The EHE Foundation (USA)
The EHE Rare Cancer Charity (UK)
The EHE Rare Cancer Foundation (Australia)
EHE Italia-Associazione Non Solo Laura ODV
EHE Canada

Quarterly Newsletter for the EHE Group
October – December 2023

the pledge

Edition 35

Contents

Front cover:

Some of the 'Remembering Steve' team

Welcome

This is the **35th edition of The Pledge,** the quarterly newsletter of the EHE Group, covering the fourth quarter of 2023. So as we say goodbye to 2023, we also want to wish all our readers a happy new year, and sincerely hope that 2024 will bring you all that you want and hope for.

We hope that you will enjoy and be inspired by the activities of the EHE Group and the global EHE community that are covered in this edition. As always, we want to say a massive thank you to all our EHE supporters who provide amazing energy, drive, and focus, and who fundraise, give their time, and so many other types of support. Without them we could not exist, and would have achieved nothing. We owe you all so much. ***"Just Live".***

Highlights

EHE Group represented at CTOS

Denise Robinson (The EHE Foundation US) and Hugh Leonard (the EHE Rare Cancer Charity UK) attended the Annual Conference of the Connective Tissue Oncology Society (CTOS) in Dublin, supporting important initiatives and speaking to key clinicians, researchers and patient advocates.

EHE-RCFA holds its AGM

Jonthan Granek, EHE Patient and Co-Founder, Director and Chair of the EHE Rare Cancer Foundation Australia chairs successful AGM for the Australian and New Zealand EHE patient community.

EHE Foundation announces 2023 Grant Awards and Giving Tuesday success

The EHE Foundation (US) were delighted to announce their 2023 grant awards to Dr Ajaybabu Pobbati, PhD at the Cleveland Clinic and Dr Munir Tanas, MD PhD at University of Iowa. Funding for these grants has largely come from grassroots fundraising, so The EHE Foundation were thrilled to also announce that their 2023 Giving Tuesday matched-funding campaign had raised over $160,000.

Italian presence grows under EHE Italia Associazione Non Solo Laura ODV

EHE Italia continues to grow with greater disease advocacy, enhanced communications with the Italian EHE community, fundraising, and clinician engagement.

Canadian campaigns continue

Canadian support continues on multiple fronts, with Michelle Hughes's **@MyJourneyToJustLive** platform and Fiona Ross continuing to deliver awareness, fundraising and huge EHE exposure.

Zebrafish progress reported by EHERCC

Ongoing research to develop a zebrafish model of EHE continues to overcome significant obstacles and is now looking to create xenotranplants (zebrafish that will host implanted human EHE cell).

Further details on these stories, and much more, can be found in this edition

the pledge

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01 Patient Support and Advocacy

Patient support within our global community predominantly comes in the form of support and encouragement provided by EHE patients to each other through the EHE Support Group closed Facebook page.

Advocacy focuses on promoting greater awareness of EHE, targeting better care and better outcomes for EHE patients globally. At the same time, the EHE Group foundations work tirelessly to champion the EHE cause, and act as a focal point for many important initiatives. The following stories cover just a few of the activities that the patient community and EHE Group are delivering.

Michelle is going to London in Ontario and London in the UK!

Since being diagnosed with EHE in August 2021, Michelle Hughes has become a tireless campaigner for the EHE cause. She is, in her own words, an Incurable Cancer Thriver, Public Speaker, and Blogger, and has established her very own brand, **@MyJourneyToJustLive.** Incredibly, Michelle now has a following of 125,000 people across all platforms.

Michelle started her campaign locally in Canada where she lives, and where she has been a prolific advocate for EHE. In October Michelle was delighted to post news of her upcoming events and activities. Michelle said:

> “Hey friends! I'm heading to London, Ontario for a keynote speaking gig and then running my first half marathon on Sunday in Niagara Falls! Together, we are spreading the ***Just Live*** message and this is just my small part.”

Michelle's media profile has also created a following internationally, with approximately 10% of her supporters based in the UK. So Michelle was super excited to confirm that she will be travelling to London, UK, in April 2024 to run as part of the EHE Rare Cancer Charity team in the London Landmarks Half Marathon. Michelle posted:

> “Hugh Leonard I'm coming! Y'all- I can't wait to make the trip over from Prince Edward Island, Canada to London, England to run in the half marathon event alongside some of you! Who will be there? 2024 is a big year for me. It's the year I was told I'd die from EHE by my first oncologist. So to celebrate my Thrivership, I have some huge goals for this year, one of which is to run the London Landmarks Half Marathon! Stay tuned!”

Hugh Leonard, Chair of the EHERCC is also very excited:

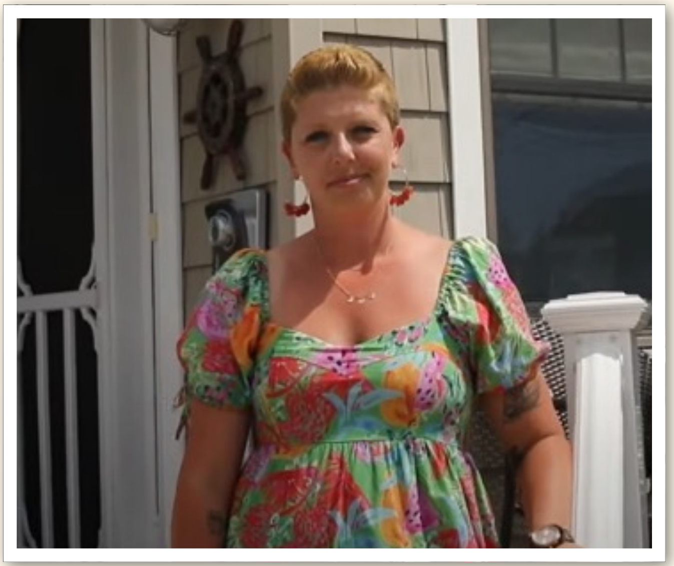
> “Patient support and advocacy comes in many shapes and sizes. Its not just about public speaking, although that is of course hugely important. It's also about patients telling their stories, about creating space and opportunities that encourage people to engage and learn about EHE, and to find out where and how they can help. It's also about patients knowing they are not alone, so being able to meet up with other patients dealing with EHE is also hugely important. Ultimately it's about hope, and nurturing a positive outlook, and this is always most effective when it is done by patients themselves. Why are we so excited about Michelle coming to London to run in the London Landmarks Half Marathon? Simply because by doing this, Michelle will be helping to tick all those boxes here in the UK, and internationally as our global community see reports of her visit. So we cannot wait to see her and her friend, Carolyn, in April. It is going to be amazing.”

Here at **The Pledge**, we are also looking forward to providing updates on Michelle's trip to the UK in April. Stay tuned, as Michelle would say. It really is going to be very exciting. And if you want to see more about Michelle and her work, then go to www.MyJourneyToJustLive.com. ■

01 Patient Support and Advocacy

Telling stories in a bookshop

Kate Czyzewski lives in the Jersey Shore community in the USA and is the Manager and Event Coordinator at Thunder Road Books. In November, she posted news that she had been the subject of a local news article talking about her role encouraging children to read books, and her life-embracing philosophy as an EHE patient.



The YouTube video was introduced by **NJ.Com**:

> “Diagnosed with an extremely rare cancer at 25, Thunder Road Books manager Kate Czyzewski’s story has had several unexpected chapters. After nearly a decade of living with epithelioid hemangioendothelioma, Kate reflects on her philosophy to embrace life by encouraging children to strengthen their love of reading so they can one day write their own stories.”

This inspiring piece explains how Kate, a teacher-turned-bookstore manager, has been instrumental in building a safe and happy environment for children at Thunder Road Books. Kate explains her passion for creating a community space where kids can be seen and heard, and advocating for children’s reading.

Diagnosed with EHE just three weeks before her wedding, nearly ten years ago now, Kate has most definitely not allowed her cancer to define her. It is clear that she has become a hugely valued member of her local community. As one person in the video explains, Kate’s very essence is felt by the community at large.

Our ***Just live*** motif epitomises the desire of EHE patients to live their lives fully, despite their sarcoma diagnosis. That spirit shines brightly in Kate Czyzewski and through her amazing work at Thunder Road Books. Keep advocating for those kids, Kate. Every community needs a Kate Czyzewski.

And here is the link to this wonderful story: www.youtube.com/watch?v=Gx-7r_tA71U. ■

Connecting our new members

One of the key goals of the EHE Group and the global EHE patient community is connecting new members with the people that can help them and support them once they have found the EHE Support Group.

In November, a new member in Italy reached out having joined the group, providing a description of their EHE journey so far and asking if there was an Italian group or Italian patients they could connect with, and finishing with a simple but very powerful comment:

> **“I thank you in advance, it is a joy to know that I finally have someone to talk to about this.”**

Jane Gutkovich was first to respond with positive news:

> **“Welcome to the group. There are many patients from Italy in this group and a separate Italian EHE FB group.”**

We love the immediacy of this sort of response, and while this may seem like a simple thing to report in **The Pledge**, we should not forget that not so very long ago, there was no connected EHE community, just a lot of individuals. We have certainly come a long way, now with a global patient community representing patients from over 80 countries, multiple foundations established, and an active programme of engagement with clinicians and researchers worldwide all working tirelessly to find new cures for EHE. So let's celebrate what that simple introduction to EHE Italia Non Solo Laua actually represents. ***Just Live.*** ■

01 Patient Support and Advocacy

Welcome new Board Member

The EHE Foundation (US) was thrilled to announce in the fourth quarter the appointment of a new Board Member to their Board of Directors:

> “The EHE Foundation was founded by patients, for patients. Continuing that tradition, we are delighted to announce that EHE patient John McFadden, Ph.D., CRNA, APRN, has joined our Board of Directors.”

With more than 35 years of experience in health care, Dr. McFadden has held positions as a nurse executive, hospital and university program accreditation surveyor, faculty member, and consultant. Today, he is Vice Provost of the College of Health and Wellness at Barry University and Professor of Anesthesiology.

Dr. McFadden has served on the board and as president of the Florida Association of Nurse Anesthetists (FANA) and as Treasurer of the Florida Association of Colleges of Nursing. At a national level, he served the American Association of Nurse Anesthetists (AANA) as a board member and as a Taskforce Chair, and member of the American Association of Colleges of Nursing (AACN). He currently serves on the editorial board of the BHSF Nursing & Health Sciences Research Journal.

Dr. McFadden has delivered more than 60 professional, national, and international presentations, workshops, journal articles, and textbook chapters. He is passionate about interprofessional collaboration and patient-focused healthcare.

New Communications & Development Manager

For the first time, The EHE Foundation (US) has a full-time Communications and Development Manager. Maggie Cameron is excited to bring her nonprofit communications experience to the Foundation:

> “Maggie will work to amplify the EHE patient voice in Foundation initiatives, and with Executive Director, Tammy Silverthorne, propel The EHE Foundation into its next chapter of growth.
>
> No stranger to EHE, Maggie is a 12+ year EHE survivor and has volunteered and consulted with the Foundation since its inception. Welcome, Maggie!”

The Pledge also wants to welcome her to the team and is excited, as the EHE global community will be stronger with Maggie involved.

Pan-European ambitions

One of the key objectives for 2024 for The EHE Rare Cancer Charity is to grow and enhance the connectivity amongst the European EHE patient community. Hugh Leonard explained:

> **“At the end of 2019 we had just started to reach out to the EHE patient community across Europe as we started to think about how to build a strong and inclusive pan-European EHE patient network. Initial responses were positive and we were excited, and then life got turned on its head with the arrival of COVID. This had multiple impacts across all societies and we felt it was not sensible or appropriate to try and build such a network in such a challenging environment.”**

The EHERCC therefore put its European collaboration ambitions on hold until the environment was more positive and settled. This also gave time for the EHE Group to progress further with its European research collaborations which were felt to provide a useful and positive foundation for re-engaging with patients across Europe. Hugh Leonard continued:

> **“The European research collaboration has progressed amazingly well and in December 2023, for example, we saw the official opening of the Pan-European EHE Prospective Registry which the EHERCC is helping to fund. This is the first such registry of its type and size for EHE anywhere in the world so is a huge achievement. 22 hospitals across Europe have joined the project which is being managed out of the Istituto Nazionale dei Tumori (INT) in Milan Italy, under the EURACAN STARTER project. So now we feel the time is right to restart the task of building an EHE patient network across Europe.”**

This was one of the topics that Hugh was able to outline when he recently had the great pleasure of meeting in London with Dora Balda. Dora is from Greece and her daughter has EHE. Hugh and Dora had a brilliant two hours talking about all things EHE. Dora’s passion and determination to make sure her daughter is Ok was phenomenal, and it was clear that she had done much reading. Hugh and Dora plan to meet again in the future. For Hugh the meeting also amplified both the need for, and the benefits that could flow from, the establishment of a coordinated European patient group.

The EHERCC hope to coordinate a European zoom call in the first quarter of 2024 to start the process. At **The Pledge**, we hope that we will be able to report on the development of this pan-European initiative in future editions of our quarterly newsletter. ■

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Studying and cancer care at the same place?!

It is not often that we have EHE patients posting news that they are studying at the same centre where they are being treated for their cancer, but that is exactly what Justin Darragh did this quarter:

> “Getting to study at the same institution where I receive care is truly a blessing. ***Just live!!!***”

Jane Gutkovich was quick to enquire what Justin would be studying:

> “Any chance you will work on EHE in the near future? That would be incredible! A short post here from you, and money, data, and tissue will flow in!”

Justin explained:

> “My Master's Degree is in molecular physiology! I'll be applying to medical school this next cycle. However, my thesis/work is mostly on acute radiation sickness and its effect on blood cells. However, I do know a number of people involved in bench work at the cancer center! Choosing a cancer-related project was just a bit too close to home for me, haha.”

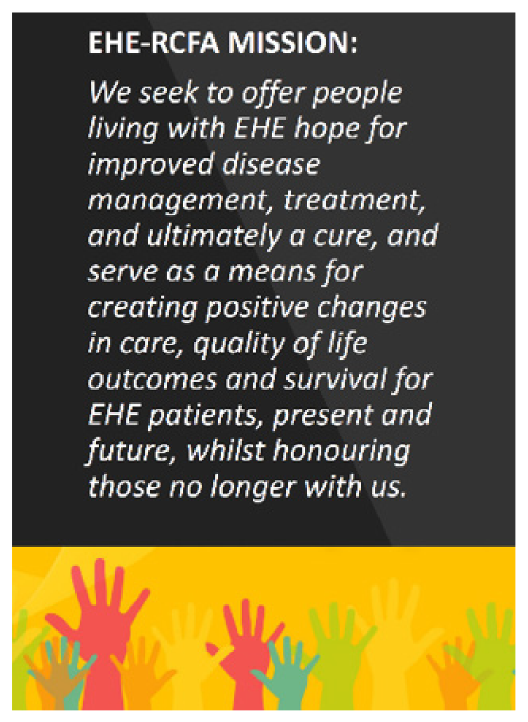
We love this story, Justin. Good luck with your ongoing education. Feel free to give us updates as you progress. We'd love to include them in future editions of **The Pledge.** ■

EHE-RCFA holds its Annual General Meeting

The EHE Rare Cancer Foundation Australia (EHE-RCFA) held its latest AGM on Sunday 3rd December. Jonthan Granek, EHE Patient and EHE-RCFA Founder Director and Chair, invited the EHE patient community to participate in what would be a virtual meeting to maximise the chance of patients across Australia and New Zealand participating.

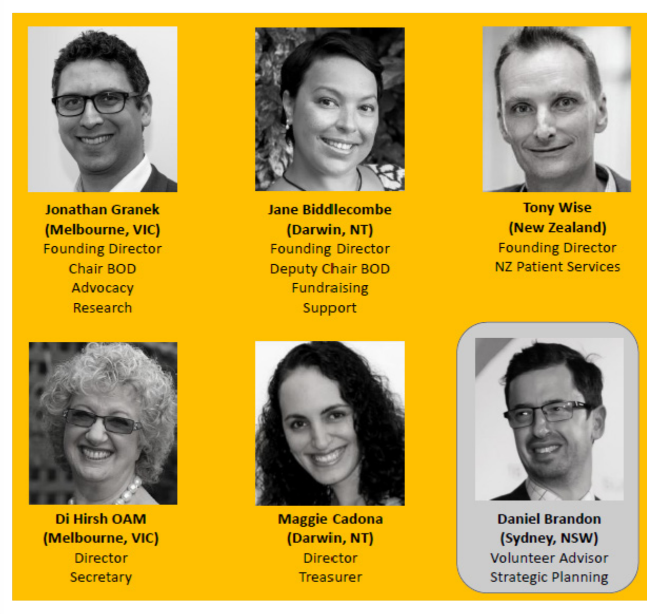
The meeting was well attended and Jonathan and the Board were able to lead participants through an extensive and inclusive agenda, showcasing the excellent work done by the EHE-RCFA over the past year.

The EHE-RCFA was also able to introduce their Board of Directors and their Medical Advisory Panel, to whom the EHE-RCFA are deeply grateful for the ongoing dedication and commitment to helping deliver the EHE-RCFA.

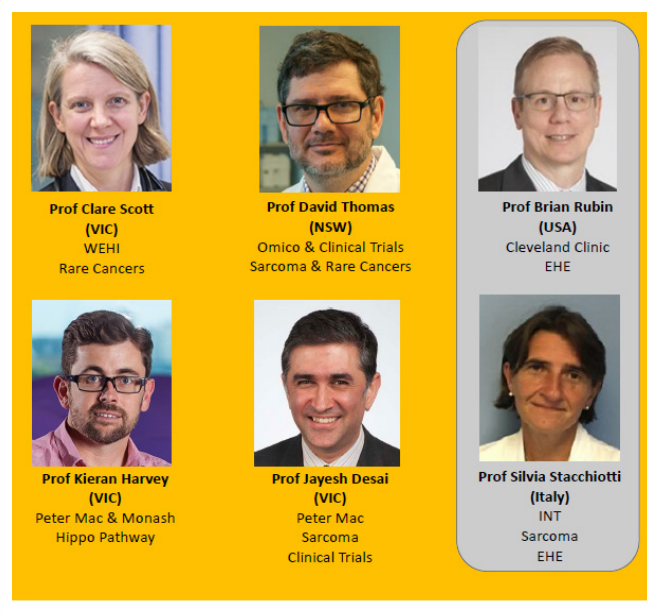


EHE-RCFA MISSION:

We seek to offer people living with EHE hope for improved disease management, treatment, and ultimately a cure, and serve as a means for creating positive changes in care, quality of life outcomes and survival for EHE patients, present and future, whilst honouring those no longer with us.



EHE-RCFA Board of Directors



EHE-RCFA Medical Advisory Panel

We want to congratulate EHE-RCFA on another wonderful year.

An important new resource

The EHE Foundation (US) posted news of an important new resource available for our EHE patient community.

New EHE patients often tell us they are overwhelmed with information when they are first diagnosed and don't know the best place to start. Many minds came together to create this new printable resource to help patients get organized before the next appointment with their doctor. Written for those newly diagnosed with EHE (and also useful for veteran EHE warriors), the new **Prepare for Your Appointment** checklist helps patients make the most of this time.


PREPARE FOR YOUR
APPOINTMENT
AFTER YOUR EHE DIAGNOSIS

BEFORE YOU GO

ASK YOUR DOCTOR

FIGHTEHE.ORG
1-877-460-4240

Check this important new resource out at: https://bit.ly/EHEchecklist.

01 Patient Support and Advocacy

Laughter with Cancer

Most people will agree that dealing day-in day-out with an ultra-rare cancer can be over-bearing at times. There is perhaps nothing better to counter this than laughter itself. Jonathan Granek had no hesitation therefore in sharing a video with the EHE community of him talking to Natalie Dewiyani at the Australia and New Zealand Sarcoma Association Conference in November. Jonathan explained:

> **“I am honoured to have had the opportunity to meet up with the extraordinary Natalia Dewiyani - champion of Laughter with Cancer and a member of the Australia and New Zealand Sarcoma Association's Community Advisory Panel. I am so glad to have you in our corner, Natalia, working to help address the needs of patients and families.”**

Natalia had recorded a short video taken at the conference in which she chatted to Jonathan as he explained his background, his diagnosis, and how he and the EHE-RCFA work to help sarcoma and EHE patients. Natalia said:

> **“Please listen to Jonathan's story, the courageous founder of EHE Rare Cancer Foundation Australia. Even when you were diagnosed with a stage 4 ultra rare cancer, your will to live and your commitment to make a difference is admirable. It's not just your cancer that is ultra rare but your generous heart is a rare gem too. If you are diagnosed with sarcoma, know that you are not alone. Are you also diagnosed or know someone with EHE? Please reach out to Jonathan. I'm so grateful I met such awesome people at the Australia and New Zealand Sarcoma Association conference.”**

Jonathan and Natalia were joined at the end of the interview by fellow EHE-RCFA Director Di Hirsh who was happy to finish by reminding everybody that the EHE Group moto is ***Just Live!*** ■

Closing the year with a huge Thank You!

Good Vibes for McKenna, established in memory of McKenna Helm, closed 2023 with a huge thank you to many people:

> “As we close out the year, our hearts are filled with gratitude. We’d like to thank everyone that has supported our vision and allowed us to truly make an impact by donating more than $29K to The EHE Foundation to support rare cancer research.”
>
> “EHE stands for Epithelioid Hemangioendothelioma and is a one-in-a-million rare cancer. McKenna truly embraced the ***“Just Live”*** lifestyle as many EHE patients do when they are diagnosed. Our hope is that you head into 2024 and ***“Just Live”*** to appreciate the small things in life and the amazing people around you.”

We also want to thank everybody at Good Vibes for McKenna, and everybody who supported their events, for doing so much to remember and celebrate McKenna and continue her support for The EHE Foundation and the EHE patient community. McKenna would be so proud of all you have achieved. ■

02 EHE Research

On the following research pages you will find updates on some of the EHE research that is ongoing, much of which is being funded by the EHE Group.

It is this research that will ultimately allow us to find new ways to treat and manage EHE.

We hope you will be inspired by the work taking place and the dedication and skill of the researchers that are delivering it.

Ikena shares encouraging data

The EHE patient community has been aware of the ongoing phase 1 trial of Ikena Oncology's TEAD inhibitor, IK-930, with updates posted by some of the EHE patients participating in the trial.


ikena ONCOLOGY

Ikena Oncology Shares Initial Positive and Differentiated Dose Escalation Data from IK-930 Phase I Trial and Reports Third Quarter 2023 Financial Results

There was, therefore, excitement in early November when Ikena Oncology formally published the initial positive results from the trial, with specific reference to epithelioid hemangioendothelioma, stating:

> **“Favorable safety profile in dose escalation shown to date; selective TEAD1 inhibition with IK-930 resulted in minimal treatment-related proteinuria without any dose reductions or treatment interruptions;**
>
> **Encouraging signs of clinical activity and tumor shrinkage in multiple patients with difficult-to-treat epithelioid hemangioendothelioma (EHE) during dose escalation;**
>
> **Additional IK-930 clinical data update planned for the second half of 2024; increased focus on enrolment of targeted populations including patients with mesothelioma and other NF2 mutant solid tumors.”**

Mark Manfredi, Ph.D., Chief Executive Officer of Ikena Oncology commented in the press release:

> **“This early look at the IK-930 dose escalation data strongly supports our differentiated approach to targeting the Hippo pathway. Importantly, following the target biology and initially focusing on EHE has allowed us to observe clinical activity of IK-930 early in our dose escalation.”**

These are indeed encouraging results for a novel drug. We look forward to being able to report in the future about both Ikena's IK-930 and the TEAD inhibitors being developed by other pharmaceutical companies.

For those interested in reading the full Ikena press release, you can find it at: https://www.globenewswire.com/news-release/2023/11/09/2777188/ ■

02 EHE Research

Highlights from CTOS 2023

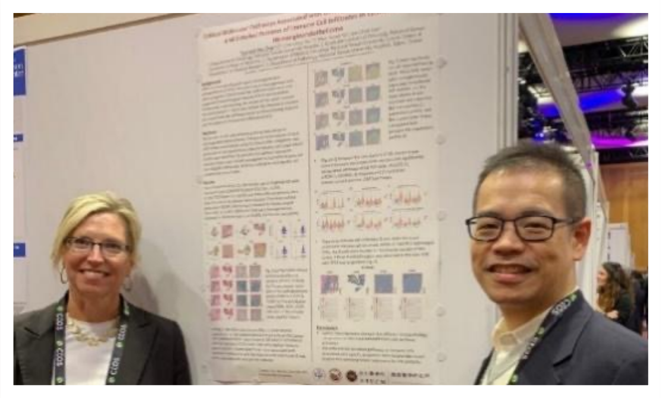
In early November, The EHE Foundation (US) Director of Research, Denise Robinson, and EHE Rare Cancer Charity Chair, Hugh Leonard, attended the Connective Tissue Oncology Society (CTOS) 2023 annual meeting in Dublin, Ireland. Every year, physicians, scientists, and advocates from around the world come together to advance patient care and increase knowledge in connective tissue tumors. EHE is a very rare type of soft tissue sarcoma that develops from the cells lining the blood vessels, classified as connective tissue.

The week began with the Ultra-Rare Sarcoma Working Group (URSWG) meeting. EHE is considered an ultra-rare sarcoma, defined as having an estimated incidence (or frequency of occurring) of less than 1 per 1,000,000 people. Dr. Silvia Stacchiotti led the meeting with Dr. Bill Tap and colleagues to discuss innovative approaches to conducting clinical trials in ultra-rare sarcomas. Thank you, Drs. Stacchiotti and Tap, and all who contributed to the meeting!

The EHE Foundation (US) and EHE Rare Cancer Charity UK met with, and are working collaboratively with, a team of clinicians, data experts, and drug repurposing experts to bring forward a clinical trial platform, PUSH – Pushing Ultra-rare Sarcoma through Hope. Denise Robinson commented:

> **“Stay tuned as this initiative grows enabling clinical trials that will investigate and find effective treatments for EHE. Many thanks to the Anticancer Fund and Italian sarcoma contingent at CTOS for bringing passion, talent, and experience to advance patient treatment options.”**

Denise also wanted to thank Dr. Tom Wei-Wu W. Chen, MD, PhD, attending physician, National Taiwan University Hospital, Taiwan (Republic of China) for his poster, “Critical Molecular Pathways Associated With Different Histopathology Features And Detailed Patterns Of Immune Cell Infiltrates In Epithelioid Hemangioendothelioma (EHE)”. Their research aims to uncover the critical molecular pathways based on histopathology features and the pattern of immune cell infiltrates in EHE. The study included four (4) EHE patients, but Dr. Chen confirmed that he envisions a larger study in the future.



Hugh and Denise also took the opportunity to meet with the team that is spearheading the current discussions with the European Medicines Agency (EMA) regarding securing approval for an extension of the label of Pfizer's drug Rapamune® (sirolimus) for the treatment of EHE. This is an important objective that could lead to open access to sirolimus for all patients in Europe, where the drug is currently only available to some patients if prescribed off-label.

Hugh and Denise agreed that CTOS was an important event in the annual calendar. Denise explained:

> "CTOS is an important opportunity to connect and collaborate with sarcoma experts who are bringing novel ideas and experience together to improve the lives of sarcoma patients. It was an honor for us to meet so many expert clinicians, researchers, and other patient advocates, who are all invested in finding treatments and cures for these complex cancers." ■

Zebrafish modelling of EHE continues

In 2018, The EHE Rare Cancer Charity (EHERCC) initiated research at the Bateson Centre at the University of Sheffield. The Bateson Centre is one of the largest and oldest zebrafish facilities in Europe, and are experts in developing models of human diseases in zebrafish. Zebrafish are used because they are cheap and quick to produce, if you are successful in creating the model you want. They are also largely transparent making it easy to see morphological changes as the fish develops.

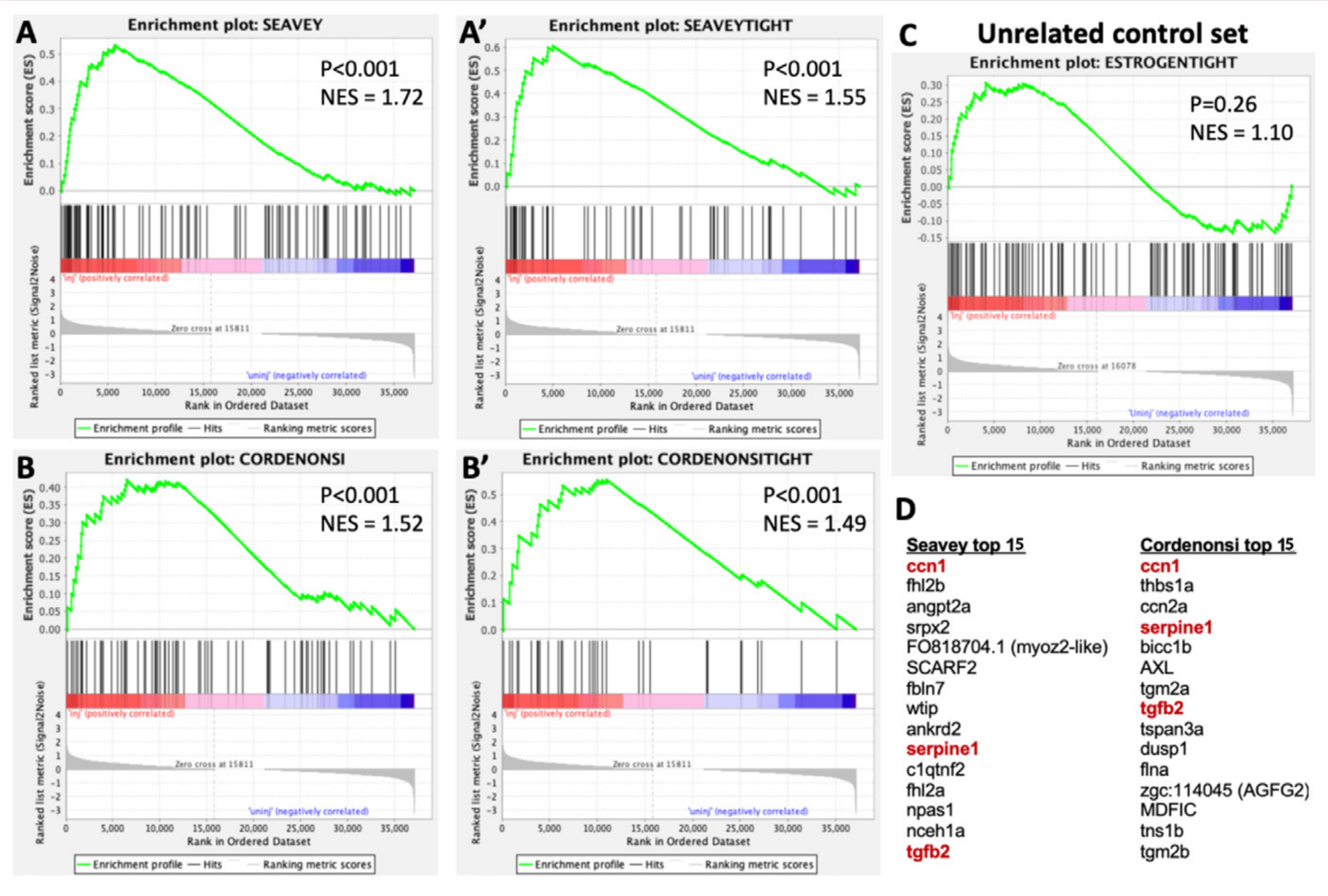
The TAZ-CAMTA1 model

Creating a human model of a rare sarcoma is not simple in a zebrafish, and the team faced many challenges early on in creating fish with EHE caused by the TAZ-CAMTA1 fusion protein. Early attempts, for example, demonstrated that the fusion protein was highly toxic to fish larvae which did not survive. This required the team to introduce the EHE chromosomal translation construct with a switch mechanism so that the TAZ-CAMTA1 could be 'turned on' once the fish had developed.

While several significant challenges were faced, the team in Sheffield continued to find solutions through extraordinary and painstaking attention to detail. At the start of 2023, the team, using a technology that analyses gene expression of all genes across the genome (RNAseq), initiated testing to see whether they could verify effects on other genes that are known to occur as a result of expression of the fusion gene in EHE, called the Seavey-set for EHE and the Cordenonsi-YAP signature set.

Testing for these effects in zebrafish however requires some detailed analysis as some human genes have two equivalent genes in zebrafish due to their partial genome duplication during evolution. This resulted in the team using a 'tight set' containing only genes with a single equivalent in both human and zebrafish, and a 'broader set' which included genes which had two equivalents in zebrafish. Subsequent testing (see Fig 1 on the opposite page) showed significant enrichment of both sets in the upregulated genes, showing that the TAZ-CAMTA1 transgene (that part of the injected construct that is inserted into the DNA) was having an effect consistent with expectations if it was working.

Testing for TAZ-CAMTA1 expression was also successful, but the team noted that the level of activated TAZ-CAMTA1 when 'switched on' was significantly lower than the level of the transgene control construct seen prior to switching. This was surprising as the analysis of downstream genes had shown a very convincing effect. Further work identified a number of possible causes for this reduced expression of TAZ-CAMTA1 associated with the TAZ-CAMTA1 construct. The team have now made modifications to the construct in new fish that are a month and half old and hope to be able to identify fish where the transgene has inserted successfully (called transmitters) by the end of March 2024.



Seavey top 15	Cordenonsi top 15
ccn1	**ccn1**
fhl2b	thbs1a
angpt2a	ccn2a
srpx2	**serpine1**
FO818704.1 (myoz2-like)	bicc1b
SCARF2	AXL
fbln7	tgm2a
wtip	**tgfb2**
ankrd2	tspan3a
serpine1	dusp1
c1qtnf2	flna
fhl2a	zgc:114045 (AGFG2)
npas1	MDFIC
nceh1a	tns1b
tgfb2	tgm2b

Fig 1: GSEA analysis results A,A') *Enrichment plots of both the "broad" and the "tight" Zebrafish-Seavey set. We expect that such genes (shown as black lines) will cluster to the left of the graph if there is TAZ-CAMTA1 activity, which can indeed be observed.* ***B,B')*** *The same can be seen for the "broad" and "tight" Zebrafish-Cordenonsi set.* ***C)*** *shows a control set (estrogen responsive genes) as an example of a negative result, black lines are not significantly clustered to the left.* ***D)*** *List of 15 most responsive genes in each set, shared genes between the sets are in red.*

The YAP1-TFE3 model

The ongoing difficulties creating animals with a high level of TAZ-CAMTA1 expression, and following discussions with the EHERCC, it was agreed that the research team should also start to try and create an inducible YAP1-TFE3 line as a potential alternative to creating an EHE model in zebrafish. YAP1-TFE3 is considerably shorter than TAZ-CAMTA1 and may be easier to express at a high level. In addition, it will also be a valuable additional model of this different variant of EHE.

Despite the work on the TAZ-CAMTA1 model, there was still concern that expressing human genes in zebrafish may lead to difficulties in obtaining high expression levels. Therefore, the team decided to make a zebrafish equivalent of the YAP1-TFE3, gene rather than use the human genes as a starting point. This involved aligning the protein sequence of zebrafish YAP1 and TFE3 with their human equivalents and determining where, in the zebrafish sequence, the two genes should be joined. An attempt to amplify these pieces from cDNA failed.

02 EHE Research

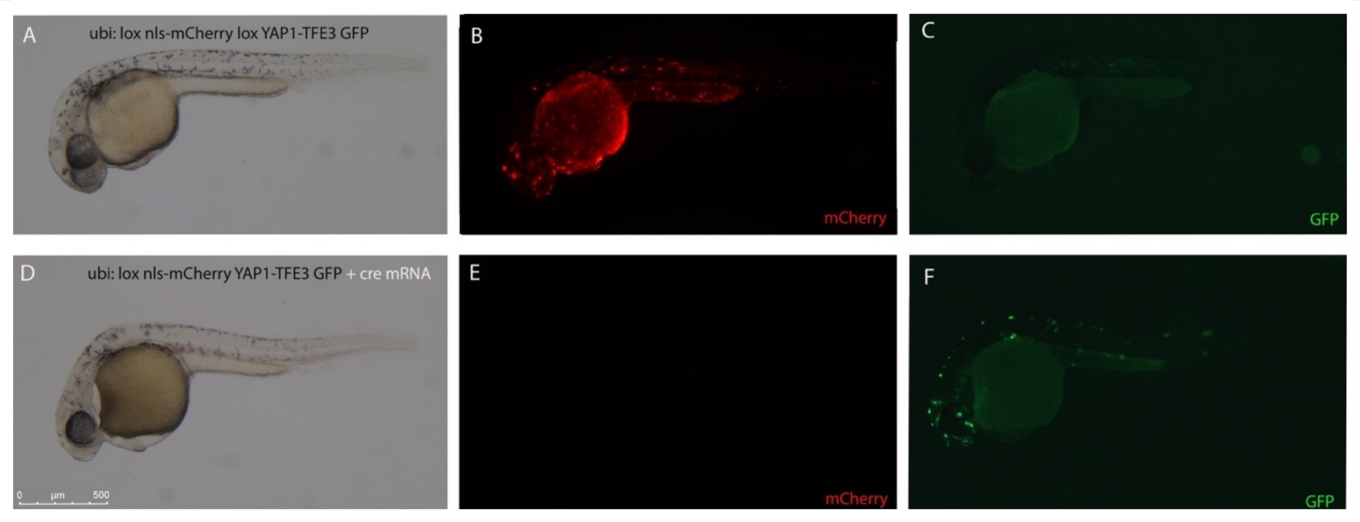


Fig 2: Switch test for YAP-TFE3 construct: *The embryo injected with the construct is shown* ***(A)****, and verified by mosaic mCherry expression observed as expected* ***(B)****, but no GFPNeon is visible showing the construct has not been induced* ***(C)****. When cre mRNA is coinjected* ***(D)*** *mCherry expression is strongly reduced* ***(E)*** *and GFPNeon can be observed* ***(F)****, showing that the switch is working.*

Further methods of creating a zebrafish equivalent of YAP1-TFE3 also experienced difficulties and it was therefore decided to synthesize the entire gene. This was done, and the resultant gene has now just been cloned into a switchable construct, as was done for TAZ-CAMTA1. The full transformation construct has been injected into embryos and the team have confirmed that the construct can be switched on by co-injection with cre mRNA as shown in Fig 2.

The team have now obtained the first transgenic embryos from this line and have started to raise larvae. To do this, the founders for this line were crossed to fli:CreGFP fish so that the larvae will have YAP1-TFE3 expression activated specifically in endothelial cells. Raising such fish was given high priority as tumour formation takes time. Approximately 20 experimental fish and 20 control fish were raised. However, the team will be generating more this year.

The team will also be doing further experiments to establish if YAP1-TFE3 is a more "potent" oncogene in fish than TAZ-CAMTA1. This has already started with the team co-injecting TAZ-CAMTA1 constructs or YAP1-TFE3 constructs, together with cre mRNA to activate the switches, and testing for levels of TAZ and CAMTA1 activity. This experiment suggested that YAP1-TFE3 is indeed more potent. In these experiments, embryos are mosaic, so only some cells in the embryo will have the oncogene expressing construct. It is therefore important to perform such comparisons on the real transgenic embryos that are now available for both TAZ-CAMTA1 and YAP1-TFE3. Once the team have embryos with the new modified TAZ-CAMTA1 construct, these can also be evaluated quickly for improvement of expression.

Using Xenotransplants; an alternative form of a zebrafish EHE model

Over the course of this project, it has become clear that getting zebrafish EHE tumours remains difficult. If tumours continue to be low in frequency or are slow to develop, it may be difficult to exploit the fish model. Therefore, following consultation with other researchers working with EHE models, the Sheffield team have contacted Dr Pasquali at the Istituto Nazionale dei Tumori (INT) in Milan in order to obtain EHE tumour cells from the EHE cell line developed by the INT research team. These cells can be transplanted in zebrafish larvae to study behaviour of these cell lines in a vertebrate in vivo environment. The two institutes are currently finalising MTAs for this transfer. Sheffield hope to have cells available in March.

Forward focus

The team in Sheffield will be continuing their work on all fronts with the following key objectives:

1. In light of the development of mouse EHE models and human cell lines, a key priority is to initiate the establishment of xenotransplantation models (injecting human cells into fish embryos) as this will provide a different form of model. If successful it also exploits the transparency and size/cost advantage of the fish system most efficiently. Once the team have established good labelling procedures, transplantation sites, cell numbers, etc. and shown that the system can work, EHERCC will discuss uses of this type of model with the Sheffield team and other EHE researchers.
2. The research team will continue to directly compare the activity of TAZ-CAMTA1, YAP1-TFE3; and modified versions of TAZ-CAMTA1 to check for comparative levels of YAP/TAZ activity. This will allow them to see whether these alternative approaches have solved the expression issues that have proved to be a significant difficulty in the original TAZ-CAMTA1 model fish. If the expression issue has been resolved, EHERCC will need to discuss with the research team and other EHE researchers how such models can best be incorporated into the overall ongoing EHE research initiative.
3. The team will continue to monitor and bank their current zebrafish lines. ■

The EHE Foundation Research Grants Program update

Through the generous financial support of its donors, EHE patient participation, and the growing community of expert researchers investigating EHE, The EHE Foundation (US) is proud to award research grants advancing the mission to find treatments and a cure for EHE.

In 2021, The EHE Foundation (US) formalized its research grants program, and the program continues to grow in researcher interest, research project applications, and total dollars granted. In the fourth quarter, as they announced their 2023 EHE Foundation Research Grant Awards, The EHE Foundation (US) thanked all who give to fund EHE research, The EHE Foundation (US) Advisory Board and the grant reviewers for their input and expertise, and especially those affected by EHE who have participated in research to help make these projects possible.

Progress reports for The EHE Foundation (US) active grants can be seen below.

Ajay Pobbati, PhD | Cleveland Clinic: Repurposing an FDA-approved Drug for EHE Treatment

The EHE Foundation (US) awarded Dr. Ajay Pobbati a grant in 2022 which was completed in the fall of 2023.

The goal was to identify an FDA-approved drug that could sequester TAZ-CAMTA1 (TC), TEAD, or both in the cytoplasm. TAZ-CAMTA1 (TC) resides in the nucleus of the cell and plays a key role in causing EHE. By relocating TC to the cytoplasm (moving it out of the nucleus), the drug would interfere with or stop the formation of EHE.

Dr. Pobbati shared in his final project report that they have identified a class of drugs as regulators of TC localization and stability. Dr Pobbati explained:

> **“When EHE cells were treated with these inhibitors, TC was mobilized into the cytoplasm and ultimately induced apoptosis (death of EHE cells).”**

Overall, approximately 4000 drugs or small molecules were screened to identify an FDA-approved drug as a potent inhibitor of TC. Future aims of this work seek to further evaluate the identified drug in mouse models of EHE. If successful, it may serve as a basis to initiate a clinical trial to test the efficacy of this drug in patients with aggressive EHE who have no effective treatment options.

We are delighted that Dr. Pobbati has generated these hopeful results, which served to support his subsequent 2023 EHE research grant application to further expand these findings. The EHE Foundation (US) has granted the 2023 award (see below), and we look forward to the team's updates in mid-2024.

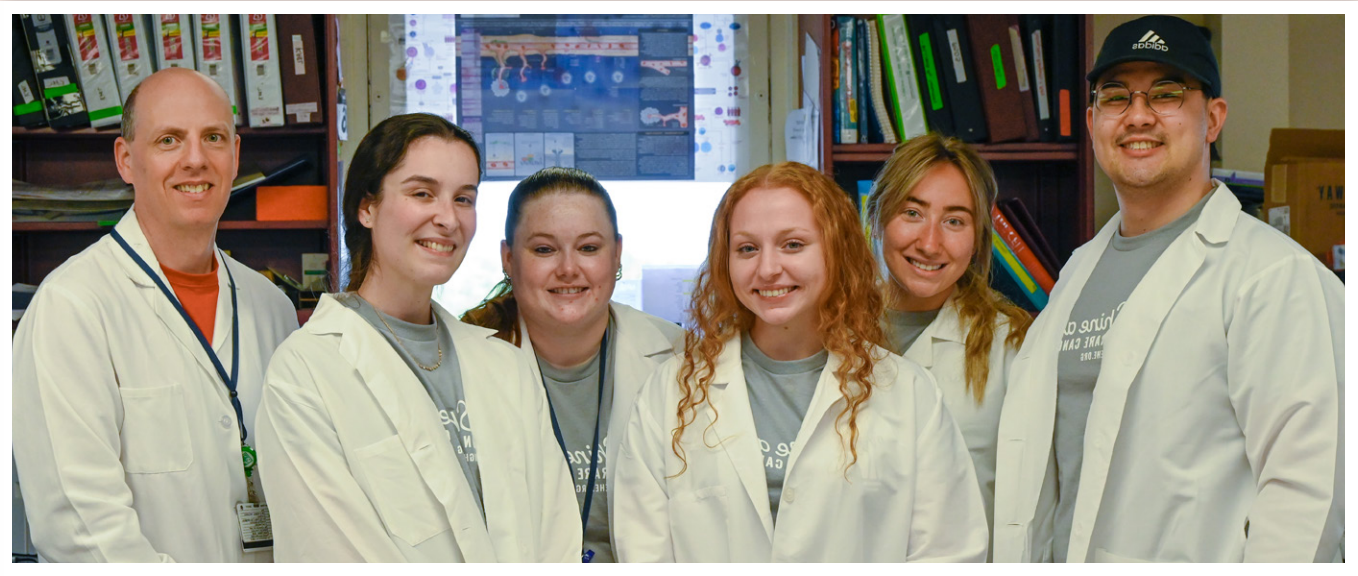
John Lamar, PhD | Albany Medical College: TAZ-CAMTA1 Regulation by the Calcium Sensor Calmodulin

The EHE Foundation (US), in partnership with the EHE Rare Cancer Foundation Australia, awarded Dr. John Lamar a 3-year grant in 2021 to investigate if a protein called Calmodulin (CaM) can repress the oncogenic activity of the TAZ-CAMTA1 fusion protein that plays a causal role in more than 90% of all EHE.

The hypothesis is that CaM binds to the TAZ-CAMTA1 fusion protein and blocks its importation into the nucleus where it would normally bind to TEADs and promote the expression of other genes that are necessary for the survival and growth of EHE cells. Initially, the project proposed using fibroblasts expressing TAZ-CAMTA1 to study CaM because there were no EHE cell lines available. However, EHE cell lines have now been established, and the Lamar Lab has spent several months optimizing their use in all the critical assays necessary for this work.

The initial results reported, using the EHE cell lines, have found that CaM and TAZ-CAMTA1 co-localize in the cytoplasm, but not the nucleus, of EHE cells. This is consistent with their hypothesis that CaM binds to TAZ-CAMTA1 in the cytoplasm and prevents it from entering the nucleus. However, although CaM is expressed in all cells, the initial work suggests that the amount of CaM produced by EHE cells is not sufficient to prevent most of the TAZ-CAMTA1 from entering the nucleus. This is why CaM is not able to prevent EHE formation and growth in cells that have a TAZ-CAMTA1 fusion.

Dr. Lamar predicts that if they can increase CaM expression in EHE cells or treat EHE cells with a peptide that “mimics” CaM, it will reduce the amount of TAZ-CAMTA1 in the nucleus and inhibit its function.



Dr Lamar (far left) and his team

John Lamar, PhD | Albany Medical College: Use of pre-clinical EHE models to identify druggable pathways to treat EHE

The EHE Foundation (US) awarded Dr. John Lamar a 3-year grant in 2022, with the goal of identifying FDA-approved drugs that inhibit EHE growth, providing the rationale to test if these drugs can be repurposed for use in EHE patients.

In Dr. Lamar's end-of-year update, he writes:

> “We have made significant progress on this project over the initial 18 months of funding. In collaboration with Dr. Brian Rubin, we have been working with the first EHE cell lines ever developed and have completed the extensive characterization and optimization necessary to effectively use these cells for this project.”

Once key assays were optimized, the Lamar Lab used these EHE cells to perform a drug screen aimed at identifying compounds that could block EHE cell viability. This drug screen revealed 17 drugs that reduce EHE cell viability without impacting the viability of normal cells. Of the 17 drugs identified, four of these drugs belong to a family of drugs that are safe and have minimal side effects in humans. Ongoing work is investigating the mechanism through which these drugs inhibit EHE cell viability.

Future work will include developing mouse models of EHE to test if these drugs can prevent EHE tumor growth and metastasis. If these tests prove that these drugs are effective in pre-clinical models of EHE, it may provide the rationale for a clinical trial to test if these drugs are effective in patients with aggressive EHE. Dr. Lamar notes that since these drugs have minimal side effects in humans, they may also provide an effective and safe alternative to the current “watch and wait” strategy available to patients with inoperable chronic or indolent EHE

02 EHE Research

The EHE Foundation Research Grants Program update

The fourth quarter saw The EHE Foundation (US) announce their 2023 EHE Foundation Research Grant Awards. Denise Robinson, Director of Research, explained:

> “We were fortunate to receive more proposals than ever to explore this ultra-rare cancer. With the guidance of our Research Committee, Advisory Board, and expert reviewers, we are pleased to announce the research grants awarded in 2023.”

Ajaybabu Pobbati, PhD | Cleveland Clinic: Harnessing FDA-approved drugs to gain mechanistic insight into the regulation of the TAZ-CAMTA1 fusion protein

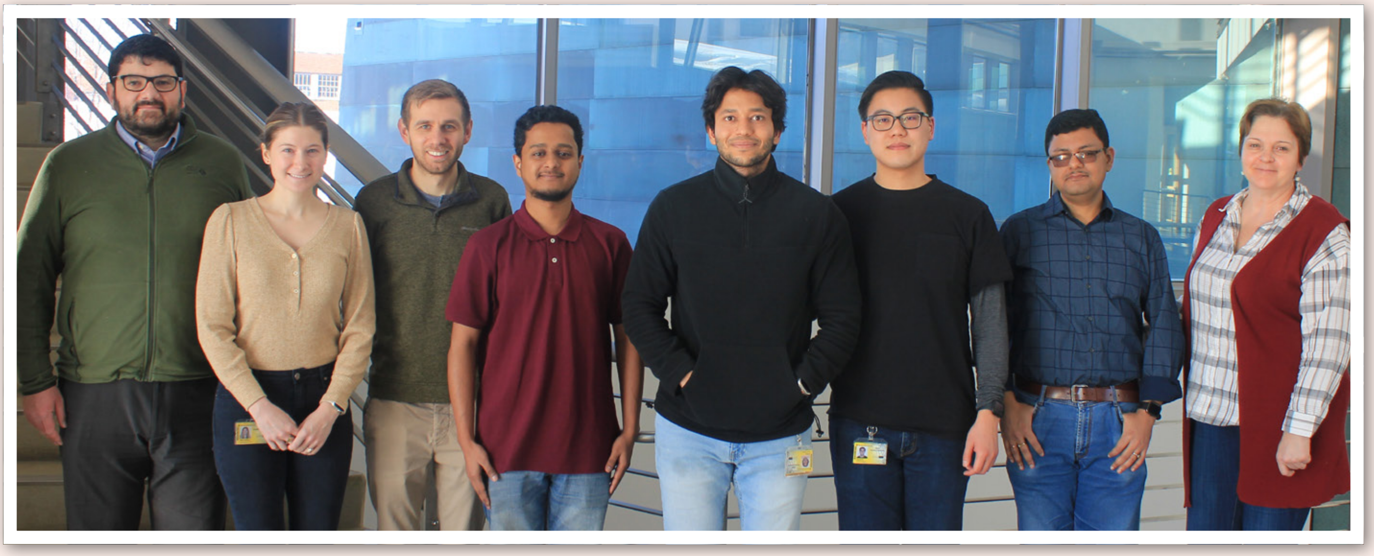
This year’s grant allows Dr. Pobbati to build upon the work funded during the 2022 Grant Cycle. The project evaluates FDA-approved drugs to understand how they could work at a molecular level to destabilize an EHE cell and cause it to degrade and disappear. Ultimately, the project aims to find an FDA-approved drug with a good safety profile that could be used to treat unresectable, aggressive EHE.

Munir Tanas, MD | University of Iowa: Creation and Characterization of an EHE Extended Primary Cell Culture

Dr. Tanas’ project was an important project to fund because it addresses a fundamental limitation in EHE research: lack of EHE cells to use for EHE research.

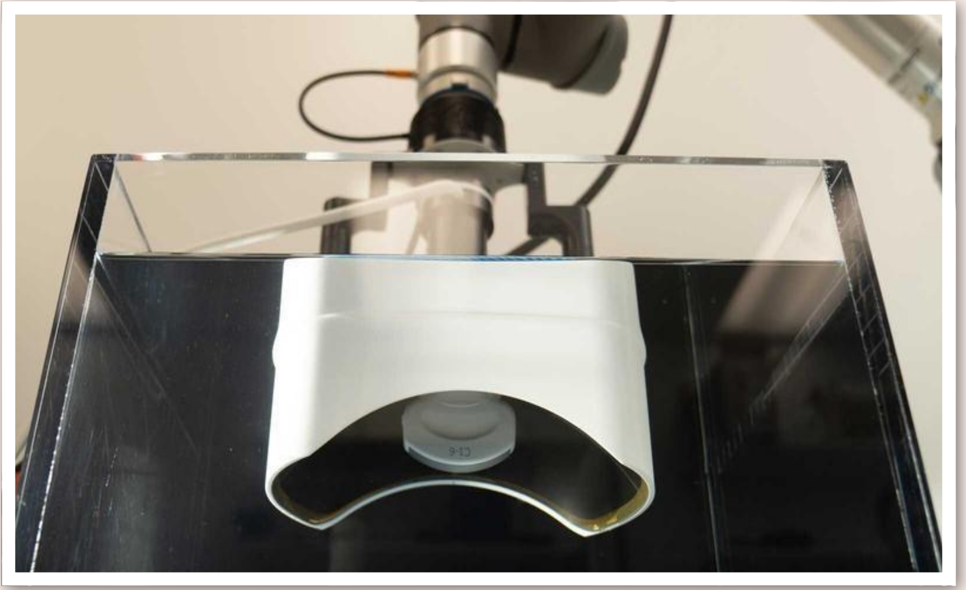
Tissue donation through the EHE Biobank collects excess tumor tissue from patients during surgical procedures. Tumor tissue is sent to key research partners, like Dr. Tanas, to create standardized EHE cell models or lines. These will then be made available to researchers worldwide. Tissue donation allows patients to directly impact the quality and pace of EHE research.

We congratulate The EHE Foundation (US) on another excellent grant round and also want to join The EHE Foundation (US) in profoundly thanking all those fundraisers who have worked so hard this year and everybody who has donated funds that enable this important annual grant program to continue. ■



Dr Tanas (far left) and his team

Excitement with new technology



The fourth quarter saw news of the FDA approval in the USA of new ultrasound technology for dealing with liver tumours. The new technology, which provides a non-invasive alternative to surgery, chemotherapy, and radiation treatments for cancer, was developed at the University of Michigan. The press release from the Rogel Cancer Center, University of Michigan, explained:

> **“Histotripsy is an exciting new technology that, although it is in early stages of clinical use, may provide a non-invasive treatment option for patients with liver cancer. Hopefully, it can be combined with systemic therapies for a synergistic therapeutic effect," said Mishal Mendiratta-Lala, M.D., an assistant professor of radiology with Michigan Medicine and principal investigator on the trial at U-M.”**

It is always exciting when pioneering research delivers new and improved treatments for cancer, and the news was picked up and posted by several EHE patients. However, while we hope that this may have application in the future for EHE, we need to recognise that to date, we are not aware of any EHE patients with liver presentation who have been involved in trials of the technology.

To read more about histotripsy go to: https://www.tandfonline.com/doi/full/10.1080/02656736.2021.1905189. ■

02 EHE Research

How you can help find a cure for EHE

Registries!

A critical component of the overall research program for any cancer is gathering data from patients about all aspects of their cancer journey. By collating, analysing and presenting this data once anonymised, patients, clinicians and researchers can begin to understand the biology of the disease, and through that process, begin to identify possible strategies for delivering better and more effective treatments.

If you are an EHE patient, please, please join the EHE Global Registry and make sure your information is helping to find a cure.

Biobanking!

Access to biological samples is also a critical component of EHE research initiatives. Tissue, fluid and blood samples provide researchers with critical access to actual EHE biological specimens that allow researchers to investigate and understand the natural history and development of EHE; investigate new hypotheses; and develop and test both new and existing drugs to see if they will help combat the disease. The EHE Group has established dedicated EHE biobanks in both the USA and the UK, and has agreed biobanking capabilities in Australia and Canada.

Today, EHE biospecimens donated by the EHE patient community are helping drive critical research:

1. EHE tumor samples are being used to deliver EHE human cell lines that will assist in the evaluation of drugs to combat EHE;
2. Tissue and blood samples have helped to identify and validate a likely biomarker of EHE.

If you are an EHE patient, please, please support EHE biobanking and make sure your samples are helping to drive EHE research.

If you need help or further information on the EHE Global Patient Registry or on how to access biobanking for your samples, please contact any member of the EHE Group or visit any of the EHE Group websites. ■

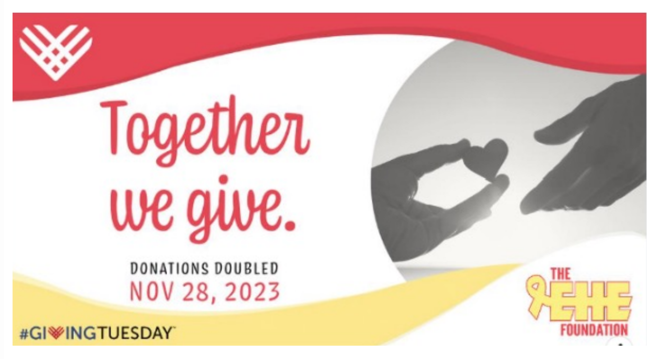
03 EHE Fundraising

Highlights of some of the fundraising activities that our supporters are delivering can be found in this section of our newsletter.

This fundraising is key to our success. It is the ‘life blood’ of our EHE Group. We thank every single person who has organised a fundraiser of some variety, supported fundraising in any way they can, or has donated to these event. We could not have achieved the progress we have without your wonderful contributions.

Giving Tuesday is another huge success

The fourth quarter saw The EHE Foundation (US) once again launch their Giving Tuesday matched-fundraising campaign. As they explained:



> **“Giving Tuesday is a day of global generosity aligned with shared values. With you, we share a vision of a world where EHE is easily diagnosed and treatable. Each day, EHE patients live with uncertainty while The EHE Foundation works hard to find answers. Now is your chance to double your donation and make a difference for those diagnosed with this one-in-a-million cancer.”**

Giving Tuesday is a global movement to celebrate and encourage giving on the Tuesday after Thanksgiving. This year, The EHE Foundation (US) Board of Directors personally guaranteed to match all donations up to $75,000, an extraordinary sum and a fantastic commitment to The EHE Foundation's core objectives.

A matched-fundraising campaign however is of no value without support from grassroots donors, and once again the EHE patient community and their support teams exceeded expectations. Many encouraged and promoted participation by sharing their EHE stories, connections, and The EHE Foundation's mission with friends, family, colleagues, and their local communities. A total of 323 individuals made personal donations to the campaign, while another 13 people organised and held their own fundraising events.

As a result, the Giving Tuesday 2023 campaign raised over $160k for EHE research. Tammy Silverthorne, Executive Director of The EHE Foundation was hugely impressed:

> **“I am blown away by the generosity of the EHE community and The EHE Foundation Board of Directors. Together, we raised over $160,000 to fund EHE research. Our work is only possible because of you, and we are grateful to have your support.”**

03 EHE Fundraising

With such a huge result, everybody wanted to express their deep and profound respect and gratitude to the Board of Directors for their wonderfully generous support, and to all those who donated to the cause.

Denise Robinson, Director of Research, also wanted to highlight why such fundraising is so important. Denise noted:

> “It is timely that The EHE Foundation’s 2023 grant awards, largely funded by the 2022 Giving Tuesday campaign, have recently been announced. The research we support may help identify potential treatments for EHE from existing drugs and may advance the creation of EHE cell lines and models needed for research. It really is hard to overstate the importance of our annual Giving Tuesday fundraising.”

We want to join Tammy and Denise in congratulating The EHE Foundation (US) Board of Directors, management team, and all the Foundation’s brilliant supporters for delivering such a successful campaign. ■

SCFC continues its fantastic support

Raising funds for EHE research requires the infrastructure to allow people to efficiently donate; be able to access the tax advantages usually available for such donations; and be confident that the funds will be properly managed and distributed. Our global community has several cases where this has been achieved by establishing dedicated EHE foundations and charities. But this is not always possible and so some patients have sought out different ways to achieve the same goals.

In Canada, Fiona Ross approached the SCFC (Sarcoma Cancer Foundation of Canada) to discuss what options might be available. The SCFC were keen to help and agreed to establish an EHE-specific fund within their structure to enable our Canadian community to raise and donate funds for EHE Research.

As “Giving Tuesday” approached, Fiona Lousie was once again reminding her fellow Canadians of this option:

> “Just a gentle reminder to any Canadians wishing to donate during "Giving Tuesday" or the holiday season that EHE research here is through the Sarcoma Cancer Foundation of Canada. You can donate via the website or by mail. Please put EHE in every box or note that you can so it is clear your donation is for our dedicated EHE account. You will get official tax receipts.”

Fiona also wanted to remind everybody that very substantial funds had already been raised and were driving an active EHE research programme in Canada. She also wanted to thank everybody globally for their past, present and hopefully future fundraising support for EHE research, wherever they live. Fiona said:

> “We are currently funding a million dollar project (only $150,000 left) for Canadian patients and research. You can find details at: http://sarcomacancer.ca/news?fbclid. Thank you to all those doing the work in the foundations, fundraising and telling their stories. It **IS** making a difference.”

If anybody has any questions about the SCFC EHE fund, how they can donate, of indeed any questions about EHE, then Fiona is happy to be contacted at fightehecanada@gmail.com.

It just remains now for us to thank Fiona and the SCFC for their great work in making it possible to raise funds and deliver EHE research in Canada. ■

Remembering Steve!

It was with sadness but also great love that Jessica James posted news in October of the ‘Shakedown for Steve’ event held in Merrionette Park, Illinois, in memory, and to celebrate the life of her brother, Steve. Jessica explained:

> “On September 22, we lost my brother to EHE ten months post-diagnosis. He was 35 years old. He was a light in this world and will be greatly missed by so many. Fifteen days after he passed, we decided to still hold a benefit in his name that was supposed to go towards paying for his medical treatments, but will now go towards The EHE Foundation - per his request. We lost Steve, but EHE has gained an army of people ready to fight this terrible disease in honor of the best guy I’ve ever known.”

The event was, not surprisingly, very well attended by so many of Steve’s family and friends. And after it was done, Jessica wanted to say a massive thank you:

> “What a long, strange trip it’s been. It seems too small to simply say thank you. To all the volunteers, the people who attended the outing, the wake, the funeral, the benefit, to those who sent their condolences or shared a story or a picture or a hug, our hearts are shattered and yet so full at the same time.”

03 EHE Fundraising

> “Thanks to the group of men in this picture (and their wives, let’s be serious), Steve’s legacy will live on. Thanks to these men and all of YOU, we sold a total of 247 wristbands for the Shakedown at Bourbon Street on Saturday, and raised more than $20,000! Steve’s wishes were to raise money for The EHE Foundation, which is where the proceeds from this benefit will go.”

> “This is not the end, but only the beginning. We will continue to carry on Steve’s legacy raising money and raising awareness for this rare cancer, EHE.”

In the true spirit of the man they honor, Steve’s family and friends are busy planning their next fundraising event, the 2nd Annual Big Steve Day on June 29, 2024, at Stoney Creek Golf Course in Oak Lawn, Illinois. ■

Milan Craft Fair another great event

Following the success of their participation in 2022, Andrei Ivanescu and Caterina Colaci from EHE Italia Associazione Non Solo Laura ODV had no hesitation in taking a stand at the L’Artigiano in Fiera International Fair for the 2023 event in December. Andrei explained:

> “This year too, like last year, our Association will participate in the L’Artigiano in Fiera International Fair held in Milan from 2nd to 10th December. We are very happy to have this opportunity once again, as last year people donated many artisan products to sell; we were able to collect many donations; and meet many new people who were passionate about our project.
>
> With four weeks to go until the start, it is really important to try to get as many people as possible to contribute: the more items we get, the more funds we can raise, and the more we can donate to research! So if you have any craft skills, or know people who would like to donate some handmade items, please contact us so we can sell them at the fair.”

The response was fantastic and once again led to a wonderful experience as Caterina explained:

> “A combination of solidarity, commitment, discovery of talented artisans, and human warmth made this year's participation an unforgettable experience. Thanks to the generosity of the participants and craft enthusiasts, we were able to achieve our goals of fundraising to contribute to EHE research and patient support.”

Everybody involved agreed that L'Artigiano in Fiera offered a unique stage to meet new people and strengthen bonds with those that they had already had the privilege of meeting last year. Andrei and Caterina continued:

> “Stalls filled with artisan creations provided the backdrop for passionate conversations, sharing life stories and nurturing human connections that go beyond commercial transactions. It was a beautiful chapter for our association. With successful fundraising, meeting new people and strengthening bonds, the association has demonstrated that solidarity, passion for craftsmanship and commitment to research can go hand in hand, creating an experience that goes beyond the confines of the fair.”

So it was with sadness but lots of pride that Andrei and Caterina posted news that the event had come to an end:

> “This concludes our second experience at L'Artigiano in Fiera! With some sadness we say goodbye to our stand, hoping to see you again next year. We would like to thank all the people who donated items for us to sell, who came to visit us during the fair, both friends and new acquaintances, and all those who supported us even from afar! We hope we can do better and better and spread more awareness about this rare disease, raise funds and support research. Big hugs to everyone!”

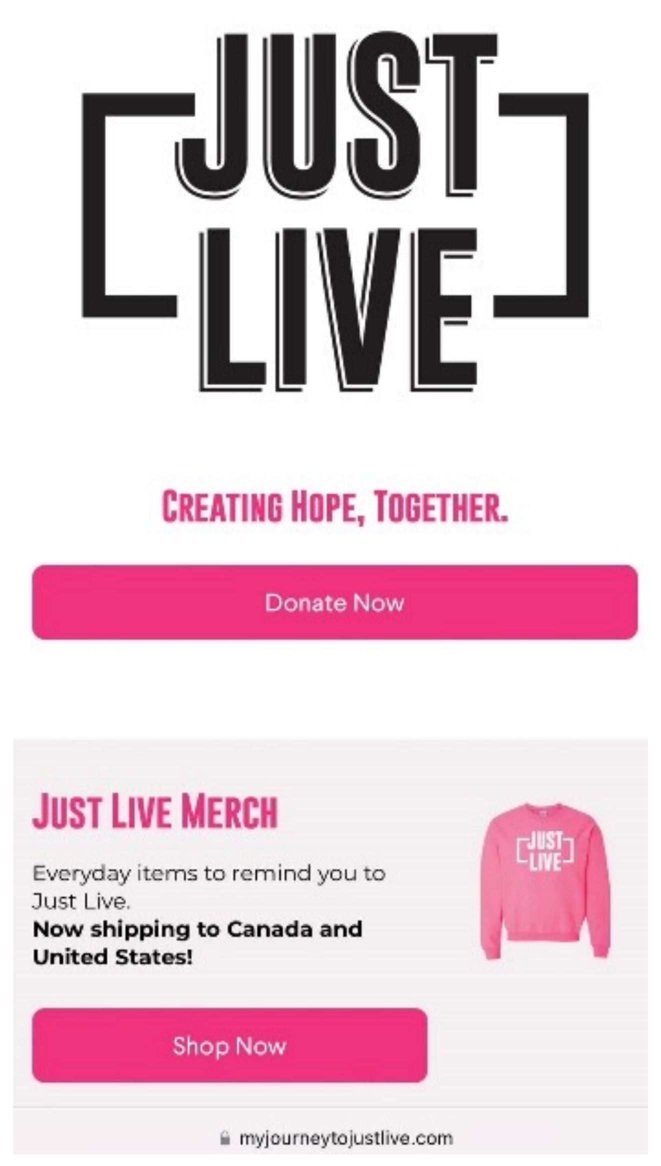
We want to congratulate Andrei, Caterina and everybody else who was involved for another wonderful and warming event. It really was a fantastic effort. ■

03 EHE Fundraising

Just Live **'Merch' on sale!**

Michelle Hughes was once again driving her fundraising activity with news that her latest ***Just Live*** merchandise had launched!

> “Hey y'all! ***Just Live*** MERCH is back and this time offering shipping across CANADA and the US! International shipping will be available soon- just working out the crazy shipping rates and trying to find a solution!”



Everyday items to remind you to Just Live.
Now shipping to Canada and United States!

myjourneytojustlive.com

Michelle included a short explanation of her story for those who were perhaps new to the group, and why every dollar raised through sales of her merch would mean two dollars for EHE research thanks to a fantastic offer to match funds raised:

> “To those new around here, I was diagnosed in Aug 2021 with innumerable lung tumours, 17 liver, 1 thigh and 1 knee tumour. I started running in Jan 2022 to set myself up for success. I take Sirolimus and Naproxen (for pain). Last Sunday I ran 10km in 50min which was a PB for me!
>
> I am hosting this fundraiser where the Sarcoma Cancer Foundation of Canada matches all donations, so each piece of the ***Just Live*** merch will produce up to $20-$40 directly for the EHE research funds! So please consider if you are looking for some ***Just Live*** clothes.”

Michelle was also excited to be able to report the year end figures:

> “The total of all merch sales in 2023 was an amazing $35,900 which with matching by the SCFC doubled to a staggering $71,800.”

Michelle also wanted to remind everybody in our global community why she was raising the funds, and also to remember one special person:

> “I do this for me, I do this for you and today, I'm thinking of the recent passing of Ashley Quehe - I'll never stop spreading our ***Just Live*** motto.”

Thank you Michelle for all you are doing. You inspire so many and act as a beacon for the EHE cause. ■

Team Mulligan drives on

Our EHE community has always recognised that EHE is a relentless adversary, and so we must be equally relentless in all that we do to combat the disease. Team Mulligan, supporting their son Joe, is a shining example of such boundless drive and determination to keep making a difference. In October, Jennifer Mulligan posted news of an evening when Joe's basketball game had been cancelled. Rather than seeing this as a disappointment, Joe simply changed course and went to the school where his father is an admin and was talking about Joe and EHE. Joe's appearance gave the evening real meaning, allowed Joe to talk about how the funds they had raised would make a difference, and to personally thank them for raising over $1,000 for EHE research.

Next, they set their sights on Giving Tuesday. With their outstanding supporters heeding the call for gifts, the Mulligans brought in close to $9000 with their Giving Tuesday campaign! With gifts in honor of Joe from family, friends, and two different school districts (North Rockland Central School District and Briarcliff Manor School District), the Mulligans were again gracious and humbled by the show of support.

Well done Joe and Team Mulligan, and a huge thanks to their fantastic supporters. ■

03 EHE Fundraising

Upcoming events

As we move into 2024, the EHE Group entities are already looking forward to their annual fundraising calendars.

The EHE Rare Cancer Charity will have a team of 50 runners taking part in the London Landmarks Half Marathon on 7th April. As readers will have seen, there is excitement this year as the team will include Michelle Hughes, EHE Champion extraordinaire from Canada, and her running partner Carolyn Dohoo. Training is well underway for all the runners. We love them for getting out there in the cold.

The EHE Rare Cancer Charity also has 20 places in the RideLondon Essex 100 cycling sportive which will take place on 26 May. The long ride is 100 miles, but there are also 40 mile and 60 mile options for those who want to help raise funds. So it you are interested in a place, please contact Hugh Leonard on his email at hleonard@ehercc.co.uk. ■

RIDE LONDON 100 MILE EVENT

SUNDAY 26th MAY 2024

WE NEED YOUR HELP AGAIN!

CAN YOU RIDE FOR US?
WOULD FAMILY MEMBERS RIDE?
WHAT ABOUT FRIENDS?
MAYBE WORK COLLEAGUES?

We thank you all for your amazing fundraising and donations. We could not have achieved the progress we have without your wonderful contributions.

04 And in other news…

And here are some examples of stories and events which may not directly relate to our group's main activities but which we feel amplify the group's motto – *Just Live*. We hope you enjoy them too.

Getting together is always special

Each quarter we see different members of our global patient community coming together and actually meeting face to face. It always creates excitement for those present, but also for the whole community as they see EHE links being established. Here are examples for this edition of **The Pledge**.

JoAnna Jones was delighted to post a photo of her meeting with Richard Harrington:

> “Me, Richard Harrington, and one of our nurses, Christian, all got to meet today! How cool!”

Meanwhile in London, Hugh Leonard posted a photo of his meeting with Dora Balda, mother of an EHE patient, and her close friend Arianna.

Hope is important

Regular contributor Carl Dixon also posted a message about HOPE:

> “One of the most powerful words you can ever keep with you for without hope many situations might just be too much to handle. Hope gives us the ability to keep pushing forward through the most difficult of times, without it all could seem lost. I keep hope with me every day, everywhere I go, keep it with you!”

And Carl was both surprised and happy when Caroline Flamand from Canada responded, posting a photo of the ‘Hope’ socks that she had made and sells in her shop

04 And in other news...

Just Live

We also enjoy posting photos from our patients that personify the ***Just Live*** motif of our global community.

In October, Tonja Pektas posted her photo of their family on a bucket-list cruise to Alaska!

> “ I hope this inspires others to ***#justlive!*** ”

Making memories in the snow

In addition to his message about hope, Carl Dixon also wanted to remind everybody of the importance of memories:

> “ I always talk about how important it is to build memories. Well today I went for a hike with the family at over 10,200 ft, so me and my older one attempted to make our first snow angels of the year!”

We look forward to sharing the next issue of The Pledge with you. We hope you have found this issue both enjoyable and informative.

Until then *Just Live!*

The EHE Foundation (USA)
www.fightehe.org

The EHE Rare Cancer Charity (UK)
www.ehercc.org.uk

The EHE Rare Cancer Foundation (Australia)
www.ehefoundation.com.au

EHE Italia-Associazione Non Solo Laura ODV
www.ehe-italia.it

EHE Canada
website not yet available