



**Boston Children's Hospital**  
Until every child is well™

# Technology & Innovation Development Office

# 2013

ANNUAL REPORT

# \$300M

NIH and Industry  
Research Funding

# \$9.6M

Gross Licensing Revenue

# \$7.4M

Net Licensing Revenue

# 29

Corporate Sponsored  
Research & Collaboration  
Agreements  
↑ 45%

# 34

License & Option  
Agreements ↑ 13%

# 144

Invention Disclosures

## About Boston Children's

Boston Children's Hospital is a 395-bed comprehensive center for pediatric health care. Boston Children's is home to the world's largest pediatric-focused research enterprise, and its discoveries have benefited both children and adults since 1869. More than 1,600 scientists, including seven members of the National Academy of Sciences, 13 members of the Institute of Medicine and 14 members of the Howard Hughes Medical Institute comprise our research community.

## About Technology & Innovation Development Office

Technology and Innovation Development Office (TIDO) helps translate the excellence of the laboratory research and clinical care at Boston Children's into lifesaving biomedical products, devices, software and procedures for the public benefit. TIDO is a team of highly motivated professionals with experience in academic and industry biomedical research, technology licensing, company startups, business and law. TIDO partners with biotechnology, pharmaceutical, diagnostic, IT and medical device companies at all stages to achieve its mission.

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TIDO reached new heights in fiscal year 2013 with respect to industry partnerships, collaborations and licenses. Notably, Boston Children's entered into a large-scale, rare disease alliance with Shire Pharmaceuticals and spun out Boston Children's molecular medicine laboratory into Claritas Genomics, an independent, first-of-its-kind, pediatric clinical genomics diagnostics company.

As the pharmaceutical industry continues to downsize R&D infrastructures and key venture capitalists pivot towards small seed investments to obtain proof of concept before series A financing, reliance on academic partnerships is growing. Locally, an increasing number of health care companies are calling Boston their home. The current landscape offers a unique opportunity for Boston Children's to forge exciting partnerships with industry and to seed new companies.

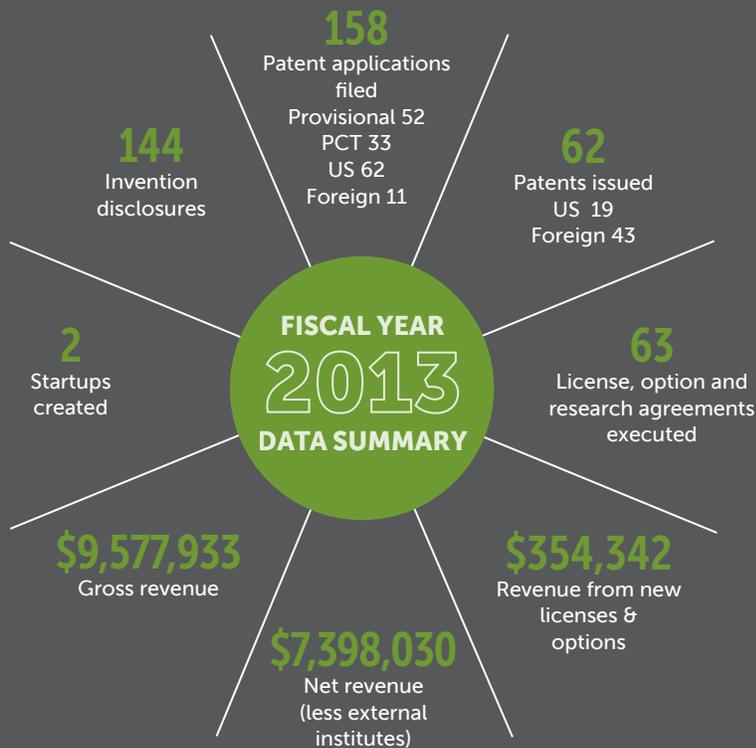
Capitalizing on this unprecedented climate, TIDO has accomplished breakthrough results in FY13 to advance Boston Children's innovations.

After six and a half years of service at Boston Children's, Erik Halvorsen stepped down from his role as our Executive Director. By transforming TIDO into a full-service technology development and licensing office, Erik leaves us well-positioned to continue to thrive in FY14.

TIDO is part of a rich ecosystem of innovation at Boston Children's that includes the Innovation Acceleration Program, the Translational Research Program and the Translational Neuroscience Center. We are proud to support the groundbreaking ideas and discoveries at Boston Children's with the mission of bringing these technologies to the patients and families that need them most.

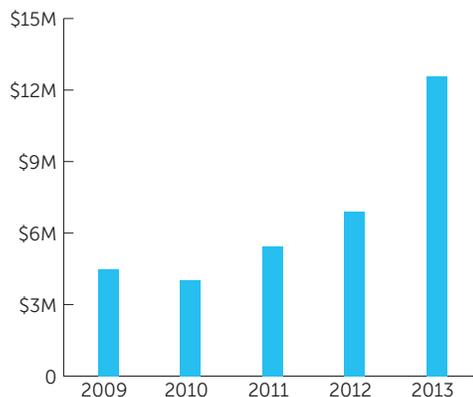
### **The TIDO Team**

# By the Numbers

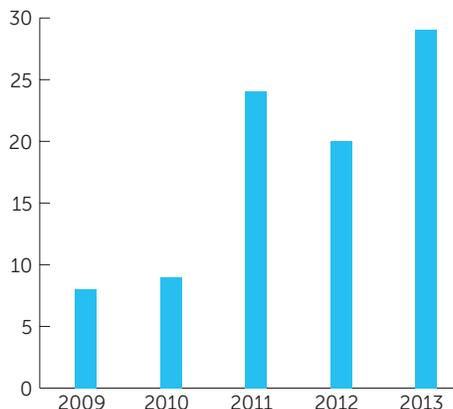


# By the Numbers

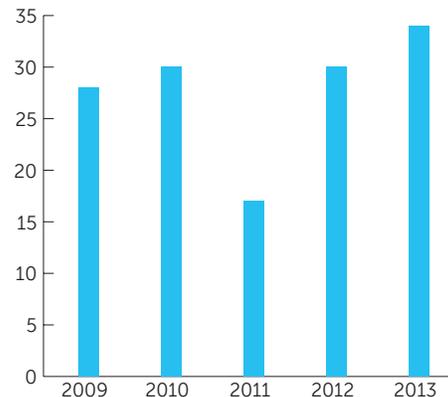
Corporate Sponsored Research Dollars



Sponsored Research and Collaboration Agreements



Licenses and Options Executed



## Issued US Patents

**Gregory, Richard; Daley, George**

8,283,331 | Methods to regulate miRNA processing by targeting Lin-28

**Murray, Martha**

8,308,681 | Device for mixing & delivering fluids for tissue repair

**He, Zhigang**

8,367,352 | Promoting axon regeneration in the adult CNS through control of protein translation

**Teng, Yang (Ted)**

8,377,463 | Methods and compositions for the treatment of open & closed wound spinal cord injuries

**Orkin, Stuart**

8,383,604 | Modulation of BCL11A for treatment of hemoglobinopathies

**Lieberman, Judy**

8,389,486 | Methods for treating hematopoietic malignancies

**del Nido, Pedro; Vasilyev, Nikolay**

8,394,015 | Instrument port for minimally invasive cardiac surgery

**Ingber, Donald**

8,394,779 | Methods of modulating angiogenesis via TRPV4

**Rao, Anjana**

8,394,778 | Regulators of NFAT and/or store-operated calcium entry

**Rao, Anjana**

8,399,185 | Regulators of NFAT

**Kohane, Daniel**

8,414,912 | Contact lens drug delivery device applied to the cornea & used to deliver medication to the eye

**del Nido, Pedro; Vasilyev, Nikolay**

8,414,607 | Miniature shredding tool for use in medical applications & methods for making

**Frank, Markus**

8,425,876 | Gene encoding a multidrug resistance human P-glycoprotein homologue on chromosome 7p15-21 & uses thereof

**Frank, Markus**

8,455,245 | ABCB5 positive mesenchymal stem cells as immunomodulators

**Kheir, John**

8,481,077 | Microbubbles & methods for oxygen delivery

**del Nido, Pedro; Vasilyev, Nikolay; DuPont, Pierre**

8,491,631 | Tissue tack

**Frank, Markus**

8,507,273 | Gene encoding a multidrug resistance human P-glycoprotein homologue on chromosome 7p15-21 & uses thereof

**Klagsbrun, Michael**

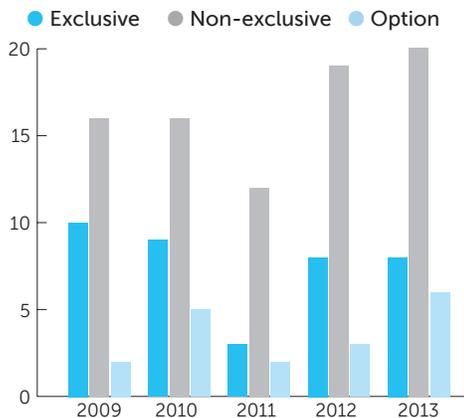
8,529,905 | Soluble inhibitors of vascular endothelial growth factor & use thereof

**Steen, Hanno; Bachur, Richard; Kentsis, Alex**

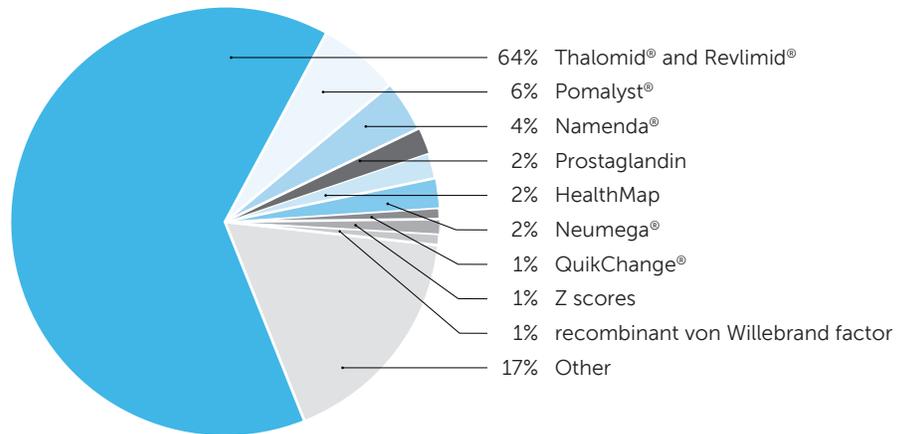
8,535,891 | Method of predicting acute appendicitis

# By the Numbers

Breakdown of License & Option Agreements



Sources of Licensing Revenue



## Issued Foreign Patents

**Zon, Leonard** Mexico  
311440 | Method to modulate hematopoietic stem cell growth

**Satchi-Fainaro, Ronit** EPO  
1494662 | TNP-470-HPMA-methacrylic acid copolymer conjugates & use thereof

**del Nido, Pedro** EPO  
1687056 | Trocar for use during endoscopy

**Springer, Timothy** EPO  
1761562 | Conformation specific antibodies

**Rao, Anjana** EPO  
1984400 | Regulators of NFAT

**Lock, James** EPO  
2015709 | Transcatheter heart valve prosthesis

**Frank, Markus** EPO  
2230253 | Antibodies against a homologue of the MDR P-glycoprotein on chromosome 7p15-21 & uses thereof

**Atala, Anthony** EPO  
2292278 | Augmentation of organ function

**Snyder, Evan** Canada  
2,313,169 | Engraftable neural progenitor & stem cells for brain tumor therapy

**Zon, Leonard** Russian Fed.  
2480213 | Method to enhance tissue regeneration

**Puder, Mark; Gura, Kathy** Canada  
2,545,752 | Treatment and prevention of liver disease associated with parenteral nutrition

**D'Amato, Robert** Japan  
5066505 | Synthesis of 3-amino-thalidomide & its enantiomers

**Springer, Timothy** Japan  
5113314 | Modified polypeptides stabilized in a desired conformation & methods for producing same

**Cima, Michael** Japan  
5265359 | Intravesical drug delivery device & method

**Teng, Yang (Ted)** Japan  
5340917 | Methods and compositions for the treatment of open & closed wound spinal cord injuries

**Zon, Leonard** Australia  
2007230902 | Method to modulate hematopoietic stem cell growth

**von Andrian, Ulrich** Australia  
2008314647 | Vaccine nanotechnology

**Corfas, Gabriel** Australia  
2009215107 | Treatments for neuropathy

**Snyder, Evan** EPO  
1267944B | Systemic gene delivery vehicles for the treatment of tumors

**Kuhn, Bernhard** EPO  
2117582 | Periostin induces proliferation of cardiomyocytes & promotes cardiac regeneration

**Zon, Leonard** China  
200780018870.X | Method to modulate hematopoietic stem cell growth

# Technology Development Fund

Boston Children's Technology Development Fund (TDF) completed its fifth funding cycle, and the advisory board selected seven projects for funding. The TDF, which was established by TIDO in 2009, invests in promising early-stage technologies to bring them to a stage where they are attractive to industry for partnering or licensing. The key to its success is an external advisory board of senior science and business mentors and a network of preferred contract research organizations to execute the project plan.

## 2013 TDF awardees and projects:

**John Kheir, MD** - Cardiology: Optimization and Testing of Polymeric, Oxygenated Microparticles as Adjunctive Therapy in Out-of-Hospital Cardiac Arrest

**Paula Watnick, MD, PhD** - Infectious Diseases: The Bacterial Biofilm Matrix as a Platform for Vaccine Development

**Charles Berde, MD, PhD** - Anesthesiology: Neosaxitoxin for Prolonged Duration Local Anesthesia (More on page 12)

**Jeffrey Burns, MD, MPH, and Traci Wolbrink, MD, MPH** - Critical Care Medicine: OPENPediatrics Virtual Dialysis Simulator (More on page 14)

**Joshua Mauney, PhD, and Carlos Estrada, MD** - Urology: Multi-Layer Silk Biomaterial for Augmentation Cystoplasty

**Pedro del Nido, MD, and Nikolay Vasilyev, MD** - Cardiac Surgery: Transapical Mitral Valve Leaflet Plication Clip (More on page 14)

**Christopher Duggan, MD, MPH, and Karen Warman, MS, RD** - Gastroenterology/Nutrition: Pediatric Nutrition Assessment



# Agreements

## **Claritas Genomics, a clinical genomics company, spins out of Boston Children's**

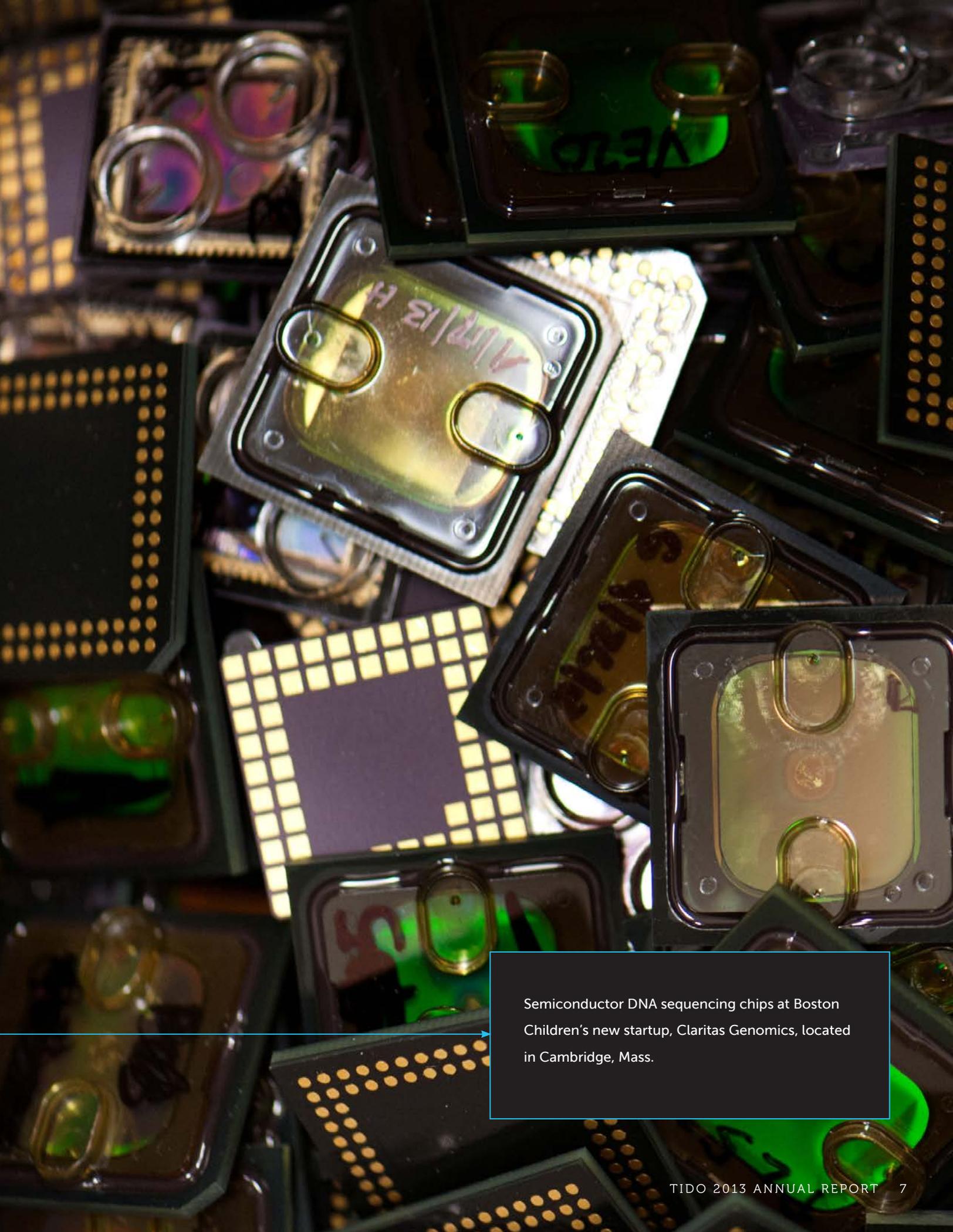
In January of 2013, Boston Children's Hospital partnered with Life Technologies Corporation to launch Claritas Genomics, a new company formed to provide genomics-based diagnostics for pediatric patients. The startup combines advanced instrumentation and data analysis with clinical interpretation by medical genomics experts at Boston Children's.

## **Three-year rare disease research collaboration program with Shire**

In early FY13, Boston Children's and Shire Plc entered into a broad collaboration partnership in orphan diseases. The goal of the alliance is to develop novel therapies to treat rare pediatric diseases with high, unmet medical need, thereby leveraging Boston Children's research expertise and Shire's development and commercialization capabilities. After the first review cycle in FY13, the joint steering committee selected two biologics research and development projects from investigators Mark Puder, MD, PhD, of the Vascular Biology Program, and Mustafa Sahin, MD, PhD, of the Neurology Department, for funding and support.

## **Pronova Biopharma enters option agreement for omega-3 therapy for fertility**

Mark Puder, MD, PhD, assistant program director of Pediatric Surgery, found that animals fed a diet rich in omega-3 fatty acids are able to reproduce with healthy offspring at advanced maternal age. Pronova has signed an option agreement with Boston Children's to develop an omega-3 therapeutic to enhance fertility. Pronova developed the first omega-3-derived prescription drug, Omacor®/Lovaza™, approved by the FDA.



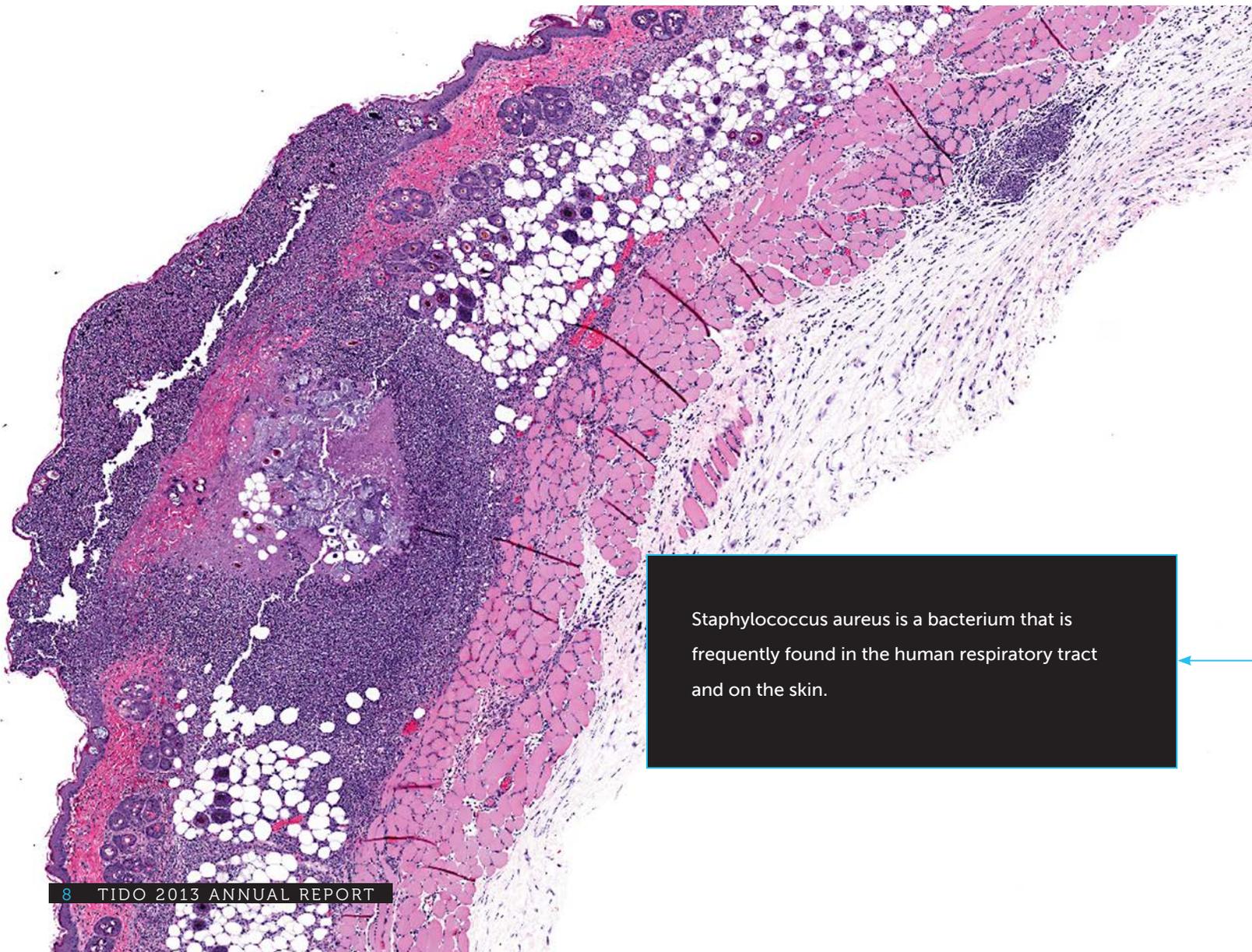
Semiconductor DNA sequencing chips at Boston Children's new startup, Claritas Genomics, located in Cambridge, Mass.

**Novo Nordisk's Diabetes and Obesity Biologics Science Forum funding awarded to Wayne Lencer, MD**

In December of FY13, Wayne Lencer, MD, chief of Gastroenterology, was awarded a two-year Diabetes and Obesity Biologics Science Forum Award from Novo Nordisk. The award, set up to fund non-clinical research related to new biologic therapeutics and targets in the field of type 1 and 2 diabetes and obesity, will be used to conduct *in vitro* and *in vivo* studies of molecular carriers for oral delivery of GLP-1 analogues for treatment of type 2 diabetes.

**Wired Informatics startup launched by Boston Children's**

Wired Informatics, LLC, was founded on technologies first developed by Guergana Savova, PhD, principal investigator in the Natural Language Processing Lab at Boston Children's. The company helps researchers, hospitals, and medical record processors efficiently extract knowledge embedded in unstructured data across the health care ecosystem by providing next-generation natural language processing and machine-learning solutions to solve clinical narrative challenges.



Staphylococcus aureus is a bacterium that is frequently found in the human respiratory tract and on the skin.

## **Takeda New Frontier Science sponsors research to discover allosteric modulators and develop Staphylococcus vaccine**

Takeda New Frontier Science and Boston Children's entered into two sponsored research agreements in FY13:

- A two-year study in the lab of Wesley Wong, PhD, an investigator in the Program in Cellular and Molecular Medicine, will use Wong's nanoscale tools as a screening platform to identify allosteric modulators, with the ultimate goal of discovering new drugs with increased efficacy, safety and potency.
- A project in the laboratory of Richard Malley, MD, senior associate physician in Medicine, will use Malley's flexible vaccine system, named Multiple Antigen Presentation System (MAPS), which simultaneously couples a polysaccharide scaffold to multiple antigens and pathogens, including Staphylococcus aureus.

### **ACT.md startup formed to improve patient care coordination**

In 2013, ACT.md was launched based on a care coordination concept developed by Isaac Kohane, MD, PhD, chair of Boston Children's Informatics Program and Kenneth Mandl, MD, MPH, director of the Intelligent Health Laboratory. Using intellectual property licensed from Boston Children's, Kohane and Mandl teamed up with entrepreneur Ted Quinn, MBA, to launch a company to develop a web and mobile platform that will transform how patients, families, and medical providers work together to deliver care in efficient and cost-effective ways.

### **SpecialNeedsWare and Boston Children's partner to deliver autism communications solutions**

SpecialNeedsWare, the maker of the AutisMate app that improves communication and life skills in autistic children, has licensed software and intellectual property developed by Howard Shane, PhD, director of the Center for Communication Enhancement and Autism Language Program. These tools include the SymbolTalk and Puddingstone software for learning skills development; the Visual Immersion Program, a learning framework to improve communication; the ALP Animated Graphics, animations to improve comprehension and facilitate expression; and the Teaching Language Concepts software, a virtual world to help children communicate and learn.

### **Biogen IDEC sponsors research to study John Cunningham virus (JCV) infection**

Biogen IDEC and Boston Children's have entered into a sponsored research agreement to study early-stage progression of JCV, the lead cause for a potentially lethal brain infection known as progressive multifocal leukoencephalopathy (PML). Use of Biogen's MS drug Tysabri® can lead to the development of PML. Tomas Kirchhausen, PhD, senior investigator in the Program in Cellular and Molecular Medicine, will study the time course and sequence of events during JCV infection, with the goal of developing strategies to prevent its spread.



A peanut allergy tolerance clinical study aims to desensitize patients by combining peanut oral immunotherapy with Xolair®.

# Clinical Trials

## **Peanut reactivity reduced by oral tolerance in an anti-IgE phase I/II clinical trial (PRROTECT)**

Food Allergy Research & Education (FARE) and Genentech have sponsored the PRROTECT study, a phase I/II placebo-controlled clinical trial. This study aims to develop a safe and rapid desensitization protocol for patients with peanut allergy by combining peanut oral immunotherapy with Xolair®, provided by Genentech. Led by Lynda Schneider, MD, director of the Allergy Program, and Andrew MacGinnitie, MD, PhD, associate clinical director of the Division of Immunology, the study is actively recruiting subjects.

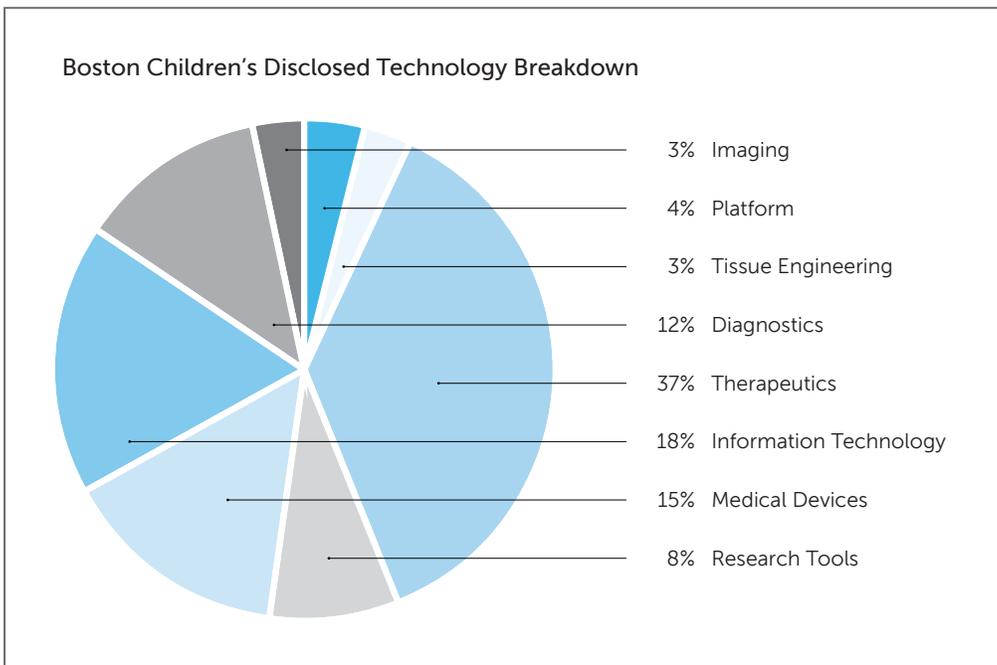
## **bluebird bio sponsors phase II/III trial for childhood cerebral adrenoleukodystrophy**

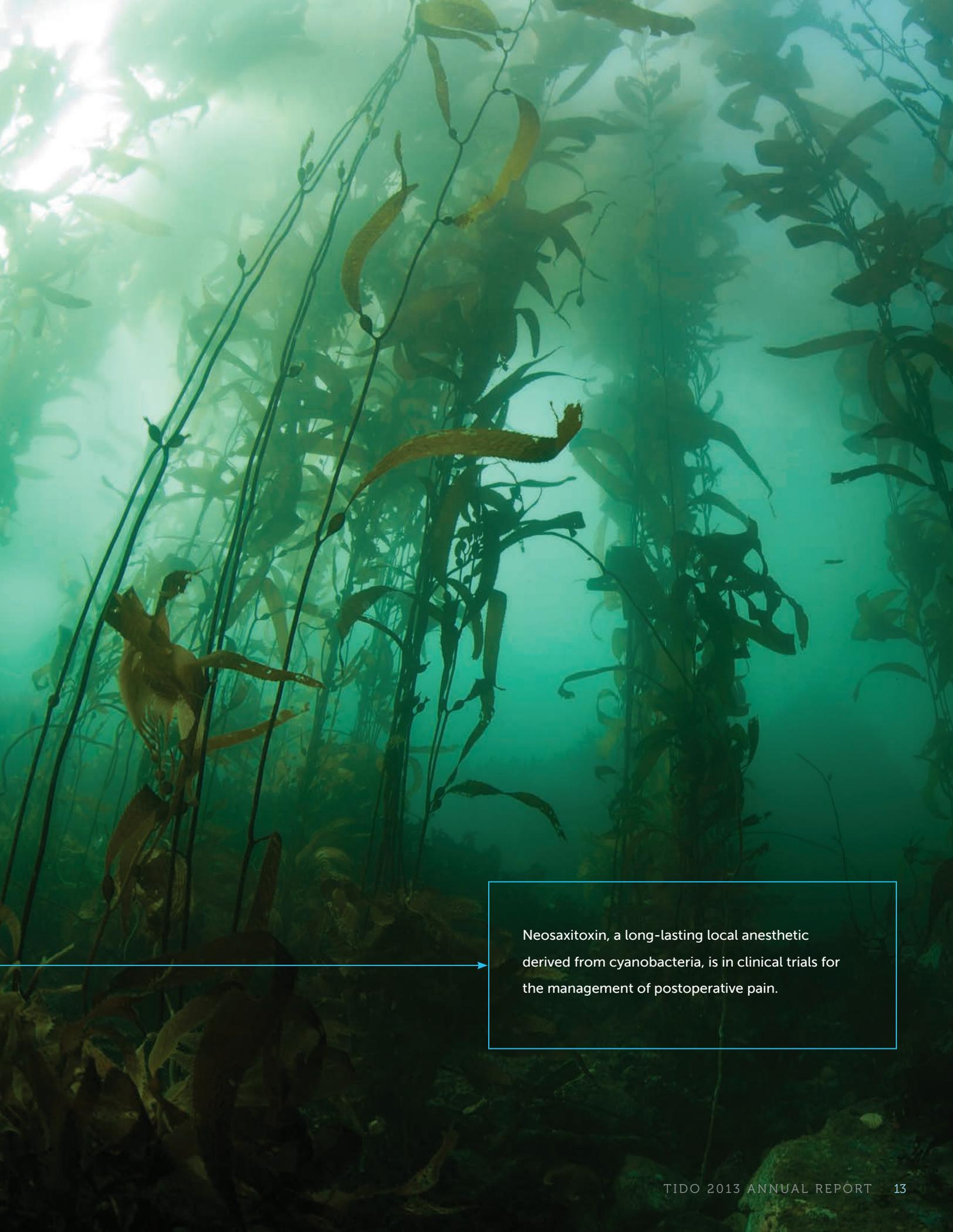
bluebird bio is sponsoring a phase II/III clinical trial designed to evaluate the efficacy and safety of its therapeutic candidate Lenti-D Drug Product to treat subjects with childhood cerebral adrenoleukodystrophy (CCALD), a fatal disease if untreated. Lenti-D Drug Product is autologous CD34+ hematopoietic stem cells transduced *ex vivo* with the lentiviral vector containing the functioning human ABCD1 complementary deoxyribonucleic acid. Led by David Williams, MD, chief of the Division of Hematology/Oncology and director of Translational Research, the trial will enroll up to 15 boys who will be monitored for 24 months following an infusion of Lenti-D Drug Product.

# Technologies

## Neosaxitoxin: Mounting a long-lasting local blockade against pain

Boston Children's Charles Berde, MD, PhD, chief of Pain Medicine, through a collaboration with Proteus SA, has led a quest to turn Neosaxitoxin—a site-1 sodium channel blocker derived from cyanobacteria—into a long-lasting local anesthetic for the management of postoperative pain. Berde and his collaborators have launched a phase I clinical trial in the US in healthy adult patients aimed at showing that Neosaxitoxin is safe at clinically relevant doses and measuring how Neosaxitoxin clears from the body. The ongoing trial will augment phase II studies already conducted in Chile showing that Neosaxitoxin can help patients undergoing surgical procedures recover quickly and experience less pain than patients treated with commercially available local anesthetics.





Neosaxitoxin, a long-lasting local anesthetic derived from cyanobacteria, is in clinical trials for the management of postoperative pain.

## OPENPediatrics: Medical technology platform to improve care of children across the globe

In September of 2013, IBM and Boston Children's announced the launch of the world's first cloud-based global medical education platform to transform how pediatric medicine is taught and practiced around the world. Conceived by Jeffrey Burns, MD, MPH, chief



of Critical Care at Boston Children's and Harvard Medical School, and developed in IBM Labs, OPENPediatrics provides information and training to medical professionals through an on-demand, interactive, digital and social learning experience. The content includes medical simulators, lectures and demonstrations from a range of international experts, training modules, best practices information and discussion functionality for users. By fusing world-class medical expertise with innovative cloud-based technology, OPENPediatrics is leveraging the accrued wisdom of the global community to improve the care of the critically ill child.

## Beating-heart cardiac surgical instruments

Pedro del Nido, MD, and Nikolay Vasilyev, MD, have a vision of conducting complex cardiac repairs in children while their hearts are still beating. These cardiac surgeons are developing miniaturized tools to enable fine surgical manipulations via a less invasive approach through the heart wall rather than open-heart surgery. The instruments being developed include the Cardioport, an imaging and instrument delivery system that includes an integrated camera and a flushing mechanism to maintain visibility and eliminate air. Surgical tools being developed for insertion through the Cardioport include the heart patch deployment system for septal defects and a mitral clip for mitral valve prolapse repair. Other procedures such as arrhythmia ablation can also be performed through the Cardioport.

## MAPS: Multiple Antigen Presentation System vaccine platform

What if you could bring together the effectiveness and low cost of a whole-cell vaccine and the safety and reproducibility of an acellular one? That's what Boston Children's Richard Malley, MD, senior associate physician in Medicine, Yingjie Lu, PhD, research associate, and Fan Zhang, PhD, have developed with the Multiple Antigen Presenting System (MAPS). The approach allows vaccine designers to simultaneously incorporate multiple protein and sugar antigens from one or more pathogens (bacteria, viruses and parasites). The resulting complex, which resembles a scaffold of sugars studded with proteins, can trigger both antibody and T-cell responses simultaneously, creating a more vigorous immune response.

# Licensee Milestones

➤ Zafgen raised \$45 million in a Series E round from a group of both private and public investors. RA Capital Management, Brookside Capital, Venrock and Alta Partners provided capital that will help fund the development of its obesity drug candidate, beloranib.



➤ SynapDx Corporation secured a \$15.4 million funding round led by Google Ventures. Foundation Medical Partners joined the financing as a new investor, alongside founding investors North Bridge Venture Partners and General Catalyst Partners. SynapDx will use the funding to complete a clinical trial studying its blood test to detect autism in 660 children between the ages of 18 months and 5 years in North America.



➤ Fate Therapeutics (FATE) went public on October 1 and raised approximately \$40 million. Fate also initiated a phase II clinical study of ProHema for the treatment of hematologic malignancies.



➤ Moderna signed a five-year strategic option agreement with AstraZeneca worth approximately \$240 million to discover and develop messenger RNA Therapeutics™. The deal gives AstraZeneca exclusive access to Moderna's mRNA therapeutic platform in the area of cardiometabolic diseases, as well as for selected oncology targets.



➤ Premacure AB was acquired by Shire in March of 2013. The deal enhances Shire's late-stage pipeline with the acquisition of a phase II protein replacement therapy being investigated for the prevention of retinopathy of prematurity.



➤ Since its launch this year, Claritas Genomics has built a partnership network that includes Cincinnati Children's Hospital and Cerner. Claritas was also awarded a Veterans Administration contract to sequence the exomes of 18,000 military veterans over 12 months.



# National Pediatric Innovation Summit Recap

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Boston Children's successfully hosted "Taking on Tomorrow," our first annual National Pediatric Innovation Summit + Awards on September 25 and 26. The two-day summit convened top health care thought leaders, including clinicians, scientists, engineers, and representatives from industry, private equity and health care policy, to take on the toughest challenges in pediatrics. More than 300 professionals participated from 23 states and as far away as Israel and China, including representatives from nine children's hospitals. Attendees voiced diverse ideas and

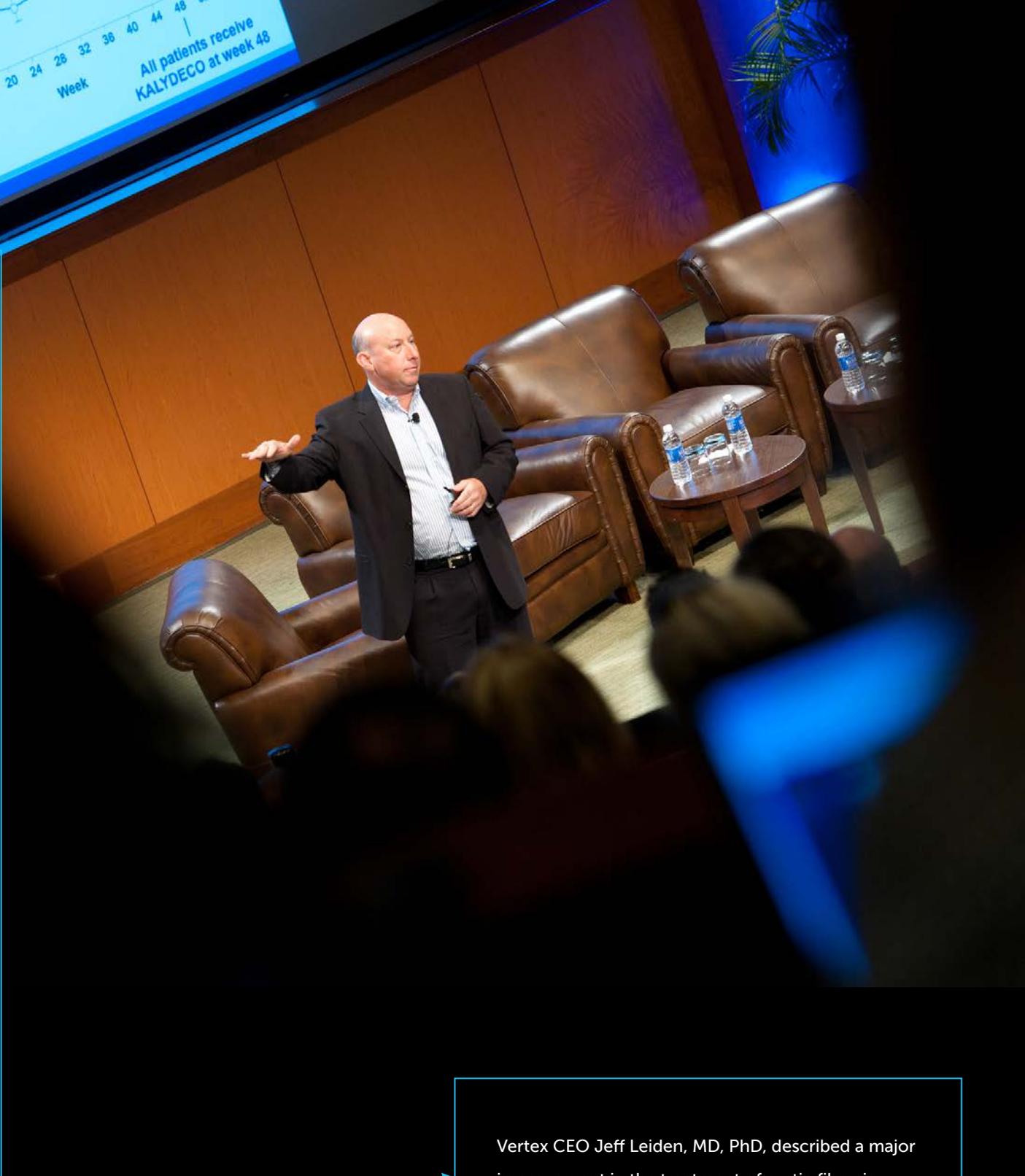
provocative questions during keynotes and panel discussions, and then dove more deeply into challenges in autism, genomics, patient engagement and how to advance innovation in pediatrics. The insights of our audience were all brought together in the pursuit of a single, shared goal—to improve care for children.

At the event, three \$50,000 Taking on Tomorrow innovation award winners were announced, based on the maturity of the technology, the commercial potential, intellectual property considerations and the strength of the development team:

- ▶ Research/Scientific Breakthrough in Autism Award: Daniel Geschwind, MD, PhD, University of California, Los Angeles, who created and leads the Autism Genetic Resource Exchange (AGRE), a large-scale, cross-institution database used by more than 150 institutions to date.
- ▶ Clinical Innovation Award: Charles Dumoulin, PhD, Cincinnati Children's Hospital Medical Center, who led a team of scientists and engineers to develop a new type of magnetic resonance imaging (MRI) system for infants.
- ▶ Community/Patient Empowerment Award: Christopher P. Landrigan, MD, MPH, and Alisa Khan, MD, of Boston Children's Hospital, Brigham and Women's Hospital and Harvard Medical School, for an interactive nightly "sign out form" for families of hospitalized children.

**Join us at Taking on Tomorrow 2014 in Boston on October 30 and 31 at the Seaport World Trade Center.**

**Go to [bostonchildrensinnovationsummit.org](http://bostonchildrensinnovationsummit.org) for more details.**



Vertex CEO Jeff Leiden, MD, PhD, described a major improvement in the treatment of cystic fibrosis patients at the National Pediatric Innovation Summit.



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Technology & Innovation  
Development Office

300 Longwood Avenue  
Boston, MA 02115

617.919.3019  
TIDO@childrens.harvard.edu

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and research technologies at  
[childrensinnovations.org](http://childrensinnovations.org)