January 19, 2025

To the California Institute for Regenerative Medicine (CIRM)
Letter of Support for the Blue Cone Monochromacy Gene therapy

I am Renata Sarno, a mother of three boys with Blue Cone Monochromacy and a sister of an adult with Blue Cone Monochromacy. This disease has been in my family for over 100 years and my grandfather also had it. In 2014, along with other families with Blue Cone Monochromacy, I formed the BCM Families Foundation, a 501 (c)(3) non-profit organization with the goal of finding a cure for Blue Cone Monochromacy.

1. Severity
First of all, I would like to tell you what Blue Cone Monochromacy is: it is a disease with severe symptoms that affects people throughout their lives, starting from the day they are born. Our children present with nystagmus at a few weeks of life, and then photophobia. We mothers then notice how low their visual acuity is, and their inability to distinguish colors. Even though we use lenses to correct their optical defect, myopia and astigmatism, our children have low visual acuity, often close to 20/400. In these 10 years of activity with the BCM Families Foundation, I have come into contact with hundreds of people affected by Blue Cone Monochromacy. Our patient registry alone contains personal information of about 100 people and family members of about 300, but the members of our social groups and national groups are many more, and we can count on a community of about 1000 patients. It is true that there is variability within all our families with cases that come very close to blindness and people with better vision, but in each of our families there are many cases of severely visually impaired people, and those who see a little better are an exception. Among the most severe symptoms after low vision is nystagmus. While the majority of us have severe symptoms for low vision, the first data on nystagmus tell us that about 60% of people maintain disabling nystagmus in adulthood, which further worsens their vision.

2. Stability
Secondly, I would like to talk to you about the stability of this disease. Many other eye diseases have a different path. The person has normal vision for a certain period of life, often a long one, and then begins to lose vision, for example central vision, and quickly and progressively loses all the vision they had. We do not, we are not lucky enough to have vision even for one day, you can think of our newborns as if they lost most of their central vision on the first day of their life, all of it immediately. And they cannot shout it out, they cannot tell you because they do not understand the difference between a before and an after. But I will shout it out to you, I am here on behalf of all our children and all the adults who live their entire lives with very low central vision that gradually fades over the years. Most of our adults, after the age of 50 or even younger, report that they no longer have daytime and central vision, that they have to wear dark glasses to be in the light, with strong photophobia. This is a severe, debilitating disease that begins on a newborn's first day and lasts a lifetime, progressively leading to the loss of retinal cone cells.

3. Community Involvement
Since 2010, I have been funding clinical and preclinical research to find a cure for Blue Cone Monochromacy and then founded the BCM Families Foundation in 2014. Since 2010 and for 14 years now, we have funded clinical studies at the University of Pennsylvania, with Dr. Samuel Jacobson until 2022 and then with Drs. Tomas Aleman and Artur Cideciyan. The initial goal was to understand if there were enough cells in the retina to be able to cure the disease with a gene therapy. This is the first question we asked ourselves. Results of UPenn studies answer positively, and therefore together with the scientists we are confident that there is a window of opportunity to treat the cone cells before their gradual and progressive loss.

We have continued the studies for 14 years and dozens of patients have participated, many children have also been examined, including my children, and I would like the effort and participation of this community of patients to be before your eyes today. It is not easy to participate, to go with visually impaired children to another city or for a visually impaired adult to travel to another city, face expenses, and spend entire days at the Scheie Eye Institute to collect important data. The exams are long, it takes a lot of patience, it is not easy to pay attention for many hours in a row, neither for adults, nor especially for children and their parents. Yet many of us, dozens and dozens, have gone, participated, donated their time, and offered their data to improve knowledge of this rare disease with the aim of a cure. Many have participated and are participating in the BCM patient registry, which today collects the personal data of more than 100 people belonging to more than 70 different families. But this community has done more: it has raised funds and financed research. Since 2010, first personally and then with the BCM Families Foundation, we have raised more than 3 million dollars and funded research, created animal models, tested AAV vectors, funded clinical studies, built and maintained the patient registry, organized national meetings for families. We have also organized 3 European meetings together with the European achromat associations to discuss gene therapies and analyze the results of their clinical trials. This community wants a cure for Blue Cone Monochromacy and has demonstrated it during all these years with support, participation, funding.

4. Why gene therapy

We have a Scientific Advisory Board and have relationships with dozens of scientists in many countries. There have been many discussions about which therapies to try, but our scientists, including Jeremy Nathans, Samuel Jacobson, Tomas Aleman, Artur Cideciyan, John Flannery, William Hauswirth, Bernd Wissinger, Susanne Kohl, Jacque Duncan, Alessandro Iannaccone and several others, all told us that the AAV gene therapy has to be considered as the primary possibility for a cure. There are currently no other options for a cure for Blue Cone Monochromacy. We have nothing else to try, except magnifying devices and eyeglass filters. Nothing. No alternatives. But we believe it is our responsibility to try, and our scientists point to AAV gene therapy as the most promising solution.

5. Achromatopsia e Amblyopia

We think that gene therapy for Blue Cone Monochromacy may have a chance of success. Amblyopia, or the effects of long-term vision deprivation on the reorganization of the visual cortex, should be different in the case of Blue Cone Monochromacy, compared to achromatopsia. These are two different diseases with different genetic causes, with different missing proteins in the phototransduction process. The opsin proteins missing in Blue Cone Monochromacy are at the beginning of the process, and this position could be an advantage. Furthermore, daytime vision and detail vision is given by the S cones for people with Blue Cone Monochromacy, even if few but present, so the visual cortex of people with Blue Cone Monochromacy is not blind to visual sharp details. Even the perception of color is partially developed in our loved ones. We therefore expect different results from those, still not definitive and not yet clear, from the trials on achromatopsia.

6. Number of patients

We know that ours is a rare disease, that the number of patients is limited and that not everyone, given the progression of the disease, will be able to be cured because the older ones will no longer have the cone cells to treat. But we also know that every year many new children are born with Blue Cone Monochromacy. We would like to give a cure to those who today are affected by this severe disease and who fall within a window of opportunity to still be cured. But we would like all the new born with this disease to have the possibility of having a cure from now on, that they do not have to have the life that we are having.

In order to cooperate with you to achieve success together in the treatment of Blue Cone Monochromacy, we are here to further testify about our disease and to hear your every need. We would like to hear what you have at heart to be confident of this funding.

1)Dr. Renata Sarno, President of the BCM Families Foundation

The following people are signing this letter with me: