

ALLIANCE TO CURE CAVERNOUS MALFORMATION



**Every donation through year's end will fund a first:
our own preclinical research program.**

Dear Friend of the Alliance to Cure Cavernous Malformation,

Because of you, 2023 was a milestone year in our mission to find a cure for cavernous malformation (CCM). I am proud to share a few highlights:

Clinical trials are going strong:

- **Ahead-of-schedule, full enrollment** of the first pharmaceutical industry-funded drug trial for cavernous malformation, Recursion's REC-994 Phase 2 Sycamore Trial for symptomatic CCM. Your support helped us mobilize our members quickly so they could join the trial, setting up a faster timeline for results to come out in 2024.
- **More industry trials are in the works.** Two more companies, Neurelis and Ovid, launched Phase 1 trials in healthy volunteers to test their CCM medicines and sought our guidance for starting Phase 2 trials in our patients in 2024.
- **We built a tool to power research.** In the last 3 years, over 500 of our members participated in the CCM Health Index, a patient-reported outcomes measure that is the only survey specific to CCM. Now, the tool is being used in the Recursion trial and will help determine whether treatments have a positive effect in other studies.

You funded strategic research grants for:

- **A non-invasive alternative to brain surgery.** In 2022, you funded a focused ultrasound research grant at the University of Virginia after other funding sources had dried up. At our 2023 Scientific Meeting, we got the results: focused ultrasound *stops lesion growth and prevents new lesion development* in mice non-invasively. Now, the National Institutes of Health has awarded UVA a large grant to continue this promising research.
- **A targeted drug-delivery approach used in other diseases.** Some of the best treatments for CCM may come from oncology, where drugs have more side effects. Side effects happen when drugs are active in parts of the body where they are not needed. This year we began funding research to use nanoparticles to encapsulate treatments for CCM and then release these medicines directly to CCM lesions.

Your support also allowed us to keep our patient community at the heart of what we do, and our outreach efforts gave hope to members like Megan (see right). Our patient support and research activities were recognized nationally in May 2023 when we won the Abbey S. Meyers Leadership Award – a prestigious honor given by the National Organization for Rare Disorders (NORD), which represents more than 300 rare disease organizations.



Megan's Journey

Megan's journey unfolded against the backdrop of familial CCM, a legacy that seemed to skip her after a childhood MRI showed no signs of lesions. However, Megan had headaches throughout her life, and over-the-counter painkillers were her daily companions. Finally, at her family's insistence, Megan sought medical help.

A CT scan revealed a concerning mass and an MRI confirmed she had at least two cavernous malformations. Megan was 25, newly married, and working 50-60 hours a week when she learned she would need brain surgery.

Since surgery, Megan has had fatigue and is unable to keep up the pace of working as many hours as she used to. Her diagnosis and surgery became a catalyst for change.

"It's made me appreciate my life a lot more," Megan reflected. The experience spurred her to pursue dreams she might have otherwise left on the backburner, like opening her own interior design business.

Megan shaved her head for the surgery rather than having a strip shaved for the incision. Now that her hair has grown long enough to obscure her scar, she feels it hides the reminder of how strong and resilient she really is.

The Alliance to Cure Cavernous Malformation is a beacon of support for Megan. "I've learned so much from the Alliance. It's so comforting to know I'm not the only one going through this," she said.

2024: We're Powering Forward with a Mouse Treatment Testing Program

We have made tremendous progress, but there is still more to do – and this is where I am asking for you to join us on the front lines of finding a cure.

There are currently more than 20 potential treatments for CCM that are sitting on shelves instead of being tested in mouse models, which is the necessary step before a treatment can be tested in a clinical trial. This is because there are simply not enough academic labs that can devote their time and space to running preclinical tests of potential CCM treatments on mice. We have never been in a position where we have the initial resources, information, and expertise to test these potential treatments ourselves.

Until now. In the next year, we will develop a program requiring **a significant multi-year commitment of financial resources**, but it's the requisite step to accelerate research. We plan to conduct **preclinical research ourselves by establishing our own colony of mice to test the most promising treatments for CCM.**

The details of our mouse treatment testing program are being worked out, but we will likely:

- 1) Fund an academic laboratory to perform preliminary cell line screening of medicines with potential based on prior research understandings.
- 2) Perform fast mouse experiments in the academic setting to determine whether a drug is worth moving forward.
- 3) Take the best candidates to a commercial laboratory with facilities to grow our mouse colony and conduct extended experiments, including watching lesions change in real time using sequential MRI.

When these drugs are effective in mice, they can then be taken up in clinical trials. Your support will allow us to fill this critical research gap in finding treatments and a cure for cavernous malformation.

All donations made through the end of the year will go directly toward testing promising treatments in mice.

2024 will be a huge year as we see the results of the Recursion and atorvastatin trials, the potential launch of two Phase 2 trials of drugs developed specifically for CCM, nanoparticle research progress, updates on gene therapy research, new care guidelines, our first family camp, the growth of our patient registry and biobank, the development of our mouse drug testing program...the list goes on! Together, we are driving these projects, united in our mission to inform, support, and mobilize those affected by CCM and drive research for better treatments and the 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.

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

With gratitude,



Connie Lee, CEO

