United States Patent [19]

Lazarus et al.

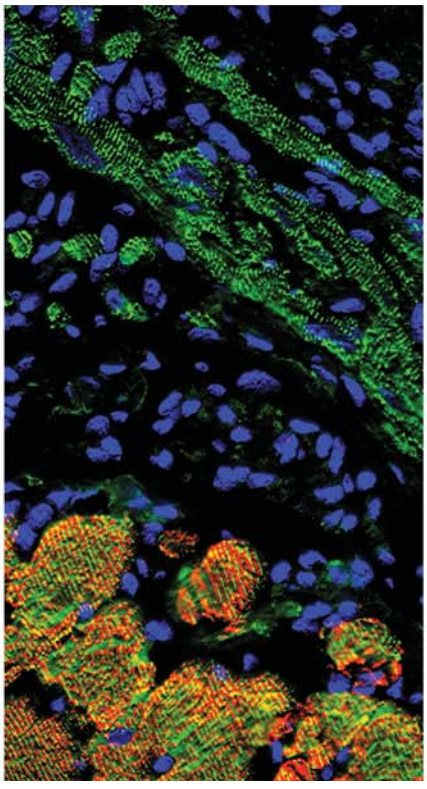
[54] **CELL FUSION**

[75] Inventors: **Herbert Lazarus**, Newton; **Jerrold F. Schwaber**, Brookline, both of Mass.

[73] Assignees: **The Children's Medical Center Corporation**, Boston; **Dana-Farber Cancer Institute, Inc.**, Newton, both of Mass.

[21] Appl. No.: **369,141**

INTELLECTUAL PROPERTY OFFICE



ANNUAL REPORT 2006

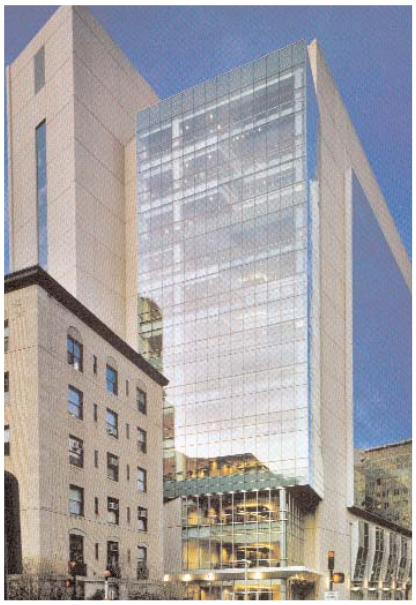
Children's Hospital Boston

A teaching affiliate of Harvard Medical School

CHILDREN'S HOSPITAL BOSTON

Children's Hospital Boston is one of the largest pediatric medical centers in the United States. Children's records approximately 17,000 inpatient and 450,000 outpatient admissions annually. Children's performs 22,000 surgical procedures and 170,000 radiological examinations every year. One hundred and sixty programs and emergency services have been developed to support outpatient services. The specialty pediatric clinics at Children's include Adolescent Medicine, Oncology, Genetics, Diabetes, Neurosurgery and Cardiology.

Children's is the most active pediatric research program in the world. Our funding base of $130 million annually supports more than 250 basic research and clinical investigators. Children's is affiliated with Harvard Medical School and the Howard Hughes Medical Institute. The hospital has over 600,000 sq. ft. of laboratory space. Areas of research expertise include vascular biology, stem cells, neuroscience, genomics/proteomics and informatics.



THE INTELLECTUAL PROPERTY OFFICE

Our goals include "100 percent case management" where the appropriate attention is given to each and every case and frequent communication is maintained with all constituents. We are entrepreneurial when warranted, creative where needed and open to suggestions and new ideas. We constantly strive to improve and welcome feedback to guide our efforts. The revenues and licenses reported in the coming pages demonstrate our success in these endeavors.

The operations and activities of Children's Hospital Boston's Intellectual Property Office (IPO) have been many and varied during fiscal year 2006 (FY06). Royalty revenues and the number of licenses increased compared to FY05. Children's joined the Harvard Stem Cell Institute and the Center for the Integration of Medicine and Innovative Technology (CIMIT). The IPO was very successful this year in developing new tools, methods and sponsorships for technology development of pediatric devices and medication formulations. Several exciting technologies are hitting milestones due to the efforts of our licensees, and truly spectacular and important new inventions have been disclosed to the IPO. Marketing to our external and internal customers is a mainstay of our program and continues to develop and mature. During the past year the IPO has reached out much more to our clinician researchers to collaborate, help obtain compounds and assist with prototype development.

IPO Activities
FY06

Invention Disclosures

The Intellectual Property Office (IPO) received 98 new invention disclosures from Children's Hospital Boston faculty, unchanged from the previous year.

FY06 Data Summary	
Invention Disclosures	98
Patent Applications Filed	125
US Applications Filed	87
Foreign Applications Filed	38
Patents Issued	35
US Patents Issued	18
Foreign Patents Issued	17
Licenses and Options Granted	27
Gross Revenues ($M)	$22.35
Net Revenue (less external institutes; $M)	$17.16
Revenue from New Licenses and Options ($M)	$1.18

Patent Filings

The IPO oversaw the filing of 125 patent applications over the course of the year. Forty-three provisional patent applications were filed. Twenty-two applications were filed for US and foreign rights under the Patent Cooperation Treaty (PCT) mechanism. Sixteen patent applications were filed in individual foreign countries.

Patent Issuances

Children's was granted 18 patents by the US Patent and Trademark Office and 17 by foreign patent offices. The Assignee designation for our patents is Children's Medical Center Corporation. These new patents are listed in Appendices 3 and 4.

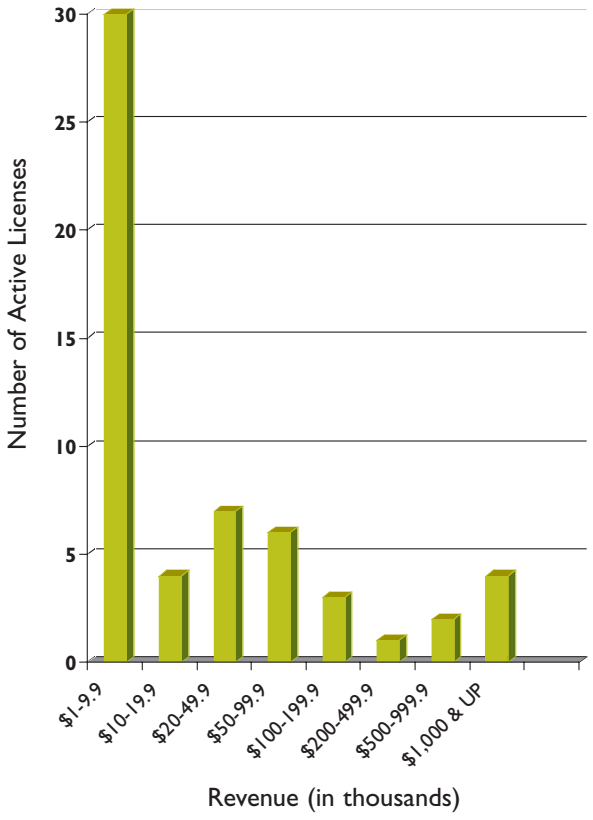
Licensing Activity

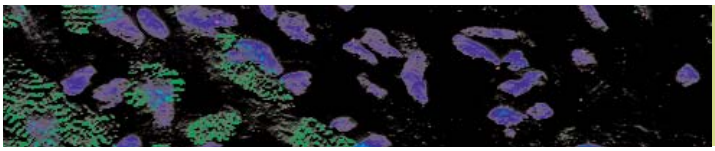
The IPO negotiated 27 license and option agreements for Children's technologies; eight exclusive licenses, 16 non-exclusive licenses and three options. The revenue recognized from these new license and option agreements was $1.18 million. The IPO's overall performance and licensing and patenting activities over the past five years are illustrated in Appendices 1 and 2.

Total Revenue

Total revenue received from all licenses has climbed in each of the past five years, and in FY06 was $22.35 million, a 27 percent increase over FY05. Of the 181 active license agreements, 57 generated revenue in FY06. Thirty of these 57 licenses brought in less than $10,000 each, but four produced over $1 million each.

Revenue-Generating Licenses FY06





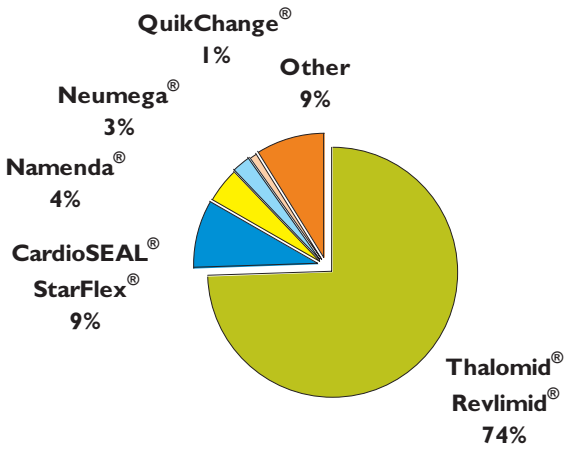
Significant Revenue-Generating Inventions

Seventy-four percent of the total revenue was generated by sales of Thalomid® and Revlimid® for the treatment of cancer. Other significant sources of revenue are royalties from the sales of CardioSEAL® and StarFlex® for minimally-invasive repair of heart defects; Namenda® for the treatment of Alzheimer's disease; and Neumega®, which stimulates platelet production and is used by cancer patients in combination with chemotherapy. Ninety-one percent of the IPO's revenue is derived from product royalties, while nine percent comes from a mixture of milestone payments, maintenance fees, license fees and other fees.

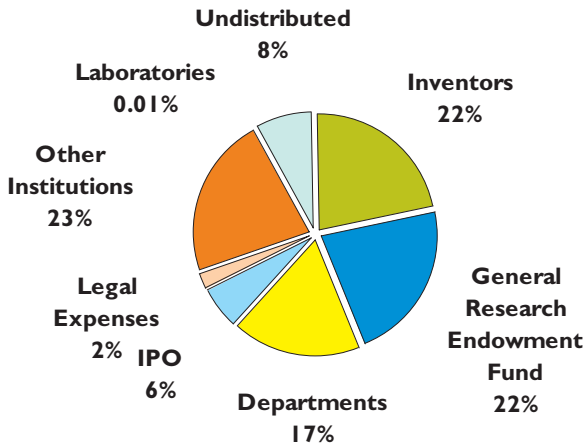
Distribution of License Revenue

Of the $22 million in total revenue, other institutional co-owners, inventors and the hospital's research endowment received approximately equal amounts, close to $5 million each. Approximately $3.8 million was shared by departments at Children's. The Surgical Research Foundation received 74 percent of this revenue. The other departments, including Cardiology, Neurology and Medicine, shared 26 percent. The IPO's operations were supported by approximately six percent of the revenues, and unrecovered legal expenses accounted for two percent. Only eight percent of the revenue received was awaiting distribution at the close of the fiscal year.

Sources of License Revenue

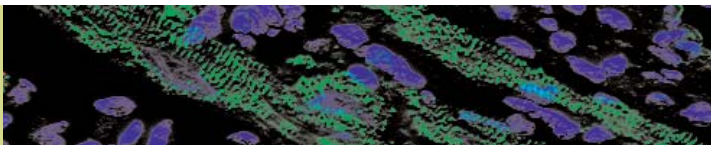


License Revenue Distribution
FY06: $22.35 Million

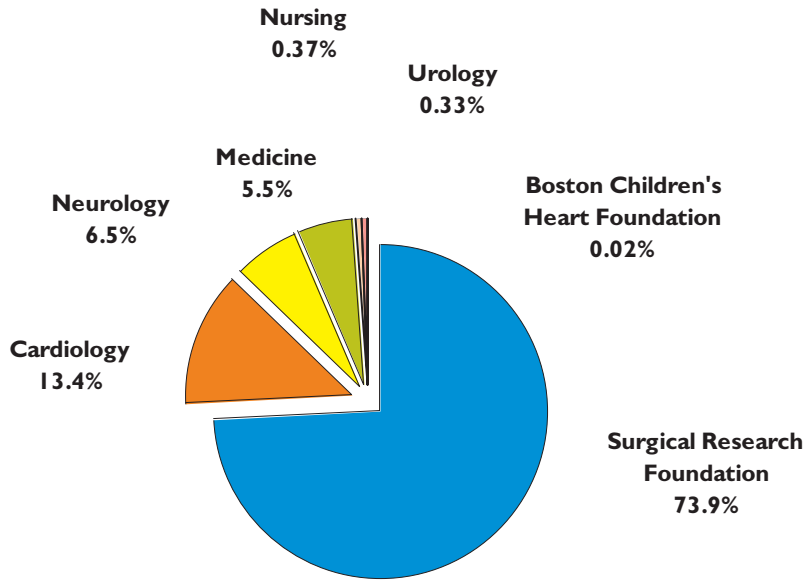


Recipients of Distributed License Revenue

Inventors	Departments	Research Endowment	Intellectual Property Office	Legal Expenses	Other Institutions	Undistributed Funds	Total
$4,875,686	$3,842,675	$4,912,813	$1,385,468	$415,971	$5,193,258	$1,724,968	$22,350,840



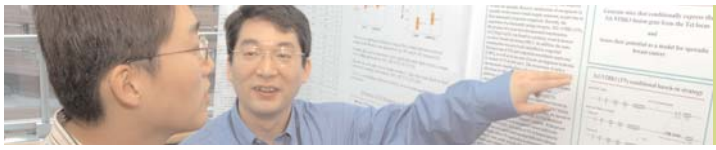
Distributions to Departments FY06: $3.84 Million



Invention Management Activity

At the end of FY06, the IPO had 412 inventions under active management. Working with David Altman, the IPO Marketing Assistant, 144 of these inventions were in marketing campaigns. Licensing managers monitored 181 ongoing licenses (distributed over 177 inventions), and coordinated the activities of outside patent attorneys to manage pending patent applications on 368 inventions and 663 issued US and foreign patents.

Invention Management Activity	
Inventions Under Active Management	412
Inventions Under Initial Evaluation	33
Inventions in Marketing Campaigns	144
Inventions in IPO Development	4
Inventions with License Pending	8
Licensed Inventions	177
Inventions with Other Institute Leading	38
Current Licenses	181
Issued US Patents	344
Issued Foreign Patents	319



LICENSE AND OPTION AGREEMENT HIGHLIGHTS

The IPO negotiated 27 license and option agreements in FY06 and three of those agreements are highlighted below.

Neuropilin Antagonist Technology to Genentech for Cancer Therapy

In November 2005, Children's entered into an exclusive license with Genentech, Inc. for anti-cancer technologies developed in the laboratory of Vascular Biology researcher Michael Klagsbrun, PhD. The approach of starving tumors of their blood supply, pioneered by Children's Judah Folkman, MD, received a boost two years ago when Genentech's drug Avastin® (bevacizumab) became the first FDA-approved cancer treatment specifically to target angiogenesis, or blood vessel growth. The Klagsbrun technologies, involving a cell receptor called neuropilin, share a similar mechanism of action with Avastin®.

In 1998, Klagsbrun and colleagues reported in the journal *Cell* that vascular endothelial growth factor (VEGF) binds not only to the VEGF receptor, but also to a co-receptor, neuropilin, originally known for its role in guiding growing nerve fibers to their appropriate destinations. Further studies showed that neuropilin acts in combination with the VEGF receptor to enhance VEGF signaling and function. This made neuropilin a good target for trying to inhibit cancer growth, and several animal studies run by Klagsbrun's team show promise in hitting that target. Klagsbrun believes that blocking VEGF from binding both to the VEGF receptor and to neuropilin may enhance anti-tumor efficacy.

Axon Regeneration Technologies to Boston Life Sciences for Central Nervous System (CNS) Therapy

Children's entered into a comprehensive licensing and sponsored research arrangement with Boston Life Sciences, Inc. (BLSI) around axon regeneration technologies. These technologies were developed in the laboratories of Larry Benowitz, PhD, and Zhigang He, PhD, who are among the first researchers to identify key factors and mechanisms that promote and inhibit axon regeneration, respectively. The complementary nature of the approaches studied by the two laboratories holds promise in advancing the development of "first-in-field" therapies targeted at restoring a variety of sensory and motor functions in patients after stroke and spinal cord, optic nerve and traumatic brain injuries.

Under the sponsored research agreements, BLSI has agreed to fund research programs for three years in the two laboratories for approaches to activate pro-regenerative pathways that stimulate axon regeneration led by Dr. Benowitz, and for approaches to deactivate anti-regenerative pathways that inhibit axon regeneration led by Dr. He. The simultaneous implementation of these sponsored research programs may open avenues for exploring combination therapies for intractable CNS disorders.

Lead Poisoning Treatment to Bezoloven

Children's entered into an option agreement with Bezoloven, a start-up company, to fund a clinical trial of a lead poisoning treatment developed by Michael Shannon, MD, Chief, Division of Emergency Medicine. Dr. Shannon has worked for years to find new and more effective treatments for lead poisoning, which is one of the most

prevalent environmental illnesses of childhood. Despite a Health and Human Services established goal of eradicating it by the year 2011, there remain an estimated 310,000 American children with elevated blood lead levels. Increasing evidence shows that identifiable physiologic disturbances occur in children with low-level lead poisoning and that chelation therapy can reverse some of these disturbances. In cooperation with Tedor Pharmaceuticals, Dr. Shannon has developed a pediatric friendly formulation of d-penicillamine for the treatment of low-level lead poisoning. Bezoloven is raising funds to conduct a Phase III trial of this product.

ONGOING AGREEMENTS UPDATE

The progress made under three ongoing agreements negotiated by the IPO prior to FY06 is described below.

Addgene Agreement Eases Research Material Exchange

In FY06 Children's researchers saw the benefits of agreements put in place by Children's IPO with Addgene, Inc. to help promote the exchange of research reagents among academic scientists. Addgene is a non-profit organization based in Cambridge, MA. They collect research reagents produced by investigators at academic and non-profit institutions (without charge to the provider), maintain the complete documentation of the material's composition, verify the material and store it in two redundant sites. The company currently collects only DNA plasmids, but they hope to extend their collection to other biological reagents. Archived plasmids are cataloged on their Web site, and can be ordered by any academic scientist for a minimal processing fee.

Addgene provides our researchers with a mechanism to document their plasmid collections and a secure off-site back-up for their collections, and eliminates the time and effort required to respond to and fulfill requests for reagents from other labs. Importantly for the IPO and other technology transfer offices involved, Addgene has implemented a simplified Material Transfer Agreement (MTA) process, with electronic approval and online access to transaction records. As a result of the IPO's work to establish a relationship with Addgene, we have greatly reduced the effort required by Children's, managing the equivalent of 97 MTAs, eliminating delays from negotiating terms, reducing the time necessary to get MTA approval and maintaining complete records of transactions.

Banking of Stem Cells at Birth for Future Use in Therapy and Tissue Reconstruction

Children's licensee, Plureon Corporation, entered into an agreement with Cryo-Cell International, Inc. for banking of Plureon Stem Cells isolated from placental tissue. Cryo-Cell, one of the world's largest private cord blood banks, announced the placental stem cell banking service in October 2005, and is preparing for its imminent launch. Parents will soon have the opportunity at the birth of their children to collect both cord blood and Plureon Stem Cells from placental tissue for their future therapeutic potential. Plureon licensed these pluripotent cells and their use from Children's in 2003. These placental stem cells have been differentiated into cells of all three germ layers, including bone, skeletal muscle, cardiac muscle, liver, nerve, fat and pancreatic cells. They have some important biological properties that make them safe and well suited to either

reconstruction of tissues or cell therapy applications. The cells have a potentially wide range of therapeutic applications and have demonstrated efficacy in disease models. The collection of the tissue does not harm the mother or the infant and the placental tissue would otherwise be discarded as medical waste. The cells are not sourced from human embryonic tissues, and researchers believe that these cells could be an alternative to embryonic stem cells in the development of human cellular therapies.

First Tissue-Engineered Bladder is Functional in Pediatric Patients

During his more than 14 years of research and medical practice at Children's, Anthony Atala, MD, saw the need for a more effective treatment for infants and children who were born with small and inflexible bladders - particularly those with spina bifida. Children left untreated and those who undergo current therapies are often plagued by significant side-effects that could eventually put the child's renal function and general health at risk. Dr. Atala first began trying to solve this problem by gathering some of the patient's own healthy bladder cells and establishing a method to expand them in large quantities in his laboratory. Then he designed a degradable scaffolding system that would enable the growth of a three-dimensional bladder-like organ, and used the patient's bladder cells to populate the scaffolding. Once the new bladder-like tissue had grown, it was surgically implanted into each patient in a way that encouraged local tissues to support its continuing maturation and growth. For the seven children whose bladders were rebuilt using this technique, the resulting regenerated organs have led to improved bladder function, reduced side effects and improved quality of life for between two and five years. The results of this ground-breaking patient study were published this year in *The Lancet* 2006; 367:1241-1246. This and other Atala technologies licensed from Children's in 2003 formed the basis of regenerative medicine company Tengion, Inc. (www.tengion.com). Tengion is working with the Food and Drug Administration (FDA) to begin clinical trials of its first product, a neo-bladder.

TECHNOLOGY HIGHLIGHTS

Three innovative technologies managed by the IPO in FY06 are highlighted below.

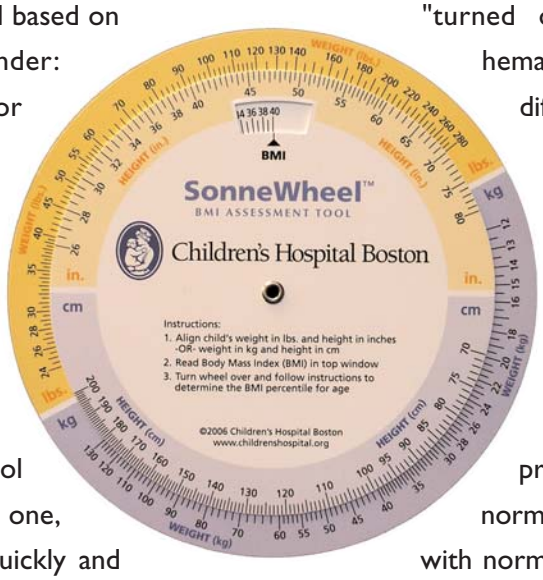
Life-Saving Treatment with Omega-3

Research in the laboratory of Children's surgeon Mark Puder, MD, PhD, focused on determining the specific component of total parenteral nutrition (TPN) that contributes to liver damage, led to a rapid change in bedside practice. TPN is the complete liquid nutritional formulation of essential proteins, lipids (fats) and sugars given intravenously to infants who are unable to feed orally. When an infant receives TPN for several months, the liver often becomes severely damaged, and the child requires a liver transplant in order to survive. The incidence of mortality without a transplant is up to 100 percent within 12 months. As soon as Dr. Puder determined that the plant-derived lipid component of TPN causes liver damage in animal studies, he focused his research on altering the type of lipid. The challenge was to identify an intravenous lipid form that would provide children with essential fats and avoid causing fatty acid

deficiency and liver damage. Children's Pharmacist Kathleen Gura, PharmD, suggested testing Omegaven, an omega-3-based product derived from fish oil. Positive results in mice permitted Dr. Puder to obtain FDA compassionate care approval to use Omegaven to treat infants experiencing liver damage due to the standard of care. To date, 28 infants have been successfully treated at Children's, and the number continues to increase rapidly both nationally and internationally due to Dr. Puder's and Dr. Gura's seminal paper published in *Pediatrics* 2006; 118:197-201.

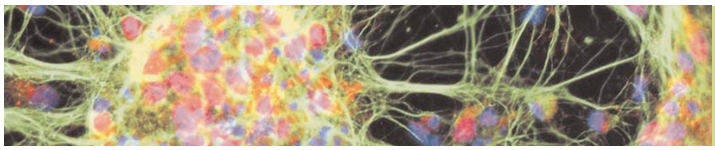
SonneWheel™

Clinicians routinely measure a child's body mass index (BMI) beginning at age 2. BMI is plotted on a standard chart, one for boys and one for girls, based on age, to monitor a child's development and track weight patterns. A plan of action is then established based on the percentile a child falls under: underweight, normal, at risk, or overweight. Currently, separate tools or formulas are used to determine the child's BMI and weight risk profile. Kendrin Sonneville, MS, RD, LDN, a dietitian at Children's, proposed a wheel-shaped prototype for a pocket-sized clinical reference tool that combines all the tools in one, allowing clinicians to determine quickly and easily a child's risk for being over or underweight. The IPO developed a product based on this proposed prototype. An internal grant from Public Affairs and the Office of Child Advocacy at Children's allowed the IPO to retain a graphic designer and printer to generate the SonneWheel™. The Public Affairs department has since given away thousands of these wheels to pediatricians to rave reviews.



Leukemia Stem Cell Identified

In his clinical practice and laboratory, Children's physician and researcher Scott Armstrong, MD, PhD, is working to find a cure for leukemia. He has created a unique model of leukemia in mice that closely mimics the human disease. Published in *Nature* 2006; 442 (7104):818-822, his intense work with the mouse model has led to the identification and confirmation of a rare population of disease-causing leukemia stem cells (LSC). These cells are most similar to a population of normal, differentiated blood cells found in healthy individuals, but they have re-activated a set of genes that are usually only "turned on" in undifferentiated progenitor hematopoietic stem cells (HSC), which differentiate to form many blood cell types. As few as four LSCs are capable of causing severe leukemia in a special strain of recipient mice, making the LSC line a powerful and important tool to identify and test new therapeutic targets. By comparing the gene expression profiles of disease-causing LSCs with the normal differentiated blood cells, as well as with normal HSCs, Dr. Armstrong has identified a group of LSC-specific, potentially therapeutic targets. This important new model system will rapidly lead to the identification of significant new drug targets that could be the basis of a cure for this devastating disease.



NEW TOOLS TO HELP DEVELOP CLINICAL PRODUCTS

Children's has approximately 400 research scientists, more than a 1,000 clinical physicians and more than 4,000 clinical staff. While Children's has enjoyed significant success moving ideas from bench to bedside, our realization of marketed products from clinical concepts and ideas has been more challenging. To support technology transfer of product ideas from the clinical staff, Jacqueline Armstrong, BEng, MBA, Nurjana Bachman, PhD, and Monique Yoakim-Turk, PhD, from the IPO created a number of new tools to foster product commercialization. These tools accelerated product development through partnerships and securing of funding for several projects.

Feasibility Studies

We tapped into the rich resource of MBA students from local business schools to complete commercial analysis and market feasibility studies of four key clinical technologies. The feasibility studies helped guide the best development approach and quantify the market potential and amount of money required to move the clinicians' inventions from ideas to proof-of-concept to commercialization.

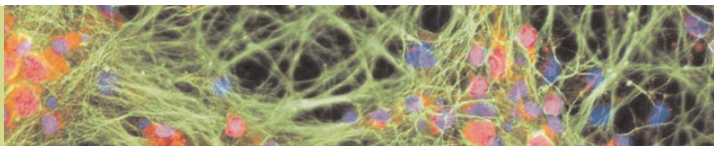
Advisory Board

An Advisory Board consisting of local entrepreneurs, venture capitalists, attorneys, engineers, physicians and others with expertise in the medical device or pharmaceutical formulation industries was convened to critique the commercial potential of several technologies, and recommend development strategies for individual technologies and product portfolios in specific disease areas. Members of the Advisory Board met with Martha Murray, MD, of Orthopaedics, Frances Jensen, MD, of Neurology and Joseph Madsen, MD, of Neurosurgery to discuss their respective technologies. One of the two meetings with Dr. Madsen was dedicated to his ideas and goals around the development of a micro-robot for neurosurgical applications. The meeting brought together members of the Advisory Board, engineering partners at Infoscitex and Foster-Miller, as well as other Children's surgeons, including Pedro del Nido, MD, Rusty Jennings, MD, and Bradley Linden, MD. The meeting resulted in a grant proposal for a new micro-robot that listed nine Children's surgeons as principal investigators or consultants. The project has since received $750,000 of funding through a Phase II Small Business Innovation Research (SBIR) grant.

Funding Sources

In the past year, we tapped into several funding sources to help develop technologies. With the assistance of a member of the Advisory Board, we developed innovative funding mechanisms and risk-sharing arrangements to support the commercialization of the lead poisoning treatment developed by Children's Chief of Emergency Medicine Michael Shannon, MD (discussed in License and Option Agreement Highlights on page 4). Nurjana Bachman, PhD, and Martha Murray, MD, applied for and were granted $25,000 from the Massachusetts Technology Transfer Center to fund continued development of a medical device prototype for delivery of a novel biologic-based joint repair technology. The device is being developed in collaboration with engineering partners at TNCO.

We have continued to support Joseph Madsen, MD and Eugene Goldfield, PhD in their collaborations with the two engineering firms Foster-Miller and Infoscitex. In conjunction with Infoscitex, Dr. Madsen and Dr. Goldfield were awarded Phase I and Phase II SBIR grants, respectively, worth more than $1 million to develop and test prototypes of medical devices.



THE STEM CELL PROGRAM AT CHILDREN'S HOSPITAL BOSTON

Dedicated faculty and staff from five cooperating laboratories at Children's, along with more than 50 affiliate members hospital-wide, have formed the Stem Cell Program. Under the leadership of Leonard Zon, MD, and George Daley, MD, PhD, the mission of the Stem Cell Program is to explore, understand and translate the promise of stem cells into clinical therapies and treatments. The IPO has supported the efforts of more than a third of the Stem Cell Program members. We have negotiated four material transfer agreement templates, two licenses, four confidential disclosure agreements and one inter-institutional agreement with various commercial and not-for-profit organizations. The goals of these efforts are to facilitate the investigators' research, the transfer of funds and stem cell lines, and the use of third party proprietary technologies. The IPO has patented three stem-cell-based technologies and marketed them to venture capital firms and companies for the purpose of promoting Children's breakthrough stem cell research. One of our goals included increasing exposure of these technologies in order to find new sponsorship and funding opportunities for the Stem Cell Program. In addition, the IPO has joined the Intellectual Property Committee of the Harvard Stem Cell Institute to enhance the development of new stem-cell-based technologies and maximize their ability to access the research community and the marketplace. An oversight committee has been formed to review potential issues and conflicts, and to define and implement the best intellectual property strategies.

CIMIT MEMBERSHIP

In October 2005 Children's became an official member of the Center for the Integration of Medicine and Innovative Technology (CIMIT). CIMIT brings together clinicians, engineers and scientists to create innovative technologies and new solutions that will improve healthcare. CIMIT fosters these collaborations through symposia, meetings and grants that fund collaborative projects between engineers, scientists and healthcare professionals. Membership in CIMIT gives Children's clinicians the opportunity to apply for research funds from CIMIT to support interdisciplinary collaborations with other CIMIT members. Intellectual property resulting from these grants is governed by a formal agreement between Children's and CIMIT that is administered by the IPO.

FACULTY/STAFF EDUCATION AND MARKETING PROGRAMS

The entire IPO staff collaborates in the department's faculty and staff education and marketing efforts, but the programs have a Resource Manager, Christine P. Nogueira, PhD, MBA, and a full time Marketing Assistant, David Altman. Our outreach efforts educate Children's faculty and staff about intellectual property and promote our investigators and technologies to the outside world.

Ongoing Education Programs

- We gave 24 presentations to Children's newly hired research personnel this year. These are aimed at educating researchers about intellectual property when they first join the staff. We encourage researchers to interact with and disclose inventions to our office with the goal of preventing future problems with Material Transfer Agreements, and premature presentation or publication of results before evaluation for patenting. This program has been running continuously for four years.

- Last May we participated in Children's annual "Research Day" by presenting a poster about the IPO's services. A new handout, "Frequently Asked Questions," was prepared and distributed to interested research staff.
- We twice presented a training module in intellectual property to hospital research administrators, covering basic principles in understanding and handling intellectual property.

New Education Programs and Events

- Peter Hodges, PhD, from the IPO, in collaboration with Paul Rufo, MD, from the Division of Gastroenterology and Nutrition, Department of Medicine, made the presentation "Patents and Your Research--Hand in Hand for Your Future" to the Children's fellows in October 2005. The goals of the presentation were to educate the audience about different aspects of intellectual property and present our office as a resource to the investigators.
- We organized and sponsored three networking events. The first was a pizza and beverage event for the Children's fellows, in collaboration with the Children's Fellows Association, in October 2005. The second was a "Cappuccino Event" for all Children's investigators in June 2006. The third event was an open house at the IPO for the Office of Sponsored Programs and the Clinical Trials Office to meet with us. All events were well attended and the licensing managers had the opportunity to answer a number of questions related to intellectual property.
- In August 2006 we launched the Intellectual Property section in the Mandatory Yearly Review for all Children's researchers. The test covers important procedural concepts involving intellectual property that all researchers should be familiar with.
- We published two articles in the Children's Research Administration online newsletter: "Protect CHB Intellectual Property: Get a Confidentiality Agreement in Place Before Meeting with a Company;" and "Material Transfer Agreement Do's and Don'ts."

Marketing to Industry

- The marketing group coordinates the IPO's marketing efforts, but all licensing managers proactively searched for opportunities to interact with industry, and to promote our inventions, investigators and office. For the third year in a row, we ran our internal Marketing Quality Improvement Program with high levels of compliance, a measurement that the intellectual property entrusted to us was marketed in a timely manner. As a group, we attended 17 conferences and participated in several courses and events to refine our knowledge of intellectual property and educate ourselves about the needs of the industry.
- We co-sponsored a booth for the second year in a row with Children's Clinical Trials Office at BIO 2006, a major meeting for the global pharmaceutical and biotechnology industries.
- We sponsored trade show booths at the annual meetings of our professional organizations: Association of University Technology Managers (AUTM), Licensing Executives Society (LES) and the combined AUTM/LES Spring Meeting.
- We hosted visits from industry and venture capital groups where we presented technologies available for

licensing and learned more about how to attract research funding to our organization.

- We shared our marketing strategies and use of our database systems with the technology transfer community by visiting Harvard University's Office of Technology Development at their invitation.

Online Presence

The IPO Web site serves as an online compendium of our procedures and policies (www.childrenshospital.org/ipo). Since many companies search the Web looking for licensing opportunities, our Web site also presents our technologies available for licensing to potential licensees. Our Web site is expanded and updated regularly.

We increased our online technology marketing efforts in FY06 by posting our technologies on the Massachusetts Technology Portal, which is an online portal where academic institutions in Massachusetts post their licensing opportunities. In addition to our own Web site, our technologies are now regularly posted on three technology exchanges: the MassTech Portal (www.masstechportal.org), TechEx (www.techex.com) and BirchBob (www.birchbob.com).

Marketing Materials

We have continuously produced new marketing materials for our portfolio of technologies and updated the existing ones throughout the year. These materials are our basic tool to reach licensees through mailings and online resources.

STAFFING

Chief Intellectual Property Officer Donald P. Lombardi resigned from Children's this year after 15 years, during which time he established the IPO as it exists today. Former Associate Director Brenda Manning, PhD, is now Director of the IPO, and three of the former Senior Licensing Managers, Christine P. Nogueira, PhD, MBA, Rudolf Slovacek, PhD, and Monique Yoakim-Turk, PhD, were promoted to group leader positions with licensing managers directly reporting.

Through the highly successful implementation of the IPO strategic plan under Donald Lombardi's direction, the IPO tripled its staff over the past six years. And through a well developed training program the staff has become one of the most well trained and best functioning groups in the technology transfer business. We will focus on the development of translational programs and commercialization strategies as growth areas in 2007.

The IPO licensing staff now consists of 12 professionals, 11 with PhDs in biological areas, two who have spent time in the academic tenure track, two with MBAs, one with an engineering degree, four who have industry experience and three who have issued patents to their names. In addition, we have developed a highly professional business office and administrative staff that ensures financial activities are executed in a timely and accurate manner.

OUTLOOK FOR NEXT YEAR

We expect licensing revenues to reach about $25 million during the coming year, continuing the increasing trend of past years. The IPO staff will be focusing on more outreach to both basic and clinical researchers, thus anticipating increased invention disclosures, collaborations and sponsored research, particularly with industry. Increased focus on commercialization strategies, training and activities will also be major goals.

APPENDIX 1

Summary of Technology Transfer Activity

(Fiscal Year 2002 through Fiscal Year 2006)

Invention Disclosures					
	2002	2003	2004	2005	2006
Total	**92**	**111**	**118**	**98**	**98**

All Agreements Negotiated					
	2002	2003	2004	2005	2006
Exclusive Licenses	7	9	7	5	8
Non-exclusive Licenses	7	11	4	13	16
Options	11	8	8	3	3
Total	**25**	**28**	**19**	**21**	**27**
Agreements Involving the Receipt of Equity	1	1	1	0	0
Amendments	8	4	4	2	5
Research Collaborations*	4	3	5	11	7
Corporate Sponsored Research*	5	6	5	6	4
Material Transfer*	173	180	203	261	285
Confidentiality*	68	49	75	95	80
Inter-Institutional Invention Administration	16	9	11	8	11
Other	4	3	5	12	5

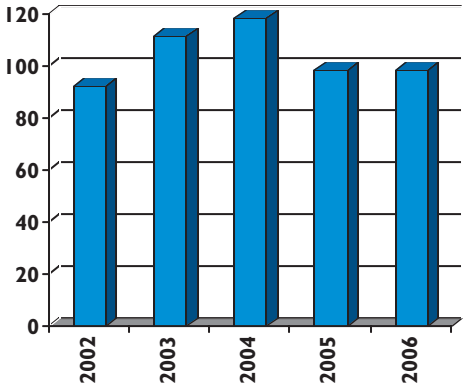
* Corporate Sponsored Research, Confidentiality, Research Collaboration and Material Transfer Agreements are negotiated in collaboration with the Clinical Trials Office (John Counts, J.D., Beth Brennan, Jay Kaplan, J.D. and Jesse Wheeler).

Gross Revenues (Millions of Dollars)					
	2002	2003	2004	2005	2006
Total	**11.8**	**13.2**	**14.1**	**17.6**	**22.4**

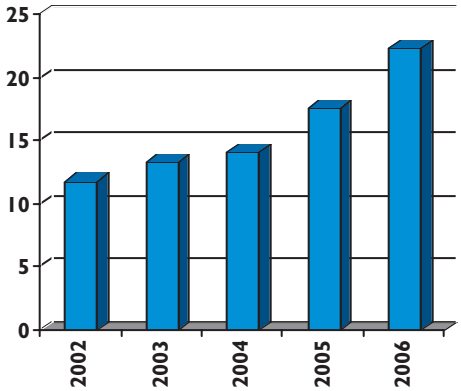
Patent Applications					
	2002	2003	2004	2005	2006
Provisionals Filed	70	29	54	55	43
PCTs Filed	31	30	14	30	22
Foreign Filed	79	64	32	15	16
US Issued	23	30	31	20	18

APPENDIX 2
Five-Year Trend of Technology Transfer Activity
(Fiscal Year 2002 through Fiscal Year 2006)

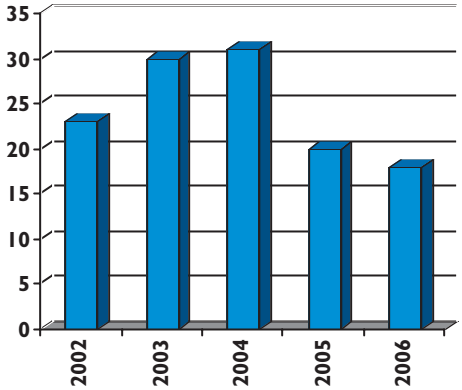
Invention Disclosures



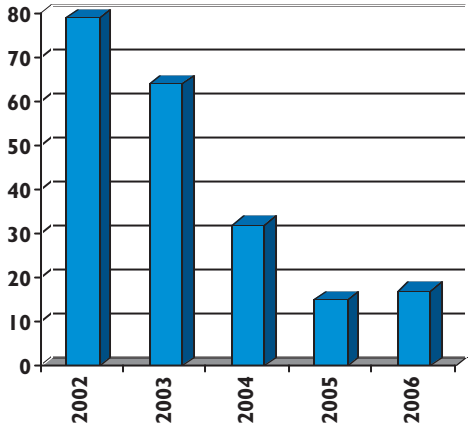
Gross Revenues ($ Millions)



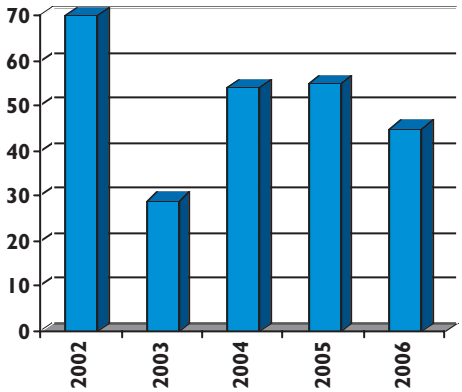
U.S. Patents Issued



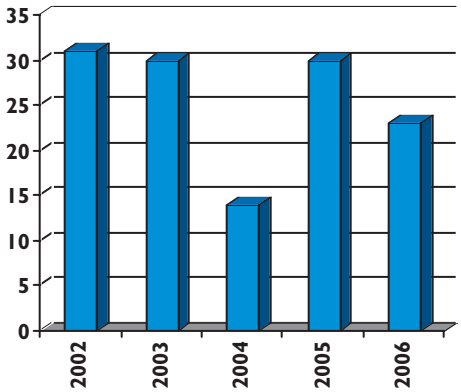
Foreign Applications Filed



Provisionals Filed



PCTs Filed

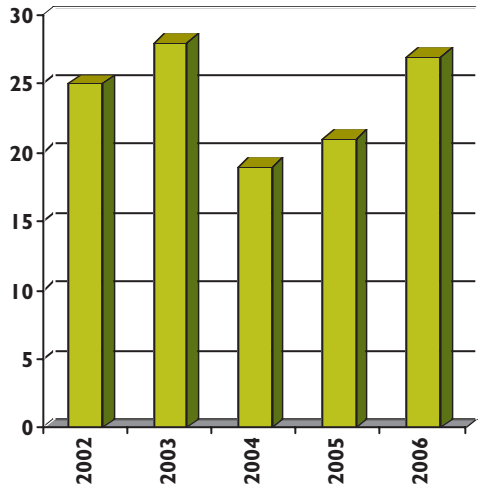


APPENDIX 2 (cont.)

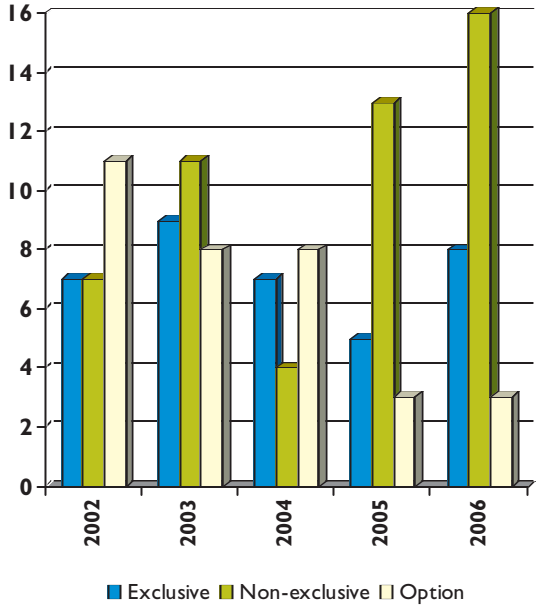
Five-Year Trend of Technology Transfer Activity

(Fiscal Year 2002 through Fiscal Year 2006)

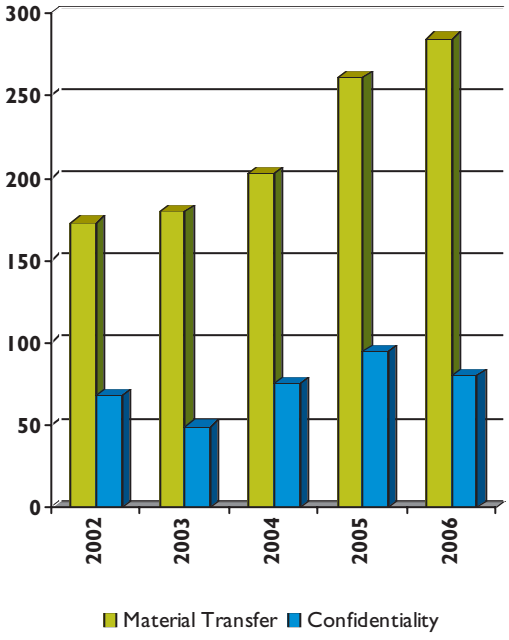
Licenses & Options Granted



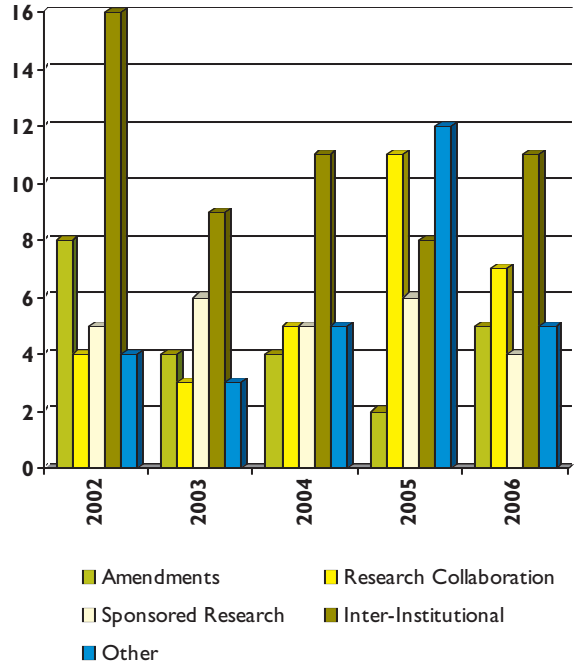
Breakdown of License and Option Agreements



Non-License Agreements Material Transfer and Confidentiality



Non-License Agreements Other



APPENDIX 3

US Patents Awarded in FY06

Children's Lead Inventor	Patent Number	Title
Atala, Anthony	7,049,057	Tissue Engineered Uterus
Ben-Sasson, Shmuel	7,037,891	Methods of Modulating G-Protein-Coupled Receptor Kinase-associated Signal Transduction
Brugnara, Carlo	6,992,079	Substituted 11-Phenyl-Dibenzazepine Compounds Useful for the Treatment or Prevention of Disease Characterized by Abnormal Cell Proliferation
D'Amato, Robert	6,977,268	Methods and Compositions for Inhibition of Angiogenesis with EM-138
D'Amato, Robert	7,112,602	Methods of Treating Undesired Angiogenesis with 2-Methyl-EM-138
D'Amato, Robert	7,081,477	Estrogenic Compounds as Antimitotic Agents
D'Amato, Robert	7,012,070	Estrogenic Compounds as Antimitotic Agents
D'Amato, Robert	7,109,187	Estrogenic Compounds as Antimitotic Agents
Folkman, Judah	7,101,979	Antibodies to Anti-Angiogenic Compositions and Methods
Gerard, Craig	7,012,133	Antibodies to C-C Chemokine Receptor 3 Protein
Gerard, Craig	6,994,977	Method of Identifying Inhibitors of C--C Chemokine Receptor 3
He, Zhigang	7,012,063	Reducing Axon Degeneration with Proteosome Inhibitors
Ingber, Donald	7,067,306	Device Containing Cytophilic Islands that Adhere Cells Separated by Cytophobic Regions
Moses, Marsha	7,078,385	Methods of Inhibiting Angiogenesis with Fragments and Homologs of Troponin Subunit I
Mulligan, Richard	6,958,226	Packaging Cells Comprising Codon-optimized Gagpol Sequences and Lacking Lentiviral Accessory Proteins
Murray, Martha	6,964,685	Biologic Replacement for Fibrin Clot
Solomon, Keith	7,098,198	Compositions of Ezetimibe and Methods for the Treatment of Cholesterol-associated Benign and Malignant Tumors
Teng, Yang Dong	7,071,194	Method for Improving Respiratory Function and Inhibiting Muscle Degeneration

APPENDIX 4

Foreign Patents Awarded in FY06

Children's Lead Inventor	Territory	Patent Number	Title
Atala, Anthony	Europe	1261692	Methods and Compositions for Reconstruction of Multilayered Tissue Structures
Atala, Anthony	Europe	1244396	Method and Compositions for Organ Decellularization
Atala, Anthony	Europe	1042019	Penile Reconstruction
Atala, Anthony	Japan	3,816,534	Bladder Augmentation Using Allogenic Bladder Submucosa
Benowitz, Larry	Korea	564789	Use of Purine Nucleosides for Modulating the Axonal Outgrowth of Central Nervous System Neurons
Brugnara, Carlo	Europe	781128	Clotrimazole Metabolites in Sickle Cell Disease
D'Amato, Robert	Europe	713393	Estrogenic Compounds as Antimitotic Agents
D'Amato, Robert	Hong Kong	HK1014504	Estrogenic Compounds as Antimitotic Agents (2-MOE)
D'Amato, Robert	Sweden	713393	Estrogenic Compounds as Antimitotic Agents (2-MOE)
Folkman, Judah	Canada	2291892	Angiostatin Fragments and Method of Use
Folkman, Judah	Israel	113,509	Pharmaceutical Compositions Comprising Fragments of Plasminogen Angiostatin Protein, Nucleic Acids Encoding the Same, and Methods of Detecting Angiostatin Protein, Nucleic Acids Encoding
Folkman, Judah	Japan	3,787,157	Angiostatin Fragments and Aggregate Angiostatin and Methods of Use
Folkman, Judah	Japan	3,840,262	Endostatin Cell Proliferation Inhibitor and Method of Use
Lencer, Wayne	Europe	1003550	Receptor Specific Transepithelial Transport of Therapeutics
Lipton, Stuart	Europe	661973	Use of Nitroglycerin Compounds to Prevent Neurological Complications
Yankner, Bruce	Australia	2003200877	Drugs for the Treatment of Alzheimer's Disease
Zetter, Bruce	Europe	1270745	Novel Thymosin-like Molecule Associated with High Metastatic Potential in Prostate Cancer

IPO STAFF INFORMATION

Brenda Manning, PhD
Director of the Intellectual Property Office
brenda.manning@childrens.harvard.edu

Christine P. Nogueira, PhD, MBA
Senior Licensing Manager, Group Leader
christine.nogueira@childrens.harvard.edu

Rudolf Slovacek, PhD
Senior Licensing Manager, Group Leader
rudolf.slovacek@childrens.harvard.edu

Monique Yoakim-Turk, PhD
Senior Licensing Manager, Group Leader
monique.yoakim@childrens.harvard.edu

Leslie Grushkin-Lerner, PhD
Senior Licensing Manager
leslie.grushkin-lerner@childrens.harvard.edu

Kathleen Bass, PhD
Senior Licensing Manager
kathleen.bass@childrens.harvard.edu

Peter Hodges, PhD
Licensing Manager
peter.hodges@childrens.harvard.edu

Jacqueline Armstrong, BEng, MBA
Licensing Manager
jacqueline.armstrong@childrens.harvard.edu

Annie Le Guern, PhD
Associate Licensing Manager
annie.leguern@childrens.harvard.edu

Nurjana Bachman, PhD
Associate Licensing Manager
nurjana.bachman@childrens.harvard.edu

Ashwini Joglekar, PhD
Associate Licensing Manager
ashwini.joglekar@childrens.harvard.edu

Abbie Meyer, PhD
Associate Licensing Manager
abbie.meyer@childrens.harvard.edu

Sharon Jordan-Prioleau, MBA
Business Manager
sharon.jordan@childrens.harvard.edu

Lisa Pight
Financial Assistant
lisa.pight@childrens.harvard.edu

Denise Wright
Administrative Assistant
denise.wright@childrens.harvard.edu

David Altman
Marketing Support
david.altman@childrens.harvard.edu

Children's Hospital Boston

300 Longwood Avenue
Boston, MA 02115

Intellectual Property Office

(617) 355-7050
IPO@childrens.harvard.edu
www.childrenshospital.org/ipo