Transfer to Transform

OFFICE OF TECHNOLOGY COMMERCIALIZATION AT NATIONWIDE CHILDREN’S HOSPITAL | 2022

When your child needs a hospital, everything matters.
OUR MISSION

The Abigail Wexner Research Institute at Nationwide Children’s Hospital is dedicated to enhancing the health of children by engaging in high-quality, cutting-edge research according to the highest scientific and ethical standards.

The Office of Technology Commercialization at Nationwide Children’s facilitates the transfer of new technologies, research and innovations to outside partners to benefit pediatric care, our community and the general public.
AFFILIATIONS

Rev1 Ventures partners with the Abigail Wexner Research Institute at Nationwide Children’s Hospital to accelerate the formation and growth of life science companies in central Ohio. Through our partnership, we seek out high growth opportunities and advise entrepreneurs who are developing innovative therapies and technologies at Nationwide Children’s. The goal is to improve children’s health in central Ohio and throughout the world by catalyzing ideas developed by innovators and researchers who may provide solutions that improve patient outcomes.

As Ohio’s bioscience, health and life sciences membership and development organization, BioOhio is focused on convening the state’s outstanding assets to accelerate the growth of its globally competitive bioscience ecosystem. High on this list of assets is pediatric research, in which Nationwide Children’s exhibits excellence every day. The Abigail Wexner Research Institute at Nationwide Children’s has been a BioOhio Leadership Member for nearly 25 years.

OhioX is Ohio’s statewide technology and innovation partnership dedicated to helping make Ohio a leading tech hub. OhioX powers connections, tells impactful stories, and advocates for growth on behalf of Ohio technology and innovation. As a founding member of OhioX, Nationwide Children’s joins industry-leading organizations across Ohio in building the future.
MESSAGE FROM LEADERSHIP

Matthew McFarland, RPh, PhD
Vice President of Commercialization and Industry Relations
Nationwide Children’s Hospital

At Nationwide Children’s Hospital, one of our pillar values is to be agile and innovative. This is evident in our culture of innovation and the work of our world class clinicians and scientists, who are considered thought leaders in their respective fields.

The Office of Technology Commercialization exists to ensure that innovative work is given the opportunity to translate beyond our walls and into the world. New technologies drive economic development in our local, national and global ecosystem, and most importantly, improve pediatric care. Gene and cell therapy, infectious disease mitigation platforms, medical devices, and advanced digital and virtual reality tools are just a few examples from our pipeline.

Over the last 15 years, we have grown our commercialization enterprise at an impressive rate by any standard. Our total deal flow for out-licensing Nationwide Children’s technologies increased by more than 900%. On average, we generated $26 million in commercialization revenue annually from 2017 to 2021. Achieving this level of commercial activity has required tremendous effort and commitment from the organization and our leadership.

While the commercial success we have experienced supports our sustainability, its returns often fall short of the total investment necessary to grow and maintain a research enterprise such as ours. So why do we do it? We do it because we are passionate about making a difference in the lives of our patients and children around the world.

I am humbled to work for an organization that demonstrates its passion through its actions. I am inspired by the ongoing investment in technology transfer at Nationwide Children’s that creates a progressive and lasting impact on the lives of children everywhere. I hope you, too, will be inspired by the stories of novel advances, exciting new technologies and job-producing startups in the following pages of this report.
DENNIS DURBIN, MD, MSCE, NAMED PRESIDENT OF AWRI

Dennis Durbin, MD, MSCE, who joined Nationwide Children’s Hospital as its first chief scientific officer in 2018, became the third president of the Abigail Wexner Research Institute (AWRI) at Nationwide Children’s on March 1, 2022. His appointment follows the retirement of John Barnard, MD, from the role.

“During Dr. Barnard’s nearly 20-year tenure, research at Nationwide Children’s grew exponentially, with a four-fold increase in National Institutes of Health funding and an expansion of our research faculty to more than 200 investigators,” says Tim Robinson, chief executive officer of Nationwide Children’s Hospital. “Dr. Barnard’s leadership brought an impressive array of discoveries that have resulted in even higher-quality patient care, including the first systemic gene therapy approved by the U.S. Food and Drug Administration (FDA), and more than 16 startup companies are translating our research into clinical practice. Dr. Durbin has large shoes to fill, but we could not have chosen a better leader to continue our legacy of high-impact research into the future.”

Dr. Barnard was a transformational leader who guided AWRI to become one of the most important research institutions of its kind in the country. Through his vision for effectively translating discoveries from the lab to patients’ bedsides, Nationwide Children’s established the OTC and developed core capabilities — regulatory affairs, animal resources, clinical research services, high-end computing and more — in house. The robust infrastructure formed under the collaborative leadership of Drs. Barnard and Durbin allows Nationwide Children’s to support every stage of therapeutic development and technology commercialization.

Commercialization success stories — novel therapies, medical devices and diagnostic tests that have been created by innovators at Nationwide Children’s and brought to market to improve care for children around the world — are a testament to the pioneering minds who helped build this ecosystem and those who will continue to support and lead it. The OTC team is excited to continue to drive technology commercialization at Nationwide Children’s under the leadership of Dr. Durbin.

“The support of institutional leadership has been a cornerstone of our commercialization success at Nationwide Children’s. The OTC is thrilled with Dr. Durbin’s appointment to this position and excited about the possibilities of what we will achieve under his leadership.”

— Matthew McFarland, RPh, PhD
Vice President of Commercialization and Industry Relations
The Abigail Wexner Research Institute (AWRI) is organized into centers of emphasis and the Institute for Genomic Medicine, all of which facilitate interdisciplinary team science by transcending traditional academic boundaries. The structure supports discovery, enabled by outstanding shared resources. Each center or institute is home to talented faculty members, staff, graduate students, residents, postdoctoral fellows and other students.

- Battelle Center for Mathematical Medicine
  Veronica Vieland, PhD, Director
- Center for Biobehavioral Health
  Cynthia Gerhardt, PhD, Director
- Biopathology Center
  Nilsa Ramirez, MD, Director
- Center for Cardiovascular Research
  Vidu Garg, MD, Director
- Center for Childhood Cancer and Blood Diseases
  Stephen Lessnick, MD, PhD, Director
- Center for Clinical and Translational Research
  William Smoyer, MD, Director
- Center for Gene Therapy
  Kevin Flanigan, MD, Director
- Center for Child Health Equity and Outcomes Research
  Deena J. Chisolm, PhD, Director
- Center for Injury Research and Policy
  Gary Smith, MD, DrPH, Director
- Center for Microbial Pathogenesis
  Lauren Bakaletz, PhD, Director
- Center for Perinatal Research
  Lynette K. Rogers, PhD, Interim Director
- Center for Regenerative Medicine
  Christopher Breuer, MD, Director
- Center for Vaccines and Immunity
  Christopher Walker, PhD, Director
- The Steve and Cindy Rasmussen Institute for Genomic Medicine
  Richard Wilson, PhD, Executive Director
  Elaine Mardis, PhD, Co-executive Director

At the Abigail Wexner Research Institute, collaboration, discovery, translation and team science define us. They are our foundation as we seek answers on behalf of children everywhere. Our researchers’ dedication and commitment to the common goal of improving the health and quality of life for children and their families enables them to work together to accomplish more than could be imagined independently. In the pages that follow are stories about the tremendous progress made possible by our culture, resources and integration with our world-class clinical teams.
RESEARCH GROWTH AT NATIONWIDE CHILDREN’S

2021 EXTERNAL AWARDS

<table>
<thead>
<tr>
<th>Source</th>
<th>2021 Funding (in millions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Program</td>
<td>$1.4</td>
</tr>
<tr>
<td>Industry</td>
<td>$15.2</td>
</tr>
<tr>
<td>Other</td>
<td>$29</td>
</tr>
<tr>
<td>Federal Other</td>
<td>$37.5</td>
</tr>
<tr>
<td>NIH Prime</td>
<td>$51.8</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>$134.9</td>
</tr>
</tbody>
</table>

RESEARCH BY THE NUMBERS

<table>
<thead>
<tr>
<th>Category</th>
<th>2019</th>
<th>2020</th>
<th>2021</th>
</tr>
</thead>
<tbody>
<tr>
<td>Principal Investigators*</td>
<td>207</td>
<td>208</td>
<td>223  *</td>
</tr>
<tr>
<td>Research Fellows</td>
<td>71</td>
<td>71</td>
<td>92</td>
</tr>
<tr>
<td>Graduate Students</td>
<td>38</td>
<td>42</td>
<td>57</td>
</tr>
<tr>
<td>Employees</td>
<td>1583</td>
<td>1534 **</td>
<td>1460</td>
</tr>
<tr>
<td>Publications</td>
<td>1357</td>
<td>1600</td>
<td>1633</td>
</tr>
</tbody>
</table>

*Includes faculty from the Abigail Wexner Research Institute and faculty from Nationwide Children’s Hospital with $50,000 or more in research funding support.

**In 2020, Andelyn Biosciences became a separate entity, resulting in approximately 100 employees moving from Nationwide Children’s to Andelyn Biosciences.
RESEARCH FACILITY HIGHLIGHTS
Research Building I (the Wexner Institute for Pediatric Research) contains 136,580 square feet of dedicated research space contiguous with Nationwide Children's clinical facilities.

Research Building II provides 164,016 square feet of additional space, including a 200-seat amphitheater, that is also contiguous with the clinical facilities.

Research Building III is 238,914 square feet and includes a 75-seat conference facility. Research Building III is certified by the U.S. Green Building Council Leadership in Energy and Environmental Design (LEED) program for sustainable building design.

MAIN CAMPUS HIGHLIGHTS
• 1,563,577 square feet of inpatient space.
• 406,751 square feet of outpatient space.
• 539,510 total square feet of research space.
• 759,447 square feet of education and support areas.
• Largest neonatal network and provider of inpatient pediatric surgeries in the United States.*

*Most recent data from CHA-member pediatric hospitals, based on highest number of ICU beds and inpatient surgeries.
RESEARCH BUILDING IV
Research Building IV is currently under construction. It will serve as a companion to Research Building III, and the buildings will be connected through a common entry atrium and on every floor, enabling the two buildings to function as one complex. The new building will add approximately 285,000 square feet to Nationwide Children’s dedicated research space. Research Building IV is anticipated to open in 2023.

“At Nationwide Children’s, we are building world-class research facilities to support our continued growth and success. Our growing facilities will help us to reach our aspirations, of developing new, life-changing therapies and creating the best possible outcomes for children around the world.”

– Dennis Durbin, MD, MSCE, president of the Abigail Wexner Research Institute
**Abeona Therapeutics**
Abeona Therapeutics, formed in early 2013 based on gene therapy technologies developed at Nationwide Children’s Hospital, is a clinical stage company initially focused on developing a cure for Sanfilippo syndrome, MPS IIIA and MPS IIIB, rare genetic disorders caused by the body’s inability to properly break down certain sugars. These diseases lead to progressive muscular and cognitive decline in children after the age of 2 years. With no cure or approved treatments, children with Sanfilippo syndrome usually die before the age of 20. Two separate multi-site phase I/II clinical trials for MPS IIIA and MPS IIIB are underway to evaluate the safety and efficacy of the treatment.

**Andelyn Biosciences, Inc.**
Andelyn Biosciences is a viral vector contract and development manufacturing organization. It was established in 2020 as a spin-out of Nationwide Children’s Hospital’s manufacturing division, which has expertise in manufacturing several adeno-associated virus (AAV) serotypes of gene therapy products.

**AveXis**
AveXis, now part of Novartis Gene Therapies, is a commercial gene therapy organization developing treatments for patients with neuromuscular diseases, including Nationwide Children’s Hospital’s licensed programs for Rett syndrome, a genetic form of amyotrophic lateral sclerosis (ALS), and spinal muscular atrophy (SMA), a motor neuron disease that is the leading genetic cause of death of children under the age of 2. The SMA gene therapy technology allows for the delivery of a replacement gene to target motor neurons throughout the brain and spinal cord. The gene therapy product for SMA, Zolgensma®, was approved in mid-2019 by the Food and Drug Administration.

**Celenex**
Celenex is a clinical stage gene therapy company targeting Batten diseases and other genetic diseases. In late 2018, Celenex was acquired by Amicus Therapeutics, a biotechnology company focusing on rare and orphan diseases. Phase I/II clinical trials for Batten diseases CLN3 and CLN6 are underway at Nationwide Children’s Hospital.

**Clarametyx Biosciences**
Clarametyx Biosciences is developing a platform therapeutic for the eradication of bacterial biofilms, which are responsible for approximately 80% of human bacterial infections. Their lead composition CMTX-101 is a monoclonal antibody that causes rapid biofilm collapse, enabling host immune clearance and potentiating antibiotic activity.
Deep Lens
Deep Lens is augmenting VIPER, one of the world’s first digital pathology cloud platforms, to include new features. For over 10 years, VIPER has allowed pathology groups to collaborate on groundbreaking cancer research across dozens of cancer types. Based on feedback from hundreds of expert global users, Deep Lens is enhancing the system to include clinical trial enrollment, AI-powered image detection and workflow support, telepathology, cloud storage and built-in APIs for integration by hardware and software vendors and biopharma companies.

ENTvantage Dx
ENTvantage Dx provides primary care physicians and otolaryngologists with rapid, in-office diagnostic tests to determine the cause of ear, nose and throat illnesses. The technology was developed as a result of the research collaboration between The Ohio State University and Nationwide Children’s Hospital, for rapid diagnosis of bacterial sinusitis. ENTvantage Dx is currently developing this technology to be used as point-of-care for patients with symptoms of sinusitis.

Invirsa
Invirsa is developing a unique, broad platform based on a naturally occurring small molecule (INV-102) that has demonstrated enhanced immune response to infection. INV-102 not only reduces viral infection, and potentially bacterial replication, it also reduces inflammation, while enhancing the body’s wound healing response. Invirsa’s technology is first being developed in the ophthalmology and pulmonary space in partnership with the Biomedical Advanced Research and Development Authority (BARDA) of the Office of the Assistant Secretary for Preparedness and Response in the U.S. Department of Health and Human Services.

LittleSeed
LittleSeed, Inc. was formed in 2018 in Powell, Ohio, with the goal of delivering clinically driven, evidence-based fun to pediatric patients. The foundational technology, Voxel Bay, was developed by a team of clinicians and game designers at Nationwide Children’s Hospital. Voxel Bay provides an interactive virtual reality platform designed to distract and calm children undergoing uncomfortable medical procedures. The Voxel Bay VR platform is being expanded to include other virtual environments and games tailored to specific needs within the pediatric environment.

LYST Therapeutics
LYST Therapeutics, based in Columbus, Ohio, was founded in 2017 to develop a platform technology for treatment of fibrotic diseases. The technology, invented by researchers in the Center for Tissue Engineering at Nationwide Children’s Hospital, is a novel immunomodulatory therapeutic antibody and has potential applications in treating stenosis, myocardial infarction and other conditions involving fibrosis.
Milo Biotechnology
Milo Biotechnology was founded in 2012 to develop a therapy that would increase muscle strength and improve the quality of life of muscular dystrophy patients and is based on a discovery by scientists at Nationwide Children’s Hospital. The therapy uses an adeno-associated virus (AAV) delivered follistatin protein, which inhibits the activity of myostatin, a protein that impedes muscle differentiation and growth. Phase I/II clinical trials evaluating the safety and efficacy of Milo’s follistatin therapy in patients with Becker muscular dystrophy, Duchenne muscular dystrophy and Inclusion Body Myositis took place at Nationwide Children’s Hospital.

Myonexus Therapeutics
Myonexus Therapeutics, a startup formed in 2017, is a clinical stage gene therapy company developing first ever treatments for limb-girdle muscular dystrophy (LGMD) types 2D, 2B, 2E, 2L and 2C based on research at Nationwide Children’s Hospital, a leader in muscular dystrophy gene therapy discovery and translational research. In early 2019, Myonexus was acquired by Sarepta Therapeutics.

NephKey Therapeutics
NephKey Therapeutics is focused on modifying existing therapeutics for use in the treatment of kidney disease in children. The company intends to protect development of a new formulation of an adult diabetes drug to treat patients with childhood nephrotic syndrome, using a 505(b)(2) new drug application (NDA) to the U.S. Food and Drug Administration (FDA). A large, multi-center clinical trial of this new formulation is under discussion with the FDA.

Scioto Biosciences
Scioto Biosciences is a clinical stage company founded in 2017 to develop treatments for diseases associated with microbial dysimbiosis. The technology platform, developed by researchers at Nationwide Children’s Hospital, is a novel formulation that primes the colony-forming mechanisms of probiotic bacteria by combining beneficial bacteria with polysaccharide microspheres. These natural mechanisms induce biofilm formation, enhance probiotic function and allow for non-spore-forming bacteria to survive passage through the gastrointestinal system. Among the first therapeutic indications being pursued is necrotizing enterocolitis, a high-morbidity disease that affects 7% of premature births.
smallTalk
Ohio-based startup smallTalk is developing the SmallTalk™ platform to enrich the neurological development of babies who don’t have regular, consistent access to their parent’s voice. Based on technology developed at Nationwide Children’s Hospital, the SmallTalk™ device is a unibody Bluetooth-enabled speaker that transmits the parent’s recorded voice with the appropriate sound characteristics to provide a clinical, therapeutic effect.

Tasseogen
The Tasseogen platform relies on the genome dashboard technology developed at Nationwide Children’s Hospital to allow researchers or clinicians to upload genome sequencing data and interactively explore the data to identify gene variants, if any, that may be causal for a patient’s disease. Tasseogen and the Information Technology (IT) Research and Innovation team at Nationwide Children’s received an Ohio Development Services Agency Technology Validation and Startup Fund (TVSF) Phase I award in 2020.

Zotarix, LLC
Zotarix, LLC, is a Columbus-based startup focused on patient safety during surgical procedures. Their first-in-kind product is a disposable medical device which provides protection against thermal and physical injury to the patient’s lips during oral surgery.
When our doctors, nurses, researchers and other staff members have an idea, they head to our Office of Technology Commercialization. Together, we take these ideas and innovations and translate them into the commercial sector, bringing about new patents, startup companies and innovations. Our team supports innovators and their ideas through every stage — from the clinic or the lab to the market and back to the bench and bedside.
In 2021, Nationwide Children’s Hospital announced the most ambitious strategic plan in its 129-year history: a five-year, $3.3 billion commitment to revolutionizing the next frontier of pediatric health and transforming health outcomes for all children.

Nationwide Children’s aggressively supports innovation and the discovery of new knowledge. In turn, successful commercialization is critical to achieving the hospital’s strategic goals.
One of the key challenges in congenital heart surgery is that current grafts used to correct heart defects are not living grafts — they don’t grow with the patient or function like a native blood vessel. In many cases, kids outgrow these grafts and require additional operations in the future.

That’s what Christopher Breuer, MD, director of the Center for Regenerative Medicine in the Abigail Wexner Research Institute at Nationwide Children’s Hospital, has spent his career trying to overcome.

Nearly 30 years ago, Dr. Breuer and Toshiharu Shinoka, MD, PhD, co-directors of the Tissue Engineering Program at Nationwide Children’s, began working together to use tissue engineering techniques in congenital heart surgery. They developed one of the first tissue-engineered blood vessels and the first tissue-engineered valve, and in 2012, just before moving to Nationwide Children’s, Drs. Breuer and Shinoka implanted the first tissue-engineered vascular graft (TEVG) in a human patient in the United States as part of a landmark clinical trial, becoming the first in the world to engineer blood vessels and implant them in human infants to repair congenital heart defects. Since then, the surgeons and their colleagues have implanted three additional TEVGs in children with single ventricle congenital heart anomalies.

A TEVG is seeded with a patient’s own cells, implanted and used as a scaffold for native tissue to grow over before the scaffold biodegrades. International clinical trials have allowed Dr. Breuer and his colleagues to meticulously fine-tune the technology, which has excellent long-term performance, grows with children as they age and preserves the natural mechanical properties of blood vessels that allow them to dilate and constrict.

Now, Nationwide Children’s is home to the first human trial approved by the U.S. Food and Drug Administration (FDA) to investigate the safety and effectiveness of using tissue engineering to repair congenital heart defects.

“The way we’ve approached bringing tissue engineering to the clinic is systematic and extremely cautious,” says Dr. Breuer, who is also the Nationwide Foundation Endowed Chair of Surgical Research and director of tis-

“IT’S BEEN ABOUT 10 YEARS SINCE I STARTED THINKING ABOUT THIS APPROACH. BUT GOING ABOUT THIS SO CAREFULLY AND WITH SO MANY INCREMENTAL IMPROVEMENTS ALONG THE WAY HAS REALLY ALLOWED THIS TO COME TOGETHER AS THE SAFEST AND MOST EFFECTIVE TISSUE ENGINEERING SOLUTION POSSIBLE RIGHT NOW.”

— Christopher Breuer, MD, director of the Center for Regenerative Medicine at Nationwide Children’s Hospital
sue engineering in the Center for Regenerative Medicine and Cell Based Therapies at The Ohio State University Wexner Medical Center. “By being this deliberate, we will end up with a safe and reliable approach.”

That thorough research has yielded another innovation that could dramatically improve the technology’s accessibility once approved by the FDA: a closed, disposable cell-seeding system.

“Our trial is going well, but even if we get approval for the current graft and don’t have a closed system, they can only be used in a handful of centers, which really limits their availability,” says Dr. Breuer.

Initial versions of TEVGs have required a highly controlled environment — a cleanroom meeting good manufacturing practice (GMP) standards, which is often staffed by dozens of people and requires a lot of money to build and even more to maintain. Even among large hospitals with established programs for the surgical treatment of congenital heart disease, many do not have GMP facilities, rendering TEVG virtually unavailable to those patients.

The closed system removes the requirement for a GMP cleanroom in order to seed the graft with a patient’s cells. A patient’s bone marrow cells can be extracted and directly transferred to the closed system, which filters the cells, seeds the scaffold and prepares the graft for implantation — all without leaving the operating room.

“The closed system speeds up the process, decreases the cost and increases safety,” explains Dr. Breuer. “And it can be done anywhere, which makes the utility of tissue engineered grafts much greater. If our system gets approved, it would be available for everyone as the first man-made graft with growth capacity, a big step in bringing tissue engineering to the clinic.”

Dr. Breuer and his team focus primarily on one application of TEVG: the Fontan procedure in children with congenital heart disease, which is performed on up to 4,000 babies in the United States each year. Once the product is available, however, Dr. Breuer believes it could be applied to other types of the nearly 10,000 congenital heart operations performed each year. With additional adaptations, the product could also be appropriate for adult cardiac populations and for use in adult and pediatric tracheas, ureters and intestines.

The system also allows for either an off-the-shelf range of graft sizes or a fully customized scaffold approach, which would allow closed graft systems to be designed to the exact size and shape required for patients based on their preoperative imaging.

This innovative solution to the challenges of non-living grafts and the costly, complex approach to current TEVG options has been long in the making but promises a widely beneficial future for the field of tissue engineering.

“It’s been about 10 years since I started thinking about this approach,” says Dr. Breuer. “But going about this so carefully and with so many incremental improvements along the way has really allowed this to come together as the safest and most effective tissue engineering solution possible right now.”

FEATURED RESEARCH

Old Drug, New Use
How an adult diabetes drug became the hottest up-and-comer in the treatment of pediatric nephrotic syndrome

Nephrotic syndrome is one of the most common kidney diseases seen in children. In most cases the cause is unknown. Nephrotic syndrome involves damage to the filtering units of the kidneys (glomeruli) leading to massive protein loss in the urine (proteinuria). This results in low protein levels in the blood (hypoalbuminemia) and swelling in the body (edema).

For decades, the condition has had one mainstay treatment: glucocorticoids. Unfortunately, about 20% of children don’t respond to glucocorticoids and follow-up options are limited. Furthermore, steroids cause immunosuppression and have other significant side effects, especially when used repeatedly or over long periods of time — so much so that clinical practice guidelines often recommend limiting steroids to the shortest possible duration.

“I’ve been studying the molecular regulation of injury to podocytes — the key cells in the kidney’s filtration barrier — for more than 30 years, looking for novel treatments for childhood nephrotic syndrome,” says William Smoyer, MD, a pediatric nephrologist who is vice president of the Abigail Wexner Research Institute at Nationwide Children’s Hospital and director of its Center for Clinical and Translational Research. “I want to find out how and why glucocorticoids work — and why they sometimes don’t — so that I can find more effective and less toxic ways to treat these children.”

Dr. Smoyer’s research team realized glucocorticoids are taken up by cells’ steroid receptors and used to turn hundreds of genes on or off. They figured there might be other drugs that could do the same — without requiring the drug’s characteristic immunosuppression for a beneficial effect.

As it turns out, an entire class of adult diabetes drugs approved by the U.S. Food and Drug Administration (FDA) get into cells by binding to a similar receptor.

“We wondered if we could use already approved drugs for adults with diabetes to treat children with nephrotic syndrome,” says Dr. Smoyer. “If we could stimulate a similar healing process in podocytes using something other than glucocorticoids, we might be able to treat people without suppressing their immune systems and with less toxicity.”

Dr. Smoyer’s team wasted no time studying these approved drugs in podocyte cell cultures in the lab. When the diabetes drug pioglitazone looked promising, they moved to animal models and found similarly encouraging results.

“To our surprise, pioglitazone could reduce proteinuria almost as well as glucocorticoids,” says Dr. Smoyer. “That’s when we realized we had the real opportunity to repurpose pioglitazone for children with nephrotic syndrome.”

Although there are few technical barriers to use of an approved drug for a different indication, the research to confirm efficacy and develop a new formulation for children with nephrotic syndrome has been hard to finance. The drug wouldn’t be classified as a “new chemical entity” with the same patent protection as a brand-new drug; pioglitazone is now made by generic drug companies only.

Dr. Smoyer’s team, however, understood the potential clinical importance of the research and started publishing and sharing the findings at professional conferences. Undeterred by funding challenges and encouraged by immediate interest on behalf of his nephrology colleagues, a promising case study and even supportive outreach from the FDA, Dr. Smoyer hatched plans for a new company dedicated to the development of pioglitazone...
as a novel, non-immunosuppressive treatment for childhood nephrotic syndrome.

The Office of Technology Commercialization at Nationwide Children’s helped Dr. Smoyer file the patent. NephCure Kidney International, an organization that supports research to find effective treatments for nephrotic syndrome and other glomerular diseases, and of which Dr. Smoyer is a long-time board member, helped facilitate connections for company leadership. And Dr. Smoyer’s new company, NephKey Therapeutics, Inc., was born.

NephKey Therapeutics intends to protect development of a new formulation of the drug, specifically to treat children, using the FDA’s 505(b)(2) pathway.

“This drug has safety data from hundreds of thousands of people, but in this case, they’re the wrong people!” says Dr. Smoyer. “The FDA is very interested in the idea of repurposing a drug to address a significant unmet medical need for children, and their support is probably the best momentum we have going for us.”

A case series reporting further promising results of the drug’s use in children with nephrotic syndrome is pending publication. The full clinical trial is already under discussion with the FDA, and Dr. Smoyer estimates the first round of clinical trial work can be completed with less than $1M in additional funding.

“It took a long time to get to this point,” says Dr. Smoyer, “but things are finally coming together. I’m first and foremost a clinician, and this has been what I’ve been working toward for my entire career: a new and better treatment option for my patients.”


“I’M FIRST AND FOREMOST A CLINICIAN, AND THIS HAS BEEN WHAT I’VE BEEN WORKING TOWARD FOR MY ENTIRE CAREER: A NEW AND BETTER TREATMENT OPTION FOR MY PATIENTS.”

— William Smoyer, MD, vice president of the Abigail Wexner Research Institute and director of its Center for Clinical and Translational Research at Nationwide Children’s Hospital
Building Baby Brains With smallTalk: From Foreign Language Learning at Home to Bridging Gaps in the NICU

The best language learners on the planet are children — especially babies. The brain is most active in creating its language center, connecting neurons and creating the highways and pathways for processing language, during infancy. In fact, language learning begins in utero. The developing brain of a fetus starts to wire language circuitry around the speech sounds and rhythms of its mother’s voice. This process accelerates when a baby is born.

The brain does more language-associated wiring during the first year of life than any other time in a person’s life. These brain changes occur rapidly as a result of exposure to adult voices speaking to the baby in “infant-directed speech,” characterized by a higher pitch and more melodic, emotional tones.

Ohio-based startup smallTalk (formerly Thrive Neuromedical) is developing the SmallTalk™ platform to enrich the neurological development of babies who don’t have regular, consistent access to their parents’ voices. smallTalk has licensed technology developed at Nationwide Children’s Hospital that delivers recorded voices to infants via devices intended for use in the neonatal intensive care unit (NICU) and at home. These devices support critical brain development for language.

Around 10% of all infants spend some amount of time in the NICU, where they may be exposed to more passing adult speech and sounds of alarms and machinery than infant-directed speech during critical periods for language-associated brain development. This lack of exposure to infant-directed speech may, in part, be responsible for the documented association between NICU care and developmental language delays.

At Nationwide Children’s, where the average stay in the NICU exceeds 100 days, researchers developed and studied an infant-safe, unibody, Bluetooth-enabled speaker device to increase babies’ exposure to their caregivers’ voices with the appropriate sound characteristics to provide a clinical, therapeutic effect. The speaker can easily fit into an incubator and uses technology and volumes safe for babies and their sensitive ears.

Beginning this year, nurses and therapists in the NICU will be able to use a specially designed iPad application to help parents or caregivers record lullabies, songs or stories. Playlists of these recordings can be transferred wirelessly to egg-shaped speaker devices placed with the babies in the NICU and played for them several times each day.

The technology has also led to the development of an innovative foreign language learning product, the smallTalk Egg™, designed to help parents expose their babies to foreign language learning before age two.

“This is the only time of life when language learning actually helps babies brains develop differently. Infants
in bilingual or multilingual household environments develop much broader speech sound recognition capabilities. By 1 or 2 years of age, they’re able to hear and verbalize more speech sounds and adapt to those languages very quickly,” says Dean Koch, CEO of smallTalk.

Infants can be exposed to these songs and stories passively, but studies have shown the most effective changes to the brain occur during interaction. Because the smallTalk Egg™ comes with a sensor device which fits into three different commercially available types of pacifiers, infants can request additional content by sucking on their pacifiers during 20-minute educational sessions. As the infant sucks, they are rewarded with 10 seconds of the foreign language lullaby, which then fades away. The baby recognizes this contingency quickly and will happily engage for a 20-minute learning session.

“Our research on brain imaging and how babies process speech sounds found that 20 sessions of 10-20 minutes over a month or month and a half is all that’s required to make a real, lasting, positive brain change,” says Koch.

The smallTalk Egg™, which will also be available this year, will allow parents and caregivers to bring this brain-enhancing technology into their homes. Currently, content is available in seven languages for use on the smallTalk Egg™, and there are plans to expand to include more languages spoken around the world.

Dean Koch, CEO of smallTalk

*Images are compliments of smallTalk.*
Novel Approaches to Gene Therapies for Patients With Rare Genetic Diseases

Paul Martin, PhD, and his lab are currently developing two novel gene therapies, including a bicistronic platform approach for arresting — and reversing — GNE myopathy disease progression, which promise to generate hope for patients with rare diseases and their families.

According to the National Institutes of Health (NIH), nearly 7,400 diseases have been identified and classified as “rare” or “orphan” — “rare” because each afflicts fewer than 200,000 people in the United States and “orphan” because drug companies, unlikely to recoup research and development costs from such small patient populations, have historically found them too uncommon to invest in. Collectively, however, these diseases affect an estimated 30 million people in the United States alone — nearly 1 in 10 — and more than 300 million people worldwide. Fewer than 10% have treatment options approved by the U.S. Food and Drug Administration (FDA).

In the 1990s, the translation of basic research on viral vectors, including adeno-associated virus (AAV) vectors, to medical applications presented an exciting new approach to treating these patients. While gene therapy faced early setbacks, there have been a number of exciting developments since. Since FDA approval of AAVs in 2017, researchers at Nationwide Children’s Hospital and beyond have been on a quest to make treatment a feasible reality for patients with rare diseases.

Paul Martin, PhD, a principal investigator in the Center for Gene Therapy in the Abigail Wexner Research Institute at Nationwide Children’s Hospital and professor of Pediatrics, Physiology and Cell Biology at The Ohio State University College of Medicine, is one of those researchers. His novel work on translational approaches is rapidly progressing therapeutics for rare genetic disorders, with the ultimate goal of reaching a population of patients who have been historically left out of drug discovery research.

Lipase A Deficiency

Dr. Martin is currently developing two gene therapies: one for lipase A deficiency and one for a slow-progressing disease of the muscle called GNE myopathy.

“Lipase A deficiency, which is sometimes also called lysosomal acid lipase deficiency, is a rare, recessive genetic disorder that leads to loss of a lysosomal enzyme that breaks down cholesterol esters into cholesterol and triglycerides into free fatty acids,” says Dr. Martin. “In its absence, the balance of fats and cholesterol are perturbed, which leads to very significant health consequences for patients such as liver disease and predisposition to heart disease and stroke.”

While individuals with a partial deficiency, or cholesteryl ester storage disease, can survive through adolescence and even early adulthood, babies born with a complete absence of the enzyme, or Wolman disease, may not be able to live longer than a few months without intervention.

The only available FDA-approved therapy for these patients is an enzyme replacement therapy that typically must be delivered by infusion every two weeks. This replacement therapy is not a curative option and is difficult to maintain as a life-long therapy for many patients.
“We wanted to develop a gene therapy that would be more efficacious and allow us to have a single treatment that leads to long term benefits for patients,” says Dr. Martin.

At this stage, Dr. Martin and colleagues are preparing a paper for publication about satisfactory results from a proof-of-concept study of their gene therapy for lipase A deficient mice. This mouse model presents symptoms that are similar to those experienced by humans with cholesteryl ester storage disease. In the mouse model, the liver can be up to five-times larger than normal due to the deposition of fat in this organ.

“We’ve been able to show in our proof-of-concept study that we can reverse that process and bring the liver back to a normal, healthy state with a single-treatment gene therapy,” says Dr. Martin.

**GNE Myopathy**

Dr. Martin is also currently focusing on diseases of the muscle, including GNE myopathy, another rare, recessive disease. A mutation in the GNE gene causes progressive muscle weakness.

Gene therapies that deliver a gene replacement to stop disease progression have been shown to be safe and effective during clinical trials for some forms of muscular dystrophy. In the case of GNE myopathy, however, AAVs could allow a copy of the GNE gene without a mutation to be inserted into a patient’s cells, actually providing GNE gene function back to the patient. This type of gene therapy could be used to treat all patients with GNE myopathy, regardless of their particular genetic mutation, and once given, could arrest disease progression for decades — even a lifetime.

Dr. Martin says this approach, however, has significant limitations.

“While gene replacement therapies can arrest disease progression, they provide little promise for reversing the disease that’s already present,” says Dr. Martin. “When a patient is diagnosed, their muscles are already weakened. After a patient’s been treated, they may not get weaker, but they probably won’t get any better either.”

The current treatment landscape for patients with muscle diseases has led Dr. Martin to develop a bicistronic, or two gene, vector. This cutting-edge platform approach pairs the existing gene replacement function with an additional component.

“Our goal is not only to provide gene replacement, which will hopefully arrest the disease, but to provide a muscle building therapy on top of that, which will replenish and renew muscle tissues so they become bigger and stronger at the same time. The net effect is that hopefully we could reverse the loss of strength in patients over time,” says Dr. Martin.

Dr. Martin and colleagues began exploring this approach to treating GNE myopathy due to the disease’s slow progression, but they plan to expand the application of this bicistronic vector technology to include other diseases of the muscle, including forms of muscular dystrophy.

— Paul Martin, PhD, principal investigator in the Center for Gene Therapy at the Abigail Wexner Research Institute at Nationwide Children’s Hospital
Natural killer (NK) cells are lymphocytes, or white blood cells, and a component of the innate immune system. They release cytotoxic molecules to help destroy cancer cells and those that have been infected with invading pathogens. Activated NK cells can minimize the side effects and lifelong impacts of chemotherapy, improve outcomes for pediatric patients who receive bone marrow transplants and help those who are immunocompromised fight viral infections. Yet NK cells have historically been underutilized as immunotherapies. These cells are resistant to gene modification, and their clinical production has proved challenging, with existing approaches for collecting NK cells being prohibitively costly and allowing only low cell numbers to be infused.

Dean Lee, MD, PhD, a principal investigator in the Center for Childhood Cancer and Blood Diseases in the Abigail Wexner Research Institute (AWRI) at Nationwide Children’s Hospital and director of the Cellular Therapy and Cancer Immunology Program at Nationwide Children’s, has aimed to combat those limitations through pioneering research and a dedication to inventing new therapies. Dr. Lee’s innovations allow NK cells to be produced as an off-the-shelf product, and his work has paved the way for ongoing translational research and improvements to care for patients with cancer.

In 2021, the Office of Technology Commercialization (OTC) at Nationwide Children’s, along with hospital and research leadership, named Dr. Lee Nationwide Children’s Hospital Innovator of the Year. Since joining Nationwide Children’s in 2016, Dr. Lee, who is also a physician in the Division of Hematology, Oncology & Blood and Marrow Transplant at Nationwide Children’s and director of the Cellular Therapy and Cancer Immunology Program at Nationwide Children’s and The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC – James), has filed:

- 23 Invention Disclosures with the OTC.
- 18 applications for Provisional Patents with the United States Patent and Trademark Office (USPTO).
- 12 International Phase Patent Cooperation Treaty (PCT) patent applications.
- 45 National Phase PCT patent applications.

The NK cell technologies developed by Dr. Lee’s lab were licensed by a startup, CytoSen Therapeutics, in 2018. In 2019, CytoSen was acquired by Kiadis Pharma, and in 2020, Kiadis was acquired by Sanofi for $358M. This rapid series of acquisitions demonstrates the value of NK cell therapies.

Dr. Lee was honored during the OTC’s Innovation Week with a special video presentation at the AWRI Annual Research Retreat.

To learn more about Dr. Lee and his research, visit NationwideChildrens.org/OTCNews

Dr. Lee and his lab were recognized by research leadership for their achievements at a reception during OTC’s Innovation Week in November 2021.
The Abigail Wexner Research Institute at Nationwide Children’s Hospital is dedicated to enhancing the health of children by engaging in high-quality, cutting-edge research to generate novel ideas. The Office of Technology Commercialization (OTC) helps develop those ideas into promising new technologies and facilitates their transfer to external partners to advance the practice of pediatrics and general health care.

Our list of technologies developed by our innovative researchers and clinicians, which ranges from early-stage technologies to market-ready products, is diverse and ever-growing. Over 70% of our patent portfolio is licensed to companies for development and commercialization, and the number of active licensing agreements grew from seven active deals in 2012 to 89 active deals by the end of 2021. In 2021, the OTC assessed over 70 new invention disclosures, filed over 125 patent applications and completed 18 licensing deals.

As a result, our comprehensive portfolio of over 130 available technologies spans a wide array of research fields and categories of market applications.

**Biomarkers:** Novel biomarkers are measurable characteristics that have been newly identified as ways to detect and measure normal biological processes, pathogenic processes or responses to interventions.

**End User Innovation:** These innovations aim to improve clinical or business practices and patient outcomes and are being developed by those who will ultimately use them.

**Gene Therapies & AAV Production:** Gene therapy is the process of replacing impaired or harmful genetic material with new material, or machinery to make the new material, to treat various conditions, including neuromuscular and neurodegenerative diseases, developmental diseases, lysosomal storage disorders, ischemia and re-perfusion injury, neonatal hypertension, cancers and infectious diseases. Inventions in this space span production methodology to vector design and delivery.

**Therapeutics:** Innovative technologies for preventing or treating diseases include cell-based treatments like engineered CAR T and NK cells, protective vaccines and small molecules effective against indications like infection, cancer and allergy, to name a few.

**Tissue Engineering:** Tissue engineering combines scaffolding, seeded cells and biologically active molecules into functional tissues. Tissue engineering holds incredible potential for repairing birth defects, allowing a patient’s own cells to be used to “grow” new tissue or organs for repair.

**Research and Clinical Tools (and Other Technologies):** Clinical and research tools augment therapeutic or scholastic activities. These can include physical items like laboratory and surgical tools as well as intangible advancements like algorithms, operating procedures and training materials.
To learn more and find the right licensing opportunity for you, visit NationwideChildrens.org/AvailableTechnologies

Innovate IP
Search our entire technology catalog/library of licensable technologies disclosed to our office. Learn more about the technologies available in each category, the inventors behind the innovations and the licensing associates who manage them.

To license a technology, contact the assigned OTC representative or email Tech.Commercialization@NationwideChildrens.org.

IN-PART
Gain member-exclusive access to information regarding revolutionary technologies and connect with our industry experts to discuss licensing and commercializing these technologies.

Technology Showcase
Each March, the OTC highlights new inventions and startup companies generated from research at the Abigail Wexner Research Institute at Nationwide Children’s Hospital through a series of special presentations at its Technology Showcase event.

View past event recordings or register for an upcoming event to learn more about the new technologies that are available to license and the inventions that are already transforming care: NationwideChildrens.org/OTC-Events
OfficE of technOlogy commercialization LEadeRship

Matthew McFarland, RPh, PhD, Vice President of Commercialization and Industry Relations
Matthew.Mcfarland@NationwideChildrens.org | (614) 722-2701

Matthew joined Nationwide Children’s Hospital as director of the Office of Technology Commercialization (OTC) in 2012 and currently serves as vice president of commercialization and industry relations. He has a diverse background in drug discovery, business development, startup generation and funding, and strategic partnerships.

During his tenure at Nationwide Children’s, the OTC has experienced an increase in annual deal flow by 900%. Matthew brokered multiple strategic partnerships for Nationwide Children’s with industry and state partners and has been substantially involved in the recruitment and establishment of industrial partners in Columbus, Ohio. He designed and implemented novel deal structures with licensing partners to foster increased engagement and deployment of development resources into the institution.

Prior to joining Nationwide Children’s, Matthew was the associate director of commercialization in the Office of Technology Commercialization at the Purdue Research Foundation, where he oversaw the management of life science technologies including small molecule therapeutics, biological therapeutics, medical devices/implants and agricultural genetics. He received a bachelor’s degree in Pharmacy from Ohio Northern University and his doctorate in Medicinal Chemistry and Molecular Pharmacology from Purdue University. He also completed a postdoctoral research fellowship in translational genetics of neuropsychiatric disorders at the Institute of Psychiatric Research at the Indiana University Medical School.

His favorite invention is penicillin.

Margaret Barkett, PhD, Director
Margaret.Barkett@NationwideChildrens.org | (614) 355-2957

Margaret joined the Office of Technology Commercialization at Nationwide Children’s Hospital in February 2010 as a licensing associate. She currently serves as the office’s director of licensing. In her role with the office, Margaret manages the assessment, protection, valuation and out-licensing of a portfolio of intellectual property assets owned by Nationwide Children’s. She is also actively involved in managing many of the office’s relationships with both internal and external stakeholders.

Margaret has a bachelor’s degree in Biology from Emory University and earned her doctorate in Molecular and Cell Biology from Boston University, where she continued her training as a postdoctoral fellow. Her doctoral and postdoctoral research in cell death biology spanned different areas including cancer biology and development. Prior to joining Nationwide Children’s, she completed a full-time, one-year technology licensing internship at Massachusetts Institute of Technology focusing on medical devices and biotechnology.

Her favorite invention is the internet.

Susannah Wolman, Operations and Business Manager
Susannah.Wolman@NationwideChildrens.org | (614) 355-2818

Susannah joined Nationwide Children’s Hospital as the business compliance and finance coordinator in July 2016 and currently serves as the operations and business manager. In her role, Susannah manages the operational side of OTC as well as the office’s financial transactions.

Susannah has a bachelor’s degree in Criminology and Psychology from Marquette University. Her favorite invention is the public library.
OUR TEAM

David Bellamy-Bise, Disclosure and Compliance Coordinator
David.Bellamy-Bise@NationwideChildrens.org | (614) 722-4163

Education and experience:
• Bachelor’s degree from Kentucky Christian University.
• Over 12 years of administrative support experience in patient care, managed care and regulatory support services.

Role and responsibilities:
• Oversight and intake of invention disclosures.
• Management of reporting federally funded inventions and patents to federal agencies.
• Licensing team support.

Favorite invention: rollercoaster

Andrew Corris PharmD, JD, Senior Licensing Associate
Andrew.Corris@NationwideChildrens.org | (614) 355-1604

Education and experience:
• Bachelor's degree in Chemical Engineering with a minor in Chemistry from the University of Pittsburgh.
• Doctor of pharmacy degree from The Ohio State University.
• Law degree from Capital University.

Role and responsibilities:
• Management of intellectual property portfolio.
• Identification of potential industry and invention partners.
• License negotiation and post-license management.

Favorite invention: Slinky™

Jocelyn Eidahl, PhD, Senior Licensing Associate
Jocelyn.Eidahl@NationwideChildrens.org | (614) 355-2848

Education and experience:
• Bachelor's degree in Biology, minor in Chemistry from the University of Akron.
• Doctorate from The Ohio State University in Pharmaceutics and Pharmaceutical Chemistry.
• Postdoctoral training in the Center for Gene Therapy in the Abigail Wexner Research Institute at Nationwide Children’s Hospital.
• Internship in the OTC.

Role and responsibilities:
• Management of intellectual property portfolio.
• Identification of potential industry and invention partners.
• License negotiation and post-license management.

Favorite invention: baking powder
OUR TEAM

Deborah Lewis, Senior Intellectual Property Coordinator
Deborah.Lewis@NationwideChildrens.org | (614) 355-4569

Education and experience:
• Paralegal certificate from Blackstone Career Institute.
• Advanced intellectual property patent paralegal certificate from IPLegalEd.

Role and responsibilities:
• Management of intellectual property and patent portfolios.
• Mediation between external law firms, inventors and licensing staff.
• Management and coordination of legal documentation.

Favorite invention: Mr. Clean® Magic Eraser™

Geena Licata, BS, Senior Intellectual Property Coordinator
Geena.Licata@NationwideChildrens.org | (614) 355-4302

Education and experience:
• Bachelor’s degree in Nutrition from Marycrest University.
• Post-baccalaureate in paralegal studies from the University of Toledo.

Role and responsibilities:
• Management of intellectual property and patent portfolios.
• Mediation between external law firms, inventors and licensing staff.
• Management and coordination of legal documentation.

Favorite invention: iPad

Matthew Moscato, Alliance Manager
Matthew.Moscato@NationwideChildrens.org | (614) 355-8784

Education and experience:
• Bachelor’s degree in paralegal studies from the University of Cincinnati.

Role and responsibilities:
• Relationship management with commercial partners.
• Mediation between stakeholders at Nationwide Children’s and commercial partners.
• Management of effective transfer of technology to commercial market.

Favorite invention: bicycle

Kyle Murrah, PhD, Senior Licensing Associate
Kyle.Murrah@NationwideChildrens.org | (614) 355-4551

Education and experience:
• Bachelor’s degree in Biological Sciences with a minor in Genetics and Film Studies from North Carolina State University.
• Doctorate in Microbiology and Immunology from Wake Forest University.

Role and responsibilities:
• Management of intellectual property portfolio.
• Identification of potential industry and invention partners.
• License negotiation and post-license management.

Favorite invention: modern plumbing
OUR TEAM

John Westerfield II, Marketing and Business Coordinator
John.Westerfield@NationwideChildrens.org | (614) 355-1850

Education and experience:
- Bachelor’s degree in Mass Communication with a minor in Journalism from Saint Joseph’s College.
- Master’s degree in Business Communication from Spalding University.

Role and responsibilities:
- Management of OTC engagement efforts with multiple stakeholders, both internal and external.
- Management of outreach and publication efforts.
- Development and execution on marketing campaigns for select high priority Nationwide Children’s technologies.

Favorite invention: printing press

Stacy Yerington, JD, Agreements Coordinator
Stacy.Yerington@NationwideChildrens.org | (614) 355-0244

Education and experience:
- Bachelor’s degree in Human Development and Family Science with a minor in Psychology from The Ohio State University.
- Law degree from the University of Pittsburgh School of Law.

Role and responsibilities:
- Negotiation and administration of Material Transfer Agreements, Data Use Agreements and Confidential Disclosure Agreements.
- Management of agreements docket.
- Licensing team support.

Favorite invention: airplane

Amy Yoder, Senior Intellectual Property Coordinator
Amy.Yoder@NationwideChildrens.org | (614) 355-3477

Education and experience:
- Bachelor’s degree in Political Science from the University of Kentucky.
- Paralegal certificate from Columbus State Community College.

Role and responsibilities:
- Management of intellectual property and patent portfolios.
- Mediation between external law firms, inventors and licensing staff.
- Management and coordination of legal documentation.

Favorite invention: waffle maker
CONTACT US:

Office of Technology Commercialization
Nationwide Children’s Hospital
700 Children’s Drive | Columbus, Ohio 43205

Phone: (614) 355-2818 | Fax: (614) 722-2716
Email: Tech.Commercialization@NationwideChildrens.org
Web: NationwideChildrens.org/OTC