



Pathway to Stop Diabetes 2015 Initiator awardee Stephanie Stanford, PhD

The goal of the American Diabetes Association's Pathway to Stop Diabetes[®] program is simple yet revolutionary:

Find a new generation of brilliant scientists at the peak of their creativity, then provide them with the freedom, autonomy, and resources to set them on the road to breakthrough discoveries.

It has been nearly a century since Drs. Frederick Banting and Charles Best made the transformational discovery of insulin. Since then, countless research breakthroughs have helped people with diabetes lead longer, healthier lives. Now, with unprecedented tools at their disposal, the next generation of diabetes researchers has the potential to make game-changing discoveries that will end the burden of diabetes.

But there is a problem. Diabetes research is critically underfunded, potentially driving talented scientists away from diabetes and jeopardizing progress.

The ADA's Pathway to Stop Diabetes program is a bold, forward-thinking initiative dedicated to bringing 100 scientists to diabetes research. Through substantial, sustained funding; access to scientific and career mentoring from current leaders in diabetes research and business; avenues for fostering meaningful collaborations; and communication outlets to convey their research, Pathway to Stop Diabetes scientists are poised to become the next generation of diabetes research leaders.

The prestigious, nomination-only Pathway to Stop Diabetes program has three distinct award categories:

Pathway Initiator - For scientists currently in training through their transition to independent research careers in diabetes

Pathway Accelerator - For scientists in the early stage of their independent research careers who show tremendous potential for answering critical diabetes-related questions

Pathway Visionary - For scientists established in fields other than diabetes who want to bring a new perspective to solving diabetes-related problems

An important facet of the program is that it invests in the person, not the project. While each individual scientist brings their own background, expertise and vision, all are steadfastly dedicated to the same goal: To Stop Diabetes.

This year, we welcomed four new corporate sponsors to Pathway to Stop Diabetes:

Abbott, Dexcom, Inc., Janssen and Pfizer Inc. They joined long-term sponsors Novo Nordisk, Eli Lilly and Company, AstraZeneca and Merck. We are confident that, with continued support from our corporate sponsors and the incredible generosity of our philanthropic supporters, we will indeed achieve our goal of bringing 100 brilliant scientists to diabetes research.

For the latest information on the Pathway program and exciting updates from Pathway scientists, visit diabetes.org/pathway.

FOUNDING SPONSORS







Type 2 Diabetes



STEPHEN C.J. PARKER, PHD University of Michigan Initiator '14



WOLFGANG PETI, PHD University of Arizona College of Medicine Visionary '14



CELINE E. RIERA, PHD Cedars-Sinai Medical Center Initiator '15



MICHAEL L. STITZEL, PHD The Jackson Laboratory Accelerator '18



SAMIE R. JAFFREY, MD, PHD Weill Cornell Medicine Visionary '18



JONATHAN V. SWEEDLER, PHD University of Illinois at Urbana-Champaign Visionary '18



SARAH A. TISHKOFF, PHD University of Pennsylvania Visionary '19

"It is an honor to be among a great class of Pathway scientists, allied in improving the lives of people with diabetes." - Matthew J. Webber. PhD

Obesity, Prediabetes and Diabetes Risk



JOSHUA P. THALER, MD, PHD University of Washington Accelerator '14



ZACHARY A. KNIGHT, PHD University of California, San Francisco Accelerator '16



PRAVEEN SETHUPATHY, PHD Cornell University Accelerator '16



PHILLIP JAMES WHITE, PHD **Duke University** Initiator '16



PAUL COHEN, MD, PHD The Rockefeller University Accelerator '17



SARAH A. STANLEY, MD, PHD Icahn School of Medicine at Mount Sinai Accelerator '17



ALEXANDER R. NECTOW, PHD **Princeton University** Accelerator '18



JOHN NELSON CAMPBELL, PHD University of Virginia School of Medicine Initiator '18

Gestational Diabetes



KATHLEEN A. PAGE, MD University of Southern California Accelerator '14



MARIE-FRANCE HIVERT, MD Harvard Medical School Accelerator '15



EBONY B. CARTER, MD
Washington University
School of Medicine
Accelerator '19

Complications of Diabetes



MICHAEL D. DENNIS, PHD Pennsylvania State University, Hershey Initiator '14



MAYLAND CHANG, PHD University of Notre Dame Visionary '15



DANIEL J. CERADINI, MD, FACSNew York University
Accelerator '16



SUI WANG, PHD Stanford University Initiator '16



JONATHAN N. FLAK, PHD University of Michigan Initiator '17



DAVID A. SPIEGEL, PHD Yale University Visionary '17

Type 1 Diabetes



THOMAS DELONG, PHDUniversity of Colorado, Denver Accelerator '15



ZHEN GU, PHDUniversity of California,
Los Angeles
Accelerator '15



STEPHANIE STANFORD, PHDUniversity of California,
San Diego
Initiator '15



ANDREW SCHARENBERG, MD*
Casebia Therapeutics
Visionary '16



ALEKSANDER D. KOSTIC, PHDJoslin Diabetes Center
Initiator '17



SUMITA PENNATHUR, PHDUniversity of California,
Santa Barbara
Visionary '17



MAUREEN MONAGHAN, PHD Children's Research Institute, Washington, DC Accelerator '18



MATTHEW J. WEBBER, PHD University of Notre Dame Accelerator '19

^{*}Relinquished as of 2017. Dr. Scharenberg is now Chief Scientific Officer at Casebia Therapeutics.

PATHWAY'S FIRST GRADUATING CLASS

In 2013, the American Diabetes Association launched the Pathway to Stop Diabetes program with a bold vision of bringing 100 brilliant scientists to diabetes research. Five stellar scientists were selected for the inaugural class, starting their grants in January 2014. They have since pursued transformational research.

This year, Pathway Accelerator awardees Dr. Kathleen A. Page and Dr. Joshua P. Thaler, and Pathway Visionary awardee Dr. Wolfgang Peti became the first scientists to complete the Pathway to Stop Diabetes program. As they have demonstrated already, they will continue to play an integral role in advancing revolutionary diabetes research.

KATHLEEN A. PAGE, MD, University of Southern California, Los Angeles, CA **Stopping the Transgenerational Risk of Diabetes**

Children of mothers who had diabetes during pregnancy are at high risk for developing obesity and type 2 diabetes. My Pathway to Stop Diabetes project has aimed to understand how "in utero" exposure to gestational diabetes results in alterations in brain pathways involved in the regulation of energy and glucose homeostasis.

With the support of this award, I have been able to invest in the use of cutting-edge imaging technologies and I initiated the largest single-center trial designed to characterize brain development and its relationship to metabolic function in pre-pubertal children at high risk for developing diabetes. This project has already led to a number of downstream studies including work aimed at identifying the impact of prenatal exposure to maternal obesity and gestational diabetes on brain development, and longitudinal studies to identify biological factors that may contribute and interact with each other to increase risk for type 2 diabetes.



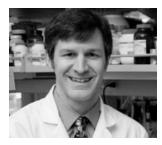
"My Pathway to Stop Diabetes award allowed me to break new ground in diabetes research to advance our understanding of early life determinants of obesity and diabetes."

JOSHUA P. THALER, MD, PHD, University of Washington, Seattle, WA

Treating Obesity and Diabetes in the Brain

The obesity epidemic is closely linked to the recent surge in type 2 diabetes, but no therapies currently exist that promote sustainable weight-loss. My Pathway to Stop Diabetes project has aimed to develop a better understanding of how the human body regulates body weight, which may enable us to act before the onset of diabetes, when complications have not yet occurred. We have provided the first substantial evidence that specific types of brain cells are critical players in susceptibility to weight gain and glucose intolerance.

This field was virtually nonexistent prior to my award and has been received with skepticism by the establishment. Without this award, our pioneering work in this area would not have been possible. Thus, I want to acknowledge the visionary roles of the ADA and the Pathway funding sponsors in creating a program to advance innovative scientists and their bold ideas in pursuit of a cure for diabetes.



"My Pathway to Stop Diabetes award provided me the opportunity to start my own lab focused on a new, challenging area of metabolic research."

WOLFGANG PETI, PHD, University of Arizona, Tucson, AZ Innovating New Approaches to Make Safer, More Effective Diabetes Treatments

When insulin signaling is disrupted, diabetes is the result. My Pathway to Stop Diabetes project has focused on using powerful molecular tools to gain fresh, essential insights into how insulin signaling becomes disrupted in diabetes, with the goal of developing a new drug and finding a cure for diabetes. This effort has already led to the identification of a drug specific for the enzyme PTP1B, which regulates insulin receptor activity. These established successes ensure our long-term commitment and, most importantly, successes for the future and hope for diabetes patients worldwide.

Without these resources, it simply would not have been possible to generate the exciting advances we have contributed to the field of diabetes. This award allowed my laboratory to push boundaries, think big and be creative, ultimately enabling us to achieve and exceed our goals set out at the beginning of the award.



"My Pathway to Stop Diabetes award allowed me not only to pursue a new area of research but also enabled me to employ novel, state-of-the-art technologies in this pursuit."

THE NUMBERS TELL THE STORY

\$51.5M

raised from corporate sponsors and individual philanthropists

invention disclosures and patent applications

110+

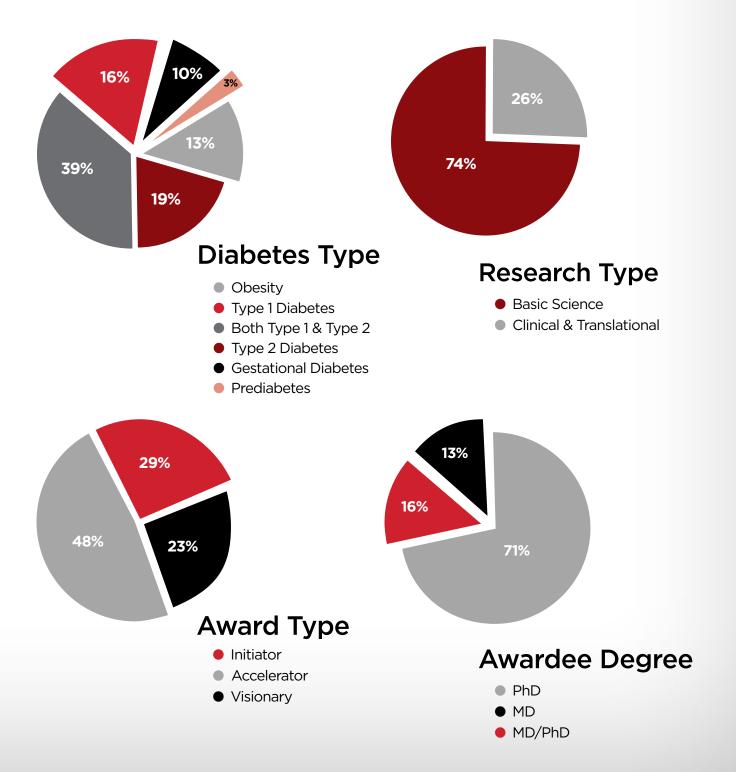
peer-reviewed publications authored by Pathway awardees

scientists selected from more than 600 applicants

average age of Pathway Initiator and Accelerator awardees compared to 44 for first time NIH R01 awardees

THE PATHWAY PORTFOLIO

Pathway scientists are selected based on their potential to become diabetes research leaders and to make significant discoveries in the field of diabetes. While each individual scientist brings their own unique vision for stopping diabetes, collectively, they address many of the key issues in prevention, management and treatment of diabetes and its complications.



DIABETES IS PERSONAL FOR PATHWAY SCIENTIST

"My passion to understand and study diabetes is built upon my personal and research experiences. I grew up in a small city close to Inner Mongolia in northern China. Over the past few decades, diabetes has become one of the most common diseases in my hometown due to the rapid economic development and lifestyle changes. More and more people are suffering from diabetes and its complications, including my close friends and family members." Pathway to Stop Diabetes 2018 Initiator awardee Sui Wang, PhD

PATHWAY SCIENTIST NAMED HOWARD HUGHES MEDICAL INSTITUTE INVESTIGATOR

Pathway to Stop Diabetes Accelerator awardee Zachary A. Knight, PhD, is investigating how the brain regulates body weight. His lab was the first to visualize hunger-controlling neurons in a living organism, which he determined become activated just seconds after the sight or smell of food. Now, Dr. Knight is determining how these neurons are regulated over the long-term, with particular interest in changes preceding obesity and type 2 diabetes.

This year, Dr. Knight was named an HHMI Investigator, one of the most prestigious honors in all of biomedical research.

He joins 300 other investigators across different disciplines, all selected based

Nobel Prize.

Pathway to Stop Diabetes 2016 Accelerator awardee Zachary A. Knight, PhD

on their potential to make

transformational discoveries

in science. To date, 29 HHMI

investigators have won a

KEY ACCOMPLISHMENTS OF PATHWAY SCIENTISTS IN 2018

Pathway to Stop Diabetes awardees represent a diverse coalition of people dedicated to furthering progress toward ending diabetes. A key way in which they accomplish this is by communicating their results to the broader scientific community, ensuring that others will build upon their findings. This year alone, they published 36 peer-reviewed articles and reviews, and presented more than 150 times at scientific conferences and symposia.

> Pathway to Stop Diabetes 2016 Initiator awardee Philip James White, PhD

TYPE 1 DIABETES

Pathway scientist Sumita Pennathur, PhD, has made significant progress toward developing an inexpensive, pain-free and disposable patch that can continuously monitor blood glucose. She has recently published a report documenting a novel way to enhance the scalability and manufacturability of microneedles for use in biomedical applications, including her glucose monitoring patch.

Kim, H., Theogarajan, L. S., & **Pennathur, S**. (Jan 2018). A repeatable and scalable fabrication method for sharp, hollow silicon microneedles. *Journal of Micromechanics and Microengineering*.

TYPE 2 DIABETES

Pathway scientist Philip James White, PhD, recently discovered how specific molecules interact to control the level of fat in the liver. Manipulation of this pathway can improve type 2 diabetes in rodents, setting the stage for the development of a medication for use in humans.

White, P. J., McGarrah, R. W., Grimsrud, P. A., Tso, S.-C., Yang, W.-H., Haldeman, J. M., ... Newgard, C. B. (June 2018). The BCKDH Kinase and Phosphatase Integrate BCAA and Lipid Metabolism via Regulation of ATP-Citrate Lyase. *Cell Metabolism*.

COMPLICATIONS OF DIABETES

Pathway scientist Mayland Chang, PhD, published results demonstrating a novel target for the treatment of diabetic foot ulcers, a leading cause of amputations in people with diabetes. She is currently developing a potential new therapy to improve the healing of foot ulcers in people with diabetes.

Nguyen, T. T., Ding, D., Wolter, W. R., Pérez, R. L., Champion, M. M., Mahasenan, K. V., ... **Chang, M.** (Sept 2018). Validation of Matrix Metalloproteinase-9 (MMP-9) as a Novel Target for Treatment of Diabetic Foot Ulcers in Humans and Discovery of a Potent and Selective Small-Molecule MMP-9 Inhibitor That Accelerates Healing. *Journal of Medicinal Chemistry.*

GESTATIONAL DIABETES

Pathway scientist Marie-France Hivert, MD, has determined the extent to which a woman's genetics alters her risk for developing gestational diabetes. Dr. Hivert found that the genetic risk for type 2 diabetes similarly applies to risk for gestational diabetes.

Powe, C. E., Nodzenski, M., Talbot, O., Allard, C., Briggs, C., Leya, M. V., ... **Hivert, M.-F.** (Dec 2018). Genetic Determinants of Glycemic Traits and the Risk of Gestational Diabetes Mellitus. *Diabetes*.

SELECT 2018 PUBLICATIONS

- 1. Chen, Z., Wang, J., Sun, W., Archibong, E., Kahkoska, A. R., Zhang, X., ... Gu, Z. (Jan 2018). Synthetic beta cells for fusion-mediated dynamic insulin secretion. Nature Chemical Biology, 14(1), 86-93.
- 2. Kycia, I., Wolford, B. N., Huyghe, J. R., Fuchsberger, C., Vadlamudi, S., Kursawe, R., ... Parker, S.C.J., Stitzel, M. L. (April 2018). A Common Type 2 Diabetes Risk Variant Potentiates Activity of an Evolutionarily Conserved Islet Stretch Enhancer and Increases C2CD4A and C2CD4B Expression. American Journal of Human Genetics, 102(4), 620-635.
- 3. Pan, W., Adams, J. M., Allison, M. B., Patterson, C., Flak, J. N., Jones, J., ... Myers, M. G. (April 2018). Essential Role for Hypothalamic Calcitonin Receptor-Expressing Neurons in the Control of Food Intake by Leptin. Endocrinology, 159(4), 1860-1872.
- 4. Luber, J. M., Tierney, B. T., Cofer, E. M., Patel, C. J., & Kostic, A. D. (May 2018). Aether: leveraging linear programming for optimal cloud computing in genomics. Bioinformatics, 34(9), 1565-1567.
- 5. Luo, S., Alves, J., Hardy, K., Wang, X., Monterosso, J., Xiang, A. H., & Page, K. A. (July 2018). Neural processing of food cues in pre-pubertal children. Pediatric Obesity.
- 6. Cardenas, A., Gagné-Ouellet, V., Allard, C., Brisson, D., Perron, P., Bouchard, L., & Hivert, M.-F. (Aug 2018). Placental DNA Methylation Adaptation to Maternal Glycemic Response in Pregnancy. Diabetes, 67(8), 1673-1683.
- Nguyen, T. T., Ding, D., Wolter, W. R., Champion, M. M., Hesek, D., Lee, M., ... Chang, M. (Sept 2018). Expression of active matrix metalloproteinase-9 as a likely contributor to the clinical failure of aclerastide in treatment of diabetic foot ulcers. European Journal of Pharmacology, 834, 77-83.
- 8. Baker, R. L., Jamison, B. L., Wiles, T. A., Lindsay, R. S., Barbour, G., Bradley, B., Delong, T., Friedman, R.S., Haskins, K. (Sept 2018). CD4 T Cells Reactive to Hybrid Insulin Peptides Are Indicators of Disease Activity in the NOD Mouse. *Diabetes*, 67(9), 1836-1846.
- 9. Rabbani, P. S., Soares, M. A., Hameedi, S. G., Kadle, R. L., Mubasher, A., Kowzun, M., & Ceradini, D. J. (Oct 2018). Dysregulation of Nrf2/Keap1 Redox Pathway in Diabetes Affects Multipotency of Stromal Cells. Diabetes. 68(1), 141-155.
- 10. Khetan, S., Kursawe, R., Youn, A., Lawlor, N., Jillette, A., Marquez, E. J., ... Stitzel, M. L. (Nov 2018). Type 2 Diabetes-Associated Genetic Variants Regulate Chromatin Accessibility in Human Islets. *Diabetes*, 67(11), 2466-2477.
- 11. Dai, W., Miller, W. P., Toro, A. L., Black, A. J., Dierschke, S. K., Feehan, R. P., ... Dennis, M. D. (Nov 2018). Deletion of the stress-response protein REDD1 promotes ceramide-induced retinal cell death and JNK activation. FASEB, fj201800413RR.
- 12. Kumar, G. S., Choy, M. S., Koveal, D. M., Lorinsky, M. K., Lyons, S. P., Kettenbach, A. N., ... **Peti, W.** (Nov 2018). Identification of the substrate recruitment mechanism of the muscle glycogen protein phosphatase 1 holoenzyme. Science Advances, 4(11), eaau6044.
- 13. Dai, W., Dierschke, S. K., Toro, A. L., & Dennis, M. D. (Dec 2018). Consumption of a high fat diet promotes protein O-GlcNAcylation in mouse retina via NR4A1-dependent GFAT2 expression. Biochimica Et Biophysica Acta. Molecular Basis of Disease, 1864(12), 3568-3576.

"The Pathway award has allowed me to conduct the high-risk, high-reward science my group is working on that would not have been funded via traditional routes such as the NIH. This funding paves a path forward for us to be able to identify mechanisms by which the gut microbiome prevents

Pathway to Stop Diabetes 2017 Initiator awardee Aleksander Kostic, PhD

autoimmune diabetes."

SUPPORTING PATHWAY TO STOP DIABETES

"At AstraZeneca, we push the boundaries of science to deliver life-changing medicines that transform the treatment of people living with diabetes, and we are passionate about supporting organizations and programs like the ADA Pathway to Stop Diabetes that share a similar mission and purpose. It is only through research that we will continue to advance that knowledge and understanding that has the potential to lead to new discoveries for people living with diabetes."

-Naeem Khan, MD, Vice President, US Medical Affairs, Cardiovascular and Metabolic Disease. AstraZeneca



"The Lebherz Family Foundation is proud to support the ADA in its quest to cure diabetes. The young scientists bring new thinking and enthusiasm to the effort and great progress is being made."

—Phil Lebherz, Lebherz Family Foundation Inc.

"At Merck we are committed to progressing diabetes research. While advancements are making a remarkable difference for patients, we recognize there is much more work to be done. That is why we are proud to support the Pathway Program and its important vision of finding the next generation of brilliant scientists to transform the future of diabetes research."

-Sam Engel, MD, associate vice president, Merck clinical research, diabetes and endocrinology



THE 2019 CLASS OF PATHWAY TO STOP DIABETES SCIENTISTS

Accelerator Awards

PROACTIVE INTERVENTION TO STOP DIABETES DURING PREGNANCY Ebony B. Carter, MD, Washington University, St. Louis, MO

Medical complications that develop during pregnancy, such as gestational diabetes, can affect the long-term health of mothers and their children. While most women with gestational diabetes return to normal immediately after delivering their babies, they remain at significantly higher risk of developing type 2 diabetes in the years immediately following pregnancy. Dr. Carter has designed an innovative and practical intervention, called Targeted Lifestyle Change Group Prenatal Care (TLC), that can be integrated in routine prenatal care. She will compare this approach to traditional prenatal care in a community of women who are predominantly low-income, African American, have high levels of obesity, and are at high-risk for developing gestational diabetes, to determine whether it improves health outcomes for both women and their children. If successful, this effort has the potential to mitigate the transgenerational risk for type 2 diabetes in high-risk populations.

A NOVEL APPROACH TO PREVENT LOW BLOOD GLUCOSE DURING SLEEP Matthew J. Webber, PhD, University of Notre Dame, Notre Dame, IN

Low blood glucose levels are a serious threat to people with diabetes—especially during sleep, when they are less aware of the condition and less able to safely counteract it by ingesting glucose. This danger leads to sleepless nights for patients and their caregivers. Using his background in materials science, Dr. Webber has outlined an innovative approach to proactively prevent the threat of low-blood glucose. His idea centers around the development of materials that can both sense glucose levels and respond to low glucose by automatically releasing the hormone glucagon. This approach will be automated and integrated into patient-friendly delivery devices, offering promise to provide a safe and care-free way to prevent potentially lethal glucose lows while mitigating a serious physical and psychological burden for people with diabetes.

Visionary Award

UNDERSTANDING THE ROLE OF GENETICS IN DIABETES HEALTH DISPARITIES Sarah A. Tishkoff, PhD, University of Pennsylvania, Philadelphia, PA

Populations of African descent, including African-Americans, have high rates of type 2 diabetes, but we don't yet understand exactly why. Dr. Sarah Tishkoff will use her expertise in the genetics of Africans to unravel the mysteries underlying this health disparity. She has identified three separate ethnically diverse African populations living indigenous lifestyles with widely different rates of diabetes. Through analyzing the differences in their DNA, immune systems and metabolism, Dr. Tishkoff seeks to understand why some indigenous populations are protected from diabetes, while others are at high risk. Understanding the risk factors for diabetes in populations of African ancestry is critical for developing better, more precise diagnostics and therapeutics and eliminating disparities in diabetes.

HONORED

"I'm humbled and honored to accept the Pathway to Stop Diabetes award. I look forward to using the Pathway award to apply diabetes prevention interventions during pregnancy that have the potential to improve health outcomes for moms and their children for years to come."

- Ebony B. Carter, MD



THE MENTOR ADVISORY GROUP

Each year, the Mentor Advisory Group, a collection of world-class diabetes research leaders, convenes to determine which applicants best embody the overarching Pathway to Stop Diabetes principles: Brilliant, Bold, Transformative. Their dedication to the program does not end there. Each successful applicant is assigned a Mentor Advisory Group mentor to help guide them to research and career success.

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Chair, Mentor Advisory Group University of Massachusetts Medical School, Worcester, Mass.

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Nabu Strategic Advisors, Los Altos Hills, Calif.

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RPORATE SPONSORS 2018 CONTRIBUTIONS TO PATHWAY TO STOP DIABETES

VISIONARY (\$2.5 Million+) **DISCOVERY (\$1.0 Million+)** INITIATOR (\$500,000+)









CORPORATE CONTRIBUTORS (\$100,000+)









"Novo Nordisk, as a Founding Sponsor has been proud to support this program which not only delivers the highest quality research in diabetes but also nurtures our most promising scientists of the future. The research carried out as part of the Pathway to Stop Diabetes is not just great ground breaking science but likely to reduce the burden of disease for people with diabetes."

-Stephen Gough MD, FRCP (UK) Senior Vice President and Global Chief Medical Officer, Novo Nordisk A/S

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Robert Singley

Bess Weatherman

^{*} Cumulative contributions through December 31, 2018 **Deceased

▲.American Diabetes Association。 Research Foundation

"As long as people continue to live with diabetes, research that leads to better outcomes is needed. Lilly supports the Pathway Program because we are committed to finding new ways to improve the lives of people who are affected by this condition. With federal funding under increased pressure, diabetes research is at risk without important initiatives such as the Pathway Program. We applaud the American Diabetes Association for its commitment to funding this important work."

-Sherry Martin, MD, Vice President, Medical Affairs, Eli Lilly and Company

* IN 2019, ELI LILLY AND COMPANY IS OFFERING TO MATCH ANY CONTRIBUTIONS FROM NEW SPONSORS UP TO \$500K *