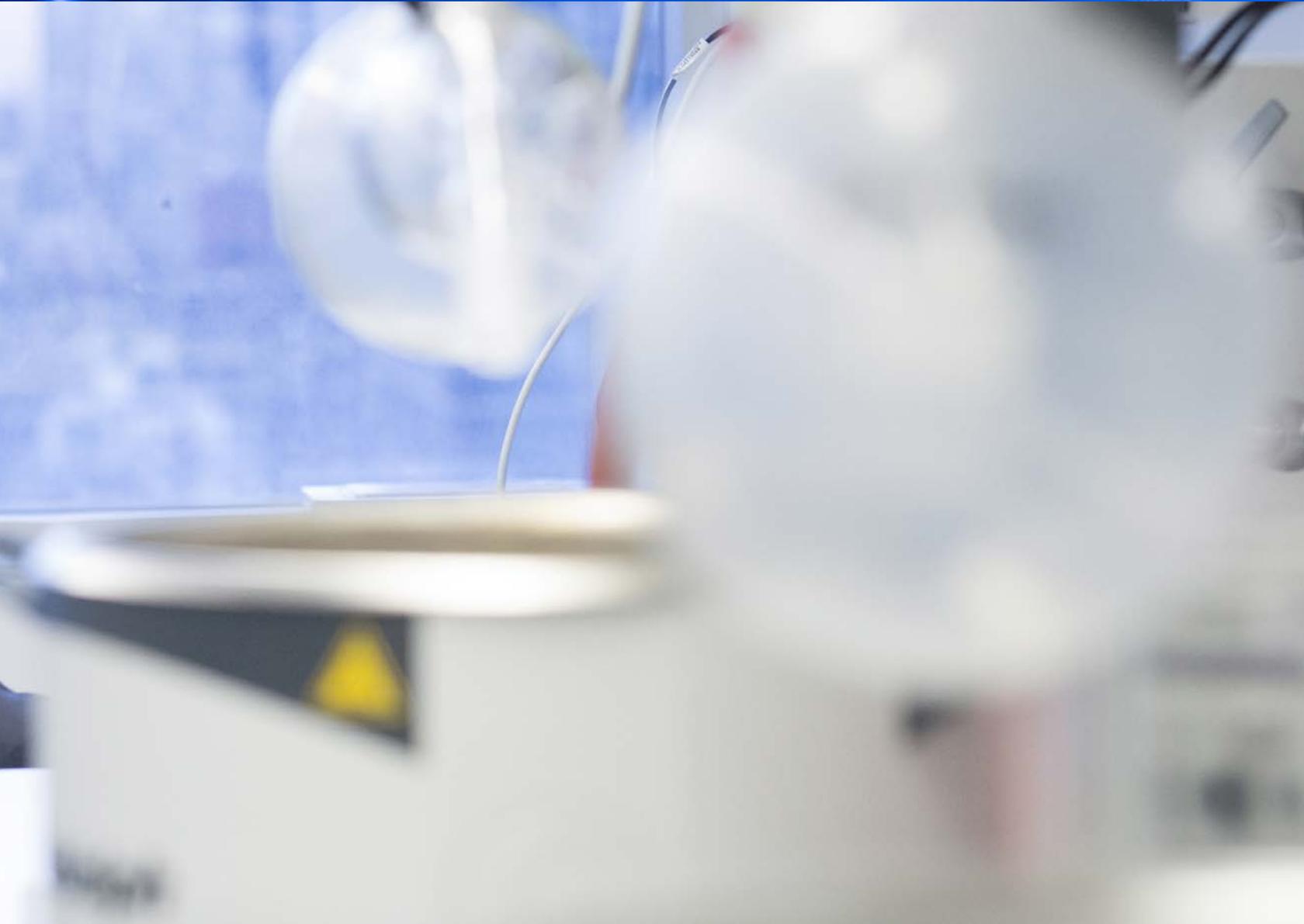


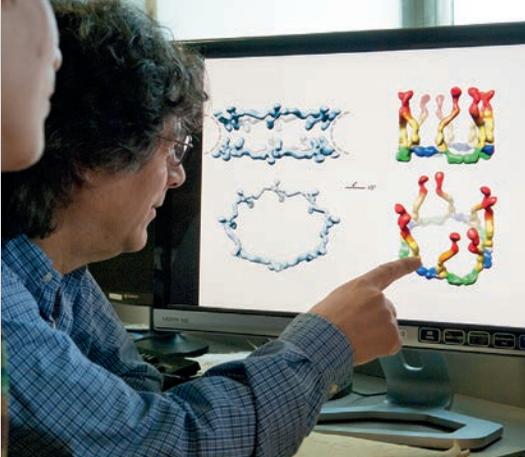


TRI-INSTITUTIONAL
THERAPEUTICS DISCOVERY INSTITUTE



encourage | empower | leverage | bridge





The mission of TDI is to **encourage** our community to advance their groundbreaking biological discoveries to *in vivo* proof-of-concept studies. TDI provides industrial-scale technical support for academic projects, making it possible to rapidly assess the utility of specific therapeutic targets in disease-relevant contexts.



TDI **empowers** the community to translate research discoveries from bench to bedside by offering a menu of services that is unprecedented in scale and scope in an academic environment. This is accomplished through a series of highly favorable academic-industry partnerships established through TDI, as well as our Innovation & Education Initiative, which provides community-wide training and support in order to maximize the impact of these partnerships on academic drug discoveries.

We achieve our mission by **leveraging** the infrastructure, staff, and intellectual capital of our academic and industry partners, as well as the generous support of philanthropists.

With the launch of key initiatives, TDI has established the first fully-funded, fully-staffed **bridge** from basic academic research discovery to human proof-of-concept demonstration.

**Basic
Academic Research
Discovery**

Tri-I Investigator identifies a new protein target implicated in human disease

**TDI Early
Project Initiative**

TDI uses outside contractors and internal expertise to quickly assess viability of the protein as a new drug target

**TDI-Takeda
Drug Discovery
Initiative**

Tri-I Investigator collaborates with TDI and Takeda to develop lead small molecule or antibody for *in vivo* proof-of-concept studies

Bridge Medicines

Upon demonstration of *in vivo* efficacy, project graduates to Bridge Medicines for development as a pre-clinical candidate

**New York-Based
NewCo**

Bridge Medicines' venture capital partners fund NYC-based company with appropriate resources to execute human proof-of-concept clinical trials

Letter from the Director



Michael A. Foley, PhD

The past year marked a period of significant growth for the Tri-Institutional Therapeutics Discovery Institute (TDI). TDI has now established the first fully-funded, fully-staffed unbroken pathway from basic academic scientific research discovery to human proof-of-concept. Working closely with our industry partner, Takeda Pharmaceuticals, we strive to break down the barriers that traditionally impede academic drug discovery by connecting academic researchers with collaborators from across the globe.

In the Summer of 2014, the TDI experiment began in earnest with the launch of the first eight small molecule drug development projects. Although our team was small, we demonstrated the ability to leverage outside resources to accelerate the pace of academic drug discovery in a nimble and cost-efficient fashion. Many of these projects are being evaluated by our new for-profit partner company, Bridge Medicines Inc., as potential licensing candidates.

In 2016, TDI was charged with a mandate to expand our portfolio in order to meet the demands of the Tri-I community. This past year has seen four major areas of growth:

- The expansion of the **Small Molecule Drug Discovery** portfolio from eight to twenty projects,
- The establishment of the **Antibody Drug Discovery Initiative** in partnership with Takeda Pharmaceuticals,
- The launch of the **Early Project Initiative**, which cultivates a pipeline of projects for both the small molecule and antibody portfolios,
- The launch of **Bridge Medicines, Inc.**, a for-profit organization that will advance successful TDI projects from *in vivo* proof-of-concept to human clinical trials.

With these key initiatives, TDI has now established a new paradigm for academic-initiated drug discovery with enormous potential implications in terms of capital efficiency and societal and medicinal impact.

Over the next year, we look forward to advancing our first projects to IND-enabling studies within Bridge Medicines. To achieve this goal, TDI will be on-boarding additional scientists with decades of experience in late-stage drug discovery. We also eagerly anticipate the breakthrough discovery efforts that will be enabled by our recent implementation of the Ablexis antibody platform. The Ablexis AlivaMab Mouse is a transgenic animal with immunoglobulin transgene function and variable gene repertoire optimized to meet the challenges of antibody drug discovery and development. The reliability and ease of use resulting from this unique and advanced design has made the AlivaMab Mouse the next-generation antibody drug discovery platform of choice for the world's leading pharmaceutical companies and for TDI.

As we look forward to the challenges and opportunities of 2017, we are deeply grateful for the support of Mr. Lewis Sanders, whose generous gifts have made possible the establishment and continued growth of TDI. We appreciate the leadership provided by our Board of Directors, whose unfailing support and vision have been crucial to our success.



Michael A. Foley, PhD
Sanders Director



Bridge Medicines: Bridging the Gap from Lab to Clinic

In October 2016, our three founding institutions joined forces with our industry partner Takeda and the healthcare investment firms Bay City Capital and Deerfield Management to establish an exciting new drug development company, Bridge Medicines, Inc. The launch of Bridge Medicines has a profound impact on TDI and our academic collaborators, as all TDI projects that demonstrate *in vivo* efficacy will have the opportunity to graduate directly to the Bridge Medicines portfolio, where they receive full financial, operational, and managerial support through Phase I human clinical trials. TDI and Bridge Medicines will work closely throughout the entire lifetime of each project to ensure seamless transfer of data and technical expertise between the two organizations. The TDI-Bridge partnership is the first academic-industry enterprise to establish an unbroken path from basic academic scientific discovery to human proof-of-concept demonstration. In 2017, we anticipate that several TDI projects will advance to the Bridge Medicines portfolio.

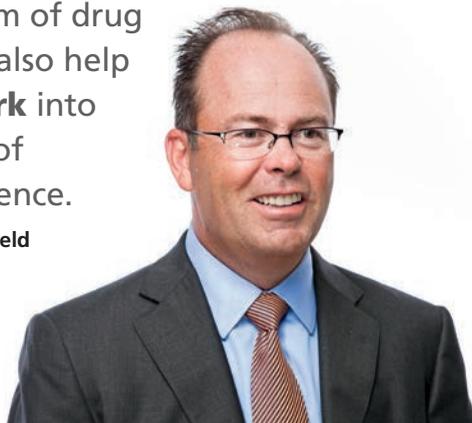


This unique academic-industry partnership advances the remarkable work of the Tri-I TDI, further **extending the ability of basic scientists...** to explore the full potential of their discoveries for the benefit of patients.

Richard P. Lifton, MD, PhD
President, The Rockefeller University

Harnessing the combined strengths of academic discovery, industrial know-how, capital and entrepreneurship, Bridge Medicines is a breakthrough in **the translation of ideas into treatments**. As Bridge Medicines changes the paradigm of drug development, it can also help **transform New York** into a world-class center of biotechnology excellence.

William Slattery, Partner, Deerfield



Ivo Lorenz, PhD, VP Biology, TDI, with Kathleen Metters, PhD, Interim CEO, Bridge Medicines



Craig Thompson, MD, President and CEO, MSKCC

As we look ahead to what's next, beyond small molecule drug discovery, this **flagship collaboration** will continue to push the boundaries of what's possible in medical research.

Andrew Plump, MD, PhD
Chief Medical and Scientific Officer,
Takeda Pharmaceutical Company



Bridge Medicines is a transformative concept for **therapeutics development that will provide enormous hope** to patients and incredibly exciting opportunities for researchers to take their discoveries into the clinic.

Augustine M. K. Choi, MD
Dean, Weill Cornell Medicine

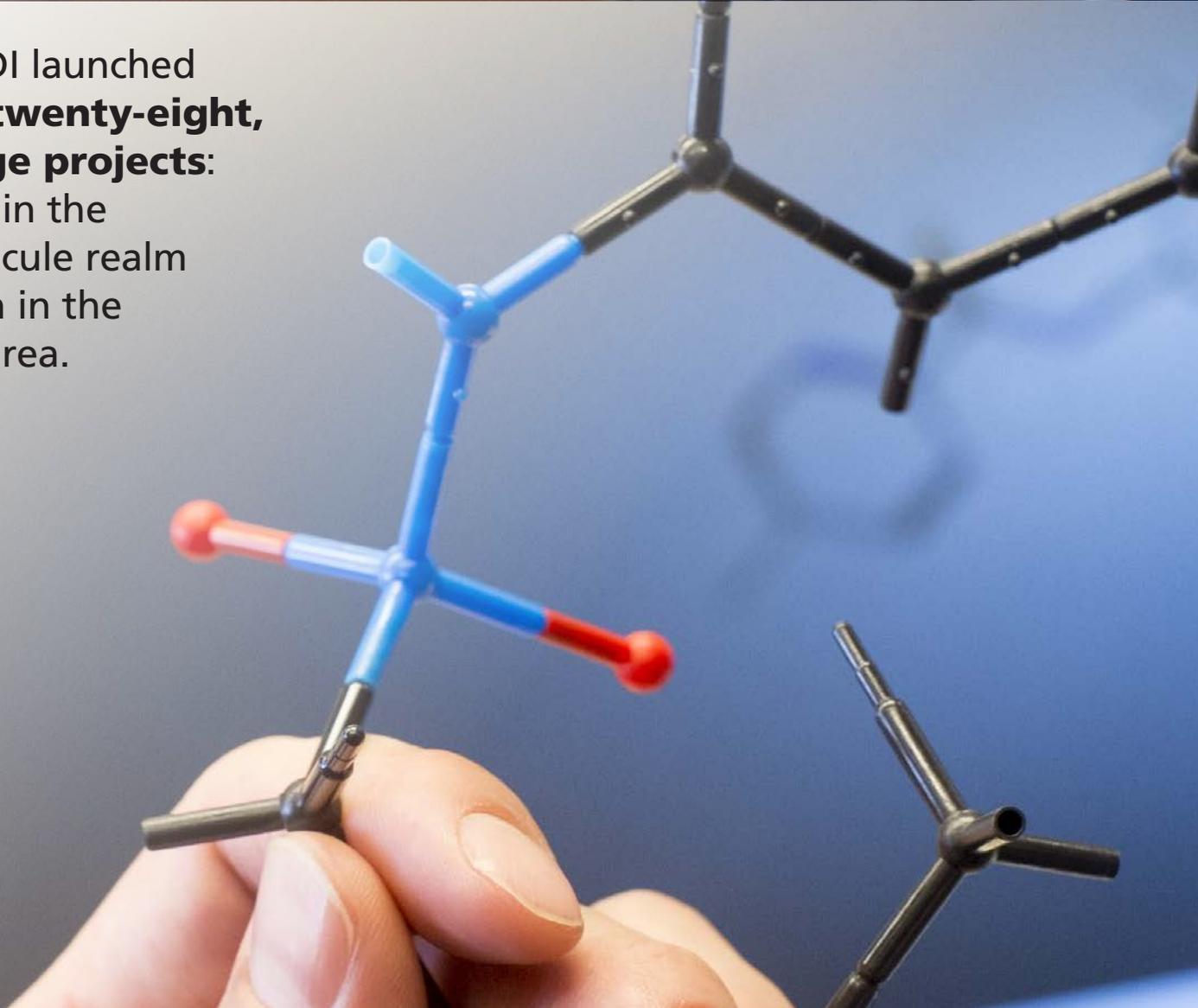


Ms. Alicia Glen, Deputy Mayor, NYC; Mr. Benjamin Kallos, New York City Councilman, District 5



Accomplishments

In 2016, TDI launched a total of **twenty-eight, early stage projects**: seventeen in the small molecule realm and eleven in the antibody area.



Accomplishments

Early Project Initiative: Cultivating Tomorrow's Pipeline

A major accomplishment of 2016 was the introduction of the Early Project Initiative, launched with the goal of generating a robust pipeline of small molecule and antibody drug discovery projects for TDI. Under this initiative, meritorious projects lacking sufficient preliminary data to join the TDI-Takeda partnership are offered project management support along with a focused menu of services, including medicinal chemistry, computational chemistry and biology, assay development, exploratory antibody generation, and high-throughput screening. The aim is to leverage TDI expertise and outside services to help the PI rapidly address key questions regarding the viability of the project; those that meet predefined criteria for success are invited to enter into the Small Molecule or Antibody Initiatives. The Early Project Initiative was launched in June 2016. Within the first six months, we initiated a total of twenty-eight early stage projects: seventeen in the small molecule realm and eleven in the antibody area.



Accomplishments

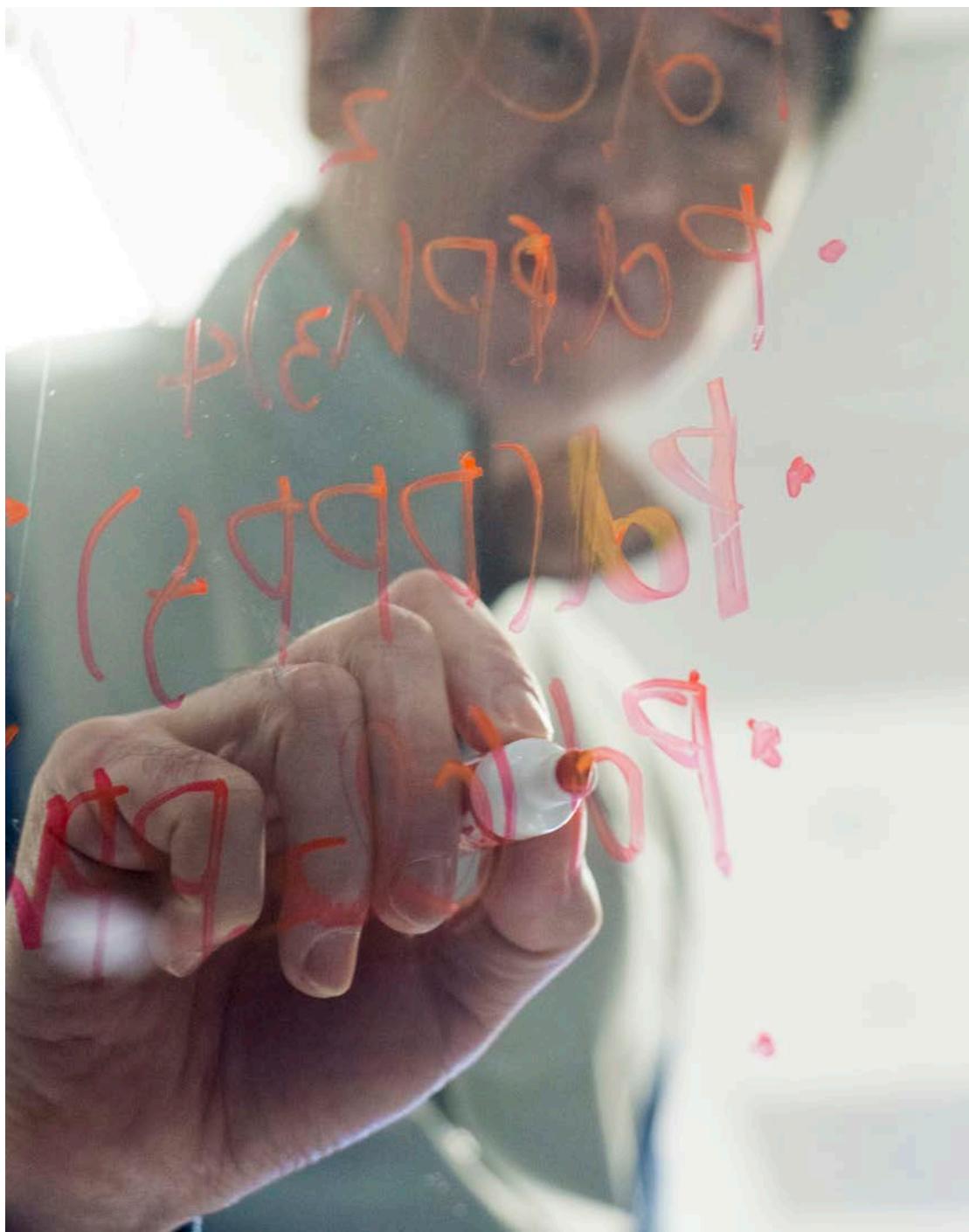
Small Molecule Initiative: Accelerating Academic Drug Discovery

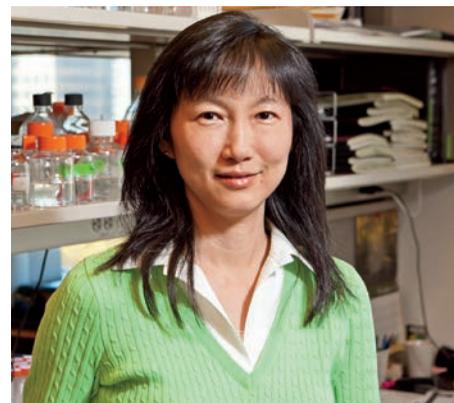
In mid-2014, TDI's Small Molecule Initiative onboarded the first cohort of eight drug discovery projects. Successful execution of these projects and the high degree of interest from the Tri-Institutional community prompted us to undertake a significant expansion of the Small Molecule Initiative. By the end of 2016, the portfolio of late-stage small molecule development projects had increased from eight to twenty. As we enter 2017, TDI is excited to be partnering with world-class scientists from across the three institutions in pursuit of groundbreaking therapeutic strategies to combat a range of diseases, from cancer to neurodegenerative disorders to infectious disease. Thus far, three projects have graduated from TDI, and four more are being evaluated in *in vivo* proof-of-concept studies.



It has been a pleasure to work with the TDI team. The resources for evaluating compounds and **the ability of the team to provide structural insight** into drug design is extremely helpful in moving hits into lead compounds.

Lewis C. Cantley, MD,
Meyer Director of the Sandra and Edward Meyer Cancer Center at Weill Cornell Medicine, Professor of Cancer Biology in Medicine



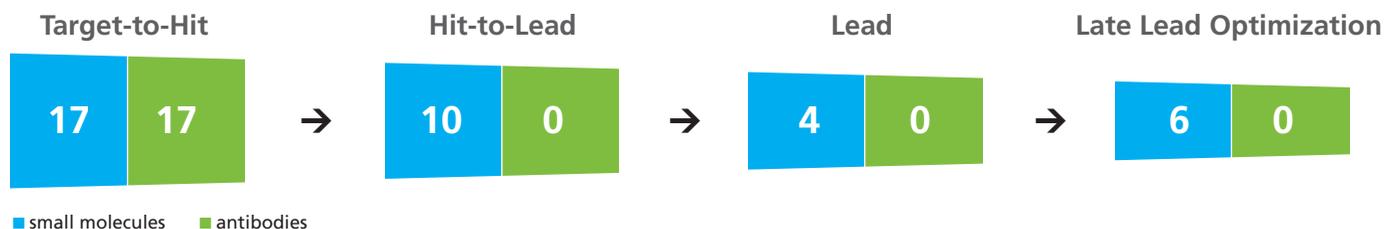


Working with TDI has enabled us to rapidly and **effectively address a difficult biological target through a multidisciplinary approach.**

Dr. Foley and his expert team of medicinal chemists have provided the rare opportunity for us to leverage industry level resources in an academic setting.

Emily Cheng, MD, PhD, Associate Member, Human Oncology and Pathogenesis Program, Memorial Sloan Kettering Cancer Center

Current TDI Pipeline: Early & Late Stage Projects



Oncology	Neuroscience	Infectious Disease	...and more
Acute myeloid leukemia B-cell lymphoma Basal cell carcinoma Brain cancer Breast cancer Lung cancer Ovarian cancer Pancreatic cancer Primary effusion lymphoma Prostate cancer Immunotherapy resistance	Alzheimer's disease Niemann Pick disease Parkinson's disease	Bacterial infection Fungal infection Malaria Tuberculosis	Autoimmune diseases Intraocular eye pressure Osteoporosis Stroke Vascular malformation



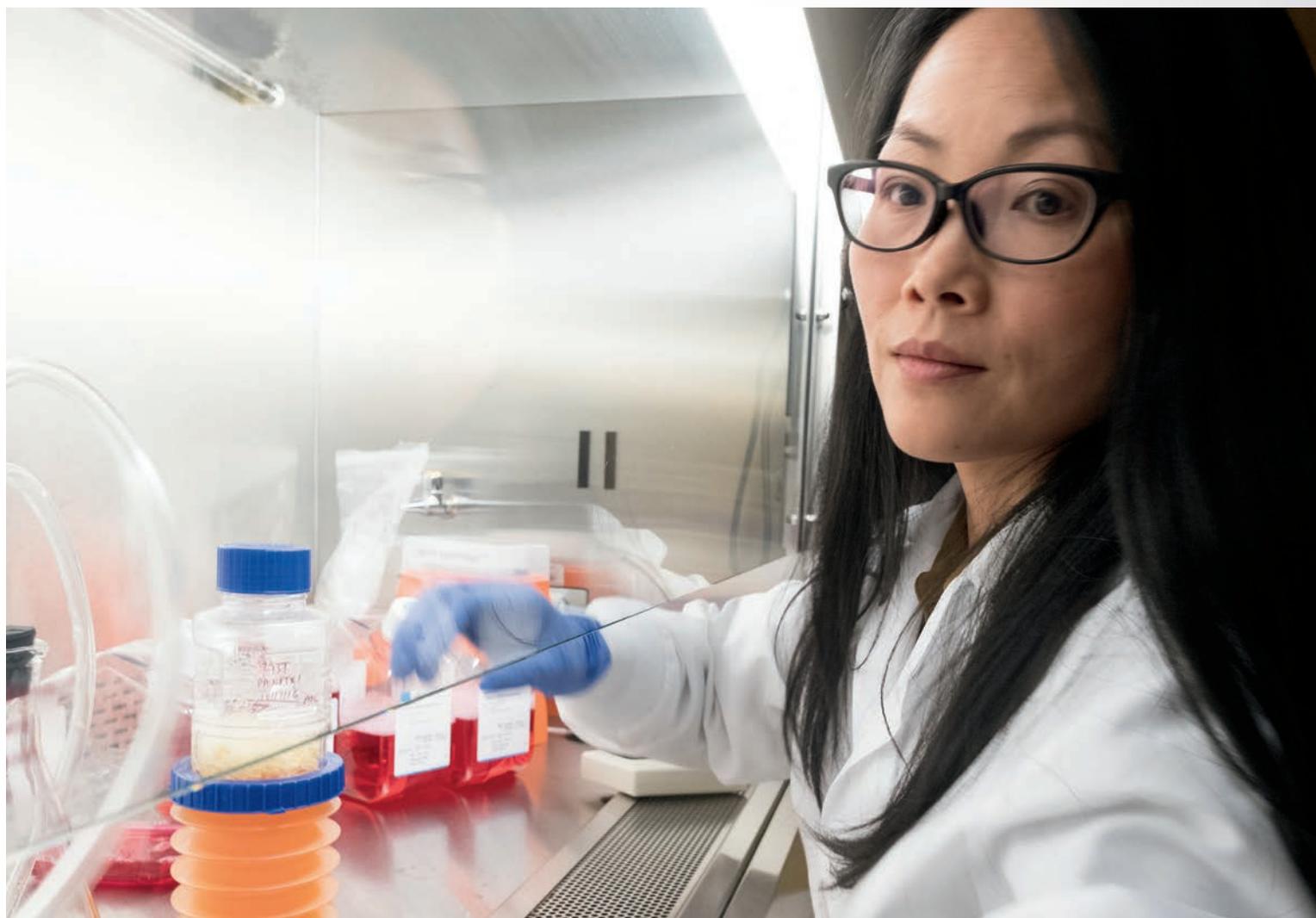
Antibody Initiative

The team is currently executing **six projects under the Antibody Initiative**, along with eleven projects under the Early Project Initiative.



Antibody Initiative: Crafting the Next Generation of Therapeutic Agents

In June 2016, TDI and Takeda finalized a major expansion of our relationship into the growing field of antibody drug discovery. In recent years, antibody strategies have gained traction due to major successes, mainly in the fields of autoimmune diseases and cancer. Antibodies often have fewer side effects than small molecule drugs because they bind very specifically and selectively to their targets. Moreover, antibodies usually last in the body for many days, which means they can be administered less frequently, adding to patient convenience. This therapeutic field is still young, and many challenges remain to be addressed. TDI and Takeda both recognize that antibody therapeutics represent an important new class of drug agents that is already transforming the biomedical community. The newly launched Antibody Initiative will position the Tri-Institutional community at the forefront of this exciting field. Over the past year, Dr. Ivo Lorenz, VP of Biologics, has established a fully-staffed Antibody discovery operation at TDI. The team is currently executing six projects under the Antibody Initiative, along with eleven projects under the Early Project Initiative.

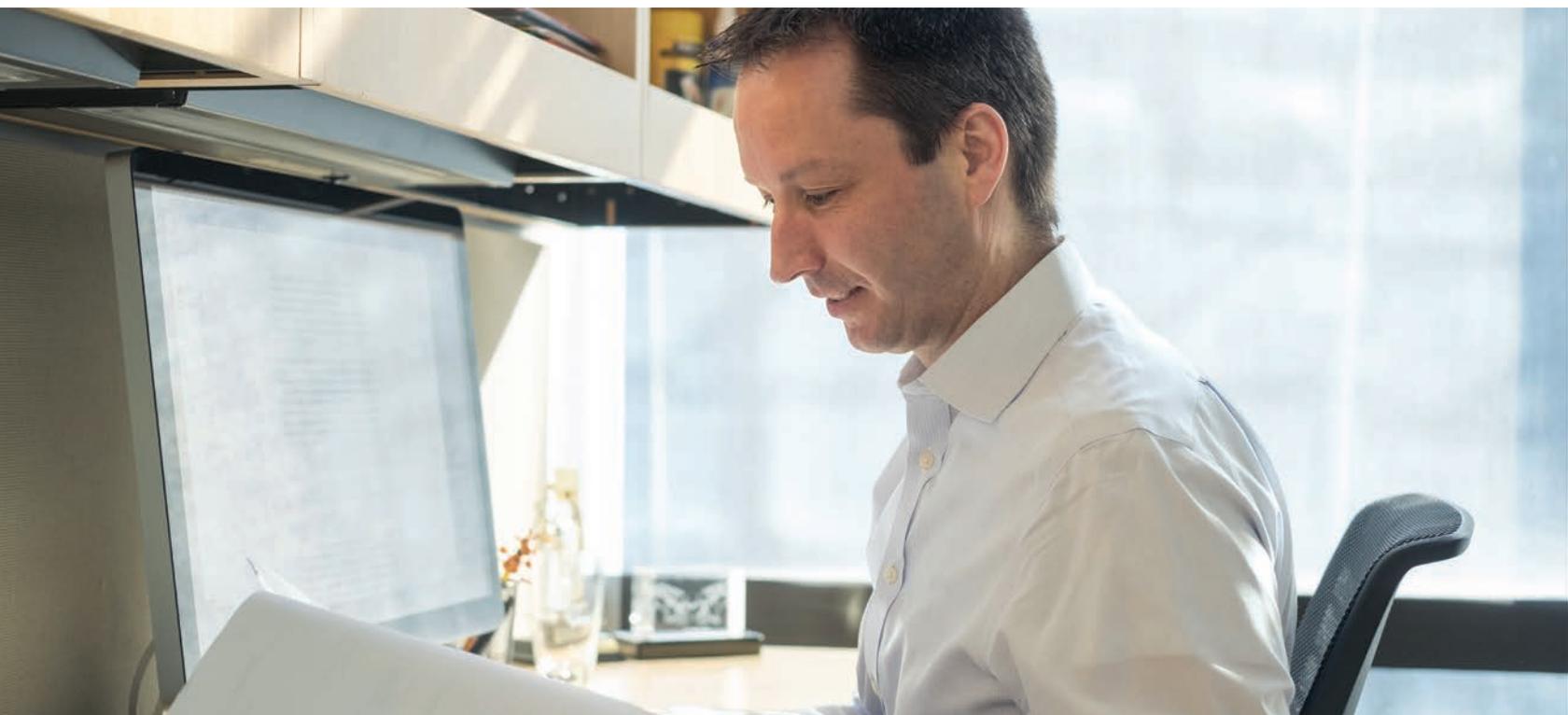


Antibody Initiative

Ivo Lorenz: Connecting Academics with Antibody Discovery Expertise

Dr. Ivo Lorenz, Vice President of Biologics, grew up in Switzerland and obtained his PhD in Biochemistry from the Swiss Federal Institute of Technology in Zürich. In 2002, Ivo moved to the United States for postdoctoral training in the Laboratory of Infectious Disease at The Rockefeller University, where he worked on the structural and biochemical characterization of an enzyme essential for the replication of hepatitis C virus. Following his postdoctoral work, he accepted a position at the International AIDS Vaccine Initiative, where he led a group studying novel approaches to develop immunogens that elicit broadly neutralizing antibodies against HIV. In 2011, Ivo joined the Biotherapeutics department at Boehringer Ingelheim, where he was the head of Immunogen Design, Immunization and Antibody Response. At Boehringer Ingelheim, Ivo led multiple projects from the oncology, immunology and infectious disease areas.

In November 2015, Ivo returned to New York City to join TDI as the Vice President of Biologics. As head of the new Antibody Initiative, Ivo quickly assembled a professional scientific staff and established TDI's new antibody laboratory in MSK's Zuckerman Research Building. In close collaboration with scientists at Takeda and Tri-Institutional faculty collaborators, Ivo and his team are already at work developing novel antibody targets across a variety of disease areas.



Being able to work with investigators from three world-class academic institutions to discover novel, **innovative therapies for a large variety of disease is a once-in-a-lifetime opportunity**. The collaborative spirit and enthusiasm that I see from faculty members, postdocs and students every day is very rewarding and encouraging.

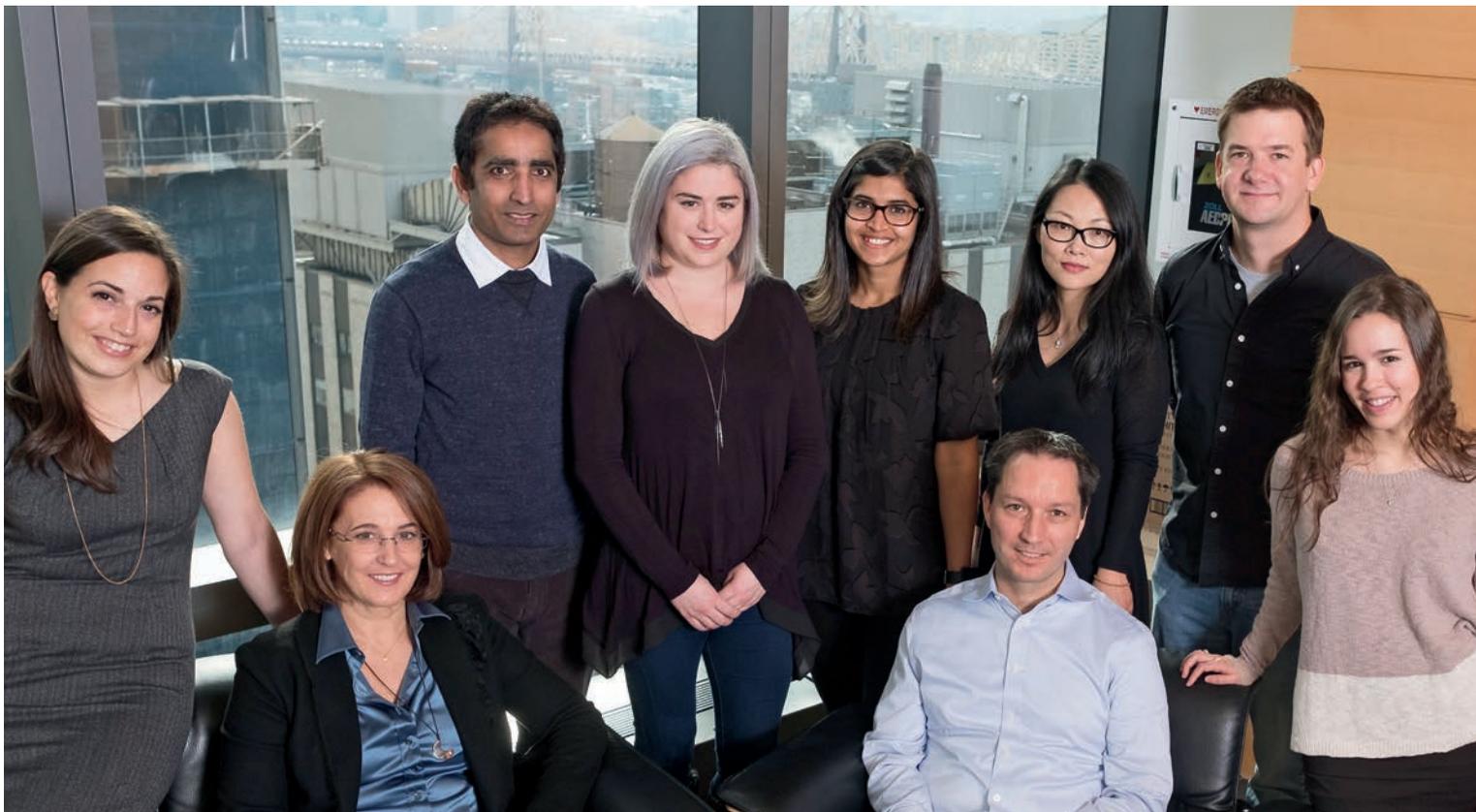
Dr. Ivo Lorenz, PhD, Vice President of Biologics



The Tri-I Therapeutics Discovery Institute has provided a highly timely, unique and important pathway for our faculty to professionally **develop innovative therapeutic agents for important human diseases**. Dozens of faculty from all three campuses are taking advantage of this hugely successful program to move novel strategies forward toward human trials.

David A. Scheinberg, MD, PhD,
Molecular Pharmacology Program, Experimental Therapeutics Center,
Leukemia Service, Memorial Sloan Kettering Cancer Center

TDI Antibody Team

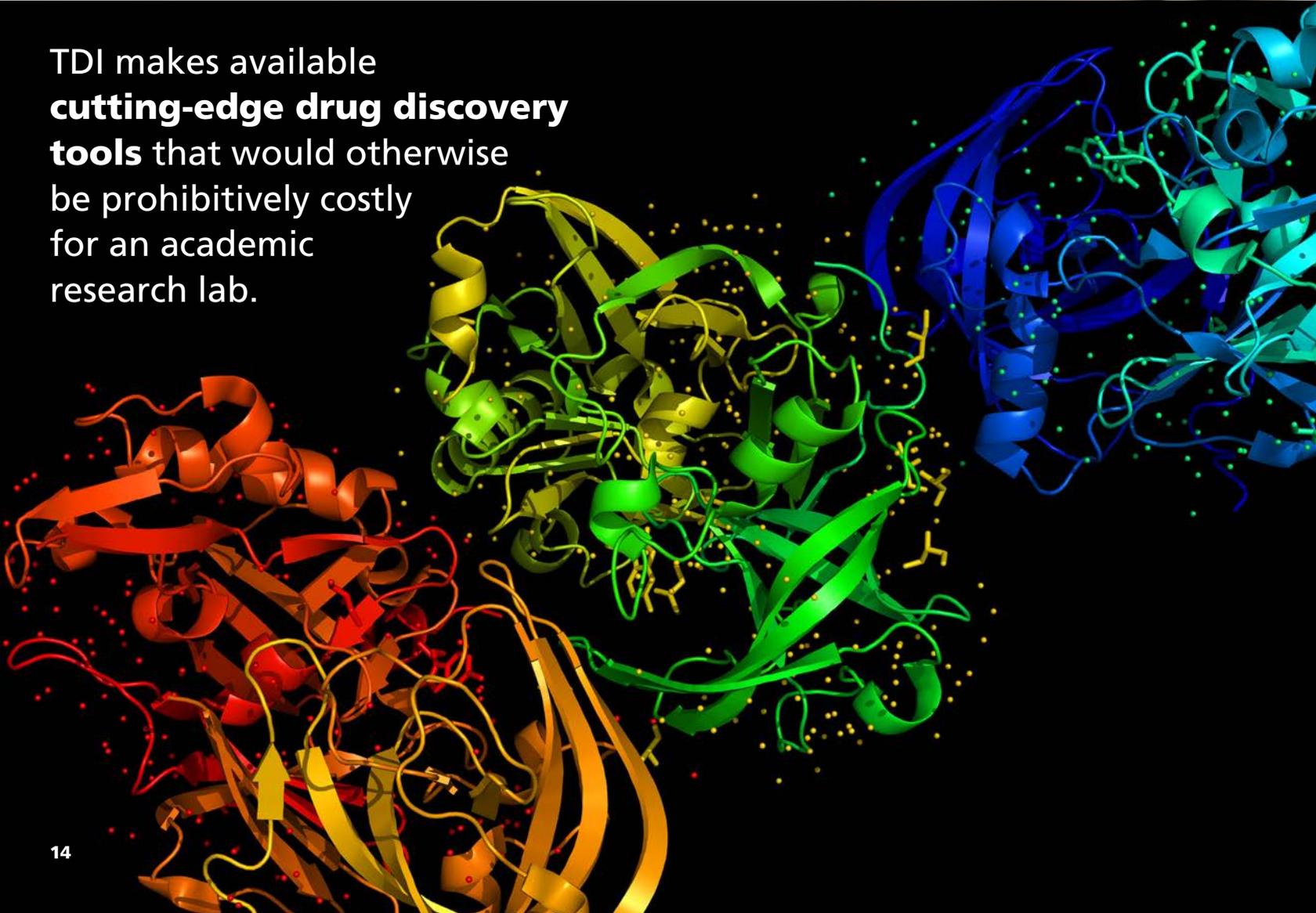


From left to right: Leanne Pedi, Abdul Khan, Mary Ann Pohl, Namita Trikannad, Chen Li, Tommy White, Kathyana Santiago
Seated: Linda Masat, Ivo Lorenz



Education & Innovation

TDI makes available **cutting-edge drug discovery tools** that would otherwise be prohibitively costly for an academic research lab.



Education & Innovation: Bringing Cutting-Edge Tools and Expertise to the Tri-Institutional Community

The Sanders Innovation and Education Initiative is a central element of TDI's mandate. TDI aims to foster a spirit of innovation across the three institutions by training Tri-Institutional researchers in state-of-the-art tools and strategies for drug discovery. Our community-wide educational initiatives include frequent trainings on Schrödinger software, an annual medicinal chemistry class, and a regular seminar series. Moreover, through a series of carefully cultivated partnerships, we make available cutting-edge drug discovery technologies that would otherwise be prohibitively costly for an academic research lab.



Mayako Michino: Accelerating Drug Discovery by Applying Computational Tools

In 2016, TDI welcomed Dr. Mayako Michino as the new Manager of Computational Chemistry. Computational technologies are a critical component of modern-era drug discovery programs. Using powerful molecular modeling software from Schrödinger, LLC, Mayako is able to accelerate key steps along TDI's drug discovery pipeline, from lead identification via virtual screening of large compound libraries to optimization of lead compound properties. Mayako comes to TDI with over ten years of experience in working with pharmaceutically relevant targets. Following undergraduate studies at Harvard University, she obtained a PhD from The Scripps Research Institute and completed postdoctoral training at the European Molecular Biology Laboratory and Weill Cornell Medicine. Immediately prior to joining TDI, Mayako was a Research Fellow at the NIH. Her research interests include molecular modeling of protein structures, prediction of ligand binding modes, and development of computational methods for application in structure-guided drug design.

Strategic Technology Partnerships: Spotlight on Cyclofluidic, LTD

TDI is committed to introducing state-of-the-art drug discovery tools to the Tri-Institutional community through industry partnerships. Among our most valued collaborators is Cyclofluidic, LTD, an innovative platform technology company located in the United Kingdom. Cyclofluidic has developed the revolutionary CycLOps™ integrated technology, which allows researchers to very rapidly advance early stage drug discovery programs through hit-to-lead optimization, tool compound discovery, and patent landscape exploration. Over the past year, a number of our Early Stage and Small Molecule projects have been the beneficiaries of this unique partnership, which has delivered promising lead compounds against a range of diseases within a very short time-frame.



Our innovative CycLOps platform ... accelerates projects from the academic research lab to the clinic. Our capabilities and **experience complement those of Tri-I TDI and enable us to play a transformative role** in bringing cures to patients in a way that dramatically increases the efficiency, and decreases the cost, of drug discovery.

David M. Parry, PhD Chief Operating Officer, Cyclofluidic, LTD



I have been amazed by the speed at which **TDI was able to bring diverse chemical resources together to address our medicinal chemistry needs**. TDI's access to a truly world-class network of synthetic resources has made our challenging medicinal chemistry problem seem simple.

Sean Brady, PhD, Associate Professor, The Rockefeller University



TDI's Strategic Partners



Preclinical drug discovery and drug development services

Absorption Systems
Agilux
Charles River Labs
Crystal Pharmatech
Cyclofluidic
Eurofins
Frontage Labs
Particle Science
Zyleris PharmaTech



Antibody discovery & development

Ablexis
Charles River Labs
ChemPartner
Creative Biolabs
GenScript
LakePharma
Proteos



Biochemical and cell-based assays

Charles River Labs
Eurofins
Horizon
Reaction Biology



Computational chemistry, biology & virtual screening

Cyclofluidic
Schrödinger



Chemical synthesis

WuXi



Structural biology, protein expression & purification

Lake Pharma
New York Structural Biology Consortium
Structural Genomics Consortium
XTAL Biostructures



Innovative screening technologies & unique libraries

HitGen
WuXi
XTAL

Strategic Technology Partnerships: Introducing Ablexis, LLC

In 2016, the TDI negotiated a non-exclusive, perpetual license agreement with Ablexis, LLC, to provide the Tri-I community with access to the AlivaMab Mouse Platform for antibody drug discovery and development.

"Ablexis is pleased to provide the Tri-I TDI access to the AlivaMab Mouse," said Larry Green, PhD, Chief Executive Officer of Ablexis. "The AlivaMab Mouse is the only transgenic animal with both immunoglobulin transgene function and variable gene repertoire optimized to meet the challenges of both antibody drug discovery and antibody drug development. The reliability and ease of use resulting from this unique and advanced design has made the AlivaMab Mouse the next-generation antibody drug discovery platform of choice for the world's leading pharmaceutical companies."

TDI will issue a request for projects from the Tri-I community early in 2017 and is thrilled to offer access to this cutting-edge technology that is revolutionizing therapeutic antibody discovery and development.

Leadership Team:

Dedicated to Bringing Value to the TRI-I Community

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This collaboration, one of Takeda's marquee alliances, is a model for how industry and academia can work together and is **the first time academia and industry have created a fully integrated chain from discovery of novel disease biology to development of drug candidate and testing of such molecules in a clinical setting.** It is thrilling to us to be partners with the Tri-I institutions in such a ground-breaking enterprise.

**Juan Harrison, Vice President, Head of Strategic Academic Alliances,
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Partner with Us

TDI is exceedingly fortunate to have some of the finest minds in the world collaborating to turn their research into next-generation drugs.

Tri-TDI brings together researchers from Memorial Sloan Kettering Cancer Center (MSK), The Rockefeller University (RU), and Weill Cornell Medicine (WCM) with collaborators across the globe to remove the barriers that impede drug discovery in academic settings. Together with our partner, Takeda, we are enabling the discovery of next-generation drugs by empowering our faculty with the tools, technology, and expertise.

With the help of your investment, we will meet this extraordinary challenge.

To be part of this project, working alongside Takeda, Deerfield, and three of the world's leading research and clinical institutions in **helping to advance translation research** and build the New York City-based biotechnology infrastructure is a great honor.

Carl Goldfischer, Managing Director, Bay City Capital



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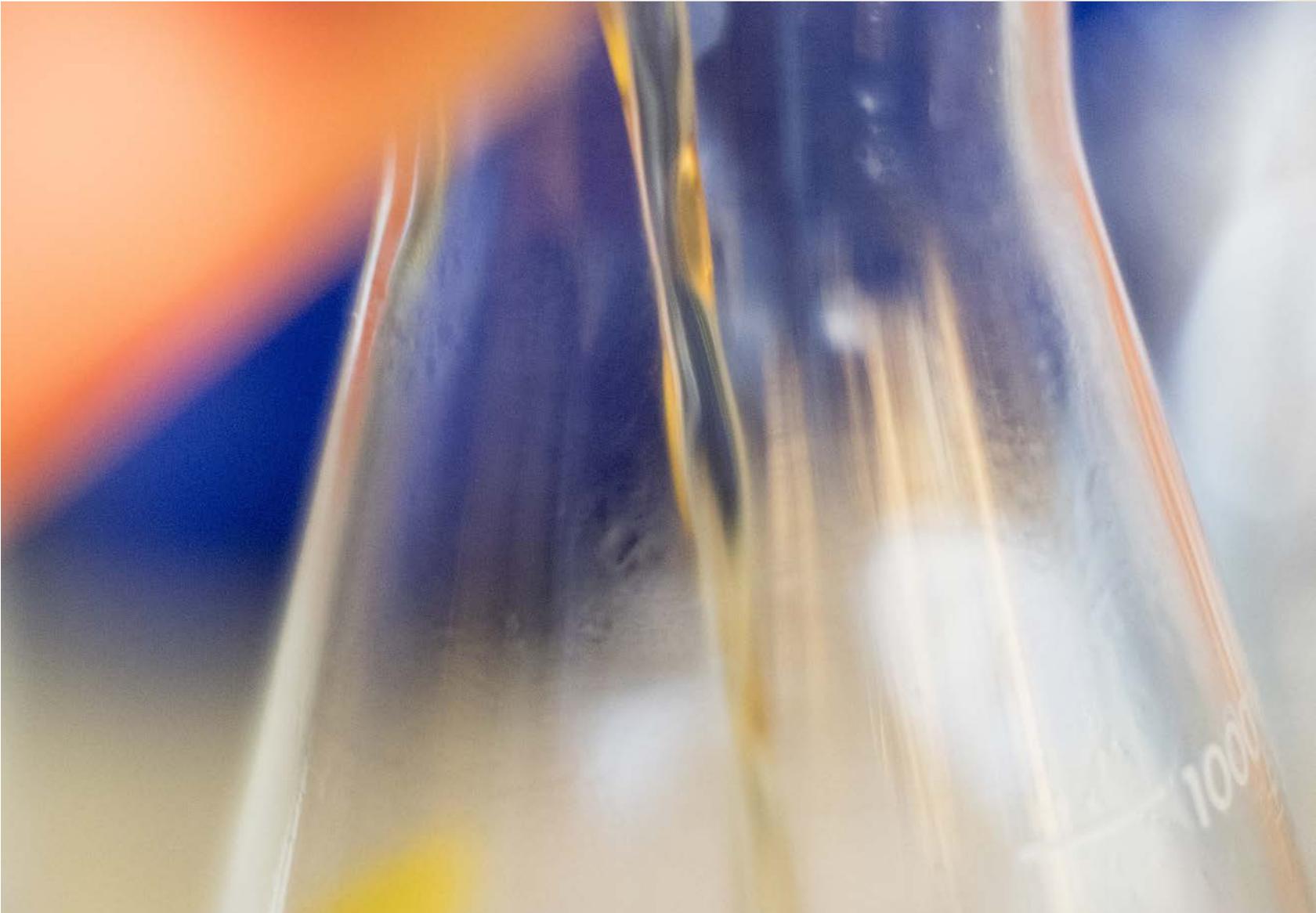
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THERAPEUTICS DISCOVERY INSTITUTE



We achieve our mission by **leveraging the infrastructure, staff, and intellectual capital** of our academic and industry partners, as well as the generous support of philanthropists.





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