



The Blavatnik Biomedical Accelerator

AT HARVARD UNIVERSITY



Accelerating Innovation to Transform Medicine



A photograph of a modern glass skyscraper. The windows of the building act as mirrors, reflecting the iconic white dome and classical columns of a historic building, likely the Harvard University Main Library. In the foreground, the dark green leaves of a tree are visible, partially obscuring the lower right portion of the glass facade. The sky is a clear, pale blue.

“Harvard University is an ideal place to bring biomedical innovations to life with its world-class research, translational expertise, strong leadership, and expansive entrepreneurial network. That combination of factors helps to ensure that revolutionary discoveries become products with transformative impact.”

– Len Blavatnik, MBA '89
Founder and Chairman, Access Industries

Bridging the Gap

Technologies developed in university labs are

embryonic: pulsing with powerful potential, but not yet ready to thrive on their own. We are keenly aware that to external partners, even Harvard's most stunning biomedical breakthroughs can be seen as too risky for commercial investment to advance their development.

Support from the Blavatnik Biomedical Accelerator to Harvard labs bridges the development gap between exploratory, early-stage research and the type of validated, de-risked technology that attracts high-caliber industry partners. When Harvard researchers have a compelling vision, a truly bold innovation to translate into patient care, the Blavatnik Biomedical Accelerator is here to say, "Yes — we see it too."

Every project in the Blavatnik Biomedical Accelerator receives strategic and financial support to advance it on a trajectory toward a crucial milestone, whether that is the validation of initial observations, achievement of proof-of-concept, or demonstration of a targeted application. At the end of a successful project, a corporate partner may join in further collaborative research at Harvard; a company may license the technology to generate new biomedical products; or investors and entrepreneurs may incorporate a new startup focused on that brilliant idea.

The end result achieves what Harvard's biomedical researchers often consider their *raison d'être*: dramatic advances in care that transform the lives of patients worldwide.

The Blavatnik Biomedical Accelerator at Harvard University was established through the profound generosity of the Blavatnik Family Foundation and the visionary leadership of Len Blavatnik, MBA '89. We are grateful and privileged to have had Len's support from the earliest days of the Accelerator. He shared with us the conviction that a program like this is not only critical to the fulfillment of Harvard's research mission, but moreover essential to fundamentally transform the practice of medicine.

We invite you to learn more about the Blavatnik Accelerator and its achievements, in the pages of this brochure.



ISAAC T. KOHLBERG

Senior Associate Provost
Chief Technology Development Officer
Harvard University





The Blavatnik Biomedical Accelerator is managed by an experienced team (*from right*): Curtis Keith, Chief Scientific Officer; Leandro Vetcher, Associate Director of Business Development; and Su Chiang, Senior Associate Director.

From Innovation to Impact

Biomedical research at Harvard has the potential to improve countless lives, revolutionize industries, and create immense social and economic value. Translating early-stage research into compelling, validated technologies, however, requires careful planning, focused resources, and a tireless pursuit of results.

The Blavatnik Biomedical Accelerator guides Harvard scientists toward translational impact by providing strategic, monetary, and advisory support for well-defined research projects. Our work is expressly aimed at hastening the pace of scientific progress, developing a shared vision with partners in industry, and ensuring that lifesaving technologies born at Harvard will become new products that impact the world for the better.

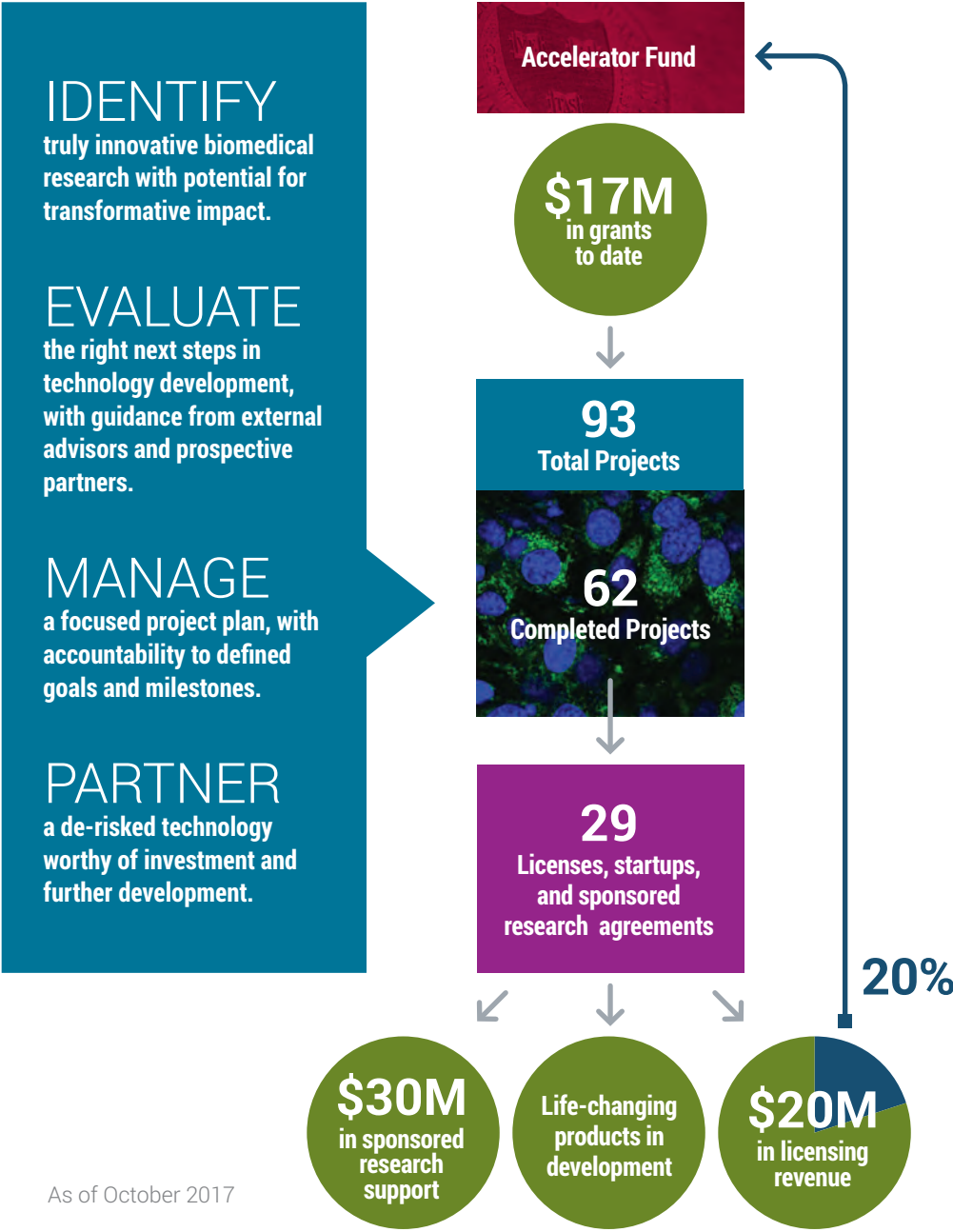
Proving the Value of Big Ideas

The Accelerator seeks to support innovative, investigator-initiated research, and to develop preliminary observations into robust intellectual property positions. Its primary goal is to advance technologies to the point where an industry partnership can commence.

We employ a proven strategy of selecting projects with significant commercial potential, and providing financial support and domain expertise to fuel translational research, proof-of-concept, and technological development. We simultaneously build relationships with industry, generating partnerships and licensing opportunities, and facilitating startup formation and investment. The Accelerator is structured as a sustainable, “evergreen” program, with revenue from successfully launched technologies cycled back to support ongoing and future Accelerator projects.

Choosing Wisely

Proposals are welcomed from Harvard principal investigators with early-stage research in a range of life science areas, including therapeutics, diagnostics, drug delivery technologies, medical devices/instruments, and enabling technologies for drug discovery. Each project is evaluated on its overall potential for impact, including its scientific and technical merit, its development needs, and the commercial prospects of the technology. Projects are selected by an independent advisory committee, and awarded grants typically range from \$100k to \$300k per project.



As of October 2017



Achievements in biomedical innovation



2013

A major gift from the **Blavatnik Family Foundation** establishes the Blavatnik Biomedical Accelerator and the Blavatnik Fellowship in Life Science Entrepreneurship

Major license and collaboration with **UCB** to develop antibodies to improve glucose regulation in diabetes

Research led by Prof. Frank Sacks shows that a subtype of HDL does not provide cardiovascular benefit, suggesting room for improvement in routine lipid profiling

2014

The Accelerator introduces Pilot-level and Development-level grants to extend its impact

Collaboration with **Roche** to develop novel Accelerator-funded antibiotics programs

BrightSpec licenses technology for chiral analysis. This enables the first product on the market resulting from Blavatnik Accelerator support

A Track Record of **Success**

First established as a pilot program, Harvard's original accelerator fund was dramatically expanded and relaunched as the Blavatnik Biomedical Accelerator in 2013 through a transformative gift from the Blavatnik Family Foundation, led by Len Blavatnik, MBA '89. Over the years, the Blavatnik Biomedical Accelerator has demonstrated consistent success in advancing breakthrough life science innovations, catalyzing major corporate partnerships, and creating new ventures.

2015

Macrolide Pharmaceuticals

launches, with \$22 million in Series A funding, to develop novel antibiotics

Research led by Prof. Susan Dymecki characterizes previously unrecognized subtypes of serotonin-producing neurons associated with disease

Prof. Matthew Shair's lab demonstrates a molecule that can halt the growth of cancerous cells through a novel mechanism

Profs. Bruce Bean and Clifford Woolf demonstrate efficacy of nociceptor inhibitors in reducing airway inflammation

2016

Magenta Therapeutics launches, with \$48.5 million in Series A funding, to transform treatment of blood diseases and immune disorders

First annual **Harvard FUSION** symposium

Major license and research collaboration with **Merck** is Harvard's largest ever

First Phase I clinical trial of a licensed Accelerator technology, announced by **Denali Therapeutics**

2017

Completed projects have attracted more than **\$30 million** in follow-on research support from corporate partners

Clinical validation of **Mellitus'** licensed diagnostic in gestational diabetes

Prof. Quan Lu's lab demonstrates that extracellular vesicles called ARMMS may be well suited to deliver drugs directly to specific tissues

Four new startups based on Accelerator technologies on track for launch in 2017



Leading the Way in Biomedical Innovation

Over the past ten years, the Blavatnik Biomedical Accelerator has enabled dozens of major medical innovations. Our projects have propelled new therapeutics, diagnostics, and medical instruments into commercial development, and continue to expand future treatment options for patients.

Accelerator-funded technologies have included treatments for metabolic disease, cancer, immuno-inflammatory disease, infectious diseases, and neurodegeneration, creating a diverse portfolio of innovations with exciting commercial potential. Roughly half of all completed projects to date have been partnered with industry—a tremendously high rate of success for academic technologies—either by forging collaborations and licensing agreements with existing biotech and pharmaceutical companies, or by forming new startups from the ground up.

These partnerships have already raised more than \$20 million in licensing revenue and more than \$30 million in industry-sponsored research funding to Harvard labs. Technology licenses also have the potential to generate significant future income via milestone and royalty payments in years to come, helping the Accelerator become self-sustaining and supporting further research on campus. We remain committed to continuing our record of success at the Accelerator through targeted translational research funding and support.

Cancer

21

- Demonstrated the role of mediator kinases in AML
- Identified inhibitors of cellular autophagy



Infectious Disease

16

- Created a platform for discovering antibiotics
- Targeted outer membrane formation in Gram-negative bacteria

Funded Projects

As of October 2017

Metabolic Disease

8

- Targeted hormone aP2 to better regulate glucose metabolism

Immuno-inflammatory Disease

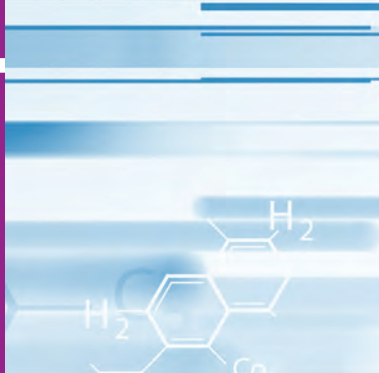
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- Demonstrated efficacy of nociceptor inhibitors in reducing airway inflammation

Regenerative Medicine

7

- Discovered a milder method of bone marrow conditioning for use in HSCT



Drug Discovery Platforms

10

- Developed a platform for incorporating fluorine into molecules to improve their properties as drugs

Devices and Instruments

5

- Developed an instrument to determine chirality of molecules

Neurology

15

- Characterized subtypes of serotonin-producing neurons
- Identified enzyme that triggers the demise of neurons in ALS



Diagnostics

7

- Developed a diagnostic for glycated CD59 to detect elevated glucose in gestational diabetes



Halting a Deadly Cancer

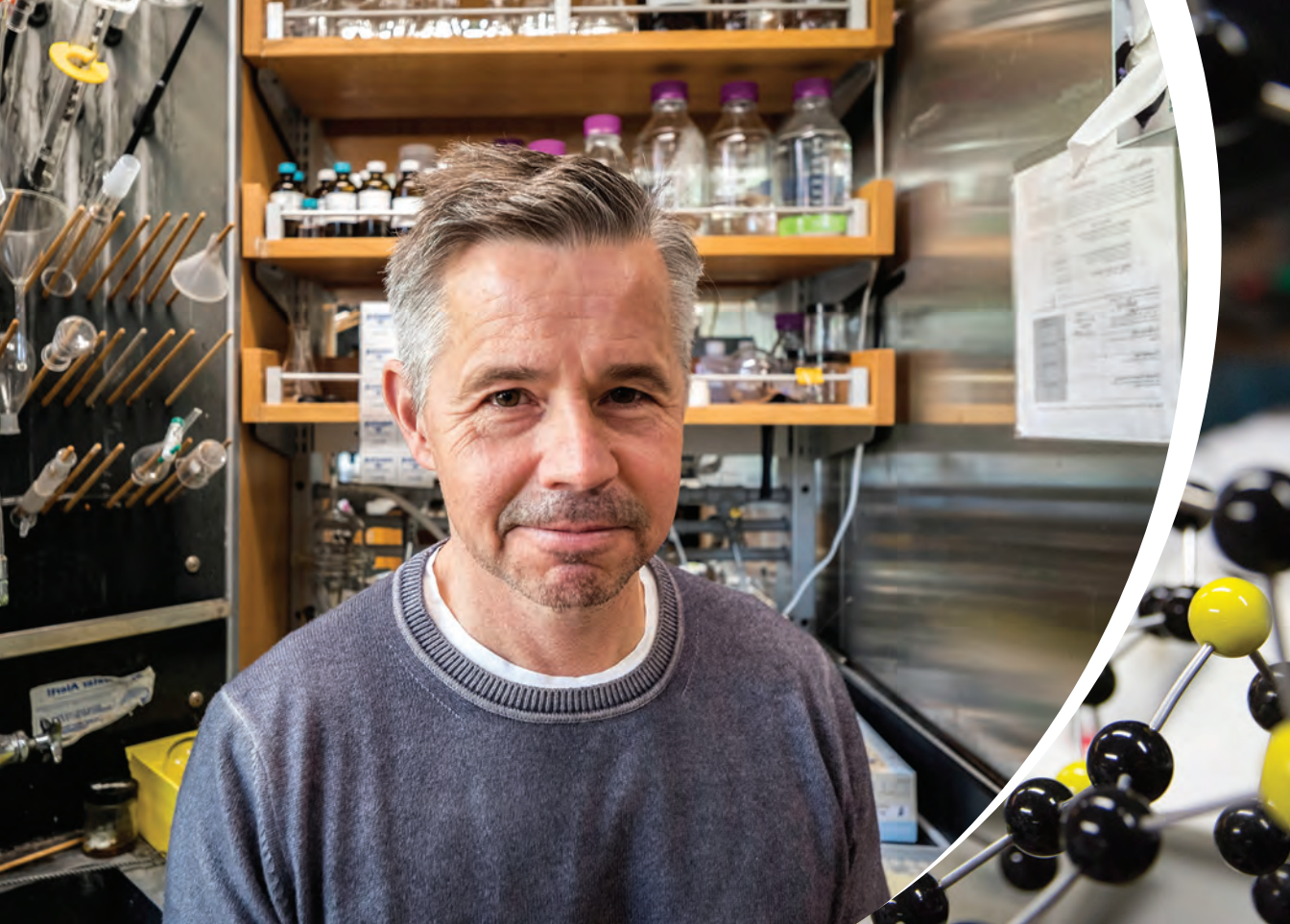
MATTHEW SHAIR

Professor of Chemistry and Chemical Biology
Faculty of Arts and Sciences

For patients with acute myeloid leukemia (AML), diagnosis can be a death sentence. This devastating blood cancer is the most common form of acute leukemia in adults, and has a five-year survival rate of only 26 percent. With support from the Blavatnik Biomedical Accelerator, Matthew Shair discovered a novel therapeutic strategy—namely, to inhibit enzymes that regulate the transcription of key genetic programs that are altered in AML and other cancers. His lab developed highly selective and potent small molecules, with favorable pharmaceutical properties, that were poised for advancement toward clinical trials.

After four years of funding from the Accelerator, his work took off. In 2016, the pharmaceutical giant **Merck** agreed to take over development, including clinical development, of the compounds identified and synthesized in his lab, and to support further research into the biology of the target enzyme. The agreement provided Harvard a \$20-million up-front licensing payment—the largest ever in the University's history—along with provisions for future development and commercialization milestones. The agreement also includes tiered royalties on any resulting products, which will ultimately help the Blavatnik Accelerator become self-sustaining.





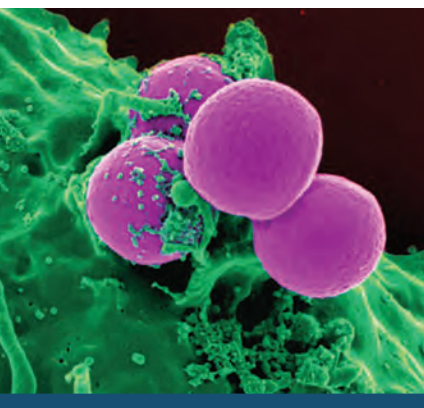
Fighting Drug-Resistant Bacteria

ANDY MYERS

Amory Houghton Professor of Chemistry and Chemical Biology
Faculty of Arts and Sciences

As new strains of drug-resistant bacteria emerge, infections that were previously simple to treat have become life-threatening. These “superbugs” infect roughly two million Americans each year, leading to thousands of deaths. Funding from the Accelerator has enabled Myers to develop a powerful platform for discovering new antibiotics, providing a means to kill off these tenacious microbes. His platform uses a novel combination of eight chemical “building blocks” to create new antibiotic compounds from the ground up. In doing so, he’s able to create drugs that the microbes have never before encountered, foiling even the most aggressive antibiotic-resistant bacteria.

Despite concerns over the spread of treatment-resistant “superbugs” nationwide, federal funding had been exceedingly difficult to secure. With Accelerator support, however, his lab was able to demonstrate synthesis and test the resulting compounds. Myers co-founded a startup based on the technology in 2015. That company, **Macrolide Pharmaceuticals**, has licensed the platform and raised \$42 million in financing (as of early 2018) to commercialize novel antibiotics for serious infections.





A Gentler Treatment for Blood Disorders

DAVID SCADDEN

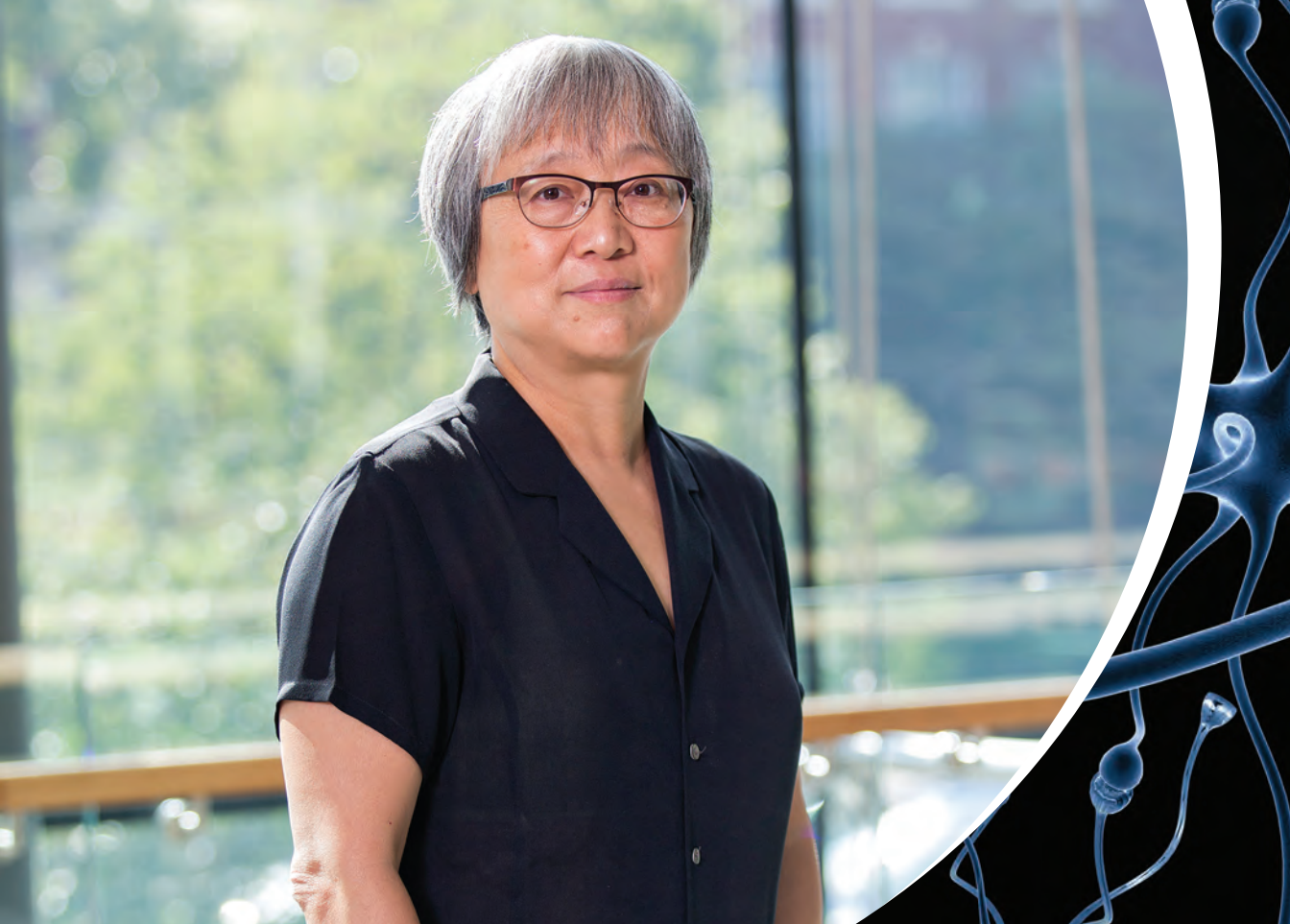
*Gerald and Darlene Jordan Professor of Medicine
Professor of Stem Cell and Regenerative Biology
Chair of the Department of Stem Cell and Regenerative Biology
Faculty of Arts and Sciences and Harvard Medical School*

Hematopoietic stem cell transplantation (HSCT), an important treatment for severe blood cancer, could one day help treat other diseases. At present, however, its widespread use is limited by toxicity associated with the conditioning that precedes the transplantation procedure.

Scadden created a new approach to the treatment that may transform blood stem cell transplants from a “treatment of last resort” into a safer, more efficient therapy. After just two years of funding from the Blavatnik Biomedical Accelerator, his lab developed milder methods to condition bone marrow in advance of HSCT, potentially allowing future use in cases of sickle-cell anemia, autoimmune diseases, and other blood disorders.

After publishing his work in *Nature Biotechnology* in 2016, Scadden co-founded a startup, **Magenta Therapeutics**, which has raised more than \$150 million in financing, as of early 2018. The company is backed by two of the top biotech VC firms in the country (Third Rock Ventures and Atlas Ventures) and an investment by Access Industries, among others.





New Ground for Neurodegenerative Diseases



JUNYING YUAN

Elizabeth D. Hay Professor of Cell Biology
Harvard Medical School

In 2015, the Blavatnik Biomedical Accelerator helped launch a small virtual startup called **Incro** to expand on research that was led by Yuan and was funded in part by the Accelerator. She had shown that compounds called necrostatins can inhibit cell death in ischemic brain injury and certain neurodegenerative diseases.

Shortly after its founding, Incro was acquired by **Denali**, one of the largest new biotech companies announced in 2015. Denali was a natural fit for the technology, bringing not only significant monetary resources but also depth and experience in neurodegenerative disease drug development. In August 2016, Denali announced that Incro's lead program—originating from the research conducted by Yuan at Harvard—was entering clinical trials. Denali's first trial for the compound was a Phase 1 healthy volunteer study to assess safety; future studies would be in patients suffering from amyotrophic lateral sclerosis (ALS) and Alzheimer's disease. This was the first time a new chemical entity from the Blavatnik Biomedical Accelerator entered human trials, clearly an important milestone for the program.



Saving Brains from Toxic Proteins

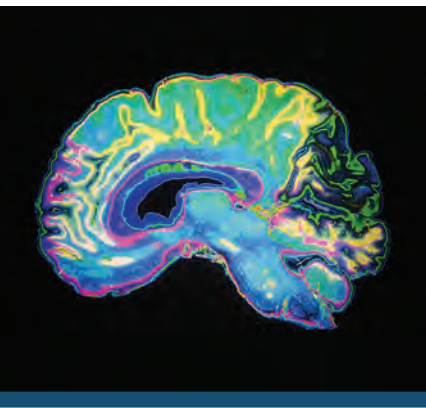
DAN FINLEY AND RANDY KING

Professor of Cell Biology and Harry C. McKenzie Professor of Cell Biology, respectively
Harvard Medical School

One of the Accelerator’s earliest business development successes

came in 2012 with the partnering of a technology created by Finley and King. Together, the researchers discovered that by inhibiting an enzyme called Usp14 that counteracts protein degradation, it is possible to enhance the cell’s removal of toxic proteins. This discovery immediately garnered interest from a number of drug companies because it suggested a new approach for treating Alzheimer’s disease, Parkinson’s disease and other diseases characterized by the accumulation of dysfunctional proteins.

Over a period of two years, the Accelerator supported development and validation of novel small molecule inhibitors of Usp14. These compounds were licensed to **Proteostasis Therapeutics**.

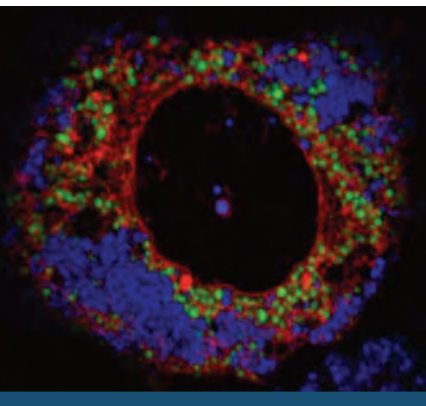




A New Treatment for Diabetes

GÖKHAN HOTAMISLIGIL
*James Stevens Simmons Professor of Genetics and Metabolism
Chair of the Department of Genetics and Complex Diseases
Harvard T.H. Chan School of Public Health*

In 2013, the Blavatnik Biomedical Accelerator entered into a major license and research collaboration with European pharmaceutical company **UCB** to develop therapeutic antibodies against a novel target associated with diabetes. The Accelerator had supported Hotamisligil's original efforts at Harvard to understand the target, a hormone called aP2 that is found in adipose (fat) tissue. His research demonstrated that aP2 plays a critical role in abnormal glucose metabolism. In collaboration with UCB, his team has developed and evaluated novel monoclonal antibodies to target aP2 and improve glucose regulation. A drug candidate has been validated in multiple rodent models of diabetes.







It Takes a Team

Bringing innovative new technologies to market

doesn't just require dogged scientific research—it often requires deep experience in the business world as well.

At the Blavatnik Biomedical Accelerator, we foster those entrepreneurial skills among the research teams we advise. We pair Harvard labs with industry consultants who have specific technical knowledge or domain expertise, and recruit experienced Entrepreneurs-in-Residence to spend time working directly with the research team, driving toward the launch of a new company.

As a result, our technologies are better positioned to succeed commercially. Moreover, Accelerator project teams benefit from professional development on a wide range of topics, including business development strategy, drug development, intellectual property strategy, regulatory affairs, and entrepreneurial financing.

The Blavatnik Biomedical Accelerator also works jointly with the Blavatnik Fellowship in Life Science Entrepreneurship. Through the Blavatnik Fellowship, selected recent MBA alumni of Harvard Business School gain experience in life science entrepreneurship through exposure to the biomedical projects at the University.

Well-connected

The Blavatnik Biomedical Accelerator resides within Harvard's Office of Technology Development, working hand-in-hand with the University's business development and intellectual property teams to guide the strategic direction of each project. This tight integration helps ensure that performance is driven toward a value-inflection point that will lead to a partnering event.



FUSION

AT HARVARD UNIVERSITY

A Unique Event for Innovative Leaders

FUSION is the annual Harvard University symposium that integrates perspectives from science and business to expand upon the promise of an emerging field. Jointly hosted by the Blavatnik Biomedical Accelerator and the Blavatnik Fellowship in Life Science Entrepreneurship at Harvard Business School, FUSION celebrates scientific advancement and economic development by convening experts to a dialogue on a theme of global importance. The first two symposia, in 2016 and 2017, addressed the topics of regenerative medicine and antibiotic resistance.

Designed to engage entrepreneurs, scientists, business leaders, and investors, FUSION creates a nexus where leaders on the front lines of invention and discovery can meet the innovators who are shaping business and policy models to commercialize life-changing science.



Accelerator Advisory Committee

The Blavatnik Biomedical Accelerator is advised by an Advisory Committee comprising academic thought leaders and accomplished members of the biopharma and life-science venture communities. This distinguished group provides critical input on project selection and oversight, helping to ensure that research work plans have been designed to drive results, add value and effectively address key criteria for licensing.

KEVIN BITTERMAN, PhD

Partner
Atlas Venture

ALEXIS BORISY

Partner
Third Rock Ventures

JON CLARDY, PhD

Hsien Wu and Daisy Yen Wu Professor of Biological Chemistry and Molecular Pharmacology
Harvard Medical School

ROSANA KAPELLER, MD, PhD

Formerly CSO
Nimbus Therapeutics

DIANE MATHIS, PhD

Morton Grove-Rasmussen Professor of Immunohematology
Harvard Medical School

CHRIS MIRABELLI, PhD

Managing Director
Healthcare Ventures

VICKI SATO, PhD

Chairman, Vir Biotechnology
Chairman, Denali Therapeutics

STEVE TREGAY, PhD

Founder, President, and CEO
FORMA Therapeutics

STACIE WENINGER, PhD

President
F-Prime Biomedical Research Initiative



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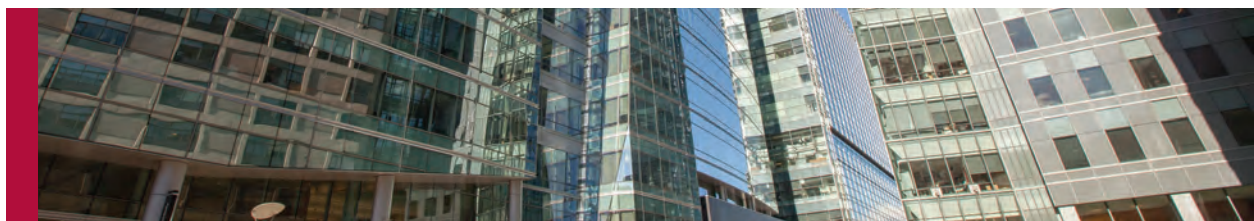


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