

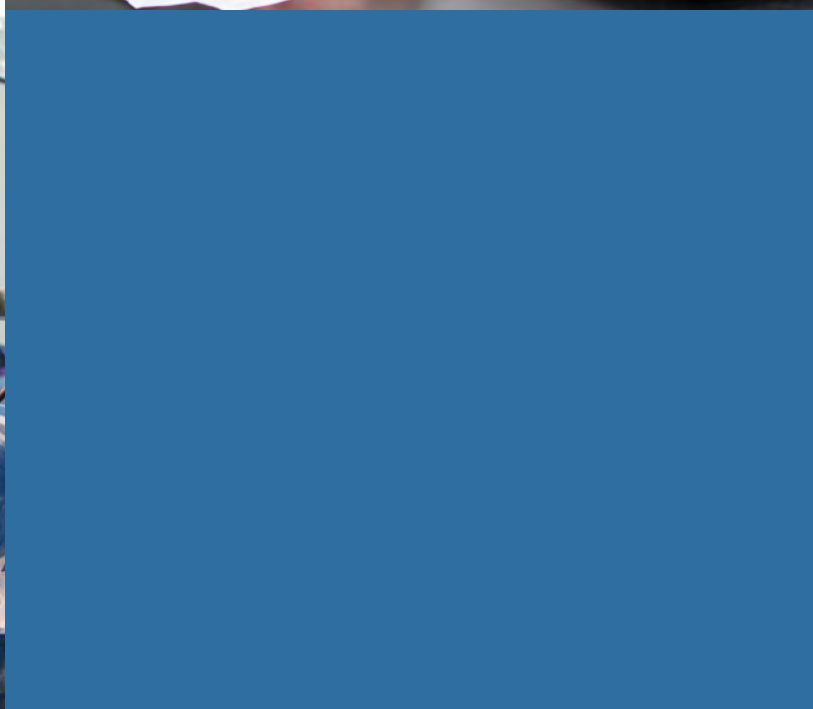


Stone
Research
Foundation

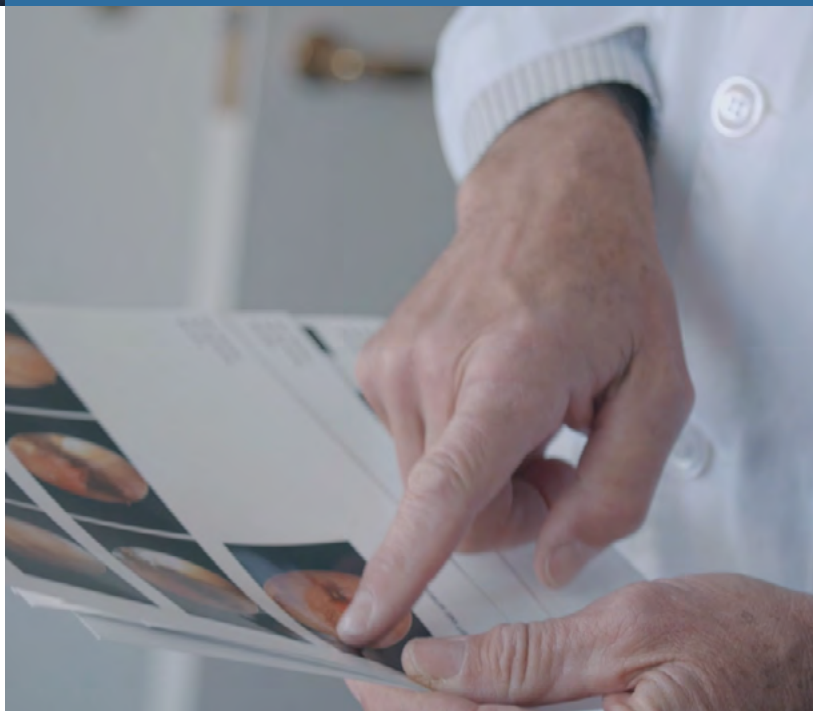
ANNUAL REPORT

Spring 2023

Our **vision** is to pioneer new orthopaedic treatments that accelerate healing, enabling people to stay active through research, development, innovation, and education.



Stone
Research
Foundation



Letter from Our Leadership

Dear Friends and Supporters,

We are thrilled to share the 2022 Annual Report for the Stone Research Foundation. Our vision is to accelerate healing from sports injuries and to treat, prevent, and cure arthritis. The goal is to keep you—and all patients—playing the sports you love for a lifetime.

During the past year, we were able to build on our 28 years of basic science and clinical experience to advance key therapies to achieve our mission. Fundamentally, cartilage is now repairable; it can be regenerated and replaced. Ligaments and tendons can now be healed with injections of growth factors. Progenitor cells can be mobilized to rush to a site of injury and arthritis to direct the healing. All of this fantastic science is now within our grasp and under our control. It will be steadily improved and used to benefit patients here and around the world. And this is not limited to humans. Performance and working dogs and horses often suffer from injuries similar to those that affect humans and require similar treatments and care for injury and recovery. Our work at the Stone Research Foundation is being applied to these athletes as well.

We are proud of these accomplishments and remain committed to our goal of facilitating more efficient and effective healing. But none of our breakthroughs would have been possible without the commitment of our donors and collaborators.

This report is our opportunity to share science and progress with you. We hope to inspire you to reach out and participate in pushing this work forward. We are deeply grateful for your continued support and dedication to our mission.

Sincerely,



Mani Vessal, MA PhD
Senior Director
Research and Operations



Kevin R. Stone, MD
Founder and CEO



2022: Year in Review and a Bright Future

Revolutionizing Articular Cartilage Repair

In 1991, Dr. Stone developed the articular cartilage paste graft technique to address the critical need for a more effective cartilage repair solution. While this treatment has shown clinical success over the past 30 years, it has not gained widespread clinical use. This is due to the lack of corporate support and the difficulty of use. However, millions of people need articular cartilage repair to recover from injury, treat pain, and avoid artificial joint replacement. We continue to improve upon Dr. Stone's technique to enhance cartilage regeneration and accelerate the recovery process.

With the help of a 1.18-million-dollar grant from the California Institute for Regenerative Medicine (CIRM), awarded to the Stone Research Foundation in early 2022, and in collaboration with Dr. Anthony Ratcliffe, we are now halfway through our two-year study aimed at enhancing the paste graft technique with the addition of hydrogel and mesenchymal stromal cells (MSCs). Our preliminary data have demonstrated that the hydrogel successfully maintains cell viability and metabolic activity within the augmented paste graft. The hydrogel will make it easier for surgeons to use the paste graft technique, while the cells may accelerate the healing.

The next *in vivo* phase of this study will examine the efficacy of our approach. Additionally, we have made significant progress by developing and testing new surgical devices to optimize cartilage regeneration and make the procedure easier for surgeons.

We have successfully met all of our first-year milestones and are on track to meet our projected goals in the second half of this study. This minimally invasive, cost-effective, and one-step solution, holds promise for widespread adoption to meet the overwhelming global need for better solutions to cartilage regeneration.



Collaborator - Anthony Ratcliffe, PhD, President and CEO of Synthasome Inc.

Investigating Articular Cartilage Paste Graft in a Large Animal Model

In parallel with our two-year study to enhance the paste graft procedure, we are funded to test this technique in an equine model. Conducting a large animal study alongside our current CIRM-funded project will successfully pave the way to launch a wide human clinical trial and apply for veterinary use in horses and dogs. We will meet with the FDA this summer, to finalize the protocol for this upcoming study. We also aim to launch this project in collaboration with Dr. David Frisbie at Colorado State University in the fourth quarter of this year.



Collaborator - David Frisbie, DVM, PhD, Dipl. ACVS, ACVS-MR - Professor of Equine Surgery at Colorado State University

Initiating the Large Testosterone Clinical Trial

Ask any patient what the worst part of their knee surgery was. The answer isn't the pain; it is muscle atrophy and the time it takes to rebuild the muscle. The atrophy starts within eight hours of surgery, due to a large surge of the hormone cortisol which binds the muscle receptors. Testosterone, given at the time of surgery, may block the cortisol binding and a percentage of the muscle atrophy. Fifteen patients have completed our pilot study, "Testosterone Therapy to Prevent Muscle Atrophy." Our data demonstrated that this therapy is safe, which allows us to proceed to a larger clinical trial pending availability of funding. This next phase of the clinical trial is designed to prove the efficacy of testosterone in reducing muscle atrophy following surgery.

Patient-Reported Outcome Studies

The SRF team tracks patient outcomes for every procedure performed by Dr. Stone. Clinical, radiological, and subjective patient-reported outcome forms are filled out by patients independent of the physician and collated in an

AI-driven patient database. By analyzing this data, the Stone Research Foundation can identify areas for improvement in the surgical techniques under study.

In 2022, our research team enrolled more than 300 patients in our outcomes study, adding to the over 3,000 total enrollments already in our database.

Outcome studies include but are not limited to:

- Anabolic & Lubrication Injections
- Articular Cartilage Paste Grafts
- Meniscus Allograft Transplantation
- MAKOplasty Robotic Partial and Total Knee Replacements
- Arthritis in the Ankle and Ankle Stability Procedures
- Rotator Cuff Repairs, Labral Repairs, and AC Joint Procedures

Nanoparticles as Promoters of Cell Growth

Cartilage can heal. However, the cellular activity of cartilage is often too low to produce an effective repair in the setting of arthritis. One question we have asked is, "Can the metabolism in the chondrocytes (cartilage cells) be boosted to produce a more rapid and greater quantity of cartilage matrix?" Working in the lab with Dr. Mark DeCoster's research team at Louisiana Tech University, a new type of copper-based nanoparticle is being tested with the cartilage tissue obtained from patients coming for total knee replacement by Dr. Stone.

Preliminary work has commenced to optimize the techniques required to induce the cells to incorporate the nanoparticles and then evaluate the cellular activity. Initial results have demonstrated increased metabolism without early cell death. We plan to test the efficacy of this technology in the paste graft technique in a lab-on-a-chip model and on an animal model in the upcoming years.



Collaborator - Mark A. DeCoster, PhD - Associate Director, Biomedical Engineering & Rehabilitation Science at Louisiana Tech University

“I don’t believe a doctor should put something in or do something to a patient without knowing the outcome or trying to study and improve it.”

-Kevin R. Stone, MD

Thought Leadership in Orthopaedic Community



The Stone Research Foundation team hosted and funded the 2022 Meniscus Transplantation Study Group meeting in conjunction with the annual meeting of the American Academy of Orthopaedic Surgeons (AAOS) in Chicago, Illinois. With more than 40 attendees from 14 countries, this was a valuable opportunity to share our techniques and surgical outcomes while learning from experts across the globe.

We attended the International Cartilage Regeneration & Joint Preservation Society Summit Meeting in Miami, Florida to enhance our knowledge on the latest orthopaedic surgical techniques. In the past 25 years we have provided opportunities for 73 fellows and interns to gain hands-on experience and learn from leading experts in the field. Through these educational programs, we are helping to prepare the next generation and shape the future of orthopaedics.



Chris Boshuizen, PhD • Aerospace Engineer & Commercial Astronaut on Maiden Flight of Blue Origin • Articular Cartilage Paste Graft & Meniscus Transplant Patient

Regeneration Scaffolds for Orthopaedic Tissues

In 1989, Dr. Stone invented the first successful collagen regeneration template for meniscus cartilage. This device successfully regenerated the meniscus cartilage in people who had previously had a meniscectomy and suffered from pain. While the device was approved for sale in the US and Europe, it did not gain widespread traction. This was due to its relatively weak structure and poor handling characteristics. SRF plans to bring 21st-century advances in collagen manufacturing and orthobiologics to produce and test novel designs that will regrow the meniscus cartilage and, potentially, ligaments and tendons. Once developed, successful devices may be eligible for licensing or startup company formation, providing an ongoing revenue stream for the Foundation.

Orthobiologics

The SRF team and clinical team at The Stone Clinic have extensive experience in the use of both growth and recruitment factors in the treatment of sports injuries and arthritis. Initial success was seen with autologous products (Platelet-Rich Plasma and Hyaluronic Acid) and birth tissues harvested from C-sections (Amniotic Fluid). Working with Dr. Daniel Grande of the Feinstein Institute, a program of sequential testing of the most promising candidates in a tissue culture and animal model, is being initiated this summer.



Collaborator
Daniel Grande, PhD - Associate Investigator
Feinstein Institute



Mike & Rose-Ann Lynch • Amateur Ballroom
Dance Champions • Robotic Partial Knee
Replacement Patient (for Mike)

Patient Success Stories



Dr. Ara Karamanian

Dr. Ara Karamanian is a radiologist in Texas. For years, he lived with knee pain that heavily impacted his daily life. After a meniscectomy, he continued to experience pain. *"I know my body, and it didn't feel right."* This led him to seek treatment with Dr. Stone for a biologic approach to repairing his knee. In 2022, he received an articular cartilage paste graft and a meniscus allograft transplant. A year after his procedure, through arthroscopic and MRI imaging, it was clear that his cartilage had regenerated. *"The articular cartilage grew in beautifully,"* says Dr. Karamanian. *"As a physician, I have an appreciation for Dr. Stone's work and skill. He took me from a point where I was in constant pain and now, I can be active again."*



Samantha Berryhill

Samantha Berryhill had been living with knee pain since 2013. As a college-level soccer player, Samantha needed a solution to her pain so she could perform at full capacity on the soccer field. In 2021, Dr. Stone performed a meniscus allograft transplant and articular cartilage paste graft for her knee. Samantha began playing soccer again just a few months after surgery and ran her first marathon seven months later. We could not be more excited and inspired by Samantha's post-operation successes.



Andrea “Andie” Haines

Since Andrea’s paste graft articular cartilage repair surgery in 2001, she has resumed road biking, commuting 10 miles each way to work. In 2014, Andrea excelled in her first triathlon, winning her age group and placing top 10 overall. She competes annually, consistently winning her age group and qualifying for USAT Nationals.

“

“Before my articular cartilage procedure, my knee was incredibly unreliable. It would frequently ‘catch,’ causing me intense pain. Determined to find the least invasive and most advanced treatment, I conducted thorough research and discovered Dr. Stone’s paste graft technique.

After diligently adhering to the post-surgery protocol for a few months, I regained the ability to walk, ride my bike, run, and fully engage in my active lifestyle. My mobility has been completely restored, enabling me to partake in sports such as backpacking, swimming, rock climbing, mountain biking, and countless other of my favorite activities.”

—Andrea “Andie” Haines

”

How Donors Make A Difference:

Articular Cartilage Paste Graft + Mesenchymal Stromal Cells + Hydrogel in an Equine Model

Osteoarthritis and trauma of articular joints can lead to long-term disability in both humans and animals and remains a major clinical problem with limited treatment modalities.

This year, we will complete our CIRM-funded project and evaluate the effectiveness of the paste graft technique in a large animal model. Thanks to a generous donation from Mike and Judy Miller and additional support from Tom O'Neal, we are ready to launch in the fall of 2023 with our collaborator Dr. David Frisbie at Colorado State University. This study will allow us to assess the quality of cartilage regeneration from our improved techniques and will provide additional support for a wide human clinical trial as well as the adoption, by the veterinary community, of this technique for healing working and competitive animals.

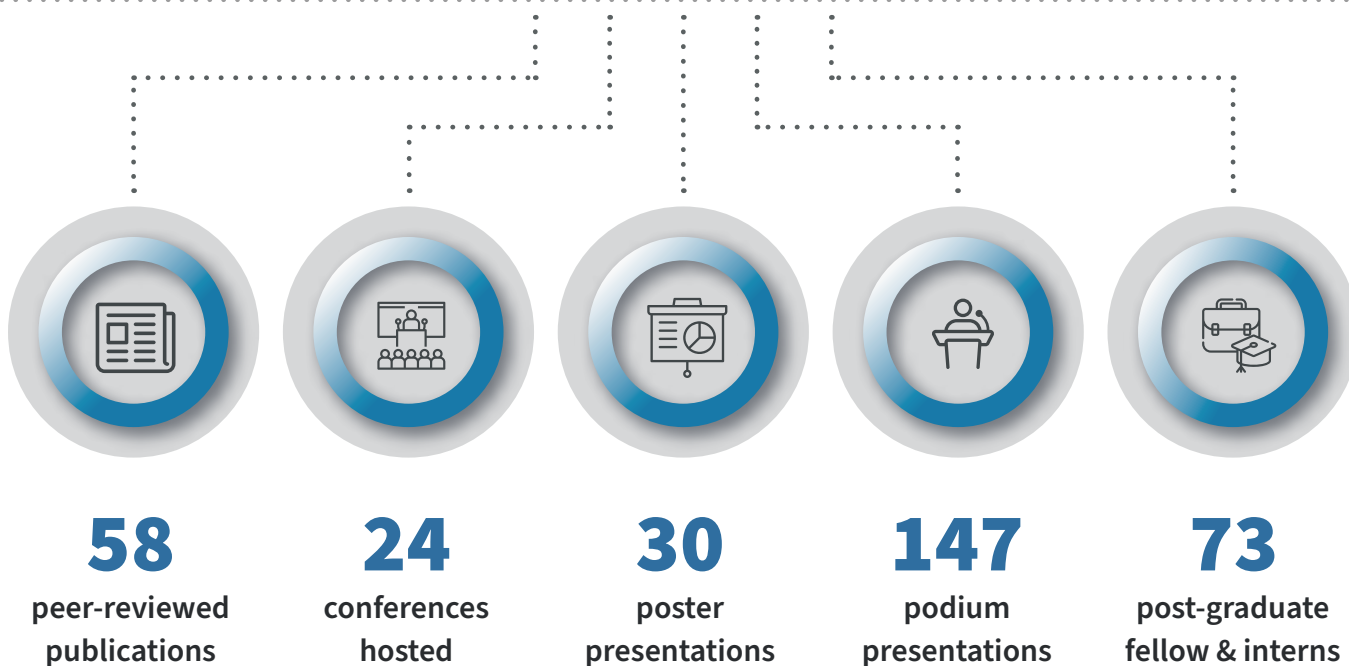


Collaborator - David Frisbie, DVM, PhD, Dipl. ACVS, ACVS-MR - Professor of Equine Surgery at Colorado State University

Donors - Mike and Judy Miller, Tom O'Neal



Contributions to the world of orthopaedic science by the SRF team:



Donor Highlights



Mark & Laura Bailey

We are grateful for our friends Mark and Laura Bailey, who have been donors to the Foundation since 2020. Both Mark and Laura have enjoyed returning to the sports they love after their care by Dr. Stone. We are grateful for their generous support and invaluable guidance this year.



Mike & Judy Miller

Mike and Judy Miller graciously funded our articular cartilage paste graft in a large animal study. This study marks a crucial milestone in our ongoing efforts to expand access to this revolutionary technique. We are thankful for their support, which has enabled us to undertake this groundbreaking research.



Rick Kimball

Rick Kimball has been involved with the Stone Research Foundation since 2006. His generosity has been instrumental to our growth and successes. His unwavering support of our research propels us closer to achieving our goals.

Brian Hinchcliffe

Brian Hinchcliffe is a new friend to the Foundation and has made a generous pledge of support. We greatly appreciate his contribution, which is providing us with the resources needed to conduct in-depth research.

Nick Woodman

As adventure lovers, Nick and Jill Woodman deeply understand the value of our research, which results in outcomes that keep people playing the sports they love forever. We are thankful for Nick and Jill's support.

Anna & Ken Zankel

The Zankel's support funded a study in which we used testosterone to prevent post-surgical muscle. They understand the frustration of having a great surgery marred by a slow muscle recovery and are determined to help the Foundation complete the definitive study to determine the efficacy of the testosterone treatment.



Richard Donovan • Bilateral Robotic Partial Knee Replacement Patient Completing 3,200 Mile Post-Op Run Across America



Kenneth St. Cyr • Pole Vaulter Competing at 2023 World Masters Association Indoor Championships • Growth Factor Injection Patient

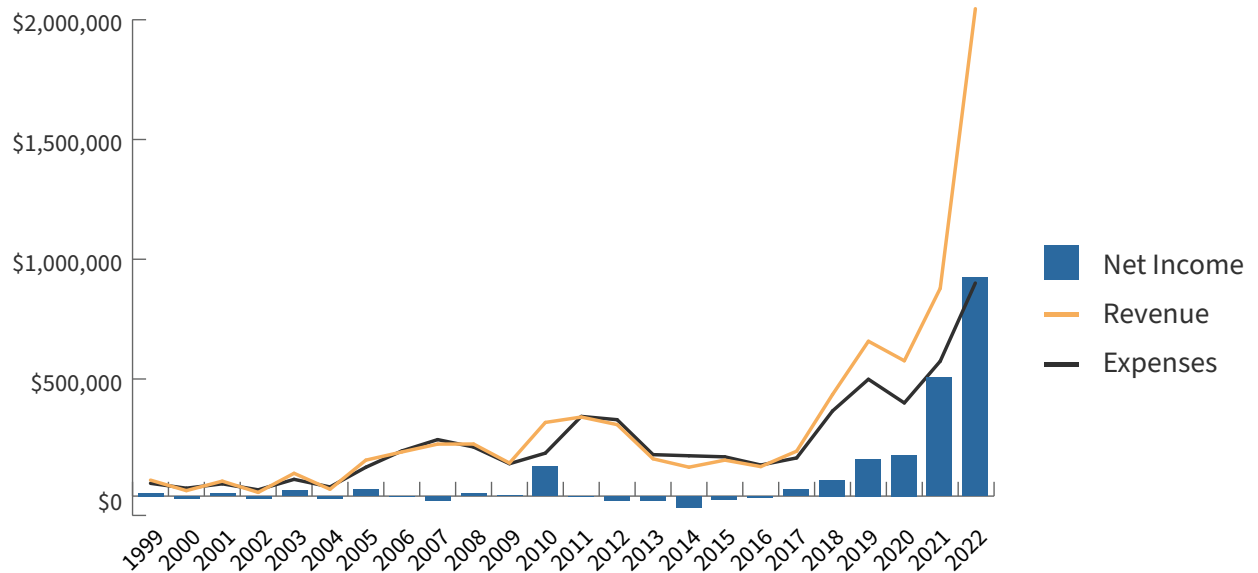
Financial Snapshot

In 2022, the Stone Research Foundation received unprecedented levels of support through donations and research grants, making it our most productive year to date. Your support can help 2023 exceed that level and deliver the care that humans—and animals—deserve. We will pursue additional funding opportunities through grants and fundraising campaigns to support our initiatives.



Tony Antonacci • Mountain Biker &
Water Sports • Robotic Total Knee
Replacement Patient

SRF Net Income 1999-2022



Stone Research Foundation Financials for 2022

Revenue

\$1,834,814

Expenses

\$913,531

Net Income

\$921,282



This year we earned Candid's, formerly known as Guidestar, Platinum Seal of Transparency. This is the highest level of financial transparency awarded by Candid.

The SRF Team & Board

Stone Research Executive Team



Kevin R. Stone, MD
Founder and CEO



Mani Vessal, MA PhD
Senior Director
Research and Operations



Dave Hopkins
Director of Communications



Lisa Evers
Senior Business Officer

Research and Development Team



Emma Miltenberger
Research Associate



Dorrell Thompson
Development Coordinator



Haley Cowles
Research Associate



Devika Kumar
Research Intern



Aliyah Davis
Research Intern

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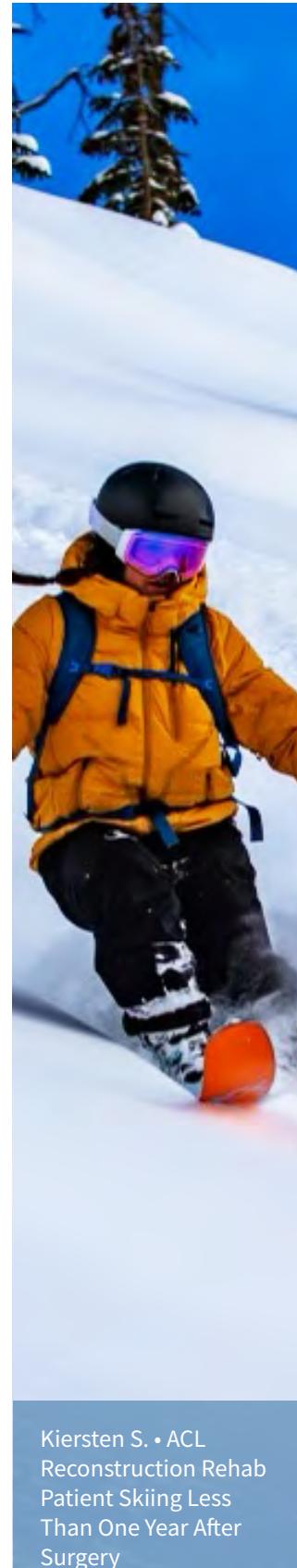
Jeff Ruberti, PhD



**William Wustenberg,
PhD, DVM**



Seth Berkley, MD



Kiersten S. • ACL
Reconstruction Rehab
Patient Skiing Less
Than One Year After
Surgery

Leadership Council of the Board

Christine Hartley (Chair)

Laura Bailey

Mark Bailey

Jennifer Brinkley

Rick Kimball

Herb Madan

Tom O'Neal

D'Arcy Roche

Ryan Stone (Advisor to Exec. Board)

Steve Tomlinson



Rick Lewon (with Dr. Stone) •
Professional Skier • Ligament
Reconstruction Patient

Thank You to All of Our Donors

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Rick Kimball

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www.stonerresearch.org**

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