

Technology & Innovation Development Office

ANNUAL REPORT





RESEARCH EXPENDITURES \$388 M

NEW INDUSTRY SPONSORED RESEARCH FUNDING \$18 M

RESEARCH AGREEMENTS 71

LICENSING AGREEMENTS 34

NET LICENSING REVENUE \$61 M*

INVENTION DISCLOSURES 129

STARTUPS CREATED 7

* Includes monetization of royalties



Wimalasema Nivanthika, Woolf Lab, F.M. Kirby Center for Neurobiology, Boston Children's Hospital



From the Director

THIS HAS BEEN A YEAR IN WHICH TECHNOLOGY COMMERCIALIZATION HAS BEEN

IN THE NEWS — unfortunately, not always for positive reasons. Academic institutions and scientists have been called out for failing to disclose their financial ties to industry, and these conflicts have cast a pall over the life-saving research done at academic institutions. I would argue, however, that our mission to treat patients is enhanced through our collaborations with industry, provided these are done in an ethical and transparent manner.

Most groundbreaking new therapies improving patients' lives today have originated from fundamental biological insights made at academic institutions. However, many of these breakthroughs would not reach patients without industry partnerships. Boston Children's is a world-leading research institution, yet despite our tremendous strengths, we are not able to bring new therapies to the market on our own. The necessary knowledge and expertise in drug development, FDA regulations, manufacturing and ultimately sales and marketing live in biotech and pharma, not academia. In partnership, we can reach the broadest group of patients.

Examples abound. Gene therapy, gene editing, RNA therapies, antibodies, CAR T-cell therapy all came from fundamental biological discoveries, made in academic institutions and commercialized through industry partnerships. Here at Boston Children's, patients with severe sickle cell disease are being treated with a novel gene therapy that is curing their painful and life-threating condition, not just treating the symptoms. This required basic insights into the biology of fetal hemoglobin, expertise in gene therapy and clinical trials, and support from bluebird bio to develop safe, clinical-grade gene therapy vectors.

Or consider mRNA therapies being developed by Moderna, a company that spun out of Boston Children's and just launched the largest biotech IPO ever. The therapies came from a fundamental insight into protein expression made by Derrick Rossi and his colleagues here at Boston Children's. Their discovery, that mRNA would retain its biological efficacy when injected into cells and produce proteins in a live animal, was the foundation of a new class of therapies now making their way through clinical trials.

Our mission to treat patients is enhanced by our collaborations with industry, not diminished. But the public's trust in academic institutions and physician-patient relationships is tantamount to our success. As we move into the genomics era, public trust and understanding will be even more critical to our ability to bring the benefits from our research to our patients. It is important to share our successes so that the public can understand that with proper ethical guidelines around academic-industry collaboration, it's the public that will benefit the most.



Irene Abrams Vice President, Technology Development and New Ventures Technology & Innovation Development Office



Significant Figures

PATENTS ISSUED 168 PATENT APPLICATIONS FILED 296 INVENTION DISCLOSURES 130 STARTUPS CREATED 7 REVENUE FROM FY18 LICENSES AND OPTIONS \$1.5 M GROSS REVENUE \$62,010,000* NET REVENUE \$61,190,000* ACADEMIC PARTNERS 220 INDUSTRY PARTNERS 298



* Includes monetization of royalties

FY18 Five-year Growth Trends

Sponsored Research and Collaboration Agreements



Industry-sponsored Research Funding



License and Option Agreements



Revenue from New Licenses



Net Licensing Revenue



* Includes monetization of royalties

FY18 Technology Development Fund

Boston Children's Technology Development Fund is dedicated to translating high-impact academic technologies into the independently-validated, later-stage opportunities sought by industry partners and investors.

The Technology Development Fund provides:

- » Mentoring and coaching through an advisory board of industry leaders in product development
- » Funds to execute the scope of work agreed upon with the mentors
- » Technical support and expertise through a network of service providers and collaborators
- » Active project management

The 2018 Awardees

Selected from 35 applications

Novel small molecule therapeutics for telomere disease Suneet Agarwal, MD, PhD, Hematology/Oncology

Targeting lysine demethylases as novel chemotherapeutics George Daley, MD, PhD and Deepak Jha, PhD, Stem Cell Program

Targeting of the YAP pathway as a novel therapeutic approach in cancer Fernando Camargo, PhD and Sophia Shalhout, PhD, Stem Cell Program

Therapeutic development of ApoM for lung diseases Timothy Hla, PhD and Steven Swendeman, PhD, Vascular Biology Program

Developing FGF21 as a treatment for retinal degeneration Lois Smith, MD, PhD and Zhongjie Fu, PhD, Ophthalmology

Device to improve heart valve repair David Hoganson, MD and Peter Hammer, PhD, Cardiac Surgery

For additional information Technology.Development@childrens.harvard.edu 617-919-1375



2009–2018 10 Years of Technology Development at Boston Children's

STARTUPS

Affinivax

Novel vaccine platform that elicits both B- and T-cell-mediated immune responses

Rebion Optical device for rapid detection of several serious eye conditions

Miach Orthopaedics A new approach for repair of torn ACLs

Nido Surgical Surgical tools for cardiac interventions

Quartet Medicine First-in-class therapies for pain management

Nocion Therapeutics Small molecule to control neurogenic inflammation

Lumos Novel central catheter for improved placement safety

Epidemico Reporting of adverse drug events

BeeVisual Blood draw learning kit

Startup in stealth mode Small molecule for treatment of obesity

Startup in stealth mode Metastatic cancer therapeutics

ESTABLISHED COMPANIES

Astute Medical Test for acute appendicitis

Grünenthal Prolonged duration local anesthetic



FY18 HIGHLIGHTS Startups

CAMP4 Therapeutics launches to discover treatment approaches for every disease

CAMP4 Therapeutics, co-founded in 2016 by Boston Children's Leonard Zon, MD (director, Stem Cell Program) and the Whitehead Institute's Richard Young, PhD, has created a unique Gene Circuitry Platform to better understand how gene



expression is controlled by signaling pathways in specific disease states. By generating proprietary genomic maps, CAMP4 can identify de-risked, druggable targets, produce actionable insights and improve therapeutic predictability, potentially addressing hundreds of diseases. The company completed a \$34 million Series A funding round in September 2018, led by Andreessen Horowitz with participation by Polaris Partners and the Kraft Group.

As part of its pipeline, the company is exploring potential therapies for Diamond Blackfan anemia (DBA), based on discoveries from both Zon and George Daley, MD, PhD (Stem Cell Program; dean, Harvard Medical School). Zon's laboratory developed zebrafish models of DBA and discovered approaches to rescue the ribosomal protein deficiency that mediated DBA. Daley, in a recent collaboration with Zon, developed a drug-screening platform using induced pluripotent stem cells from DBA patients to identify more therapeutic approaches for this congenital disorder.

Altheia Science launches to develop treatments for autoimmune diseases and cancer

Altheia Science is an Italian biotechnology company founded in December 2017 by Boston Children's Alessandra Biffi, MD, PhD (director, Gene Therapy Program) and Paolo Fiorina, MD, PhD (Nephrology Research) with the technology transfer company AurorA-TT. Altheia is focused on delivering curative cell- and gene-based therapies to patients



with autoimmune diseases, including type 1 diabetes and multiple sclerosis. The company completed a \$19 million Series A financing round in December 2018, with private investors and the Rovati family, former owners of Rottapharm.

Altheia's technology is founded on seminal research performed by Biffi and Fiorina, which the company has now exclusively licensed. Biffi's group developed methods to manipulate and administer hematopoietic and progenitor stem cells (HSPCs) for direct transplantation into the brain, publishing positive results in a mouse model of metachromatic leukodystrophy in late 2017. Fiorina's laboratory discovered that HSPCs from diabetic patients express less PD-L1 and developed methods to increase PD-L1 expression in HSPCs to reverse diabetes in a mouse model, work published in late 2017. Altheia will leverage these discoveries to create novel therapies to treat autoimmune diseases and cancer in a variety of tissues and organ systems.

Nocion Therapeutics to develop novel treatments for cough, pain and itch

Nocion Therapeutics, co-founded by Boston Children's Clifford Woolf, MD, PhD (director, F.M. Kirby Neurobiology Center), Harvard Medical School's Bruce Bean, PhD and Brigham and Women's Hospi-



tal's Bruce Levy, MD, was launched in 2018 with an exclusive license to Woolf's and Bean's know-how and patented discoveries from Boston Children's and Harvard University.

Woolf and Bean began collaborating in 2006 to explore whether a charged sodium channel blocker can specifically target nociceptors, the nerve fibers that signal pain, as well as pruriceptors, the fibers that signal itch. The two neurobiologists went on to discover potent, novel charged sodium channel blockers that act only on pain and itch fibers. In consultation with Levy, a prominent pulmonologist, the team tested the compounds in rodent models of airway inflammation and found a significant reduction in cough, a condition also mediated by nociceptors. The research received support from Harvard's Blavatnik Biomedical Accelerator and Boston Children's Technology Development Fund.

Miach Orthopaedics launches with a novel bio-engineered ACL repair approach

Miach Orthopaedics, Inc., founded by Martha Murray, MD (Orthopaedic Surgery, Sports Medicine) in 2016, develops bio-en-



gineered surgical implants for connective tissue repair needs. In September 2018, the company completed a \$22.5M series A financing round, co-led by Amzak Health Investors LLC and DSM Venturing with participation from the NFL Players Association and others.

The company was founded on more than a decade of Murray's research at Boston Children's investigating improved methods for anterior cruciate ligament (ACL) repair. The current standard of care involves replacing the ACL with a graft of a healthy tendon from another part of the leg or from a donor. These grafts are linked to a high rate of re-tearing and arthritis, particularly in

young athletes. Murray's team discovered why the ACL does not heal on its own and developed a novel method to address this: a protein-based sponge holding a small amount of the patient's own blood that is surgically implanted between the torn ends of the ACL. This provides a scaffold that allows the ACL's torn ends to heal back together, avoiding the need for a graft. The technology, named the Bridge-Enhanced® ACL Repair (BEAR®) implant, has been effective and reduced arthritis in pig studies. Safety has been demonstrated in a small human study. Now the company is performing FDA-approved clinical trials in children and adults.

Puddingstone Place uses Boston Children's technology to improve quality of life in autism

Puddingstone Place has exclusively licensed a portfolio of patents comprising the Visual Immersion System[™], a comprehensive framework and instructional philosophy for teaching communication and language skills to individuals with



autism spectrum disorder and other developmental disabilities. Howard Shane, PhD (director, Center for Communication Enhancement and the Autism Language Program) developed the system at Boston Children's and is also a company founder.

ConsortiaTX launches with exclusive license to therapeutic microbiota

ConsortiaTX, Inc., a seed-stage biotech company launched in 2017, has exclusively licensed intellectual property from Boston Children's and Brigham and Women's Hospitals developed by Talal Chatila, MD, Lynn Bry,



MD, PhD and Georg Gerber, MD, PhD. Chatila, Rima Rachid, MD, and Azza Abdel-Gadir, PhD (Division of Immunology), with Bry and Gerber, determined changes in human gut microorganisms associated with food allergies. Bry developed defined microbial species, or consortia, that confer protection when tested in a mouse model of severe egg allergy, developed in Chatila's lab. Using these consortia, the team successfully prevented the development of food allergy in these mice and reversed established disease. These studies further showed that the microbes skewed the immune response away from food allergy by inducing regulatory T cells that support tolerance of food antigens, alter gut barrier permeability and change the underlying microbiome. Leveraging this knowledge, the company will develop a live biotherapeutic product to reverse food allergies.

FY18 HIGHLIGHTS

Licenses

Harvard Pilgrim Health Care licenses KidsMD as a tool for its members

KidsMD is a digital health platform developed by the Innovation & Digital Health Accelerator (IDHA) to provide parents with trusted



content, resources and tools for their child's health and wellness, extending Boston Children's pediatric expertise beyond our walls. Through meaningful health recommendations and personalized content, parents and caregivers can make informed decisions about whether to treat their child themselves or seek additional professional care.

Harvard Pilgrim Health Care has non-exclusively licensed the platform as a resource for its members. Harvard Pilgrim Health Care and IDHA have also collaborated to develop the platform for the company's online portal.

Fresenius Kabi gains FDA approval for Omegaven

Fresenius Kabi, a health care company, licensed the use of Omegaven for the prevention and treatment of parenteral nutrition–associated liver disease (PNALD) from Boston Children's in 2010. The license



expanded this year to include parenteral nutrition–associated cholestasis (PNAC). This year, the FDA approved the use of Omegaven as a source of calories and fatty acids in pediatric patients with PNAC, a potentially fatal condition.

The treatment was developed by Mark Puder, MD, PhD (Surgery) and Kathleen Gura, PharmD (Pharmacy), who regularly saw infants on parenteral nutrition, a method of intravenous feeding, develop liver injury so severe they would need a liver transplant or die from liver failure. Fresenius Kabi was already producing and marketing Omegaven for a different indication in adults in Europe and Asia. In 2004, Puder and Gura received compassionate-use approval to run their own FDA-regulated clinical trials. In 2018, 14 years after its first successful use in infants, Omegaven was approved and may become the standard source of lipids for these devastating conditions.

FY18 HIGHLIGHTS

Sponsored Research and Collaborations

Relmada Therapeutics sponsors testing of drug efficacy in a mouse model of Rett syndrome

Rett syndrome is a rare, progressive disease with neurological abnormalities and is seen only in young



girls. There is currently no approved therapy. Michela Fagiolini, PhD (F.M. Kirby Neurobiology Center) uses an MeCP2-deficient mouse model of the disease, which shares the regression of visual function and other pathology seen in patients, to study the NMDA-receptor signaling thought to underlie the disease. Relmada Therapeutics is partnering with Fagiolini to test their NMDA receptor agonist in the MeCP2 mouse model, both before and after the onset of Rett-like symptoms. The goal is to advance the preclinical development of Relmada's drug for Rett syndrome.

Collaboration with St. Jude and others to develop novel gene therapies for sickle cell disease

Boston Children's signed a collaboration agreement with St. Jude Children's Research Hospital, Massachusetts General Hospital, the Broad Institute and NHLBI/ NIH to form the St. Jude Children's Research Hospital Collaborative Research Consortium on Novel Gene Therapies for Sickle Cell Disease. Daniel Bauer, MD, PhD (Hematology/Oncology), the principal Boston Children's investigator for the consortium, will advance his work on genome editing of the BCL11a erythroid enhancer to increase fetal hemoglobin expression as an approach to overcome the presence of sickled red blood cells in patients.

Celgene sponsors consortium to study pulmonary fibrosis

Celgene has committed over \$6 million to a research consortium dedicated to accelerating research in pulmonary fibrosis. The company is sponsoring collaborative research being performed by Carla Kim, PhD (Stem Cell Program) and six other renowned researchers. Kim and her collaborators are building off her organoid co-culture technology to develop new models of the disease process in pulmonary fibrosis and to identify targets for treatment.

Boston Children's initiates genetic study of a rare neurological disorder

Boston Children's Hospital, in collaboration with Pfizer, is searching for genetic drivers of



opsoclonus myoclonus syndrome (OMS), an extremely rare immune-mediated childhood neurological disorder. The study is part of the Boston Children's PrecisionLink biobanking and genomics effort led by Kenneth Mandl, MD, MPH (director, Computational Health Informatics Program), and is being carried out by Mark Gorman, MD (Neurology) and Sek Won Kong, MD (Computational Health Informatics Program). Gorman and Kong are recruiting carefully phenotyped OMS patients in Boston Children's Pediatric Neuro-Immunology Program, using the extensive medical informatics capability built here, to gather samples from patients and their parents for DNA sequencing. The study is designed to determine whether OMS has high-penetrance genetic drivers and has broader implications for understanding the role of the immune system within the central nervous system.

Ipsen Pharma sponsors research to develop a new botulinum neurotoxin for therapeutic use



Min Dong, PhD (Urology) and Pål Stenmark, PhD, a collaborator at Stockholm University, published their discovery of the first new botulinum toxin to be found in close to 50 years. They named the unusual toxin BoNT/X. Now the collaborators have entered into an exclusive license and sponsored research agreement with Ipsen Pharma, a global biopharmaceutical company, to scientifically de-risk BoNT/X and optimize it for therapeutic applications. BoNT/X cleaves the same nerve proteins targeted by other botulinum toxins, like Dysport® and Botox[®], but it also cleaves a unique group of proteins and thus may improve and/or expand the therapeutic use of the toxins.

Vir Biotechnology sponsors study to image and track flu in a mouse model

Boston Children's has entered into an ambitious, threeyear sponsored research agreement



with Vir Biotechnology, a company launched in early 2017 to transform the care of people with or at risk for serious infectious diseases. Vir is sponsoring a study led by Hidde Ploegh, PhD (Program in Cellular and Molecular Medicine), with collaborators at Harvard University, to use radiolabeled-virus and non-invasive live imaging techniques to track the course of influenza infection in a mouse model. The study will also track the immune response to the flu in young and aging mice. The project aims to gain insight into the mobilization and function of immune cells in vulnerable populations and identify new therapeutic approaches to combat viral infections.

Micreos sponsors study of novel antibiotic for staph infection

Micreos, a biopharmaceutical company developing antimicrobial compounds to treat infectious diseases, is sponsoring research in the laboratory of Raif Geha, MD (chief, Immunology). Geha and Manuel Leyva Castillo, PhD, an instructor in Pediatrics, will use their extensive knowledge of atopic dermatitis animal models to perform preclinical research on the company's novel topical antibiotic for Staphylococcus aureus skin infections. The study will provide insight into the kinetics of staph infection on inflamed skin.

Xintrum sponsors development of novel therapeutic approach for CNS injury



Xintrum Pharmaceuticals is sponsoring research at Boston Children's Hospital to develop novel therapies for central nervous system (CNS) injury, such as stroke. The study is being led by Zhigang He, PhD, BS (Neurology), who discovered that genetic manipulation of the mTOR pathway, namely co-overexpression of osteopontin and insulin-like growth factor 1, could sensitize mature, non-regenerative neurons to growth factors. This approach stimulated neuron regeneration and led to functional recovery in a mouse model of optic nerve injury. Now, He and his team will investigate how to translate this novel strategy into a biological drug or gene therapy approach to treat CNS injury.

FY18 New Technologies

New insights into the biology of primary aldosteronism provide a target for therapy

Primary aldosteronism (PA) is a hormonal disorder causing high blood pressure. It affects about 10 percent of all hypertensive patients, an estimated 100 million people world-wide. However, PA is markedly underdiagnosed and patients have limited medical and surgical options to address their disease. David Breault, MD, PhD (associate chief, Endocrinology) has identified a novel aldosterone regulator, FGFR2, as highly expressed in the adrenal glands in a mouse model of PA. This discovery provides an important insight into PA's pathogenesis and will potentially lead to a new class of therapies for this neglected disease.



Image: Sining Leng

Mouse model of FGFR2 knockout in the adrenal gland which shows disruption of normal morphology and impaired aldosterone production. This model provides essential proof-of-principle data to therapeutically target the FGFR2 pathway.

Novel vaccine adjuvants added to the Precision Vaccines Program portfolio

Infectious diseases remain a leading cause of morbidity and mortality among newborns and the elderly, due to differences in their innate immune systems



compared to older children and middle-aged adults, making traditional vaccines less effective. The inclusion of adjuvant molecules in vaccines can broaden, enhance and accelerate immune responses by activating additional immune pathways, yet there is an unmet need for vaccine adjuvants that are active in the very young and the elderly. Using novel human in vitro platforms, a team from Boston Children's Precision Vaccines Program, including program director Ofer Levy, MD, PhD, David J. Dowling, PhD and Francesco Borriello, MD (Infectious Diseases), has developed a portfolio of adjuvants for these vulnerable populations. Recently, the team identified three small molecules that can activate immune cells and boost influenza vaccine immunogenicity in mice using a high-throughput screening approach. They are now working with medicinal chemists and formulation experts to optimize the molecules for further in vivo testing as adjuvants.

Novel diagnostic approach for sudden unexpected death in pediatrics

Sudden unexplained death in pediatrics (SUDP) is an inclusive term for sudden deaths in children that remain unexplained by standard autopsy and death scene investigation. SUDP accounts for nearly 10 percent of all child mortality in the U.S. While SUDP is a diagnosis of exclusion, the Robert's Program on SUDP at Boston Children's considers the possibility that these deaths are instances of extreme, lethal phenotypes of undiagnosed diseases that may have genetic causes. Through a unique approach of case review and family assessment, program director Richard Goldstein, MD and colleagues compiled literature reviews, family histories and phenotypic data to identify a panel of 203 genes associated with SUDP. Work is ongoing to refine the list further. The team will use this comprehensive panel for identification, study and prevention of SUDP, recognizing the near-universal desire of families to learn more about the reasons for a child's death and to understand the potential risk to siblings.

Therapeutic development of apolipoprotein M (ApoM) for vascular diseases

Sphingosine-1-phosphate (S1P) is an important mediator of endothelial cell function through G-protein receptor activation and is chaperoned by HDL-associated apolipoprotein M (ApoM). ApoM-bound S1P is limited in several inflammatory, metabolic and vascular diseases. Timothy Hla, PhD and Steven Swendeman, PhD (Vascular Biology Program) developed a method to harness the pro-vascular and anti-inflammatory properties of the ApoM-bound S1P by fusing ApoM with the IgG constant region (ApoM-Fc), enhancing in-vivo stability where ApoM alone is insufficient. More recently, Hla and Swendeman have collaborated with Mark Puder, MD (Vascular Biology, Surgery) and Lois Smith, MD, PhD (Ophthalmology) to develop ApoM-Fc as a therapeutic for vascular diseases of the eye and lung. They have focused their efforts on bronchopulmonary dysplasia (BPD), a lifelong illness affecting preterm infants that are maintained on high-oxygen ventilation. Promising data from animal models of BPD enabled the team to be selected for a 2018 Technology Development Fund award to continue their drug development program.



Microscopic image of heart tissue after myocardial ischemia/ reperfusion injury (heart attack) in mice. Green label shows neutrophils, red label shows vessels in the heart and blue shows nuclei of cells. The mice were previously injected with ApoM-Fc which minimizes heart tissue damage after a heart attack. imMKCLs, with membranes stained orange and nucleus stained blue, normally produce some platelets as they mature into magakaryocytes, visualized here as the membrane breaks and release platelets.

> Treating the cells with one of the factors identified by Daley's team produces more mature, plateletreleasing megakaryocytes. This is a potential approach to mass produce platelets for transfusion.

mages: Arunoday Bhan

Novel approach to produce platelets for transfusion

More than 2 million platelet apheresis units are transfused every year in the U.S., a life-saving measure in the setting of inherited platelet disorders, chemotherapy, radiation therapy, bone marrow transplantation, bone marrow failure, surgery and trauma. However, banked donor platelets have major limitations, including short shelf life, potential for contamination and unpredictable activity due to donor variability. A promising alternative is the mass production of universal donor platelets from megakaryocytes derived from human induced pluripotent stem cells (a recently established cell line called imMKCL). This approach is currently limited by low yields. Researchers from the Stem Cell Program, including George Daley, MD, PhD, Thorsten Schlaeger, PhD and Arunoday Bhan, PhD, have developed a high-throughput, live-cell imaging assay to study the maturation process of megakaryocytes and identify factors that promote or restrict platelet production. To date, they have discovered two biological factors that increase platelet production from imMKCLs three-fold. They are now using their platform to screen small molecules that could be used to generate platelets for transfusion or to stimulate a patient's own platelet production.

Spotlight on Strategic Alliances

On a mission to maximize the impact of innovation on patient health, TIDO facilitates industry collaborations that translate the novel work of Boston Children's researchers into realworld applications. We have developed flexible, multi-year collaboration alliances with industry sponsors to significantly reduce the administrative and resource hurdles that can hinder collaborative scientific progress. Our partners include:



Our newest alliance, signed in 2018, is with BridgeBio Pharma, a clinical-stage company focused on developing treatments for

genetically defined diseases. The alliance will support innovative research leading to therapies for patients with genetic diseases and cancer. We are currently running our first call for proposals and look forward to a long and fruitful collaboration.



Since 2011, Boston Children's has been collaborating with Pfizer's Centers for Therapeutic Innovation (CTI) to help bridge the gap between early scientific discovery and its translation into new

medicines. The goal of this collaboration is to identify large and small molecule compounds with activity in a pathway or target of interest to a Boston Children's researcher and to Pfizer/CTI. With Pfizer's funding, scientists from both sides work collaboratively to create potential therapeutics and to advance lead molecules through drug development and potentially into the clinic. Participants in the CTI network include more than 27 academic institutions, several patient foundations and the National Institutes of Health.

Four of Boston Children's investigators have been selected for a collaboration with Pfizer/CTI:



SANOFI

This year marked the second call for proposals for the Sanofi Innovation Awards (iAwards)

program, which supports early-stage innovative and translational research. The main objective of the program is to convert successful and promising projects into sponsored research programs and subsequently create licensing and startup opportunities. In addition to providing funding for a one-year study, Sanofi scientists actively engage with Boston Children's investigators to accelerate the conversion of innovative ideas into effective and safe therapeutics for patients. Successful projects have the potential to grow into sponsored research agreements with significantly increased funding and timelines.

Four of Boston Children's investigators were awarded iAwards in 2018:



Shire

Boston Children's and Shire entered into a broad research collaboration in rare diseases in 2012. The partnership

seeks to advance new treatments for a number of rare pediatric diseases by combining the research and clinical expertise of Boston Children's with Shire's therapeutic development and commercialization capabilities. The emphasis is on drugs that could become candidates for development in under three years.

Shire has funded and collaborated with the following Boston Children's investigators:



FY18 PATENTS Issued U.S. Patents

ABCB5 positive mesenchymal stem cells as immunomodulators Frank, Markus 10,017,738

ABCB5(+) stem cells for treating ocular disease Frank, Markus 9,801,912

Antibody molecules to TIM-3 and uses thereof Umetsu, Dale 9,884,913

BPI and its congeners as radiation mitigators and radiation protectors Levy, Ofer 9,884,089

Calmodulin inhibitors for the treatment of ribosomal disorders and ribosomapathies Zon, Leonard I 9,827,252

Composition for on-demand ultrasound-triggered drug delivery Kohane, Daniel S 10,010,709

Compositions and methods for functional nucleic acid delivery Langer, Robert S 9,970,002

Compounds for the treatment of obesity and methods of use thereof Ozcan, Umut 9,925,161 9,968,575

Detecting inclusion body myositis Greenberg, Steven A 9,778,250

Detection of 5-hydroxymethylcytosine

by glycosylation Rao, Anjana 9,816,986

Detection of human somatic cell reprogramming *Daley, George Q.* 9,846,164

Diagnostic markers and therapeutic targets of Kawasaki disease Kentsis, Alex 9,869,673

Hematopoietic stem cell specificreporter mouse and uses thereofRossi, Derrick10,080,354

High-throughput mouse model for optimizing antibody affinities Alt, Frederick W. 10,034,463

High-throughput structure determination using nucleic acid calipers Shih, William 9,897,597 Hydrogel encapsulated cells and anti-inflammatory drugs Langer, Robert S 9,867,781

Induced pluripotent stem cells with synthetic modified RNAs Rossi, Derrick 9,803,177

Instrument port for minimally invasive cardiac surgery del Nido, Pedro J. 9,844,394

Insulin derivatives for diabetes treatment Langer, Robert S 9,867,869

Lin28-mediated control of let-7 biogenesis Gregory, Richard I. 9,938,354

Measuring the level of 5-hydroxymethylcytosine in a sample from a subject having cancer or suspected of having cancer

Rao, Anjana 10,041,938

MetAP-2 inhibitor polymersomes for therapeutic administration Folkman, M. Judah 9,782,489 9,789,199

Method of making a deletion in a target sequence in isolated primary cells using Cas9 and two guide RNAs Rossi, Derrick 9,822,370

Method of predicting acute appendicitis Kentsis, Alex 9,933,439

Method of preventing and treating type 1 diabetes, allograft rejection and lung fibrosis (by targeting the ATP/P2X7R axis) Fiorina, Paolo 10,071,167

Methods and apparatuses for treating vessels Lock, James 9,849,006

Methods and assays for combination treatment of cancer Kim, Carla 9,895,390

Methods and compositions for the inhibition of TRPV4 Ingber, Donald 10,047,140

Methods and compositions for the production of siRNAs Lieberman, Judy 9,840,703 Methods and compositions relating to mesenchymal stem cell exosomes Mitsialis, S. Alex 9,901,600

Methods and products for tissue repair Murray, Martha M 9,849,213

Methods and uses for ex vivo

tissue culture systems *Mammoto, Akiko* 9,951,313

Methods for inducing cardiomyocyte proliferation Wang, Dazhi 9,885,043

Methods for treatment of melanoma Zon, Leonard I 10,016,402

Modified biotin-binding protein, fusion proteins thereof and applications Malley, Richard 10,017,548

Modulation of BCL11A for treatment of hemoglobinopathies Orkin, Stuart H 9,885,041

Natural IgM antibodies and inhibitors thereof Carroll. Michael C 9.914.751

Nucleic acid-based linkers for detecting and measuring interactions Wong, Wesley P 9,914,958

Photocleavable chemical inducers of dimerization (CID) and methods of use Schwarz, Thomas 10,053,445

Regulators of NFAT Rao, Anjana 9,932,378

Role for the Perlman syndrome exonuclease Dis3l2 in the Lin28let-7 pathway Gregory, Richard I. 9,994,813

Selectively disrupted whole-cell vaccine Malley, Richard 9,827,299

Self-regulated peptide hydrogel for insulin delivery Langer, Robert S 9,994,615

Sepiapterin reductase inhibitors for the treatment of pain Woolf, Clifford 10,059,664 Systemic gene replacement therapy for treatment of X-linked myotubular myopathy (XLMTM) Beggs, Alan 9,839,677 9,895,426

Targeting ABCB5 for
cancer therapyFrank, Markus9,855,342

Targeting BCL11A distalregulatory elements for fetalhemoglobin reinductionOrkin, Stuart H9,822,355

Use of CD36 to identify cancer subjects for treatment Watnick, Randolph S. 9,921,224

FY18 PATENTS **Issued Foreign Patents**

EPO

Italv

Malta

Spain

A broadly neutralizing human antibody that recognizes the receptor-binding pocket of influenza hemagglutinin Harrison, Stephen EPO 2739312 Japan 6325979

A gene encoding a multidrug resistance human p-glycoprotein homologue on chromosome 7p15-21 and uses thereof Frank Markus Canada 2,411,101

2298799

ABCB5 positive mesenchymal stem cells as immunomodulators

Frank, Markus 2.685,492 Canada

ABCB5 targeting for cancer therapy Frank, Markus

EPO

6268237 Japan

An osmotic pump device for retention in a genitourinary site in a patient Cima, Michael India 289639

Biochemically stabilized HIV-1 Env trimer vaccine Harrison, Stephen 2340038 EPO

BPI and its congeners as radiation mitigators and radiation protectors

Levy, Ofer Australia 2012240206 China ZL 201280016834.0

Compounds for the treatment of obesity and methods of use thereof

Ozcan, Umut AL/P/2018/000593 Albania Austria 2900230 Australia 2014354831 Belgium 2900230 Bulgaria 20242 P20181879T Croatia Cyprus 2900230 Czech Republic 2900230 Denmark 2900230 2900230 Estonia 2900230 Finland 2900230 2900230 France Germany 2900230 2900230 Greece Hong Kong 2900230 Hungary 2900230 Iceland 2900230 Ireland 2900230 2900230 2900230 Latvia Lithuania 2900230 2900230 Luxemboura Macedonia P-2018/892 2900230 2900230 Monaco Netherlands 2900230 2900230 Norway Poland 2900230 Portugal 2900230 Romania 2900230 Russian Fed. 2650646 San Marino 2900230 Serbia P-1365/2018 2900230 Slovakia P-201331170 Slovenia 2900230 Sweden 2900230 Switzerland 2900230 Turkey 2900230

Device for high throughput investigations of cellular interactions

Tharin, Suzanne Canada 2,813,211

Efficient protein expression in vivo using modified RNA (mod-RNA)

Rossi, Derrick EPO 2694660 France 2694660 2694660 Germany Ireland 2694660 2694660 Italv

Fused antigen vaccines and compositions against Streptococcus pneumoniae Malley, Richard 2013209513 Australia 6379041 Japan

Hydrophobic tissue adhesives del Nido, Pedro J. Canada 2,913,338

Instrument port for minimally invasive cardiac surgery del Nido, Pedro J.

FPO 1971280

Lin28-mediated control of let-7 biogenesis

Gregory, Richard I.	
EPO	2688595
France	2688595
Germany	2688595
reland	2688595
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Technology & Innovation Development Office

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