

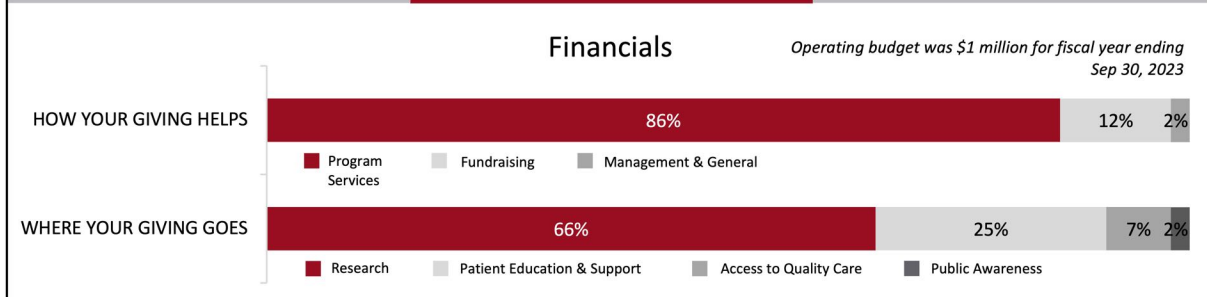
**How You've Made a Difference:
Alliance to Cure's 2023 Impact Report**



2023 HIGHLIGHTS

Better access to care. Better patient outcomes. More treatments in development than ever before.
With your support, we are in urgent pursuit of a lasting cure.

More on Alliance to Cure Cavernous Malformation's impact in 2023:
www.alliancetocure.org/about-us/impact/



Driving Research for Better Treatments and a Cure

Alliance to Cure in early planning stages of first focused ultrasound clinical trial for CCM patients

Based on positive research findings from a University of Virginia study, we are in the early stages of designing a clinical trial to test the safety of focused ultrasound (FUS) as a non-invasive treatment for cavernous malformation patients. If proven safe and effective, FUS could represent a cure for sporadic patients – those with just one lesion – and a better treatment for familial patients, who typically have multiple lesions.

Alliance to Cure is driving this project forward by assembling academic, corporate, foundation, and government partners. We are designing a trial, finding funding, and working with partners to apply to the FDA for permission to launch. If all goes as planned, we should see our first patients enrolled in 2025.

Data from preliminary research published by UVA earlier this year shows that FUS stabilized existing lesions and prevented lesion growth in cavernous malformation mouse models. UVA had designed this study to determine if FUS could safely open the blood-brain barrier and be used as a first step in developing methods for delivering medicines to brain tissue surrounding lesions.

However, researchers were surprised that temporarily opening the blood-brain barrier without delivering another treatment resulted in dramatic improvements. UVA researcher Delaney Fisher presented these findings at Alliance to Cure’s 2023 Science Meeting and Patient Conference; a recording can be found on Alliance to Cure Cavernous Malformation’s YouTube channel. UVA’s preliminary findings can also be read online at the following link: rebrand.ly/CCM-FUS-Jan2024

UVA’s groundbreaking study has also spurred \$3.1 million in additional funding from the National Institutes of Health (NIH), awarded in January, to continue studying FUS and cavernous malformation. The NIH grant will allow UVA to study how FUS can deliver gene therapy and drug compounds through the brain-blood barrier to target cavernous malformation lesions in preclinical models.

Focused ultrasound (FUS) is a non-invasive treatment technology in which sound waves are targeted to treat tumors and other conditions. FUS can be combined with microbubbles – tiny gas-filled bubbles – and used as a tool for targeted medication delivery. Microbubbles exposed to FUS can temporarily open the blood-brain barrier, which enables medicines to reach the brain. Focused ultrasound machines are available in more than 1300 hospitals globally. The technology is approved for several neurological conditions, like essential tremor and Parkinson’s disease, and is under investigation for many more.

Focused Ultrasound Quick Facts

- A painless, non-invasive treatment tool
- Looks like a helmet or MRI machine
- Sends ultrasound waves (sound waves) to a focused point in the brain
- Temporarily opens the blood-brain barrier, enabling immune system response and allowing medicine to reach damaged brain tissue
- FDA-approved to treat essential tremor, Parkinson’s dyskinesia, certain cancers; shows promise in treating Alzheimer’s and addiction
- Slows and prevents growth of cavernous malformations in preclinical models



University of Virginia focused ultrasound researchers Delaney Fisher, Tanya Cruz, Khadijeh Sharifi, and Richard Price at the Alliance to Cure 2023 Scientific Meeting.

Our Ground-Breaking Treatment Testing Program Launches

Last year, we shared our plan to begin a pre-clinical treatment testing program to address a major gap in finding treatments for CCM, and we have updates to share.

If you remember, many potential treatments for CCM have not been tested in models of CCM disease. These medicines are already on the market or in development for other illnesses and have biological justification to be tested for CCM.

Unfortunately, there is nowhere to do this. Academic labs are busy with their NIH-funded projects that will lead to publications. Pharmaceutical companies will not develop the infrastructure of CCM pre-clinical models – cell lines and animal models – to test just one drug. So, many potential treatments are waiting on shelves instead of moving toward patients.

To address this, the Alliance to Cure has taken the ground-breaking step of creating a pre-clinical treatment testing program. At this very moment, we are testing 16 compounds, alone and in combination, in various models of CCM disease. Initial testing is happening in academic labs; promising compounds will receive in-depth testing under our direction at a contracted scientific research organization (SRO). If any drug effectively slows or stops CCM in the lab, it will become a candidate for our industry and academic partners to test further in clinical trials.

"All of the treatments we are testing are approved for other conditions; they have good long-term safety profiles, are biologically relevant, and are currently *not* being tested in different labs or companies for treatment of cavernous malformation," said Dr. Amy Akers, project lead and the Alliance to Cure's Chief Scientific Officer. "The project's goal is to complement existing studies and bring additional treatments to clinical trials as quickly as possible."

Dr. Akers has been engaged in CCM research since 2005, first as a graduate student in the Duke University laboratory of Dr. Doug Marchuk, our current Scientific Advisory Board Chair, and from 2009, as our Chief Scientific Officer.

In Dr. Marchuk's lab, Dr. Akers performed experiments that confirmed that some sporadic CCM lesions have the same mutations as familial lesions, with the mutations localized to the lesion. With the Alliance, Dr. Akers serves as the liaison to and consultant for the global scientific community, has been responsible for developing our biobank, and is the project manager for our Clinical Care Consensus Guidelines. She is a co-author of 17 CCM research papers. Her role as lead for this treatment-testing project is a natural next step.

Our project has launched, with 16 initial compounds in the early stages of testing. With your continued support, by the end of this year, lab work will be in full gear, providing a resource to the field with the goal of finding a cure, faster.

Sara Sukalich, MD Joins Board



Sara Sukalich has returned to the Alliance to Cure Board, previously serving as Board Chair from 2010-2013. She is amazed at the growth and impact of the Alliance on patients, families, researchers, and the medical community

over the past two decades. Sara was diagnosed with cavernous malformations in 1994, a few months after graduating from college. Subsequently, family members in three generations have been diagnosed with the CCM1 mutation.

Sara is an OB/GYN with over twenty years of experience in medical education administration. Her career has been dedicated to physician education. She believes that training physicians to be competent, compassionate providers is the best way to positively impact patients and their families. She graduated from Harvard College and obtained an MD and Master of Medical Education from the University of Cincinnati. She is also a certified health and well-being coach. She lives in Columbus, Ohio, with her husband, son, and a clowder of cats.

Patient Registry

Growing Our Resources

The Alliance to Cure Cavernous Malformation launched a new patient registry last year and asked our members, including those already in our old registry, to join. So far, 667 patients have shared their information. If you're a patient, we hope you'll add your information at ccmregistry.org. Your experiences are critical in helping us understand the illness and advance treatments. The registry is also how you can tell us you are interested in genetic testing. The 30 minutes you spend is one of the most impactful things you can do.

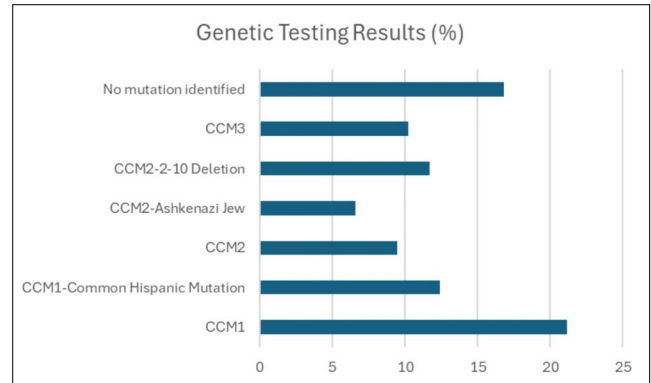
Here are some things we know about our current registrants:

Country of Residence: There are 35 countries represented in the patient registry. US (77%), Canada (4%), Australia (3%), and the UK (3%) are the top 4 countries.

Lesion Details: 24% of patients have brainstem lesions(s) (n=161). 8% of patients have lesion(s) in the spine (n=53), and 3% have skin lesions (n=22). 28% of patients reported that they currently have 1 lesion (n=188). 14% currently have 2-10 lesions (n=94). 12% currently have more than 10 lesions (n=82). 5% currently have no lesions (n=37).

Hemorrhage & Seizure History: 41% of patients have had at least one hemorrhage (n=227). 25% of patients have experienced seizures (n=170).

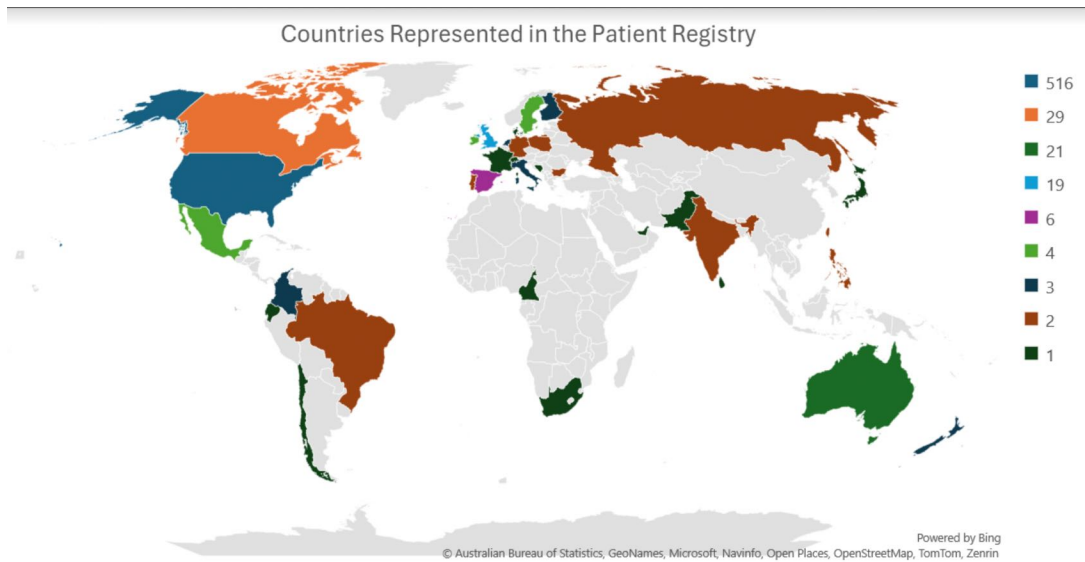
Genetic Testing: 20% of patients or a family member have received genetic testing (n=137). Below is a chart that shows the breakdown of detailed results of those who have had testing.



Clinical Trial Participation: A very small number of registry participants are enrolled in clinical trials (3% or n=23).

Current Health Status: One-third of patients reported that they are either asymptomatic or have no significant disabilities (33% or n=223). 16% of patients reported they have a slight disability (n=105), and 1% of patients reported that they have a moderate disability (n=7).

These data points are valuable to any researcher designing clinical studies and puts us in a position to be efficient and effective partners in trials.



UNM Center of Excellence holds annual patient conference, recognizes advocacy

More than 80 participants affected by cavernous malformation gathered at the University of New Mexico (UNM) Health Sciences CCM Center of Excellence on March 9 for the 2024 Patient, Family, and Provider Conference in Albuquerque, NM. The UNM Center of Excellence has held conferences almost annually since 2008 to educate patients about cavernous malformation treatment, management, and research. UNM is the only Alliance to Cure-recognized Center of Excellence in New Mexico, where the majority of cavernous malformation patients have the familial CCM1 Common Hispanic Mutation.

This year's conference included 14 speakers and featured presentations from UNM Center of Excellence and Chair of Neurology Dr. Michel Torbey, Alliance to Cure CEO Connie Lee, and Alliance to Cure Board member Christina Campos. Dr. Torbey described efforts to educate clinicians across the state about cavernous malformation, Connie shared research news, and Christina described how her family's experience with cavernous malformation inspired her involvement with Alliance to Cure and advocacy, for which she was awarded UNM's CCM Center of Excellence Advocate of the Year.

This advocacy in New Mexico has resulted in a 3-year \$720,000 appropriation from the New Mexico state legislature to support cavernous malformation programming through UNM. These funds are being used to develop educational materials, enable New Mexicans' access to free genetic testing to confirm diagnosis, and conduct outreach to patients and clinicians across the state.

For more information about the CCM1 Common Hispanic Mutation, visit www.alliancetocure.org/genetics/common-mutations/ccm1-common-hispanic/



A group of attendees at UNM Center of Excellence's 2024 Patient, Family and Provider Conference poses with Alliance to Cure National Community Development Specialist Linda Fuchser (third from left).

Alliance to Cure to create a clinical trial education course for New Mexico Community Health Workers

In preparation for the start of upcoming clinical trials in New Mexico, the Alliance to Cure Cavernous Malformation is creating a comprehensive course for Community Health Workers (CHW). New Mexico is largely rural with sparse healthcare infrastructure, and CHWs are the front line of health education in many communities. New Mexico has the highest prevalence of CCM in the world.

The goals of the program are to offer CHWs the information they need to introduce their community members to the idea of clinical trials. Additionally, the training will cover the clinical features of CCM and explore the genealogy of at-risk families.

We anticipate the program will be eligible for Department of Health continuing education credit. It will be offered through Teachable and via Zoom. As part of the course, CHWs will be armed with infographics they can share with their community

The University of New Mexico is a CCM Center of Excellence and plans to host upcoming clinical trials.

Improving Cavernous Malformation Care

Many cavernous malformation patients receive delayed diagnoses and ineffective treatment because the condition is not well known, even within the medical community. Alliance to Cure works to improve access to quality cavernous malformation care.

Updated CCM Clinical Care Consensus Guidelines nearing completion

Alliance to Cure is working with our medical advisors and invited experts to update the peer-reviewed Angioma Alliance CCM Clinical Care Consensus Guidelines, first published in the May 2017 issue of Neurosurgery. The definitive guide for clinicians treating cavernous malformation patients, the Clinical Care Consensus Guidelines offer detailed recommendations on diagnosis, treatment, and monitoring. Since their first publication in 2017, the guidelines have been cited by more than 300 scholarly articles.

The updated guidelines will include expanded spinal and pediatric CCM coverage, diagnostic guidelines, and recommendations from the latest research. They are expected to be published later this year.

The current Clinical Care Guidelines are at www.alliancetocure.org/for-professionals/clinicians/ccm-care-guidelines/

Breaking Barriers program to partner with Centers of Excellence

Our Breaking Barriers program, with funds from Justworks Spring Forward award, is partnering first-year medical students from Morehouse School of Medicine with 8-week summer research placements at our Centers of Excellence.

Students with an interest in neuroscience will be placed at Cincinnati Children's Hospital, Boston Children's Hospital, and Duke University to participate in cutting-edge science. Our aim is to diversify neuroscience, leading to better care for all.

Texas Children's Hospital becomes CCM Clinical Center, first hospital in Texas recognized for expertise in cavernous malformation care

Alliance to Cure welcomed Houston's Texas Children's Hospital on April 10 into our network of cavernous malformation Centers of Excellence and Clinical Centers. A CCM Clinical Center, Texas Children's is the first hospital in Texas to be recognized by the Alliance to Cure for offering interdisciplinary, specialized cavernous malformation care and providing standards of care that meet or exceed the CCM Clinical Care Consensus Guidelines.

Texas Children's is the 20th hospital to join the network and the fourth to specialize in pediatrics. The hospital is the primary pediatric training site for Baylor College of Medicine. Texas Children's conducts genetic research through its Neurological Research Institute (NRI), specifically around pediatric cavernous malformations.

Alliance to Cure aims to place expert cavernous malformation care within a reasonable travel distance for every American through its network of Centers of Excellence and Clinical Centers.

In-depth article on cavernous malformation published in New England Journal of Medicine

Dr. Edward Smith, Chair of the Alliance to Cure's Medical Advisory Board and Director of the CCM Center of Excellence at Boston Children's Hospital, wrote a peer-reviewed overview of cerebral cavernous malformation published on March 14 in the New England Journal of Medicine, a prestigious journal reaching one million readers a week, including clinicians of all disciplines. The review, "Cavernous Malformations of the Central Nervous System," can be accessed by creating a free account at www.nejm.org/doi/full/10.1056/NEJMra2305116. Patients may share this article with medical providers to increase understanding and help guide treatment.

Finding expert surgical care through Alliance to Cure

After years of numbness, aches, and misdiagnoses, an excruciating bout of leg pain brought Ana to a doctor's office in Anchorage, Alaska, in March 2023. An MRI showed a bleeding cavernous malformation in Ana's spinal cord, and Ana's doctor recommended she have an experienced neurosurgeon remove the lesion.

Ana searched online for more information about her new diagnosis.

"I found the Alliance through Facebook, thank God," she says. She also found the list of Alliance to Cure's recognized Centers of Excellence, including Stanford Health in Palo Alto, California. Ana referred herself there to find out more.

"I have never worked with a medical center that was so on top of things," says Ana. Centers of Excellence have specialized teams that follow the national Cavernous Malformation Clinical Care Guidelines. They also treat more cavernous malformation patients than typical hospitals, and Ana learned that the Stanford team was experienced in performing spinal cord surgeries, the rarest type of lesion.

Even at a Center of Excellence, "to make that decision to have surgery is really difficult," Ana explains. A risk of spinal cord surgery was paralysis from the waist down, but opting not to have surgery could have resulted in a paralyzing stroke if Ana's cavernous malformation continued to hemorrhage.

Ana decided to have her surgery done by the specialized team at Stanford in August 2023 rather than wait for a potential emergency surgery scenario in Alaska. The Stanford neurosurgery team removed the lesion without serious complications.

Nine days after the surgery, Ana was able to walk with a walker.

"Everyone was floored by how soon I was walking," she said. "I think a lot of that is going to Stanford, going to the best."

Ana is also thankful for Alliance to Cure.

"There's so much good information," she says. "The support groups has really been a lifesaver for

me." Ana has even found family through Alliance to Cure: she met another Facebook community member who not only shares the CCM1 Common Hispanic Mutation with Ana, but a set of great-grandparents.

Seven months post-surgery, Ana is home in Anchorage with her husband and two young children, back at her job as the Deputy Director of Business Solutions and Data in the company's IT department where she has worked for nearly 18 years. She is still recovering, but she can walk with a cane, and she feels thankful.

"I lived," she says. "Somebody went into my spinal cord, and I survived it. They went into my motherboard, my processor, and I survived it."



After learning about Alliance to Cure and its recognized Centers of Excellence, Ana had surgery at Stanford Health to remove a hemorrhaging spinal cavernous malformation that threatened paralysis. Stanford is part of Alliance to Cure's network of Centers of Excellence and Clinical Centers, 20 hospitals recognized by Alliance to Cure for providing high-quality, interdisciplinary care for cavernous malformation patients.

Alliance to Cure Celebrates Rare Disease Day

Alliance to Cure organized parties hosted by our volunteers nationwide to raise awareness of cavernous malformation for Rare Disease Day on February 29, 2024. Patients met each other – for many, it was the first time they had met anyone else with cavernous malformation – and colored the stripes of toy zebras, the mascot of Rare Disease Day. The adorable toy zebras were provided by Recursion, our partner in the first industry-sponsored clinical trial for a cavernous malformation drug that is expected to report results at the end of 2024.



Albuquerque, NM



Memphis, TN



Carlsbad, CA

Upcoming Events

National Events

3rd Annual Strides to Cure CCM: June 2023

We are celebrating Cavernous Malformation Awareness Month with our 3rd Annual Strides to Cure CCM, our national virtual walk to honor patients and families everywhere. Walk, run, or roll wherever you are, join a team in your area, or organize your own team. Sign up to receive updates about this and other events at www.alliancetocure.org/sign-up-for-updates/

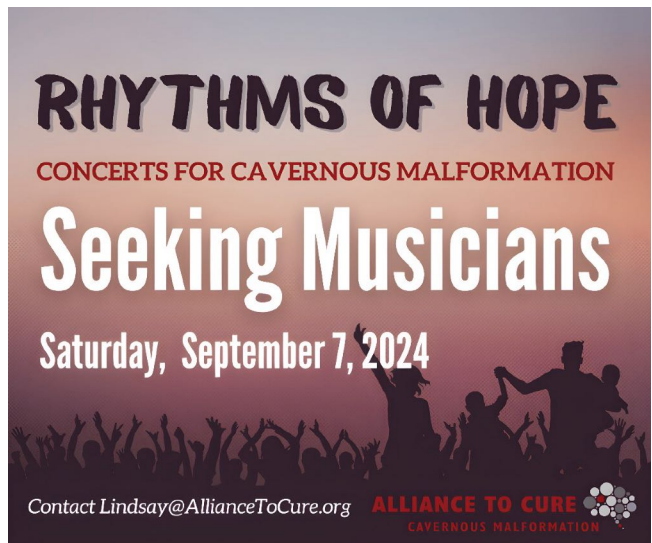
2024 Patient Conference

This year's patient conference will be held in Toronto, Canada, on July 26-27 in conjunction with the Alliance to Cure's 20th Anniversary International Scientific Meeting. We look forward to an exciting first day of expert presentations and a second day of social activities, including a picnic and an outing to a Toronto Blue Jays baseball game. The meeting will be recorded for those who aren't able to attend.

Find more details and register at angioma.networkforgood.com/events/67058-2024-patient-conference.

Family Weekend Fully Registered

Our first-ever family weekend, to be held on June 28 – July 1 in Silver Bay, NY, is fully registered. We look forward to hosting 60+ Alliance to Cure kids and adults for a long weekend of community and fun. This event is made possible thanks to the support of an individual donor and our sponsors – our families appreciate you!



Rhythms of Hope Needs Your Musical Talent

We are seeking talented musicians to volunteer their time for our upcoming hybrid annual fundraising and awareness event on September 7th.

We have something extraordinary up our sleeve, and we need your help! Let us know if you or someone you know is a talented musician!

Virtual and in-person performance opportunities are available.

Contact Lindsay@AllianceToCure.org



Regional Events

Rocking for a Cure

You are invited to the 2nd annual Rocking for a Cure fundraising event hosted by the Baron family in Gambrills, Maryland, on June 1st.

The all-ages, FAMILY-FRIENDLY event features:

- Live music by Blues in a Blender (bluesinablender.com/)

- Silent Auction & Raffles

- Karaoke and more

For more details and to purchase tickets, visit angioma.networkforgood.com/events/68057-2nd-annual-rocking-for-a-cure



Bi-Coastal Golf Scrambles

East Coast and West Coast: two opportunities to participate in a golf scramble to benefit the Alliance to Cure.

What is a golf scramble? Each golfer on the team hits a tee shot. The team then selects the best tee shot, and all four golfers hit their next shot from that spot. This process continues until the ball is holed out.

Follow the links for details and registration:

East Coast: Chip in for a Cure

Join us on the prestigious PB Dye golf course in Ijamsville, Maryland, on May 20th:

angioma.networkforgood.com/events/65720-chip-in-for-a-cure-golf-scramble

West Coast: Swinging for a Cure

Join us at Twin Oaks Golf Course in San Marcos, California, on May 23rd:

angioma.networkforgood.com/events/66324-swinging-for-a-cure

Thank you to our sponsors!



Where the world comes for answers



How You Can Help

Volunteer: Share your talent and time in any number of ways including Community Alliances, peer support, events, legislative advocacy, and much more: www.alliancetocure.org/care-community/community/volunteer/.

Donate: Your contributions help fund our research initiatives toward a cure and our patient support programs. To donate, please send a check or money order in the enclosed envelope or visit our website at www.alliancetocure.org to donate with a credit card.

Sponsor: Sponsorships can maintain essential programs or help us expand our support for the patient and research community. Sponsors are acknowledged with logo placement, naming opportunities, or appropriate other recognition. Contact us at info@alliancetocure.org to learn more about these opportunities and valuable benefits for your company.

Our Mission and Goals

It is our mission to inform, support, and mobilize those affected by cavernous angioma and drive research for better treatments and a cure. We do this by developing and executing strategic, creative, high-return interventions as a model for rare diseases:

1) **Facilitate and participate in cavernous malformation research to achieve a complete understanding of the disease** and facilitate clinical drug trials and other treatment improvements. We do this through our Accelerating Cures program, Scientific Meetings, patient registry and biobank, genetic testing program, research collaborations, and outreach to special populations.

2) **Provide disease and resource information** to educate and improve the lives of people affected by cavernous malformation, caregivers, health professionals, researchers, policymakers, the media, and the general public. We achieve this through our website, publications, webinars, conferences, and media appearances.

3) **Foster and promote a caring community to provide support.** We offer live and online support opportunities and broad international outreach.

4) **Get people involved in advocacy and active participation toward a cure.** Involvement can include activities like research participation, Community Alliances, our upcoming Patient-Expert Certification, legislative advocacy, and public events.

5) **Build and sustain a broad base of funding sources to support our mission and goals.** We count on you!

About Alliance to Cure Cavernous Malformation



Alliance to Cure Cavernous Malformation is a non-profit, international, patient-directed health organization created by people affected by cerebral cavernous malformations (also known as cavernous angiomas or CCM). Our mission is to inform, support, and empower individuals affected by cavernous malformation and drive research for treatments and a cure. We are monitored closely in our educational efforts by a Scientific Advisory Board comprised of leading cerebrovascular neurosurgeons, neurogeneticists, and neurologists.

Alliance to Cure Cavernous Malformation

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Follow Us on Social Media

www.AllianceToCure.org

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Instagram, TikTok: @AllianceToCure



A copy of the latest financial report, registration filed by this organization and a description of our programs and activities may be obtained by contacting us at: Alliance to Cure Cavernous Malformation, 520 W 21st St STE G2-411, Norfolk, VA 23517, info@angioma.org. If you are a resident of one of the following states, you may obtain financial information directly from the state agency. Angioma Alliance d/b/a Alliance to Cure Cavernous Malformation, EIN 02-0600697, complies with state charitable registration requirements.

- Florida – A COPY OF THE OFFICIAL REGISTRATION AND FINANCIAL INFORMATION MAY BE OBTAINED FROM THE DIVISION OF CONSUMER SERVICES BY CALLING TOLL-FREE, WITHIN THE STATES, 800-435-7352 (800-HELP-FLA) OR BY VISITING www.800helpfla.com. REGISTRATION DOES NOT IMPLY ENDORSEMENT, APPROVAL OR RECOMMENDATION BY THE STATE. Florida Registration CH20096
- Georgia – A full and fair description of our programs and our financial statement summary is available upon request at our office and email indicated above.
- Colorado – Colorado residents may obtain copies of registration and financial documents from the office of the Secretary of State, 303-894-2860, www.sos.state.co.us/ Reg. No. 20063003635.
- Maryland – For the cost of copies and postage, from the Office of the Secretary of State, State House, Annapolis, MD 21401.
- Michigan – MICS # 35000
- New Jersey – INFORMATION FILED WITH THE ATTORNEY GENERAL CONCERNING THIS CHARITABLE SOLICITATION AND THE PERCENTAGE OF CONTRIBUTIONS RECEIVED BY THE CHARITY DURING THE LAST REPORTING PERIOD THAT WERE DEDICATED TO THE CHARITABLE PURPOSE MAY BE OBTAINED FROM THE ATTORNEY GENERAL OF THE STATE OF NEW JERSEY BY CALLING 973-504-6215 AND IS AVAILABLE ON THE INTERNET AT: <http://www.state.nj.us/lps/ca/charfrm.htm>. REGISTRATION WITH THE ATTORNEY GENERAL DOES NOT IMPLY ENDORSEMENT.
- New York – Upon Request, Attorney General Charities Bureau, 102 Broadway, New York, NY 10271
- North Carolina – Financial information about this organization and a copy of its license are available for the State Solicitation Licensing Branch at 919-807-2214. This is not an endorsement by the state.
- Pennsylvania – The official registration and financial information of Angioma Alliance may be obtained from the Pennsylvania Department of State by calling toll-free within Pennsylvania 800-732-0999. Registration does not imply endorsement.
- Virginia – State Division of Consumer Affairs, Department of Agriculture and Consumer Services, PO Box 1163, Richmond, VA 23218.
- Washington – Secretary of State at 800-332-4483 or <http://www.sos.wa.gov/charities/>. REGISTRATION WITH A STATE AGENCY DOES NOT CONSTITUTE OR IMPLY ENDORSEMENT, APPROVAL OR RECOMMENDATION BY THAT STATE.