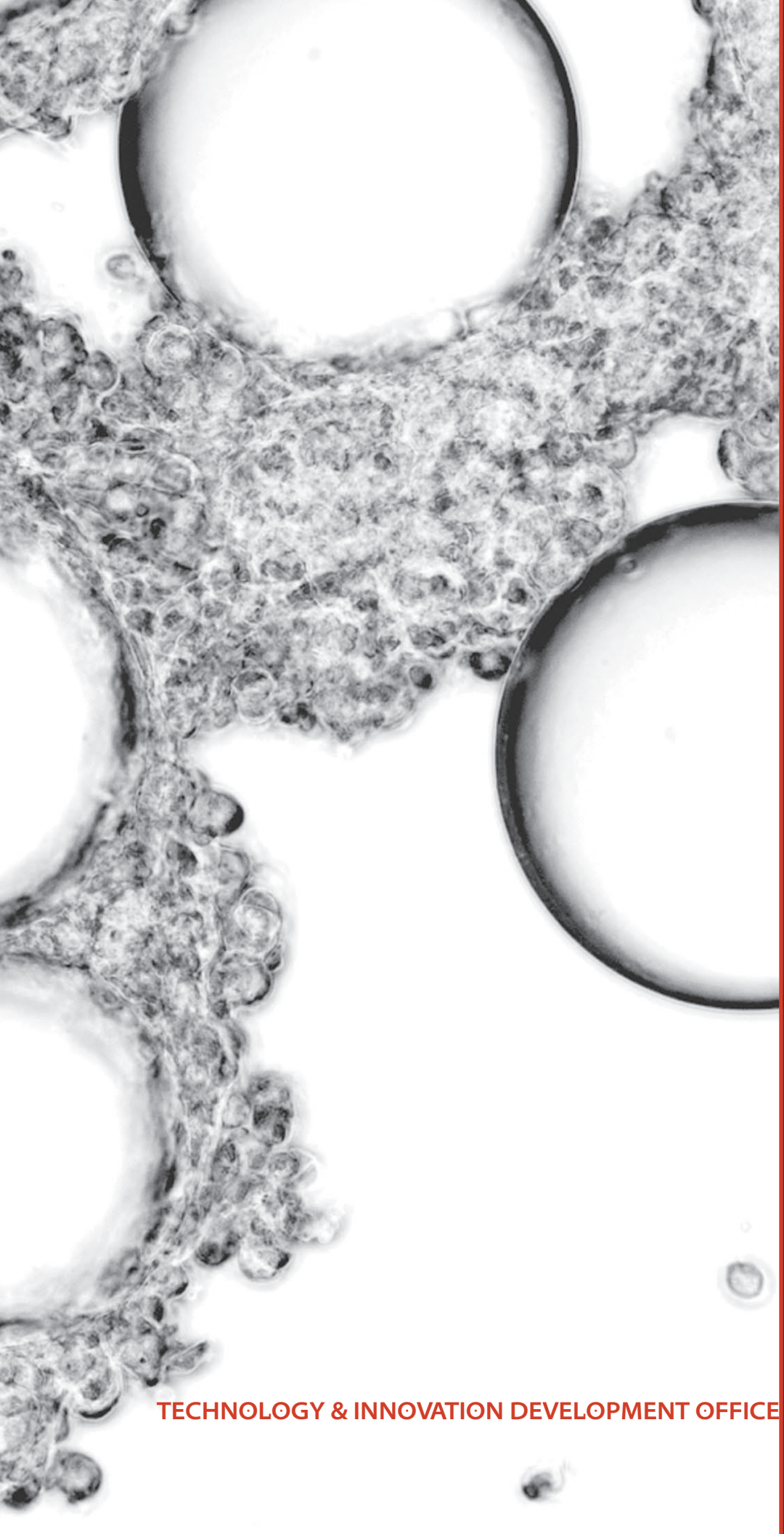


Children's Hospital Boston

TECHNOLOGY & INNOVATION DEVELOPMENT OFFICE 2011 ANNUAL REPORT

THE TIDO TEAM

DIRECTORS

Erik Halvorsen, PhD
Executive Director of TIDO
Managing Partner, Technology Development Fund

Kathleen Bass, PhD
Associate Director of TIDO

PATENTS & LICENSING:
LICENSING MANAGERS

Alexander Augst, PhD
Associate Licensing Manager

Connie Caron, MBA, Patent Agent
Licensing Manager

Ryan Dietz, JD
Director, Office of Technology Development at Children's Program in Cellular and Molecular Medicine/The Immune Disease Institute

Abbie Meyer, PhD
Licensing Manager

Maude Tessier, PhD
Licensing Manager

Alan Yen, PhD
Licensing Manager

PATENTS & LICENSING:
CONTRACTS & INTELLECTUAL PROPERTY

Christopher Geehan, JD
Contracts & Intellectual Property Specialist

Stanley Tabi, JD
Patent Coordinator

Rajinder Khunkuhn, JD
Patent Specialist

TECHNOLOGY DEVELOPMENT

Monique Yoakim-Turk, PhD
Partner, Technology Development Fund
Associate Director of TIDO

Meridith Unger, MBA
Principal, Technology Development Fund
Associate, Business Planning & Analysis

BUSINESS DEVELOPMENT & MARKETING

Nurjana Bachman, PhD
Associate Director, Strategic Initiatives and Business Development

David Altman
Senior Marketing and Communications Specialist

Keeley Wray
Senior Market Research Analyst

CLINICAL TRIALS OFFICE

Elizabeth (Lianne) Cleary, JD
Contracts Associate

Abbey Coffin
Contracts Specialist

Allison Hannibal
Business Analyst

Fernando Vallés, JD
Contracts Associate

BUSINESS & ADMINISTRATION

Sharon Jordan-Prioleau, MBA
Business Manager

Lisa Pight
Financial Assistant

Katherine Fox
Administrative Associate

LETTER FROM THE EXECUTIVE DIRECTOR

Differentiation

Collaboration

Diversity

Team

Famous American industrialist, innovator and pioneer of the automobile industry Henry Ford once said, ***"Coming together is a beginning. Keeping together is progress. Working together is success."***

The Technology & Innovation Development Office (TIDO) came together around a core of what was the Intellectual Property Office in 2007. In a change that represented more than just an update to the office name, the group of talented individuals with varied backgrounds and experience were organized into new functional groups that could better support Children's Hospital Boston's research and innovation. Over the course of a few years we added expertise in **Business Development** (forming collaborations with companies), **Marketing** (detailed market/product analysis and use of cutting edge social media outlets), **Technology Development** (investment fund and advisory board of industry leaders), and the **Clinical Trials Office** to our core **Patents and Licensing**. This was the beginning. A novel combination of people, skills, resources and processes that could help the institution translate its world-class research and innovation into new products that could improve and even save lives.

In Henry Ford's world of the automobile, he was able to align teams of workers and standardize processes to such a degree that it led to the creation of mass production through assembly lines. Translating biomedical research and innovation into products may not be as linear as an assembly line, but the use of workers with specialized skills and roles operating as a unified team with a common goal certainly resonates even today and is an underlying strength of TIDO.

In the last year, TIDO has made progress on many fronts in support of its mission. Business Development efforts led to several research collaborations, notably Children's entry into Pfizer's Centers for Therapeutic Innovation and a major research effort to develop new drugs for muscular dystrophy (both highlighted on page 6). The marketing team has harnessed the power of new communication tools such as Twitter, Facebook and the Vector blog to present Children's to a much broader audience and create ongoing dialog. The Technology Development Fund just entered its fourth year and awarded $1.1 M to 12 projects in 2011. Over the last three years, the fund has committed to awards totaling $3.7 M for 29 projects at Children's. These investments have helped advance these technologies and have led directly to $5.4 M in follow-on funding and several license agreements with corporate partners to develop commercializable products.

The trend we have increasingly seen over the past few years—namely, the growing interest among big pharma and large biotech collaboration and co-development over direct licensing of early stage intellectual property (IP)—certainly held true this past year. With 24 research collaborations and 43 clinical trial agreements (an increase of 167 percent and 39 percent, respectively, over last year) we anticipate that most future licenses to big pharma will come from jointly created IP arising from collaborations. Co-development and collaboration with commercial partners will be the new normal when it comes to advancing research discoveries to new products—and is an expansion of the team concept already in place.

It may not be Henry Ford's assembly line, but the necessary components are in place here to continue to move important pediatric innovations forward to the point where they can become products to improve the lives of our kids. All teams need a common goal—and I think this is one we can all support.

Erik Halvorsen, PhD
Executive Director of TIDO
Managing Partner, Technology Development Fund

TIDO ACTIVITIES

INVENTION MANAGEMENT ACTIVITY

Inventions under active management	794
Inventions in development	19
Current licenses	301
Issued U.S. patents	450
Issued foreign patents	640

FY11 DATA SUMMARY

Invention disclosures	134
Patent applications filed	149
Provisional	49
PCT	28
U.S.	52
Foreign	20
Patents issued	52
U.S.	32
Foreign	20
Licenses & options granted	17
Gross revenue	$10,571,051
Net revenue (less external institutes)	$7,517,132
Revenue from new licenses and options	$419,446

RECIPIENTS OF DISTRIBUTED LICENSING REVENUE

Inventors	$2,615,586
Departments	$1,942,738
General Research Endowment	$2,366,024
TIDO	$719,932
Legal expenses	$144,939
Other institutions	$3,053,919
TOTAL	$10,571,051

With more than $253 M in annual funding and 800,000 square feet of space, Children's Hospital Boston has the world's largest and most active pediatric research enterprise. Our investigators—basic scientists, clinical researchers, epidemiologists and more—are Harvard Medical School faculty dedicated to accelerating the pace of medical discovery from brainstorm to bench to bedside. The National Institutes of Health is our largest research sponsor. The hospital is home to nine members of the National Academy of Sciences, nine members of the Institute of Medicine and 11 investigators supported by the Howard Hughes Medical Institute, the nation's largest private nonprofit source of funding for biomedical research and science education. Children's 1,100 scientists are experts in many fields.

INVENTION MANAGEMENT ACTIVITY

In FY11, TIDO had 794 inventions under active management. Licensing managers supervised 301 ongoing license agreements, and, with the support from outside patent attorneys, managed 880 pending patent applications on 370 inventions and maintained 1,090 patents issued in the U.S. and other countries.

PATENT FILINGS

TIDO filed a total of 149 patent applications in FY11. Forty-nine were provisional patent applications and 28 were filed for U.S. and foreign rights under the Patent Cooperation Treaty mechanism. Fifty-two applications were filed in the U.S. and 20 in individual foreign countries.

PATENT ISSUANCES

In FY11, Children's was granted 32 patents by the U.S. Patent and Trademark Office and 20 by foreign patent offices. Children's patents are filed with the Assignee designation of Children's Medical Center Corporation. These new patents are listed in Appendix 3.

INVENTION DISCLOSURES

TIDO received 134 new invention disclosures from Children's clinicians and researchers, a 15 percent increase over FY10.

LICENSING ACTIVITY

TIDO negotiated and executed 17 license and option agreements for Children's technologies: four exclusive licenses, 11 non-exclusive licenses and two options. These new agreements led to $419,446 in revenue for the hospital. TIDO's overall performance, including licensing and patenting activities over the past six years, is illustrated in Appendices 1 and 2.

RESEARCH AGREEMENTS

TIDO negotiated and executed 906 research agreements in FY11: forty-three clinical trial agreements, 839 academic and industry material transfer agreements and 24 corporate sponsored and collaborative research agreements. The total budgeted costs of the clinical trial agreements were approximately $4.4 M.

TECHNOLOGY DEVELOPMENT FUND

The Technology Development Fund (TDF) awarded $1.1 M to 12 projects during the FY11 funding cycle. TDF received 52 letters of intent, a 27 percent increase over FY10. To date, TDF's investment of roughly $1.2 M in FY09-FY10 has been leveraged into $5.4 M in follow-on funding from government, foundation and philanthropic sources. Eighteen contract research organizations were subcontracted on FY09-FY10 projects and five projects are being co-developed with key academic and industry partners (see page 4). TDF's first licensed technology, a blood draw educational kit, achieved commercial launch at the end of 2011 (see page 8).

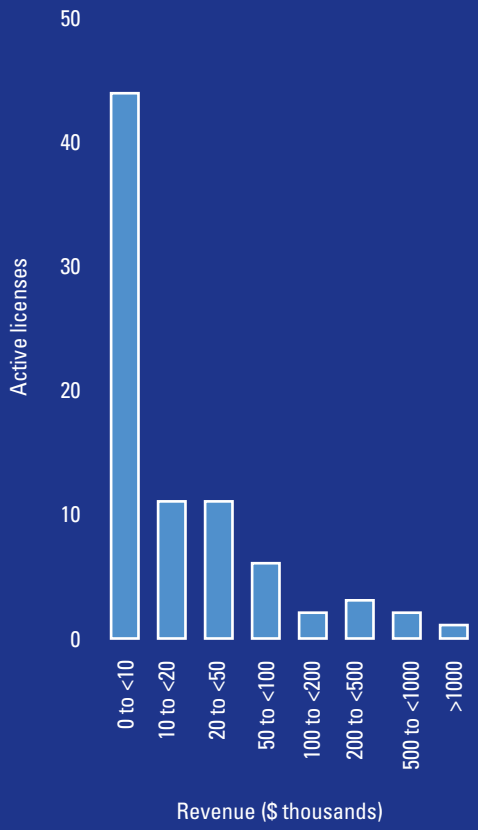
DISTRIBUTION OF LICENSING REVENUE

Children's received $10.6 M in gross revenue from all licenses in FY11, a decrease from the previous year. The hospital realized $7.5 M in gross revenue after distribution of $3.1 M to other institutional co-owners. Of the net $7.5 M, $2.6 M was distributed to the inventors and $1.9 M to their respective departments and laboratories. The hospital apportioned the remaining $3 M to the General Research Endowment, unrecovered legal expenses and TIDO's operations.

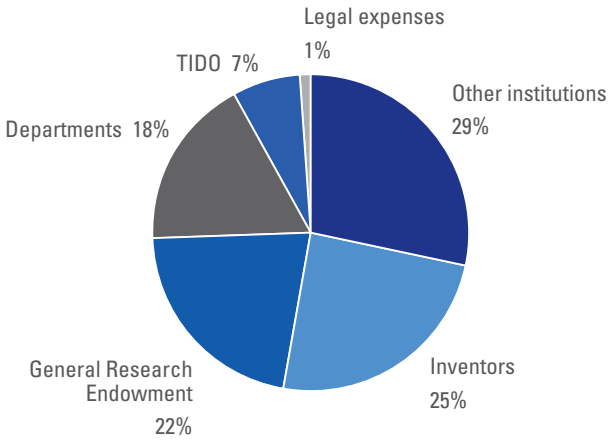
SIGNIFICANT REVENUE-GENERATING INVENTIONS

Seventy percent of the hospital's net licensing revenue was generated by sales of THALOMID® and REVLIMID® brand drugs for the treatment of cancer. Other significant sources of revenue were royalties from the sales of Namenda® for the treatment of Alzheimer's disease; Neumega®, which stimulates platelet production and is used in combination with chemotherapy by patients with cancer; the dystrophin diagnostic test offered by Athena Diagnostics; and milestone payments on Pomalidomide, a cancer drug in clinical trials.

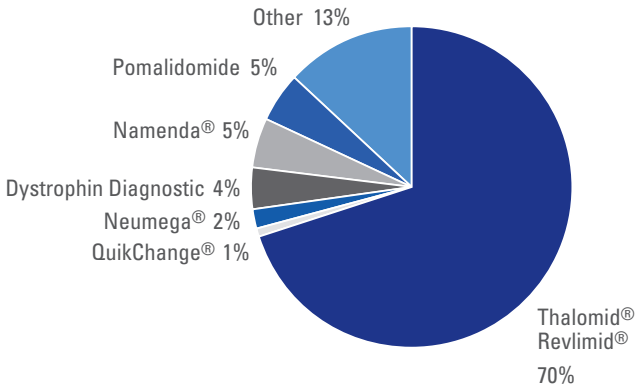
REVENUE-GENERATING LICENSES FY11



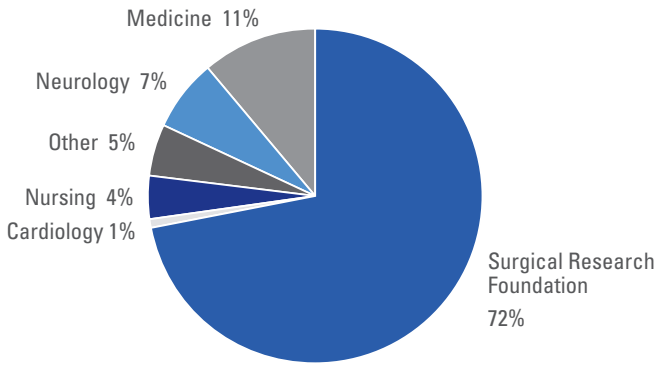
NET LICENSING REVENUE DISTRIBUTION FY11: $7.5 MILLION



SOURCES OF LICENSING REVENUE



DISTRIBUTIONS TO DEPARTMENTS FY11: $1.9 MILLION



TECHNOLOGY DEVELOPMENT FUND

Development of projects funded in FY09-FY10 continued in 2011 with $1.2 M invested by the end of FY11, attracting $5.4 M in follow-on funding from public, private and philanthropic sources. Data generated through FY09-FY10 funded projects resulted in four publications, 10 manuscripts and six new patent applications.

Children's Hospital Boston awarded a total of $1.1 M to support the development of 12 projects in the third year of its Technology Development Fund (TDF). This application cycle was marked by a 27 percent increase in the number of applications as well as a significant increase in the diversity of technologies proposed, with a new emphasis on healthcare information technology applications. FY11 marked the first license of a TDF-funded technology that achieved commercial launch at the end of 2011 (see Bee Visual story on page 8).

In addition, TDF formed strategic partnerships with internal and external programs to advance three of the Children's technologies chosen for funding in the past two years:

• Debra Weiner, MD, PhD, director, Pediatric Emergency Medicine, received an award in 2009 to support her BEAPPER project, a smartphone application to enhance communication in the Emergency Department. The project received a FastTrack Innovation award from Children's Innovation Acceleration Program in 2011. The combined resources from both programs supported a team of software programmers who built the user interface and linked the program to the hospital's information technology system. The Children's Emergency Department is currently testing the application.

• Christian von Hehn, MD, PhD, research fellow, and Clifford Woolf, MB, BCh, PhD, director of the F.M. Kirby Neurobiology Center, received a 2010 award for the development of ion channel blockers to disrupt neurogenic inflammation. The project—being conducted in collaboration with Bruce Bean, PhD, professor of Neurobiology at Harvard Medical School—is being co-funded by a Harvard University Biomedical Accelerator Fund award. The team combined resources from the two institutions to generate new chemical entities that were tested in various animal models of neurogenic inflammation. The results are being prepared for publication.

• Children's and the Center for Integration of Medicine and Innovative Technology (CIMIT) joined forces to co-develop a dehydration diagnostic device initially invented in 2010 by Vassilios Bezzerides, MD, PhD, clinical fellow in Pediatrics. The team is leveraging CIMIT's engineering expertise and Children's clinical expertise to redesign and clinically test the device.

Monique Yoakim-Turk, PhD

PROJECTS SELECTED IN 2011:

PROMININ-1: TOPICAL TREATMENT FOR CHRONIC WOUNDS
Avner Adini, PhD, and Robert D'Amato, MD, PhD, Vascular Biology Program

A short peptide derived from Prominin-1 dramatically improves vessel formation by potentiating endogenous VEGF binding to its receptor. Drs. Adini and D'Amato showed an acceleration of diabetic wound healing over the control in mouse models. The 2011 grant will fund formulation and pharmacokinetic work.

LODAMIN: ORAL ANTI-ANGIOGENIC THERAPEUTIC
Ofra Benny-Ratsaby, PhD, and Robert D'Amato, MD, PhD, Vascular Biology Program

Lodamin is a polymer-conjugated form of TNP-470—one of the most potent anti-angiogenic agents ever discovered—rationally designed by Dr. Benny-Ratsaby and the late M. Judah Folkman, MD, to overcome TNP-470's poor pharmacokinetics and reversible neurotoxicity. Lodamin is orally available and has demonstrated broad-spectrum anti-angiogenic activity in a range of *in vitro* assays and murine primary cancer models. Compared to anti-VEGF, Lodamin was able to repress lesions in a mouse model of age-related macular degeneration. Also funded in 2009 to develop a reproducible and scalable synthesis protocol, the 2011 grant will support pharmacokinetic work to support an IND package.

NEOSAXITOXIN: PROLONGED-DURATION LOCAL ANALGESIC
Charles Berde, MD, PhD, Department of Anesthesiology

Neosaxitoxin (NeoSTX) is a member of the family of site 1 sodium channel toxins, which have been shown by Dr. Berde and colleagues in both preclinical and clinical studies to be active for up to twice as long as current analgesics. NeoSTX also does not show neurotoxicity, cardiotoxicity or other side effects typical of traditional anesthetics and analgesics. This project received funding in 2010, and the 2011 grant will fund remaining preclinical studies recommended by the FDA at a pre-IND meeting in November 2010.

MEDWATCHER: CROWDSOURCING FOR DRUG SAFETY SURVEILLANCE
John Brownstein, PhD, Children's Hospital Informatics Program

Nearly half of all Americans currently take a prescription drug, yet the public remains largely unaware of medication safety concerns. Dr. Brownstein and colleagues are developing MedWatcher to engage users (both the public and healthcare practitioners) in issues of drug safety, providing up-to-date safety advisories and a reporting tool for direct submission of adverse drug events by the user. The 2011 grant will fund development of the user interface and back-end data interoperability (see page 6).

CARDIOPORT FOR TRANS-APICAL CARDIAC INTERVENTIONS
Pedro del Nido, MD, and Nikolay Vasilyev, MD, Department of Cardiac Surgery

Enhancing their portfolio of inventions for performing beating heart surgery, Dr. del Nido and his team have designed a cardiac port with an air purging system and a one-way valve that prevents air emboli and minimizes blood loss during trans-apical cardiac interventions. The port has the added functionality of an optical window that allows continuous visualization inside the beating heart. The grant will support functional prototype optimization of the visualization system as well as reduction of the cardioport's diameter.

EDMC: WEB-BASED DISEASE MANAGEMENT SYSTEM
Eric Fleegler, MD, MPH, Division of Emergency Medicine, and Eugenia Chan, MD, MPH, Division of Developmental Medicine

eDMC is a multi-modal patient management system for children with attention deficit hyperactivity disorder (ADHD). eDMC systematically monitors patient symptoms, functioning and learning, medication use and side effects as well as family and patient quality of life. By centrally gathering this information, eDMC will allow practitioners treating ADHD to access a robust set of clinical data and significantly increase efficacy and efficiency of ADHD care. The 2011 grant will fund expansion of the proof of concept software to enhance accessibility and user experience.

ABCB5: MAB THERAPY FOR METASTATIC MELANOMA
Markus Frank, MD, Division of Nephrology

ABCB5 is expressed selectively on cancer stem cells that are resistant to conventional forms of therapy, but which are critical drivers of tumor initiation and metastatic disease progression. Dr. Frank has shown that targeted killing of cancer stem cells in melanoma through ABCB5 monoclonal antibody-dependent cell-mediated cytotoxicity significantly inhibits human xenograft tumor growth in immunodeficient mice established either with patient tumor cells or established melanoma cell lines. The 2011 grant will be used to generate a panel of fully human ABCB5 antibodies.

HEART VALVE LEAFLET UTILIZING A NOVEL FIBER ARRANGEMENT
Peter Hammer, PhD, Department of Cardiac Surgery

Dr. Hammer has created a novel heart valve leaflet using polymer and reinforcement fibers that promises to achieve the durability of mechanical valves without their risk of thrombogenicity. Dr. Hammer's valve mitigates this risk through the fiber pattern's unique control of valve function and stress distribution. The 2011 grant will fund design, manufacturing and testing of a series of valve prototypes.

INTRAVENOUS OXYGEN DELIVERY VIA MICROBUBBLE TECHNOLOGY
John Kheir, MD, Department of Cardiology

Dr. Kheir has shown that intravenous delivery of oxygen via microbubbles can rapidly increase plasma oxygen concentration to reverse acute hypoxia. Notably, near-normal levels of oxygen were maintained in a rabbit during a 15-minute period of asphyxia. If successful, this technology could have clinical advantages over CPR, intubation and mechanical ventilation. The project was the recipient of 2009 and 2010 grants, and the 2011 funding will support optimization of the microbubble formulation.

DIAGNOSTIC FOR KAWASAKI DISEASE
Susan Kim, MD, MMSc, Department of Rheumatology

Kawasaki Disease (KD) is a pediatric autoimmune disease that causes inflammation of blood vessels and which, if left untreated, can lead to coronary artery aneurysms in up to 25 percent of affected children. There is currently no diagnostic test for KD. Dr. Kim has identified several novel protein markers in the urine of KD patients, two of which have been validated in a 60 patient study. The 2011 grant will be used to further assess the specificity and predictive utility of these proteins in diagnosing KD.

CYSTATIN B: NOVEL PROGNOSTIC BIOMARKER FOR BLADDER CANCER
Bruce Zetter, PhD, Vascular Biology Program

Dr. Zetter and his team, in collaboration with investigators at Massachusetts General Hospital, have discovered a novel cancer urinary biomarker. Called cystatin B, the marker has been found to be a powerful, non-invasive and predictive marker of transitional cell carcinoma in the bladder. Dr. Zetter has shown that cystatin B correlates with tumor grade and stage, and is predictive of future disease recurrence and progression. The 2011 grant will support validation of cystatin B in a larger patient cohort using a quantitative assay.

GLYCO-TRAP: NOVEL GLYCOPROTEIN CAPTURE AND ANALYSIS DEVICE
Richard S. Lee, MD, and Hui Zhou, PhD, Department of Urology

Glyco-Trap, developed by Dr. Lee and colleagues, is a novel device technology that can sequentially release, capture and purify both glycans and protein fractions of a sample to facilitate subsequent structural characterization of both fractions: a critical tool for quality control analysis of biopharmaceutical product production, amongst other research and development applications. The 2011 grant will fund development and optimization of a Glyco-Trap device prototype to evaluate commercial potential.

LICENSES & COLLABORATIONS

COLLABORATIONS AND SPONSORED RESEARCH AGREEMENTS

NOVEL COLLABORATIVE RESEARCH AGREEMENT FOR MUSCULAR DYSTROPHY THERAPEUTICS WITH PFIZER

Pfizer and Children's have launched a new collaborative program aimed at identifying potential drug therapies for Duchenne muscular dystrophy (DMD). At the heart of the collaborative research agreement is a novel exchange of expertise that brings the respective strengths of academia and industry together in a framework that could benefit DMD patients in the future.

To have Pfizer show this level of interest in DMD is very exciting, and I am pleased to have this opportunity for us to put our complementary resources to work together.

–Louis Kunkel, PhD

The agreement focuses on the work of the laboratory of Louis Kunkel, PhD, director of the Program in Genomics and discoverer of the dystrophin gene that underlies the biology of DMD. In March 2011, Dr. Kunkel and colleagues announced the results of their efforts to screen 1,200 chemicals already approved for human use in a zebrafish model of DMD for any that might have a restorative effect on muscle tissue. Dr. Kunkel's team found that several had the desired effect in the zebrafish model, including compounds owned by Pfizer.

Through the agreement, Pfizer will, via its Orphan and Genetic Diseases Research Unit, provide Dr. Kunkel access to select proprietary compounds, as well as relevant data about these compounds. Pfizer is also committing internal resources to the project.

In collaboration with Pfizer, Kunkel's laboratory will test the compounds provided by Pfizer in the DMD zebrafish model, with an eye toward identifying candidates for further preclinical development.

"This agreement brings together the best of two worlds, namely Pfizer's ability to develop promising new compounds and our ability to test them in physiologically relevant models," Dr. Kunkel said. "To have Pfizer show this level of interest in DMD is very exciting, and I am pleased to have this opportunity for us to put our complementary resources to work together."

CHILDREN'S JOINS PFIZER'S CTI PROGRAM

Over the past 12 months, Pfizer has built collaborations with a number of premier academic medical centers, including Children's. In June of 2011, Pfizer launched the Boston branch of its Centers for Therapeutic Innovation (CTI), fostering independent collaborations with seven Boston institutions. The CTI aims to facilitate and support joint drug discovery and development from the conception of an idea through early clinical trials. Pfizer will provide Children's with its complementary knowledge, resources and infrastructure to support a number of Children's therapeutic projects.

Louis Kunkel, PhD

The CTI has a 50/50 mechanism for sharing the decision-making responsibility through its joint steering committee, which governs all aspects of the collaborations. Also, both parties work together to design projects through early human clinical trials, ensuring that only truly translational projects will be selected to move through this program and allowing Pfizer's unique strengths and infrastructure to be brought to bear.

As the only pediatric hospital in the CTI to date, Children's is optimistic that some of the projects supported through this program will lead to treatments for pediatric genetic conditions. Pfizer's recently created Orphan and Genetic Disease Unit will be represented in the partnership.

THE FDA AND CHILDREN'S TO DEVELOP A MOBILE APPLICATION FOR REPORTING ADVERSE MEDICAL DEVICE EVENTS

The U.S. Food and Drug Administration (FDA) uses several tools to help identify safety problems associated with medical devices. One of those

tools is its adverse event reporting system, which collects reports from manufacturers, user facilities, physicians, and voluntary reporters.

The bulk of reports received by the FDA are mandatory reports generated by manufacturers, importers and user facilities as required by federal law (21 CFR Part 803 and Part 519 of the U.S. Food, Drug & Cosmetic Act), but some are generated from individuals, such as medical practitioners or patients.

Meanwhile, broad adoption of Internet and mobile technologies has enabled a new class of real-time reporting systems where consumers can play a direct role in providing information regarding their experiences.

To encourage more participation from the public, John Brownstein, PhD, director of the Computational Epidemiology Group within the Children's Hospital Informatics Program, has been working alongside doctoral candidates Clark Freifeld at Boston University and Nabarun Dasgupta at the University of North Carolina to develop a mobile application and software called MedWatcher.

Medwatcher will engage the public in device safety and enable the users to report medical device adverse event information directly to the FDA. This tool represents a departure from the current method of receiving voluntary reports from user facilities, practitioners and patients, and provides significant advantages in scalability, coverage, timeliness and transparency.

The FDA and Children's are collaborating to develop this mobile tool to better engage users in issues of device safety, providing both current safety advisories and a reporting tool for direct submission of device events by the user. The system is designed to enhance the FDA's surveillance and regulatory efforts by generating intelligence about emerging medical device risks, especially for widely used devices.

COLLABORATION WITH THE LEUKEMIA & LYMPHOMA SOCIETY TO IDENTIFY LEUKEMIA THERAPEUTIC CANDIDATES

David Williams, MD, chief, Division of Hematology/Oncology and director of Translational Research at Children's, is working with The Leukemia & Lymphoma Society (LLS) in a collaborative effort to identify and evaluate new therapeutic candidates for leukemia. Together, Dr. Williams and LLS are searching for molecules that inhibit Rac, a member of the Rho GTPase family. Dr. Williams has previously published that Rac is a key regulator of the engraftment and mobilization functions of hematopoietic stem cells. Further, dysregulation in Rac function is a key molecular switch in leukemia. Utilizing unique models and assays performed by Dr. Williams' team and candidate molecules identified in *in silico* screening assays by LLS, the collaborators will evaluate future hits to find promising new leukemia therapies.

PFIZER ENTERS COLLABORATION TO BETTER UNDERSTAND THE PHARMACOGENETIC RESPONSE TO GROWTH HORMONE

Joel Hirschhorn, MD, PhD, director, Center for Basic and Translational Obesity Research, and Andrew Dauber, MD, MMSc, attending in Endocrinology, are collaborating with Pfizer scientists Laura Audi, MD, Pediatric Endocrinology Research Unit, and Antonio Carrascosa, MD, chief of the Pediatric Endocrine Service, Fundació Hospital Universitari Vall d'Hebron Research Institute, Barcelona, to study the pharmacogenetics of growth hormone responsiveness using genome-wide association analysis and target gene sequencing.

The knowledge gained from this study may enable clinicians to target growth hormone therapy to those who would yield the greatest benefits, and may help identify genetic subgroups of patients who would represent a new indication for growth hormone therapy. Finally, this study may identify novel genetic causes of short stature, which could represent new targets for growth-promoting therapies.

LICENSES

STARTUP SYNAPDX EXCLUSIVELY LICENSES AUTISM DIAGNOSTIC DISCOVERIES

SynapDx Corporation exclusively licensed worldwide rights to Children's discoveries to accelerate the development of its blood-based tests to enable the early detection of autism spectrum disorders (ASDs). The discoveries were developed through the collaboration of two leading Children's researchers: Louis Kunkel, PhD, director of the Program in Genomics, and Isaac Kohane, MD, PhD, chair of the Children's Hospital Informatics Program. ASDs are currently estimated to affect 1 in 110 children in the U.S. according to the Centers for Disease Control and Prevention. SynapDx hopes to provide laboratory-testing services to physicians who evaluate children for developmental disorders, with the goal of enabling earlier detection of autism.

MODIFIED RNA TECHNOLOGY LICENSED TO STARTUP MODERNA THERAPEUTICS

In December of 2010, the Program in Cellular and Molecular Medicine at Children's and the Immune Disease Institute (PCMM/IDI) exclusively licensed a "modified RNA" technology developed by Derrick Rossi, PhD, investigator in the PCMM, to a startup company, Moderna Therapeutics Inc., co-founded by Dr. Rossi, Professor Robert Langer, Massachusetts Institute of Technology (MIT), Kenneth Chien, MD, PhD, Massachusetts General Hospital, and Flagship Ventures, a venture capital firm headquartered in Kendall Square, Cambridge.

This technology, named one of *TIME Magazine's* "Top 10 Medical Breakthroughs for 2010," uses chemically modified RNAs to reprogram cells to serve as other cell types, and can reprogram various adult cells into pluripotent stem cells. It establishes a broad and powerful platform for producing novel research tools as well as developing therapeutics in regenerative medicine.

INVIVO THERAPEUTICS EXPANDS EXCLUSIVE LICENSE

Children's expanded its exclusive license with InVivo Therapeutics to include two new fields of use. InVivo, founded in 2005, had previously licensed Children's biopolymer technologies that protect and support nervous system tissue. The technology was developed by Yang (Ted) Teng, MD, PhD, Department of Neurosurgery, Professor Robert Langer, MIT, and Eric Woodward, MD, New England Baptist Hospital, for use in treating spinal cord injury.

The expanded license allows InVivo to develop products to treat nerve damage in the CNS, the optic nerve and retina, and certain areas of the peripheral nervous system. After demonstrating successful functional recovery in a non-human primate study, InVivo filed an IND in July 2011 for a biopolymer scaffold implant to treat spinal cord injury. The revolutionary pilot trial will be an open-label study of 10 patients with acute spinal cord injuries.

THERABIOLOGICS EXCLUSIVELY LICENSES STEM CELL TECHNOLOGIES FOR TREATING BRAIN CANCERS

TheraBiologics, Inc. has exclusively licensed Children's stem cell technologies for treating brain cancers and other invasive and metastatic solid tumors.

Brain tumors affect over 23,000 patients and accounted for over 13,000 deaths in the U.S. in 2011. They are also the leading cause of death from solid tumor cancers in children. Secondary brain tumors from metastases to the brain from melanoma, lung cancer and breast cancer account for 98,000 - 170,000 cases per year in the U.S. and 20 percent of cancer deaths annually.

In the late 1990's, former Children's researchers Evan Snyder, MD, PhD, and Karen Aboody, MD, along with collaborators from the University of Pennsylvania, the University of British Columbia, and Massachusetts General Hospital, created engraftable human neural stem cells (NSC) and cell therapy methods to treat brain tumors. They also showed data supporting the use of intravenously administered NSCs as delivery vehicles to target therapeutic agents to metastatic tumor sites selectively.

TheraBiologics was recently founded by Dr. Aboody to develop new cancer treatments. In 2010, the FDA approved an IND application by Dr. Aboody and City of Hope to begin a Phase I clinical trial in recurrent glioma patients under a dose escalation protocol. This trial is currently ongoing.

LICENSES WITH PRODUCTS LAUNCHED IN FY11

ISPAWN ZEBRAFISH BREEDING TANK PRODUCT LAUNCHED

Developed by Christian Lawrence and Isaac Adatto of Children's Aquatic Resources Program and the laboratory of Leonard Zon, MD, director of Children's Stem Cell Program, the iSpawn is a specialized breeding tank designed to take advantage of the zebrafish's natural preference for breeding in shallow water. Originally, Adatto built a tank with a sliding insert using a five-gallon bucket, some mesh, hot glue, and a hacksaw. It worked well enough that Adatto and Lawrence decided to scale it up into something that would be efficient enough for lab use.

Adatto and Lawrence worked with a plastics fabricator to develop several large-scale prototypes, and then with TIDO to license the design to Tecniplast, a manufacturer of animal care equipment for research. The company, which will further develop and market the iSpawn, unveiled its design at the 2011 European Zebrafish Meeting in Scotland.

The system holds much promise for genetic and stem cell researchers who use zebrafish. In a June 2011 *PLoS ONE* paper, Adatto et al. directly compared the iSpawn's performance with that of the standard breeding practice, looking at parameters such as the time needed to conduct a large-scale collection and the numbers of embryos collected. The iSpawn allowed the team to collect double the number of fish embryos in a quarter of the time and less than one-fifth the amount of lab space.

BEE VISUAL EXCLUSIVELY LICENSES BLOOD DRAW EDUCATIONAL TOOL TO REDUCE ANXIETY IN CHILDREN

Children with autism and other developmental conditions are often nervous when faced with medical procedures such as blood draws. These children may refuse or make it very difficult for clinicians to carry out this procedure.

To address this problem, Ellen Hanson, PhD, director of the Neurodevelopmental Disorders Phenotyping Program, and Lenny Rappaport, MD, chief of the Division of Developmental Medicine and director of the Developmental Medicine Center, developed an educational kit to aid parents in preparing children for the procedure. The kit consists of a storybook describing the blood draw procedure and a simple medical kit with example tools like those used in the clinic to help parents condition the children. The educational material has been shown in clinical studies to significantly reduce the stress in these children.

Children's collaborated with Bee Visual, LLC of Southborough, MA to translate the research material developed by Drs. Hanson and Rappaport into a commercial kit that is being sold widely to parents. The kit is available for purchase at www.beevisual.com.

Ellen Hanson, PhD

CLINICAL TRIAL AGREEMENTS

Our collaboration leverages Children's clinical research know how with our complementary late stage drug development expertise to help patients with autism and other neurodevelopmental disabilities.

–Randall Carpenter, MD
President and CEO
Seaside Therapeutics

Ramzi Nasir, MD, MPH

VGO COMMUNICATIONS TELEMEDICINE ROBOT STUDY

Hiep Nguyen, MD, co-director of the Center for Robotic Surgery, has been using robotics to enhance his urological surgery procedures for years, but his newest interest is in developing new ways to use robots outside of the operating room. Dr. Nguyen teamed up with VGo Communications to use their VGo, a 4-foot tall, remotely controlled robot on wheels with video conferencing capabilities, to communicate with and remotely monitor patients post-surgery. The approach—featured in the *Boston Globe* and by ABC News— spares the patient and family from making additional visits to the hospital, while allowing the doctor to visually evaluate recovery. This is an early pilot study in telemedicine at Children's, and will evaluate the impact of the robot solution on both the cost of post-operative care as well as patient satisfaction.

Hiep Nguyen, MD

CLOSED-LOOP INSULIN THERAPY TRIAL TO TREAT DIABETES

Management of type 1 diabetes in young children is complicated due to their unpredictable eating patterns, erratic activity levels and need for small doses of insulin. Andrew Dauber, MD, MMSc, attending physician in Endocrinology, and Garry Steil, PhD, research scientist, have designed and initiated a clinical trial to compare closed-loop insulin delivery to standard insulin pump therapy in children under age 7. Closed-loop insulin therapy—which to date has never yet been explored in this age group— involves the integration of continuous glucose monitoring with continuous insulin delivery via an insulin pump using an algorithm that calculates insulin dosage. This system essentially serves as an artificial pancreas. Study partners Abbott Diabetes Care Inc., Animas Corporation and HemoCue, Inc. are providing the devices required to carry out the trial.

Andrew Dauber, MD, MMSc

AUTISM SPECTRUM DISORDER CLINICAL DRUG STUDY

Ramzi Nasir, MD, MPH, assistant in Medicine, and other investigators from the Division of Developmental Medicine are embarking on an industry-sponsored clinical trial that will assess arbaclofen, provided by Seaside Therapeutics, for the treatment of autism spectrum disorders (ASDs). If successful, this study could translate into a better understanding of how to treat ASDs and other neurodevelopmental disorders.

CLINICAL TRIAL TO SLOW THE PROGRESSION OF INTRALUMINAL MULTIVESSEL PULMONARY VEIN STENOSIS

Intraluminal multivessel pulmonary vein stenosis (PVS) is a rare but deadly condition that affects infants and young children. The only known "cure" is lung transplantation, which has its own serious risks and a poor prognosis, with a three to five year survival rate. The cause of PVS is unknown; however, the progressive vessel obstruction seen in this condition is known to be caused by uncontrolled growth of

myofibroblasts, which express the biologic markers PDGFR and VEGFR on their surface.

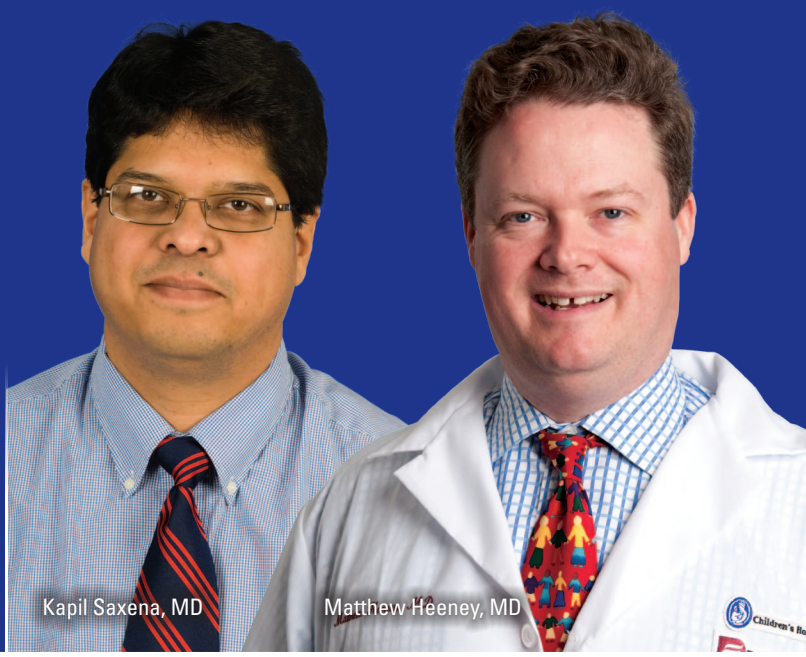
Based on this knowledge, Kathy Jenkins, MD, MPH, senior associate in Cardiology, and Mark Kieran, MD, PhD, director of Pediatric Neuro-Oncology, are studying the use of Gleevec® (which targets PDGFR), manufactured by Novartis Pharmaceuticals; with or without Avastin® (which targets VEGFR), manufactured by Genentech, to treat the progression of intraluminal multivessel PVS in patients. This is the first clinical study of its kind to use anti-cancer agents to treat this condition.


Kathy Jenkins, MD, MPH

CLINICAL STUDIES TO TEST LONGER LASTING DRUGS IN PATIENTS WITH HEMOPHILIA

Hemophilia is a group of hereditary genetic disorders that impairs the body's ability to control bleeding. Specifically, hemophilia A is an X chromosome-linked bleeding disorder that primarily affects 1 out of 5,000 males. It is caused by mutations and/or deletions in the Factor VIII gene, which results in a lack of Factor VIII activity.

Investigators Kapil Saxena, MD, associate director, Boston Hemophilia Center, and Matthew Heeney, MD, director, Clinical Hematology, are embarking on industry-sponsored studies focusing in hemophilia A. In particular, their attention has been drawn to a new set of hemophilia therapies, that they believe will last longer in the circulation, requiring fewer infusions and allowing doctors to treat patients with hemophilia A more effectively. Success in these studies could help doctors reduce the number of bleeding episodes patients experience while helping improve their joint health.


Kapil Saxena, MD

Matthew Heeney, MD

CHILDREN'S HOSTS FIRST RARE DISEASE SYMPOSIUM

TIDO and Children's Manton Center for Orphan Disease Research hosted Children's first Rare Disease Symposium on November 17, 2011. The day-long symposium highlighted researchers and clinical investigators whose work focuses on understanding rare diseases and developing ways to treat them.

Pediatrician-in-Chief Gary Fleisher, MD, opened the symposium by outlining the breadth of Children's research enterprise, its unique patient population, and the resources and drive with which Children's investigators pursue the development of treatments for their patients. The meeting was designed to encourage conversations between Children's investigators and industry partners with the goal of building partnerships that enable promising discoveries to become clinical treatments. The conference led to several of the academic-industry collaborations that are highlighted in this report.

We were honored to have the individuals listed (right) as speakers at the inaugural symposium.

Scott Armstrong, MD, PhD - Associate in Medicine, Division of Hematology/Oncology
Alan H. Beggs, PhD - Director, The Manton Center for Orphan Disease Research
David Clapham, MD, PhD - Chief, Basic Cardiovascular Research Laboratories
George Q. Daley, MD, PhD - Director, Stem Cell Transplantation Program, Division of Hematology/Oncology
Elizabeth Engle, MD - Associate in Neurology, Ophthalmology and Medicine
Gary Fleisher, MD - Physician-in-Chief, Pediatrician-in-Chief and Chairman, Department of Medicine
Raif Geha, MD - Chief, Division of Immunology
Ellis Neufeld, MD, PhD - Associate Chief, Division of Hematology/Oncology
Luigi Notarangelo, MD - Director, Research and Molecular Diagnosis Program on Primary Immunodeficiencies, Division of Immunology
Mustafa Sahin, MD, PhD - Director, Multi-Disciplinary Tuberous Sclerosis Program, Department of Neurology
Yang Shi, PhD - Merton Bernfield Professor of Neonatology, Division of Newborn Medicine
Edward Smith, MD - Director, Pediatric Cerebrovascular Surgery, Department of Neurosurgery and the Vascular Biology Program
Christopher Walsh, MD, PhD - Chief, Division of Genetics
Matthew Warman, MD - Director, Orthopaedic Research Laboratories, Department of Orthopaedic Surgery
David Williams, MD - Chief, Division of Hematology/Oncology, Director of Translational Research

APPENDIX 1 SUMMARY OF TECHNOLOGY TRANSFER ACTIVITY FY06–FY11

INVENTION DISCLOSURES

	2006	2007	2008	2009	2010	2011
TOTAL	98	94	116	128	117	134

GROSS REVENUES ($M)

	2006	2007	2008	2009	2010	2011
TOTAL	22.4	18.1	16.3	14.3	12.6	10.6

ALL AGREEMENTS NEGOTIATED

	2006	2007	2008	2009	2010	2011
Exclusive licenses	8	7	5	10	9	4
Non-exclusive licenses	16	19	14	16	16	11
Options	3	3	3	2	5	2
TOTAL	27	29	22	28	30	17
Corporate sponsored research and collaborations	11	18	9	8	9	24
Clinical trials	34	36	32	58	31	43
Material transfer	285	398	603	617	860	839
Confidentiality	80	64	74	71	130	122
Amendments	5	4	9	9	2	4
Agreements involving the receipt of equity	0	1	1	2	0	0
Inter-institutional invention administration	11	11	4	14	13	20
CRO agreements	-	-	-	-	8	15
Other*	5	6	4	6	16	21

* Includes project, royalty sharing and consulting agreements, and memoranda of understanding

PATENT APPLICATIONS FILED

	2006	2007	2008	2009	2010	2011
Provisionals	49	47	69	63	42	49
PCTs	25	24	26	33	27	28
U.S.	49	33	30	44	45	52
Foreign	27	18	22	29	9	20

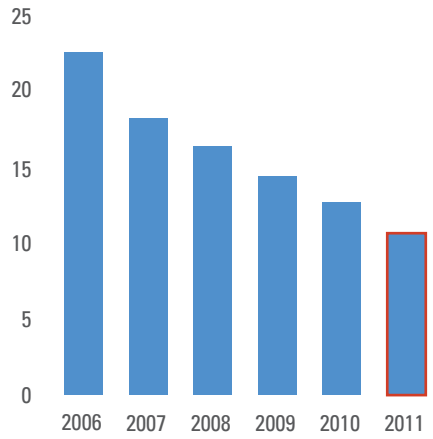
TECHNOLOGY DEVELOPMENT FUND

	2009	2010	2011
Letters of intent	27	41	52
Funded projects	11	12	12
Total money awarded	$1.2 M	$1.4 M	$1.0 M
Projects with renewed funding		3	3
Money spent to date*	$780,000	$400,000	**
Follow-on funding *	$4.6 M	$785,000	**
Significant collaborations *	1	3	**
Follow-on publications (published and manuscripts)*	6	8	**
Follow-on patent applications *	4	2	**
Network of CROs	-	9	18

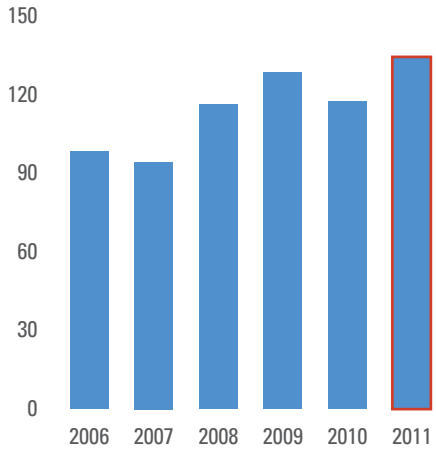
* By funding year ** To be determined

APPENDIX 2 SIX-YEAR TREND OF TECHNOLOGY TRANSFER ACTIVITY FY06–FY11

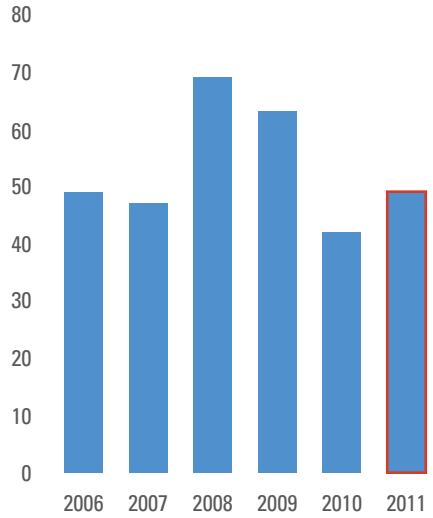
GROSS REVENUES ($M)



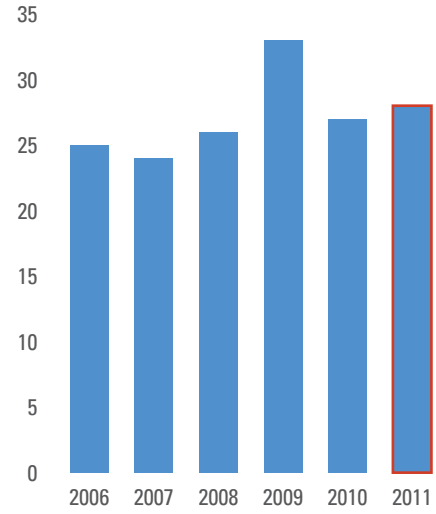
INVENTION DISCLOSURES



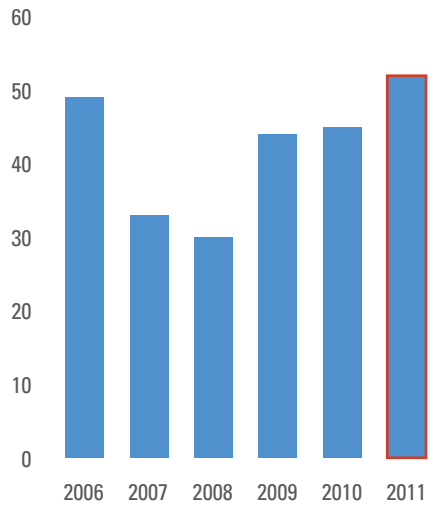
PROVISIONALS FILED



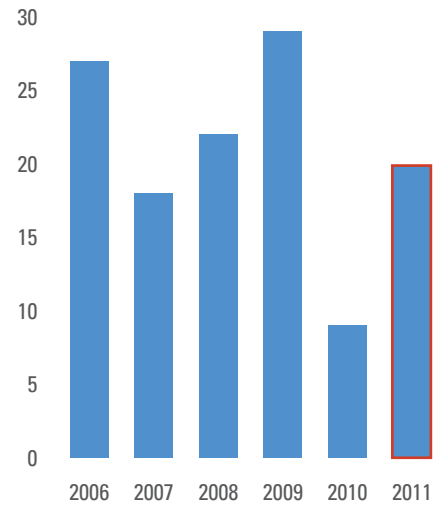
PCTS FILED



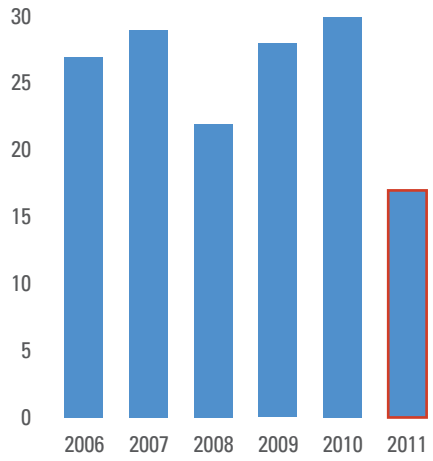
U.S. PATENTS FILED



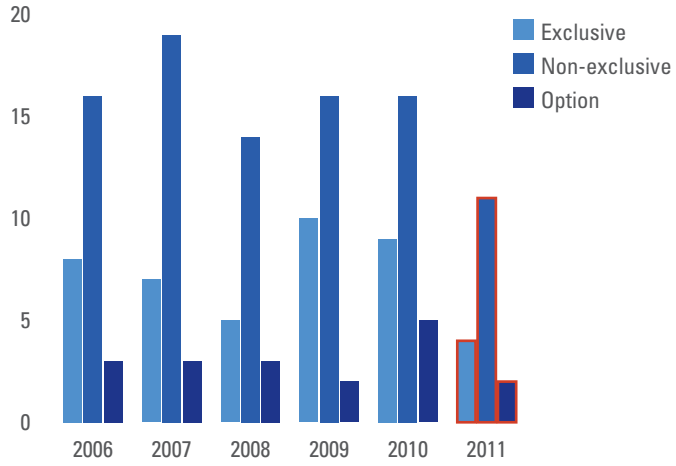
FOREIGN APPLICATIONS FILED



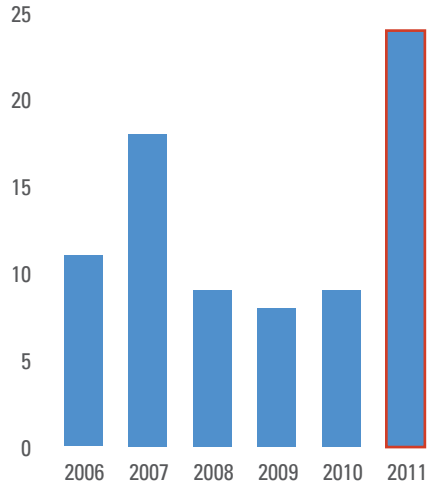
LICENSES & OPTIONS GRANTED



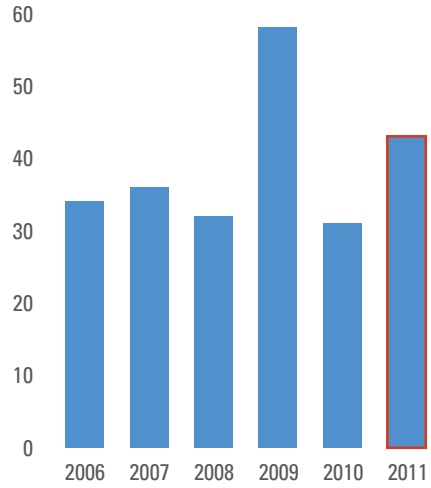
BREAKDOWN OF LICENSE & OPTION AGREEMENTS



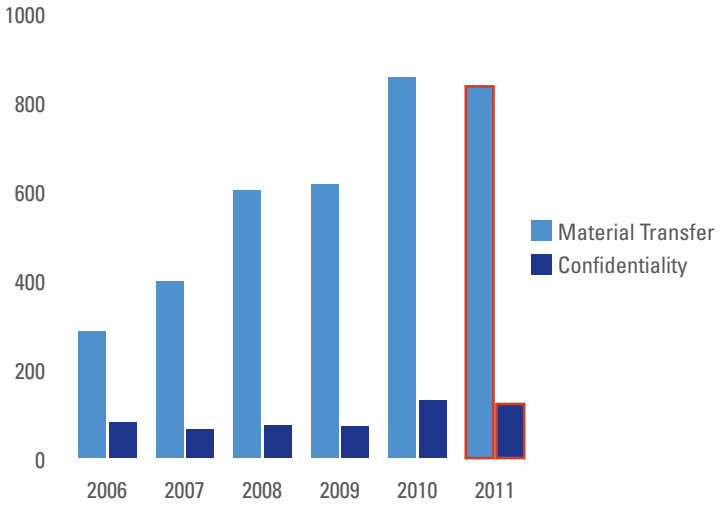
SPONSORED RESEARCH & COLLABORATION AGREEMENTS



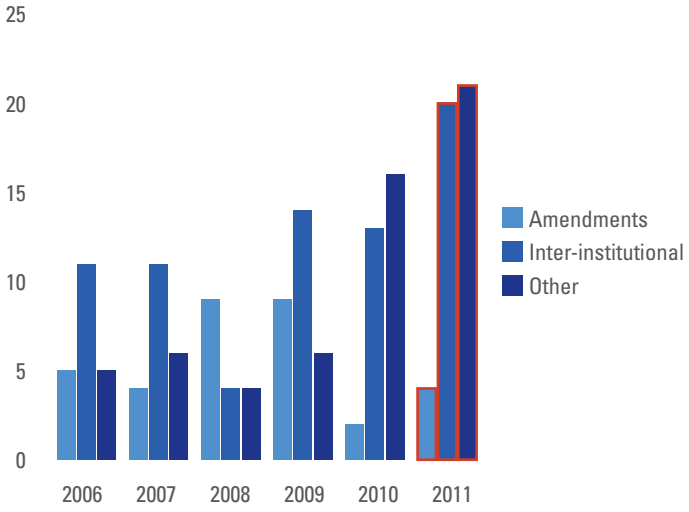
CLINICAL TRIAL AGREEMENTS



NON-LICENSE AGREEMENTS: MATERIAL TRANSFER & CONFIDENTIALITY



NON-LICENSE AGREEMENTS: OTHER



APPENDIX 3 PATENTS ISSUED IN FY11

UNITED STATES

LEAD INVENTOR	ISSUE DATE	PATENT NUMBER	APPLICATION TITLE
Atala, Anthony	9/20/11	8,021,876	Methods of isolation, expansion and differentiation of fetal stem cells from chorionic villus, amniotic fluid, and placenta and therapeutic uses thereof
Springer, Timothy	9/20/11	8,021,668	Integrin alpha L I domain mutants with increased binding affinity
Wu, Bai-Lin	8/23/11	8,003,326	Method for diagnosing autism spectrum disorder
Zetter, Bruce	8/9/11	7,993,863	Methods for diagnosis and prognosis of cancer
Breuer, Christopher	7/26/11	RE42,575	Engineering of strong, pliable tissues
Atala, Anthony	6/28/11	7,968,336	Methods of isolation, expansion and differentiation of fetal stem cells from chorionic villus, amniotic fluid, and placenta and therapeutic uses thereof
Springer, Timothy	6/28/11	7,968,284	Modified polypeptides stabilized in a desired conformation and methods for producing same
Breuer, Christopher	6/21/11	RE42,479	Engineering of strong, pliable tissues
Mulligan, Richard	6/14/11	7,960,525	Gene repair involving *in vivo* excision of targeting DNA
Hunter, David	6/14/11	7,959,292	Vision screener
He, Zhigang	6/14/11	7,959,901 B2	EGFR inhibitors promote axon regeneration
Lieberman, Judy	5/17/11	7,943,589	siRNA microbicides for preventing and treating diseases
Benowitz, Larry	5/3/11	7,935,680	Methods for modulating the axonal growth of central nervous system neurons
Frank, Markus	4/19/11	7,928,202	Targeting ABCB5 for cancer therapy
Springer, Timothy	4/19/11	7,927,591	Conformation specific antibodies
Williams, David	3/29/11	7,915,384	Chimeric peptides for the regulation of GTPases
Puder, Mark	3/1/11	7,897,591	Method of treating fatty liver disease
Springer, Timothy	2/1/11	7,879,577	Modified polypeptides stabilized in a desired conformation and methods for producing same
Folkman, M. Judah	1/11/11	7,867,975	Therapeutic antiangiogenic endostatin compositions
Corfas, Gabriel	1/4/11	7,863,295	Treatments for neuropathy
Moses, Marsha	12/28/10	7,858,324	Cyr61 as a biomarker for diagnosis and prognosis of cancers of epithelial origin
Mayer, Bruce	12/7/10	7,846,746 B2	Methods of analysis and labeling of protein-protein interactions
Murray, Martha	11/23/10	7,838,630	Biologic replacement for fibrin clot
Alt, Frederick	11/23/10	7,838,503	Methods for extending the replicative lifespan of cells
Ingber, Donald	11/16/10	7,834,884	Method and apparatus for displaying information
Hirschhorn, Joel	11/9/10	7,829,281	Compositions and methods for obesity screening using polymorphisms in NPY2R
Von Andrian, Ulrich	11/2/10	7,825,088	Methods for the treatment of multiple myeloma
D'Amato, Robert	10/12/10	7,812,169	Method of synthesis of 4-amino-thalidomide enantiomers
Atala, Anthony	10/12/10	7,811,332	Reconstruction method for urological structures utilizing polymeric matrices
Rogers, Gary	10/12/10	7,810,501	Orthotic device for preventing and/or correcting deformational posterior plagiocephaly
Paige, Keith	10/5/10	7,807,150	Injectable composition containing crosslinkable material and cells for forming animal tissue
Atala, Anthony	10/5/10	7,806,937	Creation of tissue engineered female reproductive organs

FOREIGN

LEAD INVENTOR	ISSUE DATE	PATENT NUMBER	COUNTRY	APPLICATION TITLE
Snyder, Evan	8/12/11	4800544	Japan	Systemic gene delivery vehicles for the treatment of tumors
Zon, Leonard	8/10/11	2425876	Russian Federation	Method to modulate hematopoietic stem cell growth
Folkman, M. Judah	7/20/11	1783215	EPO	Angiostatin and method of use for inhibition of angiogenesis
D'Amato, Robert	7/5/11	2,457,319	Canada	Synthesis and anti-tumor activity of nitrogen substituted thalidomide analogs
D'Amato, Robert	6/14/11	2,430,669	Canada	Synthesis of 3-amino-thalidomide and its enantiomers
Snyder, Evan	5/10/11	2,406,664	Canada	Systemic delivery of neural stem cells to treat cancer
D'Amato, Robert	4/5/11	2,514,681	Canada	Methods and compositions for inhibition of angiogenesis
Paige, Keith	2/25/11	4690648	Japan	Injectable polysaccharide-cell compositions
Atala, Anthony	2/16/11	1448247	EPO	Creation of tissue engineered female reproductive organs
Atala, Anthony	2/16/11	1448247	France	Creation of tissue engineered female reproductive organs
Atala, Anthony	2/16/11	60239217.9-08	Germany	Creation of tissue engineered female reproductive organs
Atala, Anthony	2/16/11	1448247	Netherlands	Creation of tissue engineered female reproductive organs
Atala, Anthony	2/16/11	1448247	United Kingdom	Creation of tissue engineered female reproductive organs
Folkman, M. Judah	1/21/11	4666767	Japan	Deglycosylated kringle 1-5 region fragments of plasminogen and methods of use
Zetter, Bruce	12/1/10	1842065	EPO	Methods for diagnosis and prognosis of bladder cancer
Zetter, Bruce	12/1/10	1842065	France	Methods for diagnosis and prognosis of bladder cancer
Zetter, Bruce	12/1/10	1842065	Germany	Methods for diagnosis and prognosis of bladder cancer
Zetter, Bruce	12/1/10	1842065	United Kingdom	Methods for diagnosis and prognosis of bladder cancer
He, Zhigang	11/18/10	2006269616	Australia	EGFR inhibitors promote axon regeneration
Benowitz, Larry	10/8/10	4601816	Japan	Use of purine nucleosides for modulating axonal outgrowth of CNS neurons

Q & A: DAVID MARGULIES, MD

EXECUTIVE DIRECTOR OF THE GENE PARTNERSHIP AT CHILDREN'S

The ultimate goal of the Gene Partnership is to better understand the role of genomic measurements in understanding disease and creating precision treatments for individuals.

–David Margulies, MD

The Gene Partnership (GP), now underway at Children's Hospital Boston, is a multidisciplinary program for enhancing research, improving patient care and accelerating the translation of genetic and genomic insights into clinically relevant information. The GP's long-term vision is to combine analysis of phenotypic data with that of the full genome, and use the integrated knowledge to inform and guide patient care. David M. Margulies, MD, executive director of the Gene Partnership, is creating a blueprint and leading a team of thought leaders with expertise in genome-guided medicine.

Dr. Margulies is no stranger to Children's. He was the hospital's first Chief Information Officer from 1986 to 1990, and went on to launch several successful companies. In 2001, he and other colleagues from Children's created Correlagen Diagnostics (now a part of LabCorp), where he led the development of automated genetic testing systems. Now he has returned to Children's, bringing his academic and commercial experience and success to bear in the service of the GP.

TIDO is honored to have had the chance to interview Dr. Margulies and discuss his vision for the GP, as well as the impact that it and other programs could have on the future of healthcare.

WHAT DOES THE FUTURE STATE OF MEDICINE LOOK LIKE, AND HOW WILL THE GENE PARTNERSHIP HELP US GET THERE?

Systems biologist Leroy Hood has described the future of medicine as "predictive, preventive, personalized and participatory." It is based on a clearer understanding of the interactions of complex elements that underpin health and disease. This future *systems biomedicine* hopes to explain the impact of genetic variation along with environment. In practice, we may be able to understand the behavior of a specific cancer and use this information to choose more effective treatments. In short, we should be able to characterize a patient's expected response to drugs and many uncommon illnesses may, finally, be understood and treated.

The Gene Partnership is assembling the basic tools and methods of systems biology, creating new ones and setting out a blueprint to apply them to both research and the practice of pediatric medicine at Children's.

WHAT IS THE OVERARCHING GOAL OF THE GENE PARTNERSHIP?

The ultimate goal of the GP is to better understand the role of genomic measurements in understanding disease and creating precision treatments for individuals. Over time, we are building a large cohort of patients and families and analyzing both genomic and phenotypic data to uncover meaningful insights about the root causes of disease. While we build critical mass toward that goal, we will also utilize the infrastructure and methods that power the GP to bring immediate benefits to patients and the research community.

WHAT IS THE GENE PARTNERSHIP'S STRUCTURAL AND PROCESS BLUEPRINT?

The GP is focused on obtaining extensive genomic data (DNA sequence, RNA sequence and epigenetic measurements) from large numbers of consented patients and family members with well-characterized disease phenotypes and

electronic medical record data. We will seek to correlate genome-derived and phenotypic measurements with other known data to evaluate specific research hypotheses, and will use the findings to diagnose and guide treatment decisions. Finally, we will also use advanced bioinformatic techniques for non-hypothesis driven exploration of this copious data set.

All of this work is taking place in the context of a collaborative arrangement between families, patients and researchers in which patients are informed in real-time of advances in knowledge related to their genetic profile.

WHAT WILL THE GENE PARTNERSHIP DO IN THE SHORT TERM?

In the early years, the GP will focus on several specific clinical and research projects: safer use of prescription medications, selection of cancer chemotherapy regimens most attuned to the specific state of an individual's cancer, genomic sequence-based definition of previously undiagnosed serious illnesses in children and piloting of multimodal assessment of children with autism spectrum disorders.

This is just the beginning, as a number of other projects are in the early planning stages. In each project, the GP team will address consenting, phenotyping, specimen collection, genomic analysis and interpretation. All will be done in a manner that advances the specifications and features of the Partnership's methods and systems for use on other projects.

WHAT OPPORTUNITY DOES COLLABORATING WITH THE GENE PARTNERSHIP REPRESENT FOR PARTNERS OUTSIDE OF CHILDREN'S?

The infrastructure we are building will be a powerful generator of new knowledge. Because it is based on detailed data from a large population – data that can be navigated in a way that protects patient privacy – it represents opportunities for collaborators of all types in academia, government and industry.

On the therapeutic development side, the tools will be useful for stratifying patients for clinical trials, performing *in silico* phase IV clinical studies, quickly identifying adverse events and finding relevant biomarkers.

For diagnostics, the practice of large-scale medical genomics will not only identify new genes and rare variants associated with disease, but also uncover unique combinations of gene variants associated with more subtle phenotypes and suggest which treatment options would be more or less appropriate.

All of our data will build upon and add to the bodies of genomic data currently available to the public, as we fully recognize that the true power of genomics lies in the aggregation of data from extremely large populations. Children's now has the pieces in place to obtain, analyze and report these data for the benefit of patients.

SELECTED PRODUCTS ON THE MARKET & IN CLINICAL TRIALS

	PRODUCT	COMPANY	PHASE 1	2	3	Mkt
THERAPEUTICS	**Revlimid** – Various indications	Celgene				
	Thalomid – Multiple Myeloma	Celgene				
	Namenda – Alzheimer's Disease	Merz				
	Neumega – Thrombocytopenia	Pfizer				
	Omegaven – Parenteral Nutrition Associated Liver Disease	Fresenius Kabi				
	Pomalidomide – Multiple Myeloma	Celgene				
	Von Willebrand Factor – Hemophilia	Baxter				
	FcRn-Factor VIII & Factor IX – Hemophilia	Biogen IDEC				
	IgF-I – Prevention of complications of preterm birth	Premacure				
	dmPGE2 – Stem cell stimulation	Fate Therapeutics				
DIAGNOSTICS	**Dystrophin Diagnostic** – Duchenne MD	Athena Diagnostics				
	INF2 DNA Sequencing Test – Focal Segmental Glomerulosclerosis	Athena Diagnostics				
MEDICAL DEVICES	**Cannula Needle Set** – Fetal surgery	ATC Technologies				
	Merge EchoIMS – Pediatric echocardiography	Merge Healthcare				
	Plagio Cradle – Treating early signs of Plagiocephaly	Boston Brace				
	Neo-Urinary Conduit – Patients requiring a urinary diversion following bladder removal	Tengion				
PATIENT AIDES	**Patient Communication Board**	Vidatek, LLC	No FDA trials needed			
	Blood Draw Learning Kit – Preparing kids with Autism for doctor visits	Bee Visual, LLC				
	When Things Go Right: Patient Safety Best Practices in Action (video)	HCPro				
	Raising Your Celiac Child-Guidelines for a Gluten-Free Life (video)	Children's				
	SonneWheel – Pediatric BMI assessment tool	Children's				
RESEARCH TOOLS	**QuickChange Mutagenesis Kits**	Agilent Technologies				

TECHNOLOGY & INNOVATION
DEVELOPMENT OFFICE

Technology & Innovation Development Office
Children's Hospital Boston
300 Longwood Avenue
Boston, Massachusetts 02115

617.919.3019

TIDO@childrens.harvard.edu

childrensinnovations.org