The theme of this year’s annual report, “Incredible,” is inspired by the new PBS documentary, *Incredible Aging: Adding Life to Our Years*. The special features 14 AFAR experts, representing grantees, board members, and scientific leadership—some of whom are seen above. PBS reached out to AFAR because our researchers could lend the brightest insights into the most exciting innovations driving healthy aging. This is a testimony to the impact that our investigators are making in the field and in our lives. We dedicate this report to their incredible talent.
AN INCREDIBLE FUTURE FOR HEALTHY AGING

For more than three decades, the American Federation for Aging Research (AFAR) has been a global leader in advancing evidence-based science that increases our understanding of the basic biology of aging and how diseases are influenced by the underlying processes or “hallmarks” of aging.

In this report, we highlight three extraordinary scientists who are driving innovative age-related research that received early support through an AFAR grant.

Their stories also highlight how AFAR grants become seed funding to take research to the next level through significant funding from the National Institutes of Health (NIH). In a single decade—from 2005-15, for example—76 AFAR grantees went on to receive R01 grants, the NIH’s core research grants. Hundreds of other AFAR grantees over the years have received R01s and numerous other esteemed research awards.

Likewise, AFAR’s proven track record in administering complex scientific programs has led to two exciting new partnerships with the NIH’s National Institute on Aging (NIA). We were selected to be the first Coordinating Center for the Nathan Shock Centers of Excellence in the Basic Biology of Aging initiative, and with Wake Forest School of Medicine, we will coordinate a new NIA Research Centers Collaborative Network (RCCN) among the NIA’s six aging center programs. For both of these NIA-supported programs, AFAR is providing critical support by conducting high-level communications, meetings and symposia, webinars, and grant reviews.

AFAR’s sustained commitment to rigorous research into the basic biology of aging has created a sound foundation for our next trailblazing phase: translating this core knowledge into exciting new pharmaceutical and clinical interventions. The most prominent and promising of these efforts is the Targeting Aging with Metformin (TAME) Trial, which continues to gain momentum under the leadership of AFAR Deputy Scientific Director Nir Barzilai, M.D. (See p. 8 for more on TAME.)

AFAR’s latest strategic plan, completed by our Board of Directors in 2017, is firmly focused on this new frontier of translational research. This plan reaffirmed our mission while mapping out new special initiatives on preclinical research and bio-behavioral science, nutrition, and exercise.

AFAR accomplishes this all with an administrative efficiency that has earned us the highest, 4-star ranking from Charity Navigator (the nation’s largest and most-utilized evaluator of charities) for five consecutive years. And we could not support and drive the future of healthy aging without the dedication and hard work of our Board and staff, volunteer scientific committee members, funding and program partners, and generous supporters.

We look forward to an incredible future of healthy aging.

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Naked mole rats and bowhead whales may seem to have little in common. But they share two important distinctions in the eyes of Vera Gorbunova, Ph.D.: both live relatively long lives, and both are resistant to cancer.

A professor of biology and associate professor of oncology at the University of Rochester, New York, Dr. Gorbunova believes that understanding the mechanisms that have naturally evolved in long-lived animals to protect them from cancer may have a profound effect on the field of human aging.

This vision has led her to build a new approach to aging research: one that uses the tools of comparative biology not only to describe the differences between species but also to identify the mechanisms that cause those differences.

“Sometimes nature may be smarter than us,” she says. “In animal studies, we can find things that could potentially be very relevant and applicable to humans.”

For example, the naked mole rat’s resistance to cancer is “controlled by a very unique molecule called hyaluronan that’s secreted by its cells. Human cells
also secrete it, but naked mole rats make 10 times more of it. Plus, the molecules are much longer than they are in humans.”

Dr. Gorbunova’s lab engineered a mouse that expresses the naked mole rat gene, which has shown health benefits in the mouse. Her lab also is developing pharmacological strategies on how to mimic the same condition in a patient using a small molecule.

This unique, comparative approach to cancer research is grounded in the 2005 grant she received from AFAR to study changes in the levels of DNA double-strand break repair proteins during aging and cellular senescence.

Receiving the AFAR grant during her first year as an assistant professor was particularly formative to her research path. “In your early years as a faculty member, you are evaluated by your institution and the field. You have to prove yourself.”

The AFAR grant allowed her to gather the preliminary data needed to obtain a grant from the NIH, which “really took these studies to the next level.”

With the NIH support, she developed a mouse model to study changes in DNA repair during aging. This eventually led to the discovery of a protein—sirtuin 6, or SIRT6—that can actually prevent the decline of DNA repair. This can be used potentially in therapies to prevent damage to the genome.

Today, Dr. Gorbunova’s lab also studies DNA repair in breast cancer cells in order to identify common alterations in repair pathways. She and her colleagues are using a comparative approach to identify tumor suppressors that evolved in long-lived and large animal species to protect them from cancer.

“It’s rewarding to see how the research funded by an AFAR grant so early in my career has evolved, and exciting to see how this research in the biology of aging and the biology of cancer can help extend health-span and suppress cancer.”
EXPLORING NORMAL COGNITIVE DECLINE UNCOVERS RESILIENCE AGAINST ALZHEIMER’S

While much research on Alzheimer’s has centered on people who already have the disease or are at risk, Catherine Kaczorowski, Ph.D., has focused instead on resilience. She is intrigued by how the brain ages when Alzheimer’s does not develop.

At The Jackson Laboratory in Bar Harbor, Maine, her research seeks to answer the question: Will preserving normal brain aging completely preserve cognitive health in Alzheimer’s disease, or are there other mechanisms that people with Alzheimer’s disease need to have addressed in order to extend their cognitive lifespan as well?

“My research focus really all stems from the very first grant I received from AFAR and The Rosalinde and Arthur Gilbert Foundation to study genetic diversity,” she says. “Every single success that I can think of right now started with my New Investigator Award in Alzheimer’s Disease. I just wouldn’t have pursued this research question if it weren’t for that grant.”

For more than 10 years, The Rosalinde and Arthur Gilbert Foundation has funded the New Investigator Awards in Alzheimer’s Disease program, supporting 52 investigators across the United States and Israel.
With the support of a New Investigator Award in 2014, Dr. Kaczorowski envisioned a research path “to accelerate our identification of new therapeutic targets for cognitive decline and Alzheimer’s.” The grant supported a study on hundreds of mice, which generated baseline data on cognitive testing and RNA sequencing over the lifespan of the animals.

The award also provided professional and personal validation, knowing her proposal was selected by AFAR’s experienced and prestigious scientific review committee. “It was invaluable to have the best aging researchers in the world tell me my research was good.” (She now serves on the selection committee for the Glenn/AFAR Postdoctoral Fellowship for Translational Research on Aging grant.)

The New Investigators community also has energized Dr. Kaczorowski. AFAR organizes the annual New Investigators meetings, where grantees present their findings and often form collaborations. “Discussions at the meetings have challenged me to push my research, and my colleagues really have inspired my commitment to Alzheimer’s.”

To date, Dr. Kaczorowski has leveraged the New Investigator award into two large Research Project Grants, known as R01s, from the NIH. The most recent—a five-year, $5.4 million grant awarded in September 2017—will support her cognitive resilience research, looking at why some people with a family history of Alzheimer’s disease, and even brain changes associated with the disease, manage to maintain cognitive abilities.

“Better understanding cognitive longevity and resilience in normal aging brains might very effectively delay the onset of neurodegenerative diseases in general. I hope my research can lead to new therapeutic strategies that can benefit people who are at high risk for normal age-related cognitive decline, but also diseases like Huntington’s and Parkinson’s.”
To many, Felipe Sierra, Ph.D., is one of the most recognized and respected champions of geroscience: an interdisciplinary field that aims to understand, at the molecular level, the relationship between biological aging and age-related diseases and other conditions that diminish our quality of life.

“The idea is that because aging is the major risk factor for these diseases, investigators doing disease-specific research should consider the effects of aging in their work. And that will hopefully lead to translational discoveries,” he says.

It is Dr. Sierra’s aim “to galvanize the research community” to fully embrace the research opportunities unlocked by addressing multiple age-related diseases at once instead of focusing on each individual disease.

As director of the Division of Aging Biology at the NIA of the NIH, he was instrumental in developing the Trans-NIH Geroscience Interest Group, which engages 20 different NIH institutes to regularly meet and collaborate.
To date, Dr. Sierra has organized two well-attended geroscience summits. To expand awareness of geroscience globally, he is planning other major meetings in the next few years around the world, including Europe, Australia, South America, and the United States.

The long-range, big picture vision that Dr. Sierra brings to geroscience was sparked early in his career, thanks to an AFAR grant.

A 1993 AFAR Research Grant helped him advance his pioneering research with the T-kininogen gene that he first isolated at Nestlé, where he was the first to apply differential screening to look at gene expression in the livers of older rats. Sierra used the AFAR grant to produce preliminary data, which he leveraged to get funding from the NIA.

“I know very well now how hard it is to get money from the NIA,” he notes. “I think that funding from AFAR is a major stepping stone for many people in the field.”

Following a shared appointment as an associate professor at the Lankenau Institute for Medical Research in Pennsylvania and the University of Chile in Santiago, Dr. Sierra joined the NIA as a program director within the Division of Aging Biology in 2002 and became director of that division in 2006—an impressive path since he received an AFAR grant over a decade earlier.

“As a young investigator, an AFAR grant strengthened my research and led me to receive funding from the NIA. Decades later, I am working at the NIA and witnessing every day how AFAR grantees are shaping the field and collaborating to move ahead exciting and necessary ideas like geroscience.”
Through decades of AFAR-supported research, we have learned that targeting the biology of aging can delay the onset of age-related diseases and conditions, which in turn increases healthspan—our years of good health as we age. This is the premise of the Targeting Aging with Metformin (TAME) Trial.

Scientists have accumulated compelling evidence that metformin—a safe, FDA-approved, first-line drug that has been used to treat type 2 diabetes for decades—can alter the molecular processes of aging. Through this mechanism, metformin may substantially reduce the risk of not only type 2 diabetes, but also cancer, cardiovascular disease, cognitive decline, and total mortality. The primary endpoint for TAME is to demonstrate that targeting aging extends healthspan.

Led by AFAR Deputy Scientific Director Nir Barzilai, M.D., the TAME Trial will be conducted at 14 centers nationwide over six years. It will be a double-blind, placebo-controlled trial, which means that the diverse participants (approximately 3,000 men and women without diabetes, ages 65-80) will be split into two groups. One group will receive metformin while the other will get a placebo, and neither the scientists conducting the trial nor the participants will know who is in the “test group” and in the “control group.”

If metformin is shown to slow the accumulation of age-related diseases, TAME will have a direct and immediate impact on approaches to preventing age-related chronic diseases in persons at high risk. This will profoundly change health care delivery and reduce costs.

“Metformin is not a magic pill,” says AFAR Scientific Director Steven N. Austad, Ph.D. “But it is a tool that can provide a proof-of-concept that by targeting aging, healthspan can be increased, paving the way for a new indication from the U.S. Food and Drug Administration (FDA) for drugs to prevent age-related diseases.”

That FDA indication would unleash the pharmaceutical industry’s considerable ingenuity, innovation, and resources on developing new and better compounds to extend healthy lifespan.

There is already significant momentum around TAME. Wake Forest University has agreed to serve as the Data Coordinating Center, while Merck KGaA, based in Darmstadt, Germany, will provide both metformin and the placebo.

AFAR is helping manage the TAME Trial’s development and is also spearheading fundraising efforts for this initiative, which will cost an estimated $75 million. Two major donors are committed—British philanthropist Jim Mellon and an anonymous, U.S.-based “angel” supporter.

“It will take a concentrated, coordinated effort across the public, private, and philanthropic sectors to raise the money needed for this crucial study,” Dr. Barzilai says. “If TAME shows that we can slow the accumulation of age-related diseases through a drug that targets the processes of aging, it will be the most important medical intervention in the modern era since antibiotics.”
This year, AFAR supported 71 investigators with more than $3,240,000 in funding through our Biology of Aging and Physician Training grants portfolio.

Since 1981, AFAR has provided nearly $175 million to more than 4,400 talented investigators and students.

**BIOLOGY OF AGING GRANTS**

AFAR's Biology of Aging grant programs fuel the pipeline of researchers working to understand the basic biology of aging and age-related diseases in order to extend our years of health and decrease periods of sickness. Several grant programs help early career scientists acquire the knowledge, skills, and experience they need to obtain higher-level grants as they build a body of research. Just as critical are grants tailored to mid-career and senior investigators, which allow them to remain focused on aging as they develop their research programs. AFAR's Biology of Aging grants maintain a core investment in basic biomedical research while helping advance translational interventions that are moving from labs into our lives.

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AFAR GRANT REVIEWS

Every year, AFAR’s nationally respected and scientifically rigorous grant reviews help ensure that only the most promising science receives our support. Members of our Scientific Review Committees are accomplished scientists representing a wide range of expertise in biomedical research on aging. They volunteer their time and expertise to review hundreds of grant applications each year and select scientists and research projects that have the greatest likelihood of making significant contributions to help us stay healthier longer as we grow older. Many are also past AFAR grantees, and they play an important role in identifying the talent and research that AFAR supports. We are grateful for their contributions, which are essential in shaping the impact and reputation of AFAR’s grant programs.

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The Glenn Foundation for Medical Research has partnered with AFAR for more than 30 years. We are grateful for its support, and we applaud its commitment to extending the healthy productive years of life through research on the mechanisms of biological aging.
PHYSICIAN TRAINING GRANTS

AFAR’s Physician Training grant programs help medical student and faculty researchers become academic and clinical leaders prepared to meet the increasing health care needs of an ever-growing older population. Across the country, few medical schools offer mandatory courses or rotations in geriatrics, yet there are nearly 50 million adults age 65 and older in need of specialized care. The necessity to sensitize physicians to the needs of older patients could not be clearer, and AFAR’s physician training grants strengthen the research that will improve care for older Americans and help us all stay healthier, longer.

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2017 Beeson Scholars are fully funded through the National Institute on Aging (NIA) of the National Institutes of Health (NIH). The Beeson annual meetings are supported through The John A. Hartford Foundation and the NIA.

MEDICAL STUDENT TRAINING IN AGING RESEARCH (MSTAR) PROGRAM

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Funded by the Kathyrn Wriston Fund, Jean and Louis Dreyfus Foundation, Lile and John Gibbons, John and Rebecca Mach, and Norman Volk.
Special Report: Centers of Excellence Program Still Pays Dividends

A special report was published in the Journal of the American Geriatrics Society in 2017, highlighting the history, impact, and legacy of The John A. Hartford Foundation Centers of Excellence (CoE) in Geriatric Medicine and Geriatric Psychiatry program.

The CoE program was launched in 1988, and funded by The John A. Hartford Foundation. It supported 1,164 fellows and junior faculty with a total investment of $57.7 million over the next 28 years. AFAR served as the CoE National Program Office from 1998 until the initiative’s closure in 2016.

“It’s fair to say that much of the success of academic geriatrics and the stature of geriatrics in American medical schools today can be attributed to the CoE program,” notes David B. Reuben, M.D., the senior author of the paper. “It successfully increased geriatrics-prepared faculty who achieved promotion and institutional retention, success in winning competitive research grants, and positions of leadership.”

“The CoE program initially aimed to address a critical shortage of faculty with expertise in geriatrics,” says Daniel Kaplan, Ph.D., the paper’s first author. “Remarkably, 97 percent of respondents have remained involved in aging and geriatrics in some capacity.”

“By integrating geriatrics expertise into the training of generations of physicians, the Centers of Excellence program has improved the quality of care for older Americans,” notes AFAR Medical Officer Richard W. Besdine, M.D., who served as Co-Chair of the CoE Program Advisory Committee. “It’s clear that the CoE program created a rich legacy in the field of academic geriatrics that will continue to pay dividends for years to come.”
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AFAR is deeply grateful to our donors for their generous support. Their continued contributions enable us to fulfill our mission and strengthen our programs.
BIOTECHNOLOGY LUNCHEON

On July 25, AFAR hosted The Architects of Aging, a luncheon symposium and awards ceremony honoring leaders in biotechnology and healthspan, at the Westin St. Francis in San Francisco.

We presented the Honorary Leadership Award to Nathaniel “Ned” David, Ph.D., Co-Founder and President of UNITY Biotechnology, and the Chairman’s Award to Edward Lanphier, Founder of Sangamo Therapeutics, Inc.

Both awardees spoke passionately about AFAR’s impact on the foundation, and future, of healthy aging. “Were it not for AFAR and its far-sighted vision going back three decades, UNITY in its current form wouldn’t exist,” said David.

An expert panel followed, featuring AFAR Deputy Scientific Director Nir Barzilai, M.D.; 1990 AFAR grantee Judith Campisi, Ph.D., of the Buck Institute for Research on Aging and UNITY Biotechnology; Jan van Deursen, Ph.D., of the Mayo Clinic and UNITY Biotechnology; and Eric Verdin, M.D., of the Buck Institute for Research on Aging.

The event also recognized our annual scientific awards. 1995 Beeson Scholar and current Board President Mark S. Lachs, M.D., M.P.H. received the Irving S. Wright Award of Distinction. Dongsheng Cai, M.D., Ph.D., of Albert Einstein College of Medicine received the Vincent Cristofalo Rising Star Award in Aging Research. Doctors Lachs and Cai also presented lectures at the 21st World Congress of the International Association of Gerontology and Geriatrics (IAGG).

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David A. Sinclair, Ph.D.
Richard G.A. Faragher, Ph.D.
Hume R. Steyer, J.D.
Alexandra L. Gatje
Rudolph E. Tanzi, Ph.D.
Michael W. Hodin, Ph.D.
Pol Vandenbroucke, M.D.
Thomas G. Kahn, C.F.A.
Joyce M. Yaeger
Peter Kimmelman
Stephanie Lederman, Ed.M.

James L. Kirkland, M.D., Ph.D.
Executive Director

President Elect

2017 STAFF

Stephanie Lederman, Executive Director

Elizabeth Pritchett-Montavon,
Finance Director
Grant Programs Assistant

Riki Blum, Finance Director
Karen Wenderoff, Director of Development

John Chaich, Director of Communications
Odette van der Willik, Deputy Executive
Catherine Cullar, Administrative Manager
Director and Director, Grant Programs
Hattie Herman, Program Officer
### SUMMARIZED OPERATING RESULTS

#### OPERATING REVENUE

<table>
<thead>
<tr>
<th>Description</th>
<th>Amount</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contributions</td>
<td>5,257,464</td>
<td>89%</td>
</tr>
<tr>
<td>Investment Income, Net</td>
<td>30,465</td>
<td></td>
</tr>
<tr>
<td>Endowment Earnings</td>
<td>396,620</td>
<td>7%</td>
</tr>
<tr>
<td>Government Grants</td>
<td>207,763</td>
<td>4%</td>
</tr>
<tr>
<td>Other</td>
<td>33,326</td>
<td></td>
</tr>
<tr>
<td><strong>Total Operating Revenue</strong></td>
<td>5,925,638</td>
<td>100%</td>
</tr>
</tbody>
</table>

#### EXPENSES

<table>
<thead>
<tr>
<th>Description</th>
<th>Amount</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research Grants and Scholarships</td>
<td>4,304,658</td>
<td></td>
</tr>
<tr>
<td>Meetings and Public Education</td>
<td>581,335</td>
<td></td>
</tr>
<tr>
<td><strong>Total Program Expense</strong></td>
<td>4,885,993</td>
<td>82%</td>
</tr>
<tr>
<td>Management and General</td>
<td>547,255</td>
<td>9%</td>
</tr>
<tr>
<td>Fundraising</td>
<td>533,554</td>
<td>9%</td>
</tr>
<tr>
<td><strong>Total Supporting Expense</strong></td>
<td>1,080,809</td>
<td>18%</td>
</tr>
<tr>
<td><strong>Total Operating Expense</strong></td>
<td>5,966,802</td>
<td>100%</td>
</tr>
</tbody>
</table>

**Total Operating Income**: (41,164)

### SUMMARY OF BALANCE SHEET

#### Assets

<table>
<thead>
<tr>
<th>Description</th>
<th>Amount</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash</td>
<td>5,690,559</td>
<td>22%</td>
</tr>
<tr>
<td>Contributions Receivable</td>
<td>6,088,719</td>
<td>24%</td>
</tr>
<tr>
<td>Investments</td>
<td>12,294,338</td>
<td>49%</td>
</tr>
<tr>
<td>Other</td>
<td>1,336,780</td>
<td>5%</td>
</tr>
<tr>
<td><strong>Total Assets</strong></td>
<td>25,410,396</td>
<td>100%</td>
</tr>
</tbody>
</table>

#### Liabilities and Net Assets

<table>
<thead>
<tr>
<th>Description</th>
<th>Amount</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research Grants and Scholarships Payable</td>
<td>2,463,536</td>
<td>10%</td>
</tr>
<tr>
<td>Other</td>
<td>117,267</td>
<td></td>
</tr>
<tr>
<td><strong>Total Liabilities</strong></td>
<td>2,580,803</td>
<td>10%</td>
</tr>
</tbody>
</table>

#### Net Assets

<table>
<thead>
<tr>
<th>Description</th>
<th>Amount</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unrestricted</td>
<td>5,652,503</td>
<td>25%</td>
</tr>
<tr>
<td>Temporarily Restricted*</td>
<td>12,965,815</td>
<td>57%</td>
</tr>
<tr>
<td>Permanently Restricted Endowment</td>
<td>4,211,275</td>
<td>18%</td>
</tr>
<tr>
<td><strong>Total Net Assets</strong></td>
<td>22,829,593</td>
<td>90%</td>
</tr>
</tbody>
</table>

#### Total Liabilities and Net Assets

<table>
<thead>
<tr>
<th>Description</th>
<th>Amount</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Liabilities and Net Assets</strong></td>
<td>25,410,396</td>
<td>100%</td>
</tr>
</tbody>
</table>

*Funding pledged in support of future programming

The above summarized financial information is derived from the organization’s audited financial statements, which are available at www.afar.org and upon request.

For the fifth consecutive year, AFAR has earned a 4-star rating from Charity Navigator, America’s largest and most-utilized independent evaluator of charities. This is the highest possible rating and shows that AFAR adheres to sector best practices and executes its mission in a financially efficient way. Attaining a 4-star rating verifies that AFAR exceeds industry standards: Only 9% of the charities Charity Navigator evaluates have received at least five consecutive 4-star evaluations, indicating that AFAR outperforms most other charities in America.
AFAR offers a range of giving opportunities for your consideration:

- Make a gift to underwrite or endow a **named research grant**. Naming opportunities in support of AFAR Research Grants, New Investigator, or disease-specific grants are available at multiple levels of giving.

- Make a gift to our **annual fund**, the central vehicle through which our core research grant program is funded. Gifts may be made annually, or consider becoming a sustaining donor through our monthly or quarterly gifts program.

- Sponsor an **MSTAR (Medical Student Training in Aging Research) scholar** in your local community and help us fill the urgent need to train more physicians to care for our expanding older population.

- Sponsor a **scientific conference** or public educational program. Sponsorship opportunities are available at many levels.

- Make a **planned gift** as a member of the Irving S. Wright Legacy Society.

- Make a **memorial** or a **tribute gift** to honor a loved one or special occasion.

- Make a **gift of stock** or other tangible property. This is a win-win: while supporting aging research, you avoid paying capital gains taxes.

- If you wish, gifts can be made through your **donor advised fund**.

We welcome the opportunity to speak with you about how your gift can help support AFAR’s researchers who are building the future of healthy aging.

If you would like more information or would like to discuss ways to support AFAR, please contact Karen Wenderoff, director of development, at 212.703.9977 or karen@afar.org.

**To make a gift online, please visit AFAR’s secure website at www.afar.org/give.**
Special thanks to all of the featured experts for lending their time and insights to this report.

AFAR 2017 Annual Report Creative Team: John Chaich, MFA - Design; SCP Communications - Copywriting; and Elizabeth Hanson - Copyediting.

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