

# ALLIANCE TO CURE CAVERNOUS MALFORMATION



**Every dollar donated through the end of the year  
will fund research grants toward a cure**

Dear Friend of the Alliance to Cure Cavernous Malformation,

This was the year the seeds you've helped us sow began to bear fruit. While we have continued to expand our patient support and education programs, in this letter, I'd like to highlight the progress we've made toward a cure.

In the last year, not just one or two, but **three clinical trials** have reached significant milestones:

- The very first medicine created just for CCM, Recursion's REC-994, entered trials with our patients! There are now 11 sites around the United States actively recruiting patients with our help. This is a pivotal moment for finding better treatments.
- The Italian safety trial of the beta blocker propranolol is complete, and results will be published in early 2023. If propranolol appears safe for people with CCM and shows signs of effectiveness, researchers can move the trial to an expanded next phase.
- The atorvastatin trial, the second trial of a repurposed medicine, has finished enrollment. Patients in the trial will now take the medicine for 2 years.

Because of your donations, we have begun to fund research directly. Our first research grant of \$87,000 was awarded to the University of Virginia to support their work in developing **focused ultrasound** as a non-invasive treatment for CCM lesions. These funds will be used to test the safety and efficacy of focused ultrasound in mouse models of the disease. Please see our Fall newsletter for more details. If the tests are successful, UVA will be able to apply for expanded funding from the National Institutes of Health and move one step further to treating patients.

We have been using the funds awarded to us by the Chan Zuckerberg Initiative to expand our **biorepository and patient registry**, with the first samples collected at our recent patient conference. These new samples will be used to develop biomarker panels to predict who is at risk for CCM hemorrhage and to create easier and less expensive diagnostic techniques. CZI funds also have added momentum to the development of CCM Centers. In the last year, we've added 4 CCM Clinical Centers and 4 Centers of Excellence. We are making it easier to find multi-disciplinary, expert care everywhere, and, with these Centers, we're creating a **network of potential clinical trial sites** that we can activate as trials expand.

(Continued on reverse)



**Christina and Joe Campos**

"Our journey starts quite a few years ago. We live in Santa Rosa, a small rural community in eastern New Mexico, where they identified many people in our community that are part of the Common Hispanic Mutation lineage," shared Christina Campos. "My husband Joe got tested first. He was positive. Both of my daughters are positive, too".

In 2018, Joe started exhibiting problems with his vision. "He was diagnosed with a very large lesion— about 4 cm dead center in the brain. By the time we got him into pre-op, he was no longer able to walk on his own. My three kids propped him up to walk him into the Barrow for his surgery."

The surgery was a success although it took six weeks before Joe could come home. After surgery, Joe had many skills to relearn. He had reverted to Spanish and needed to remember English. He had to relearn how to use his hands. The hemorrhage and surgery affected his eye, and Joe had trouble walking. Christina notes, "With CCM, it's not even the number of lesions in your brain — it's the bleeds and where they are. It's all about real estate. It's all about location. His was in a terrible location, but we are grateful for the recovery he has had so far."

Christina's family is committed to bringing awareness to CCM to change the future for her daughters. "We educate, talk about it, share information, and are as open as possible so that people are comfortable learning more."

Christina and Joe's story is featured in the Alliance to Cure Cavernous Malformation documentary, *Eloquent*, released in theaters and available for private showings this year.

Because of your donations, we are building a **database of mouse models** of CCM that includes 13 labs from around the world who have agreed to join the consortium we formed early this year. Our database is already fueling collaborations between labs as they share mouse model resources and giving us insights to decide where to direct funding. When complete, the mouse database will offer the information we need to create a multi-institutional plan to test a variety of medicines in the best models.

Finally, through a grant from the United Kingdom, we are planning a multi-national trial that will allow us to test multiple treatments at once. The trials will share a placebo arm, an efficient use of our patient participants. This trial structure is called a **platform trial** and requires international institutions and industry partners to collaborate in new ways. Supporting this effort are Dr. Rustam al-Shahi Salman, Dr. Issam Awad, Dr. Roberto Latini, Dr. Helen Kim, and the office of New Mexico Senator Ben Ray Lujan, who suffered a stroke himself early this year.

### Our Plan Going Forward

This year's victories give us momentum, and we plan to expedite the work toward a cure. Here is how you can help. **Every dollar donated to the Alliance to Cure Cavernous Malformation through the end of the year will fund research grants toward a cure.** We will award funding to high-risk/high-reward projects with the most significant potential to move the field forward quickly. Your support will allow successful projects to establish a proof of concept which will lead to larger funding. In some cases, your support may help rule out approaches – this is important, too.

### Sample Projects

With your help, we can fund the exploration of **advanced drug delivery** methods to get treatments directly to lesions. This work goes hand-in-hand with the recent discovery of the cancer-like biology of CCM. If we need to resort to cancer drugs to shrink lesions, we want a way to isolate the activity of the drugs to the lesion itself to prevent side effects. Targeted drug delivery research and implementation are already well underway in other diseases. It's time for us to figure out how to make it work for CCM.

We also would like to fund early work for potentially curative treatments like **novel gene therapy methods** and **miRNA interventions**. Because the CCM genes are large, familial CCM is not amenable to whole gene replacement therapy using current methods. Instead, researchers are developing targeted technologies that can read past mutated genes to restore normal function. We also are soliciting proposals to test compounds with the potential to regress lesions by altering the relationship between miRNA and the proteins involved in CCM. These are cutting edge projects that could leapfrog us ahead.

### Finally

In 2022, we entered our 20<sup>th</sup> year and changed our name. Where we once were Angioma Alliance, we are now the Alliance to Cure Cavernous Malformation. This new name reflects the promise we make to each other to work together for a cure. During this giving season, please join us in ensuring the promise of a cure by making a **tax-deductible, year-end donation**. You can mail a check using the enclosed donor envelope or donate online at [AllianceToCure.org/Donate](https://AllianceToCure.org/Donate).

Thank you for your support throughout the year and your trust in us. Together, a cure is within our reach.

With gratitude,



Connie Lee, CEO

