated polymer mixture, which is injected into a blood vessel. After injection, the liquid firms up into a gel, fully blocking the vessel and stopping the flow of blood. The material contains a positively charged polymer and a negatively charged polymer mixed in water. It also contains the metal tantalum, which enables doctors to see what happens after it's injected, using X-ray fluoroscopy.

Prior to entering the body, the ionic properties of the polymers prevent them from binding to each other and solidifying. "It stays in a liquid form in the syringe, and it stays in a liquid form in the delivery catheter," Ginster said. "Once in the bloodstream, however, the chemical environment inside the body allows the polymers to cling together, forming a malleable gel. As it solidifies, the gel follows the flow of the blood vessel, conforming to the exact shape and size of the vessel to form a plug that blocks off the route. "We refer to it as an electrostatic gel," Ginster said, "that is the final product that sits in the vessels."

The advantage of liquids is that they conform to the shape of the vessel and provide a long-lasting stoppage, but current liquid embolization products are tricky to prepare and use safely. "One is essentially super glue," Ginster said. "It works very well in certain areas, but you could glue catheters in place if you aren't careful." The second main type of liquid requires a highly toxic solvent and is unpleasant for the patient.

"Our product has a totally different solidifying mechanism of action," Ginster said. "It's a much easier product to prepare and to deliver from the physician standpoint than other products that are out there today." The inclusion of tantalum gives it better visibility inside the body than many of these existing products, which can be hard to track after insertion.

Jim Hotaling

When Dr. Jim Hotaling says he has "done a bunch of different things to optimize care for men's health and male fertility," he really means it. As a urologist at University of Utah Health, he sees patients, performs surgeries, runs big data research groups and commercializes technologies based on that research. From studying the genetics of **male infertility** to developing an FDA-approved, at-home urologic test, his work all comes back to that goal of optimizing care.

His research into genetics and male fertility led him on an interesting path as he sought out grants. Hotaling initially applied for around 10 different grants to support his early efforts to understand how gene mutations affect both male infertility and overall health, but despite getting close a few times, the research never received funding. At the time, they were "working with The Utah Population Database (UPDB) at Huntsman Cancer Institute and using more of a sort of demography, big data set analysis," he said.

In order to get the funding he needed, it turned out Hotaling needed to pivot. He partnered with Aaron Quinlan, a U professor of human genetics and biomedical informatics, and Ki Aston, the IVF laboratory director at the U, to take a different approach and delve more deeply into the genetics. With Quinlan and Aston's help and this new direction, the project was "funded the first time we submitted it," he said.

Studying the genetics of infertility is challenging because there's no infertility gene, and even if there was, Hotaling said it would "take itself out of the gene pool." The team is now looking at the genetic underpinnings and risk factors as well as environmental exposures to understand who is at risk of having genetic issues that could lead to infertility.

With this research, Hotaling hopes to help "infertile men have kids and help them have the healthiest kids they can." As a clinician with experience starting two companies based on his research, Hotaling has a unique perspective into what patients need and how he can help both as a doctor and as an entrepreneur. "I had to call a patient this morning and say, 'You're never going to have your own kids.' And there's nothing that makes you feel like a bigger failure that that," he said. "What motivates a lot of this is that human moment."

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