BLU GENES
FOUNDATION

ANNUAL REPORT 21

blugenes.org

Letter from the Executive Director

Just a few short years ago, a hope of treatment for Tay-Sachs disease was not on the horizon. Parents of children diagnosed with this rare and devastating genetic disease were told that the best they could do was keep their child comfortable and make the most out of every day they had together.

That option wasn't enough for Sam and Maria Crignano when their granddaughter, Siena, was diagnosed just after her first birthday. They founded Blu Genes specifically to support the tremendous amount of research focused on rare genetic disorders that, because such work impacts only a small number of people per disease, struggled to secure the grants needed to allow the work to progress.

It is because of the generosity of donors like you that Blu Genes has made a real and tangible difference in propelling genetic research forward in just four short years. Our first funding project at the University of Massachusetts (UMass) drove research to clinical trial, leading to a potential treatment option for infants diagnosed with Tay-Sachs. It would not even be in today's landscape without your support.

For our current funding initiative, we have joined with the world-renowned Hospital for Sick Children (SickKids) to advance cutting-edge gene editing research aimed at correcting the mutations that cause Tay-Sachs. This research could be the key to effective treatments, and even a cure. More so, it may serve as a foundation for understanding how to use gene editing for other genetic mutations, potentially acting as a building block toward treatments for other currently fatal rare genetic diseases.

We are forever grateful for your unwavering support, particularly during these last two pandemic years when we couldn't always hold our signature events or say "thank you" in person. Your ongoing support during this time has meant we have been able to continue to push boundaries; because every day not moving forward is a day lost for the families who will benefit from our efforts.

Thank you to our Board, who has determinedly guided us, and to our scientific advisory committee who continues to work tirelessly to uncover the promising, yet underfunded, genetic research that has the potential to make a great impact.

Finally, thank you to our sponsors and donors for putting your trust in us to change the landscape and improve the future for children and families with Tay-Sachs and other rare genetic diseases.

Nicola Dent
Executive Director

The Story of Blu Genes Foundation

For the first few months of her life, Siena was just like other infants — she was growing well and hitting her milestones. Her mom, Sara Margani, kept the two of them busy with music and swim classes, walks to the park and visits with friends.

But by six months, Sara began noticing subtle developmental delays in Siena.

"My most vivid memory is after a swim class when one mom sat her child, who was a little younger than Siena, on the floor," recalls Sara. "I was shocked that the child just sat there because whenever I put Siena down, I had to pack pillows around her to keep her from falling over. As a mom, I just knew that something wasn't right."

Soon after, Siena was diagnosed with Tay-Sachs disease. Doctors didn't expect her to live long enough to celebrate her fifth birthday.

"We were essentially told that there were no treatments, no therapies and nothing we could do," says Sara. "Doctors basically told us to take her home, love her and watch her decline. We didn't accept that, so we started doing our homework."

Soon after, Sara's family founded Blu Genes Foundation for just that purpose — to find and fund the promising genetic research that, due to a lack of financial resources, was simply sitting on a shelf. Rare genetic diseases, like Tay-Sachs, affect families around the world but because the conditions aren't well known and affect just a small percentage of the population, research into treatments and cures don't receive the same level of funding as other diseases.

"When we embarked on the Blu Genes mission, we learned that research for Tay-Sachs was so far behind where it could be. There were other (Tay-Sachs) foundations providing patient advocacy and support, but the research to treat the actual disease was pathetically underfunded," says Sara.

Blu Genes' first funding project was at the University of Massachusetts (UMass): a gene therapy research project that had proven promising, but scientists had been waiting years for the funding needed to take it to clinical trial. Blu Genes' $1.8 million commitment did just that. (Read more about the UMass research on page 6.)

Siena became one of the first people to receive a conservative dose of the treatment after being approved by the FDA for "expanded access" to the clinical trial. (Expanded access allows for patients to access pre-clinical trial therapies when premature death is likely without early treatment.) The dose was conservative because she was considered to be too far along in disease progression. She is now more stable, no longer suffering from seizures, and with more control of her eye movements, says Sara.

In early May, Siena and her family celebrated her sixth birthday.

"I'm confident that (the gene therapy clinical trial) has helped her get to where she is today," says Sara.

Ultimately, Blu Genes' goal is to not only support the development of promising treatment options for families like Siena's, but to fund the groundbreaking research that can one day provide options for families living with other rare genetic diseases as well.

"There are a lot of families who are given terrible news every single day about genetic diseases we've never heard of. We want to be able to give those parents choice and options for treating their children, instead of simply being told to take their child home and do nothing. That would be a really big deal for any parent of a child with any disease."


“We were told that there were no treatments, no therapies and nothing we could do.”
- Sara Margani

UMass Research Leads to Potential Tay-Sachs Treatment

At the University of Massachusetts (UMass) Medical School, Prof. Miguel Sena-Esteves and his colleagues had been studying Tay-Sachs and gene therapy treatments for over a decade, specifically looking at the ability to harness the adeno-associated virus (AAV) to fix a Tay-Sachs genetic mutation. People living with Tay-Sachs are missing the gene that produces the HEXA enzyme that breaks down GM2 gangliosidosis, a waste product in the brain. A build-up of GM2 damages and kills brain cells, causing a neurodegenerative decline that leads to death.

Prof. Sena-Esteves and Dr. Heather Gray-Edwards developed a treatment that would turn on the ability of the brain cells to produce the HEXA enzyme. However, this promising research was crawling along due to a lack of funding.

At Blu Genes, we recognized that this research could help children living with Tay-Sachs in the immediate future, so for our first funding project, Blu Genes committed the required $1.8 million investment to propel this groundbreaking research from the preclinical phase to in-human trials.

In 2020, the treatment was approved by the FDA as an Investigational New Drug (IND), which cleared the way for human trials. The positive results of the UMass research and early trials caught the attention of Sio Gene Therapies, a clinical trial company that licensed the research and conducted further trials with more patients and stronger doses.

In February 2021, Sio Gene began treating its first infantile Tay-Sachs patient in a Phase I/II trial for the AXO-AAV-GM2 therapy. To date, seven children have received treatment as a result of this clinical trial. Meanwhile, the FDA has granted Fast Track Designation, Orphan Drug Designation and Pediatric Disease Designation for the treatment of Tay-Sachs (as well as Sandhoff disease, another type of GM2 gangliosidosis disease), helping to get this life-saving therapy to the families that desperately need it.

The Sio Gene licensing has now ended, but it allowed for great leaps forward in developing and launching this first in-human clinical trial. UMass remains committed to moving this research and this trial forward to the finish line, where the treatment could be available in a clinic for patients diagnosed with Tay-Sachs.

When Blu Genes was founded just four years ago, there were no treatments for patients diagnosed with Tay-Sachs disease. With the success of this UMass trial, today there is real hope.

Beyond Tay-Sachs

Sio Gene Therapies also supported the advancement of another gene therapy that built on the success of the Tay-Sachs treatment with a similar therapeutic for GM1 gangliosidosis, a fatal lysosomal storage disorder that progressively destroys nerve cells in the brain and spinal cord. Interim data presented at a conference in October 2021 showed promising results: Six out of seven patients had no signs of disease progression as of their assessment at the start of 2022. Preliminary data like this offers hope that there may soon be a therapy for children with GM1 gangliosidosis.

Funding Cutting-Edge Research at SickKids

Fresh off the successes of our UMass research partnership, we began searching for another promising project in need of a funding commitment. We found one close to home, joining with the world-renowned Hospital for Sick Children (SickKids) in Toronto.

Leveraging the resources of the top-ranked pediatric healthcare centre in the world, and thanks to generous support from donors like you, we're funding a dedicated team to conduct cutting-edge gene editing research aimed at correcting the mutations that cause Tay-Sachs.

With our two-year, $360,000 funding commitment, Dr. Zhenya Ivakine and his team are utilizing an advanced gene editing technology known as CRISPR/Cas9. Replicating the naturally occurring immune responses in bacteria, this technology is designed to remove DNA mutations and, in the case of this research, replace them with a corrected gene.

These therapeutic technologies have taken decades to develop to this point of investigation, and we are thrilled to have the opportunity to support the advancement of research that could be the key to effective treatments, and even a cure.

The groundbreaking research underway by Dr. Ivakine's team will give us a clearer understanding of how Tay-Sachs progresses, which can inform the development of the CRISPR/Cas9 gene editing treatment. Once the treatment proves to be effective in this preclinical research, Dr. Ivakine's team will be able to move on to secure approval for clinical testing in people.

Translational genomics, such as this Blu Genes-funded study, is a shift from one-size-fits-all therapeutics, to treatment that is precisely tailored to each disease mutation of genes or even each child's individual genes. SickKids, and Blu Genes, understand that using tools and technologies that offer unprecedented opportunities for more rapid, accurate and cost-effective treatment has the potential to transform the lives of children facing rare diseases.

What is CRISPR/Cas9 and How Does it Work?

CRISPR stands for Clustered Regularly Interspaced Short Palindromic Repeats, which is a DNA sequence that some bacteria use to fight viruses. (Yes, even bacteria have to take on viruses.)

When bacteria are infected with a virus, they insert a piece of the virus's DNA into their own so they can recognize the virus in future. If that virus, or a similar one, attacks again, the bacteria produces an RNA segment that attaches itself to the virus's DNA, deactivating it.

CRISPR/Cas9 technology harnesses this naturally occurring process. Using a Cas9 enzyme and guiding RNA, researchers are working on targeting specific pieces of our genetic code, in order to precisely cut the DNA and correct a disease-causing mutation.

Dr. Ivakine and his team are specifically working on targeting the most common HEXA genetic mutation that causes Tay-Sachs. The goal is to provide preclinical evidence of a CRISPR/Cas9-based correction that effectively and efficiently treats Tay-Sachs and has the potential to be a cure.

Our Events

BLU & YOU

In a year when pandemic shutdowns forced us all to stay home, we still found a way to bring the style and elegance of our signature Tea for Blu event directly to our donors' doorsteps.

Tea for Blu is a beautiful springtime afternoon of socializing, traditional tea service, fun activities and special guests to help fund the advancement of Tay-Sachs disease research. After being cancelled in 2020, the event was re-imagined as Blu & You in 2021 as we delivered premium loose-leaf tea, scones and fine jams to event participants' homes throughout the spring. Corporate sponsors also received a beautiful handcrafted candle by a local Toronto artist as a token of our appreciation.

The event raised over $80,000 in support of groundbreaking genetic research.

Our annual Tea for Blu returned on May 29, 2022 at the King Edward Hotel in Toronto.

We are forever grateful for the generosity of all of our Blu & You donors. It's because of you that we can fund the research that creates hope and opportunities.

VELO BLU

On a sunny September day, riders and guests joined us for our signature event, VELO BLU, a charity ride and celebratory day through Niagara-on-the-Lake to help us raise vital funds that could transform the lives of chidren with Tay-Sachs disease.

The 2021 ride challenged cyclists along a scenic route through the region, culminating at Peller Estates Winery for a celebration with great food, wine and company, as well as a sense of accomplishment. The event exceeded fundraising goals, raising close to $250,000.

Thank you to our presenting sponsor, **Greybrook Realty Partners**, and to all of our sponsors, donors, riders and guests who made VELO BLU 2021 a great success. We look forward to seeing everyone back in September 2022.

Thank You to our 2021 Donors

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Anonymous - Corporate
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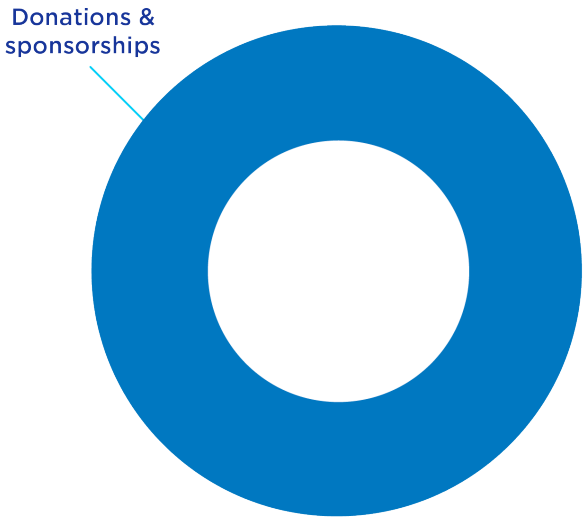
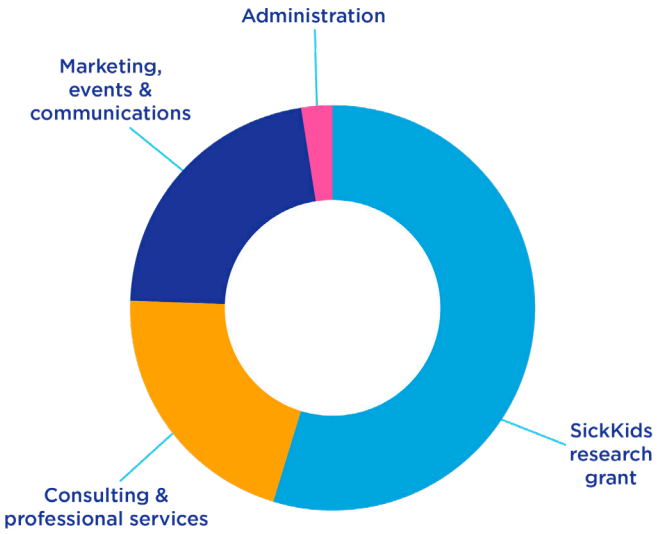
Financial Summary

2021 REVENUE



2021 REVENUE ALLOCATION



Revenue Breakdown

Donations & sponsorships:	$319,316

Revenue Allocation Breakdown

SickKids research grant:	$179,013
Marketing, events & communications:	$72,016
Consulting & professional services:	$68,000
Administration:	$7,790

For complete audited statements, visit www.blugenes.org or email nicola@blugenes.org

Look to the Future

VISION FOR TOMORROW

It's because of generous donors like you that Blu Genes is able to strategically invest our philanthropic resources in world-class genetic research, offering hope to patients and families with Tay-Sachs disease where currently there is none. Today we are supporting the groundbreaking studies and clinical trials that, not long ago, were thought to be a far-off dream.

Building on this momentum, we will continue to develop relationships with other organizations focused on Tay-Sachs, and other rare genetic diseases, in order to better understand and support the needs of patients and families. Patient support and advocacy groups have been working in this space far longer than we have, and we are stronger when we work together.

Our goal is to fund treatment options and a potential cure for Tay-Sachs disease, but we have no intention of stopping there. With your support, we will continue taking the bold steps to find and fund the promising genetic research that will make a real and tangible difference in the lives of patients and families living with dozens of other genetic disorders.

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Blu Genes Foundation is raising funds to advance gene therapy research and find a cure for genetic disorders, beginning with Tay-Sachs disease. We believe in offering hope where currently there is none.

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