



**Methuselah
Foundation**

**The Past
Fifteen Years**

**Return
on Mission
Report
2003-2018**



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Making **90**
the new **50**
by **2030**



Introduction Message from our Foundation's CEO



I am happy to report that
we are winning!

Dave Gobel
CEO



It has always been the fervent desire of the Methuselah Foundation to find itself with nothing left to accomplish. Over the years, we have been focused on seeking the point of greatest leverage to prevent or reverse the damage associated with aging.

We treat aging the way a medieval diamond cutter would face the challenge of cleaving one of the most valuable and hardest substances known to man. In an era where tools were primitive, the gem cutter would carefully examine the internal crystalline structure, as well as the faults in the diamond. After careful and methodical analysis, the gem cutter would strike the diamond with a cleaver, which would result in the large diamond breaking into predictable and useful smaller pieces, ready for polishing and setting in jewelry.

Aging has been, not just an engineering problem, but a cultural one. One of our "first strikes at the diamond" was aimed not just at scientific progress, but also at publicly celebrating advances in the field. This was the Methuselah Mouse Prize, designed to reward scientific advances and simultaneously overcome the reluctance of the biogerontology community to deliberately explore extending healthy human lifespan.

As a social engineering effort, the prize has been spectacularly successful. Efforts to engineer life extension have gone from practically zero dollars worth of investment when we began, to well over a billion dollars in investment. When we started, the very idea of working on increasing the human lifespan would result in career suicide. Now, the worldwide community is publicly focused on extending lifespan and reversing aging.

Due to these early successes, more and more investors are giving attention and funding to our space. In anticipation of this sea change, the Methuselah Foundation created the Methuselah Fund to help curate and direct investments into projects and startups that will move the needle in the near future as we prosecute our mission to extend healthy human lifespan. None of this would have happened without the incredible support of our donors over the years.

In the following pages, you will see highlights of our work through the years. We hope you enjoy some of the diamonds that we have been polishing over the years in pursuit of our shared goals as we move towards **the crowning achievement of having made 90 the new 50 by 2030.**

History of the Methuselah Foundation



Mission

Methuselah Foundation is a biomedical charity co-founded by David Gobel and Dr. Aubrey de Grey. Our mission is to make 90 the new 50 by 2030. We chose that mission because it's falsifiable – it keeps us committed to “return on mission.” Having a falsifiable mission keeps us focused. It drives a mindset based in urgency and action. We never want to become the type of charity that exists for existing's sake!

Approach

Our approach is to put the mission first and money second. We look for high-leverage interventions that spur concrete progress in the short term, and synergistic ripple effects over time. We have built a record of spotting and betting early on people and projects that, with our significant incubation and strategic services, go on to realize remarkable results.

Against Odds

When we began in 2001, it was widely considered both immoral and a fool's errand to work on extending healthy human life. For scientists, it was academically dangerous to even discuss the possibility. Seventeen years later, Methuselah, its partners and donors have played an unmistakable role in transforming the scientific and cultural outlook.

Return on Mission: *"How many lives are saved and how many people are not suffering that otherwise would have suffered..."* -DAVID GOBEL

Pathfinding Strategies of the Methuselah Foundation

Our strategies are meant to be accessible to everyone since elegantly simple ideas can move masses.



New Parts for People

Technologies that will create new organs, bones, vasculature (with the probable near-term exception of the brain).



Get the Crud Out

Safely remove senescent and other destructive biological structures, intercellular damage or waste (i.e. amyloid), etc.



Restore the Rivers

Restore the circulatory system to full competence.



Debug the Code

Restore the body's informational integrity and its accurate replication.



Restock the Shelves

Replenish building blocks such as stem cells and immune system antibodies.



Lust for Life

Restore the capacity for joy. For instance, rejuvenated senses and athletic competence.

Progress 2003-Today

Marshaling the movement to undo aging
(Mprize, SENS, *Ending Aging*, The 300):

2003-2009

2003



INTRODUCED the world's first longevity prize, Methuselah Mouse Prize (Mprize). Conceived by David Gobel and Dr. Aubrey de Grey, Mprize stimulated and honored advancements in new life extension therapies by awarding two cash prizes: one for breaking the world record for the oldest-ever mouse, and one for the most successful approach to rejuvenating the health of old mice. The prize for longevity was first won by a team led by Dr. Andrzej Bartke of Southern Illinois University. The prize for rejuvenation first went to Dr. Stephen Spindler of the University of California, Riverside. Additionally, in 2009, the first Mprize Lifespan Achievement Award went to Dr. Z. Dave Sharp of the University of Texas Health Science Center at San Antonio for extending the lifespan of already aged mice using the pharmaceutical rapamycin.

FISCALLY SPONSORED Dr. Aubrey de Grey's Strategies for Engineered Negligible Senescence (SENS), a long-term research framework to develop regenerative therapies that repair seven major classes of cellular and molecular damage associated with aging. SENS-related research programs were established by Methuselah Foundation at Arizona State University, Rice University, and the University of Cambridge. The SENS program spun out from our foundation in 2009 as the SENS Research Foundation (SENSRF), with ongoing support from Methuselah.

Progress

2003-2009

2003+



SPONSORED and later funded six SENS-focused events between 2003-2009. Hosted at the University of Cambridge, the SENS events became the leading series of conferences dedicated to tackling aging through rejuvenation biotechnologies. They have played a central role in building an international network of researchers and research programs that approach aging as a solvable engineering challenge. The series continues under SENSRF's Undoing Aging Conference.

Progress

2003-2009

2004



CREATED The 300, a group of up to 300 individuals pledging \$25,000 each to help Methuselah advance the defeat of aging. David Gobel's idea for the Methuselah 300 came from the 300 Spartans who held the pass at Thermopylae in 480 BC. Those men did not survive themselves, but their deeds were a rallying symbol for the people of Greece to repel the Persian invaders. In similar regard, The 300 have stepped forward to serve as the bold few committed to extending healthy life – even as that aim was mocked by the press and scientific establishment over the last decade.

Progress

2003-2009

2005

PROPOSED (by Dave Gobel) the “SENS Challenge” to Jason Pontin, editor in chief of MIT Technology Review, after the magazine published a pejorative profile of de Grey and SENS, along with Pontin’s column calling de Grey a “troll.” MIT and Methuselah pledged to pay \$10,000 respectively to any molecular biologist(s) who could demonstrate that SENS “is so wrong that it is unworthy of learned debate.” Three qualifying submissions were reviewed by a distinguished group of judges (Rodney Brooks, Anita Goel, Vikram Kumar, Nathan Myhrvold, and J. Craig Venter). As Pontin wrote in his summary, the unanimous view was that no submission met the “criterion of the challenge and disproved SENS.”



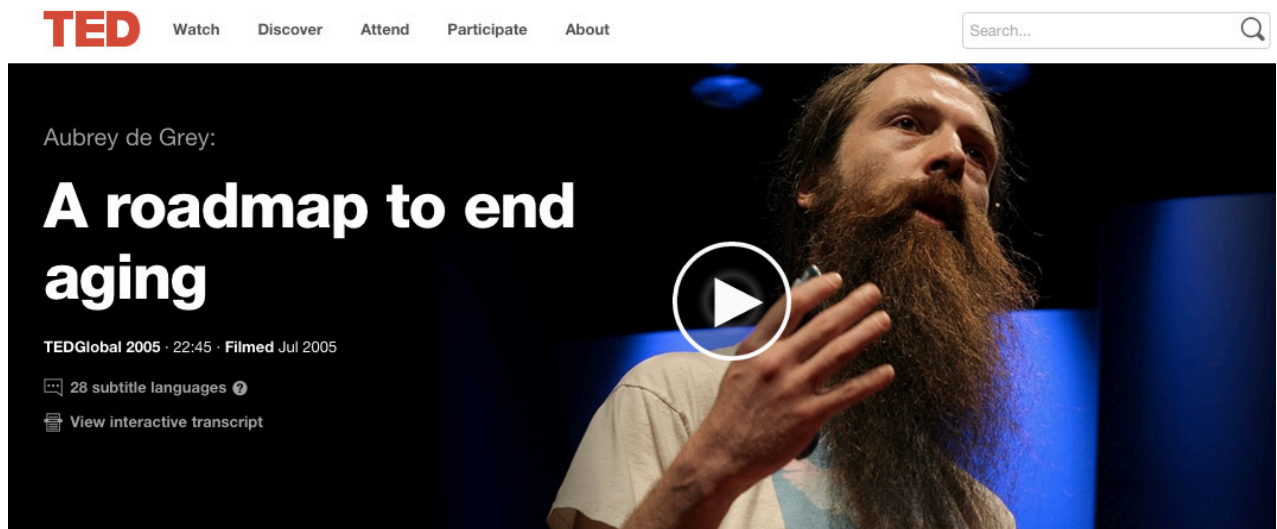
2006

CONTRIBUTED funding (\$100,000) and direction to launch the Supercentenarian Research Foundation (SRF) with Dr. L. Stephen Coles and Dr. Elliot Bergman. Instead of exploring why supercentenarians lived so long, we wanted to know, if you live that long, what do you die of? Thanks to the work of Coles and Robert Young, an answer was learned: senile systemic amyloidosis (SSA), more commonly known as wild-type transthyretin amyloid. As humans age, the transport protein Transthyretin begins to unravel and stick to the inside of blood vessels, restricting blood flow and subsequently causing heart failure. This appears to be a leading cause of death among supercentenarians.

Progress

2003-2009

2008



The screenshot shows the TED website interface. At the top left is the TED logo, followed by navigation links: Watch, Discover, Attend, Participate, and About. On the right is a search bar with the placeholder text "Search...". Below the navigation is a video player for a TED talk by Aubrey de Grey. The video title is "A roadmap to end aging". The video is from TEDGlobal 2005, is 22:45 long, and was filmed in July 2005. Below the title, there are two icons: a subtitle icon with the text "28 subtitle languages" and a transcript icon with the text "View interactive transcript". The video player shows a man with a long beard (Aubrey de Grey) speaking, with a play button overlay in the center.

CATALYZED global awareness for longevity research, thanks to the Mprize, its scientists and donors, the best selling book *Ending Aging*, and de Grey's public advocacy (whose beard deserves special mention). Methuselah Foundation was the first charity to mobilize the movement to undo aging. We built and defended the scientific case for approaching age-related damage as an engineering problem. We changed the conversation and made longevity research a fundable area.

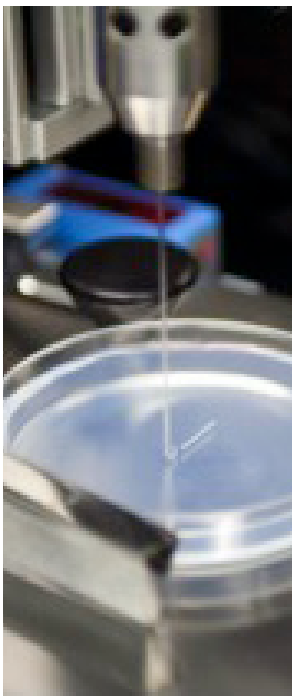
Progress 2009-Today

Making 90 the new 50 by 2030 (incubation, New Organ, Methuselah Fund, The 300)

2009-PRESENT

2009

BECAME the first outside investor in Organovo, which designs and creates 3D human tissues that for the first time enable drugs to be tested on functional human tissues before ever administering them to a person; and in the future will enable therapeutic tissues to be implanted into the body to repair or replace damaged or diseased tissues. They've introduced the first architecturally-correct human liver and kidney tissue assays, with the potential to improve drug development dramatically by reducing the cost of toxicology tests and eliminating the need for animal testing.



Progress

2009-Today

2010



INVESTED early in Silverstone Solutions – founded by David Jacobs and acquired by BiologicTx in 2013 – to turn their kidney-pair-matching software, MatchGrid, into a cloud-based service. Hospitals and transplant organizations are using MatchGrid to rapidly match living organ donors with patients who have willing but incompatible donors – what’s known as kidney-paired donation. This enables more patients to receive a living donor kidney instead of waiting 5-10 years for a cadaver organ. Over 1,000 lives have been saved, and thousands more will be in the years ahead.

Progress

2009-Today

2011



LAUNCHED the New Organ Alliance, a collective initiative of key partnerships and prizes advancing the bioengineering and banking of tissues and organs for restoring health and reducing the global organ shortage. Conceived by David Gobel, New Organ is at the center of coordinating greater effort to industrialize the dream of “new parts for people.”

Here’s why we have the New Organ Alliance: “It seems to me that our priorities are misplaced and I like to call this ‘suffering from species insanity.’ It is insane that as a species we’d spend \$200,000+ to restore a car like a Shelby Cobra, and yet all that car’s creator Carroll Shelby could get were junkyard parts. His heart came from someone deceased – it wasn’t new. His kidney came from his wonderful son, but it wasn’t new, and it didn’t fit. None of these parts fit. And most people in need don’t even have the chance to get a junk part.” –DAVID GOBEL

Progress

2009-Today

2013

CREATED the world's first organ bioengineering prize, the New Organ Liver Prize, in partnership with the Institute of Competition Sciences. With 13 active teams, the challenge prize will award \$1 million to the first team that creates a regenerative or bioengineered solution for keeping a large animal alive for 90 days without native liver function.

"The Founding Fellows of the Tissue Engineering & Regenerative Medicine International Society (TERMIS) strongly endorse New Organ. Regenerative medicine has made significant advances in the past 15 years and the New Organ Liver Prize is a golden opportunity for the next leap forward. The public and the medical community will realize a remarkable clinical benefit with the availability of 'off the shelf' livers obviating the need for donor organs, and the medical health care system will simultaneously benefit. We hope this forward-looking effort sets the standard that inspires other initiatives to focus the resources of regenerative medicine on solving major health care challenges."

LAUNCHED a \$500,000 partnership with Organovo to place their 3D bioprinters in research labs as a springboard to create bioprinted tissues for surgical transplantation. Recipients include: Yale School of Medicine (Dr. John Geibel), UCSF School of Medicine (Dr. Edward Hsiao), and Murdoch Children's Research Institute (Dr. Melissa Little).

AWARDED a grant to Dr. L. Stephen Coles, co-founder and executive director of the Gerontology Research Group and noted researcher on supercentenarians (people aged at least 110). The grant explored new methods of personalized gene sequencing and pre-testing of potential chemotherapy courses in immunodeficient mouse models.

Progress 2009-Today

2014

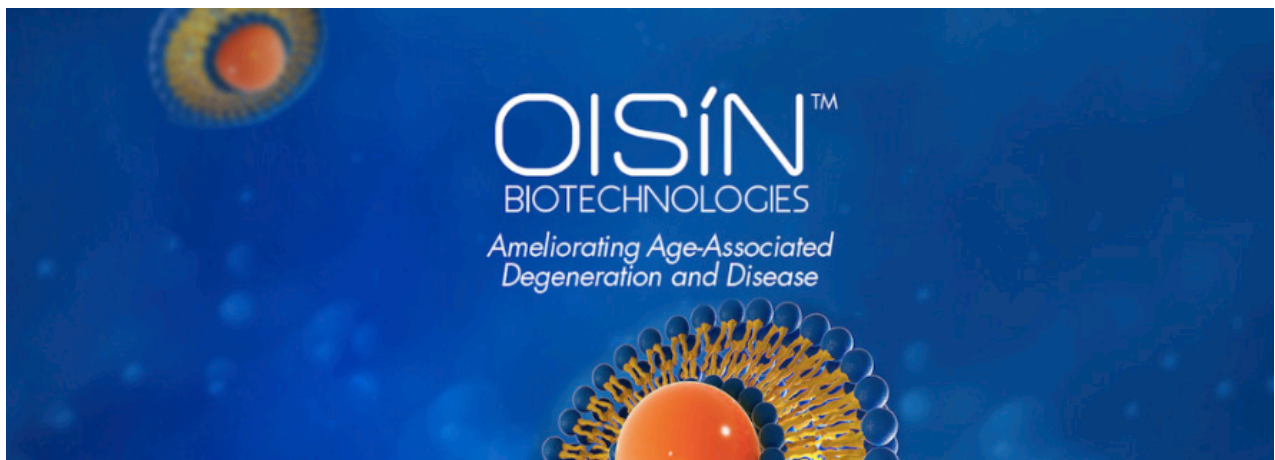


FISCALLY SPONSORED and contributed to the Organ Preservation Alliance, a charity working to accelerate organ banking. They've had a number of successes: organizing the first Organ Banking Summit, facilitating events in Washington, DC (e.g., a DARPA-led workshop), co-creating the first Organ and Tissue Preservation Community of Practice with the American Society of Transplantation, and contributing to new grant programs from the DoD for organ preservation research, representing over \$15 million in new funding for this neglected field. Recently, they hosted the Organ Banking Summit at Harvard Medical School and received \$2 million from the Pineapple Fund.

AWARDED a Methuselah Prize (\$10,000) to Dr. Huber Warner for founding the National Institute on Aging's Intervention Testing Program, a gold-standard assessment of treatments attempting to slow aging in mice.

Progress 2009-Today

2014+



BECAME the founding investor in Oisín Biotechnologies. Oisín aims to show degenerative aging conditions can be ameliorated through the safe removal of death-resistant cells (i.e., senescent cell clearance). Over the last decade, Methuselah has promoted this approach under the SENS strategy, and it's now showing results. In February 2016, e.g., Mayo Clinic researchers reported extending the life of mice by up to 25% through senescent cell clearance.

"We invested in Oisín because of the promise of their targeted approach to removing senescent cells without causing collateral damage or side effects. We think of this as 'getting the crud out,' one of our key themes." –**DAVID GOBEL**

PROVIDED web marketing for Oisín as part of our incubator services, along with strategic advice, e.g., company structure, regulatory pathway, Series A conditions, etc.

GAVE a grant to Oisín to find out if its platform technology could effectively and selectively destroy prostate cancer cells. The research led to spectacular results and is being pursued by a spin-off company known as Oisín Oncology, incorporated in late 2017.

Progress

2009-Today

2015



FUNDED the sequencing of the bowhead whale genome at the University of Liverpool (published in *Cell Reports*, January 2015). The bowhead whale is the longest-lived mammal, capable of living over 200 years, making its genome and transcriptome (i.e., messenger RNA) a valuable source of biological data for longevity studies. An assembly of the bowhead whale genome has been made available online to encourage further research.

Progress 2009-Today

2015+



CO-ORGANIZED the White House Meeting on Regenerative Medicine and the landmark Organ Bioengineering & Banking Roadmap Workshop – supported by the National Science Foundation – in May 2015. Key challenges, milestones, and metrics were identified for a coordinated effort to accelerate solutions to the organ shortage.

FUNDED development of the beta roadmap report “Solving the Organ Shortage through Organ Banking and Bioengineering.” This report was guided by expert input from the May 2015 roadmap workshop, co-organized by New Organ and Organ Preservation Alliance (with sponsorship from the National Science Foundation and Methuselah), in conjunction with an organizing committee of leading scientists, patient advocates, and government representatives. Two follow-up perspectives were published, “Bioengineering Priorities on a Path to Ending Organ Shortage” (*Current Stem Cell Reports*) and “The Promise of Organ and Tissue Preservation to Transform Medicine” (*Nature Biotech*).

Progress 2009-Today

2015+



BEGAN memorializing The 300 members with a monument located on a breathtaking hillside at St. Thomas in the U.S. Virgin Islands, just as the original 300 Spartans were commemorated with a monument at Thermopylae.



Progress

2009-Today

2015+



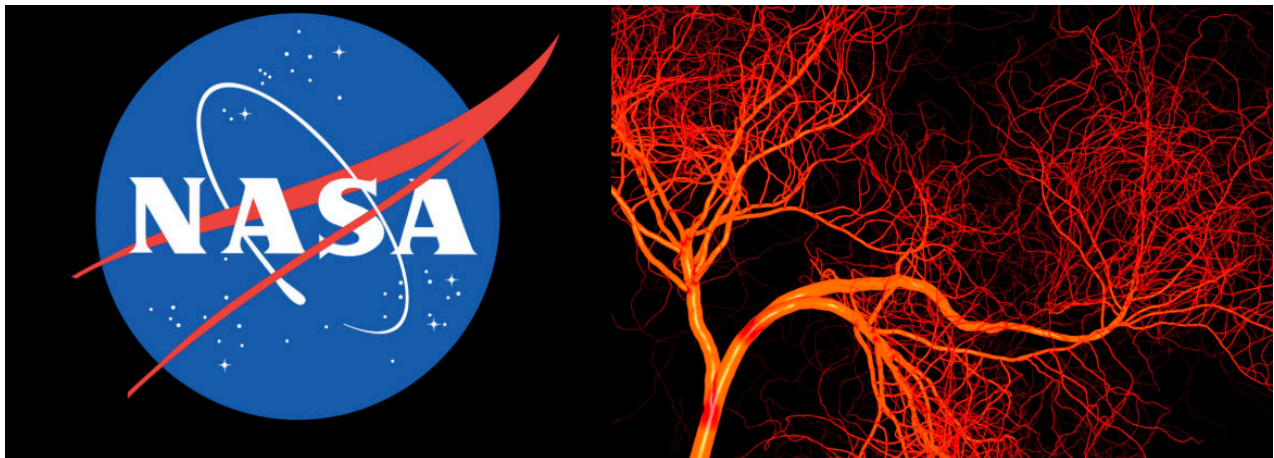
MADE the founding investment in Leucadia Therapeutics. For 25 years most research has viewed plaques and tangles in the brain as the cause of Alzheimer’s disease. This has led to a string of failed clinical trials. Leucadia’s research is showing that plaques and tangles are the *effect* of a more serious *underlying condition*. They are developing a therapeutic device to restore cerebrospinal fluid (CSF) flow across the cribriform plate, with the aim of improving the clearance of toxic metabolites from the regions of the brain affected earliest by Alzheimer’s disease.

PROVIDED a grant to Ichor Therapeutics, which used C60 (carbon buckyballs) to double the median lifespan in a mouse model with acute myeloid leukemia (AML), a lethal blood cancer with only a 24% five-year survival rate. Methuselah’s grant is funding a large-scale efficacy study to assess the validity and safety of the results via Ichor’s initial study.

Progress

2009-Today

2016



PARTNERED with NASA to launch the Vascular Tissue Challenge at the White House Organ Summit: a \$500,000 prize for creating thick, microvascularized tissues that remain functional and alive for over 30 days. Solving this key challenge will enable industrializing tissue and muscle patches that restore function. The Center for the Advancement of Science in Space (CASIS) is providing \$200,000 to support related research at the ISS's National Laboratory.

ORGANIZED the Vascular Tissue Challenge Roadmapping Workshop at NASA Ames, attended by 100 leaders with participation from NIH, NSF, VA, NASA, and DoD. This event mapped out challenges, pathways, and milestones toward overcoming the thick-tissue vascularization barrier – the primary impediment delaying the development of effective tissue engineering therapies. An expanded roadmapping summit was hosted at NASA Ames in 2018.

FUNDED Dr. Max Peto's work on Litmon, a mailing list for monitoring longevity-related scientific literature. His daily reporting is shared with longevity investigators and 300 members, and helps us identify investment opportunities.

Progress

2009-Today

2017



LAUNCHED the Methuselah Fund – an LLC subsidiary of Methuselah Foundation – to invest in more mission-critical startups, beginning with Leucadia and building upon prior success with Silverstone and Organovo. The fund’s “mission capital” helps early-stage companies avoid compromising and pivoting away from our mission, which has been a common occurrence with traditional venture capital pressuring for financial returns. We focus on potential breakthrough biotech platforms that are just about to leave the R(earch) stage of R&D and enter the D(velopment) phase.

PROVIDED branding and marketing for Leucadia as part of our incubator services (creating leucadiatx.com), along with strategic advice, e.g., company structure, regulatory pathway, Series A conditions, etc.

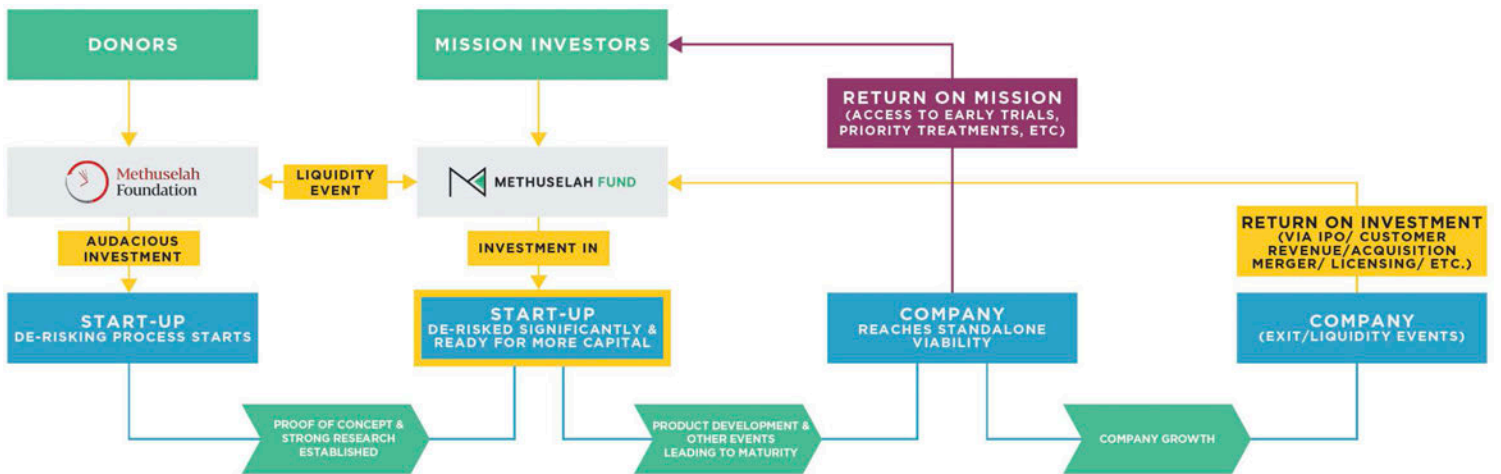
GAVE a grant to Leucadia Therapeutics in support of a small animal study to test their hypothesis regarding a root cause of Alzheimer’s disease, along with the continued development of their novel therapeutic device. We also assisted in closing their pre-Series A funding round. Each investor was a member of the Methuselah Fund.



M Fund Ecosystem's Dynamics



METHUSELAH FUND





Methuselah Foundation

Thanks for reading.
We hope to hear from you!

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