



**Rare Cancer Charity UK**  
Annual Report and  
Financial Statements 2022





## Epithelioid Haemangioendothelioma (EHE)

# EHE Facts

A **destructive vascular sarcoma** that is found in the walls of blood vessels

Commonly appears in **liver and lungs** but can appear anywhere

Can present as **indolent** (passive) or **aggressive**

Typically more aggressive in **young people**

**Can re-present** after long period with no disease

Often presents with **multiple tumours** called 'multifocal'





May turn **aggressive at any time** without warning

Clinical signal that onset may be tied to **pregnancy** and **puberty** in young women

Living with EHE causes **enormous psychological stress**

Affects both males and females but is **more prevalent in women**

One of the **world's rarest cancers**, with approximately 20 patients per year in the UK

**No recognised treatment**, so treatment is by trial and error

**No known cure.** Aggressive disease is **normally fatal**

Find out more at: [www.ehercc.org.uk](http://www.ehercc.org.uk)







# Annual Report and Financial Statements 2022

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# Message from the Trustees

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**The renewed energy and focus from our patient community seen in 2021, post-COVID, continued with record numbers of supporters wanting to run and cycle for the Charity in the London Landmarks Half Marathon and the RideLondon 100 cycling sportive, respectively.**

**The EHE research we are funding continued to produce positive results with our ongoing European collaboration expanding and the PhD we funded in Manchester coming to a successful conclusion. The international EHE research programme we support has also continued to grow and produce important results.**

Our patient support and advocacy activities have also continued. Patient support and information sharing has been provided on a patient-to-patient basis through the group's global EHE Patient Support Facebook page. At the same time, every opportunity has been taken to engage with the general public, regulators, hospitals and other key stake holders to ensure that awareness of our EHE global community and the Charity continues to grow.

2022 also marked the start of a number of key initiatives to review the Charity's activities and structures with a view to strengthening our teams, recruiting volunteers, working with specialists, and engaging with key hospitals and research centres. All of this work is focused on further strengthening and expanding our operations so that we can support our patient community better, raise more funds, drive more research, and so bring forward the new drugs and treatments that are so badly needed to help those diagnosed with EHE.

As we prepare this annual summary of our activity and achievements, we are once again reminded that the activities we are proud to report have only been possible because of the extraordinary commitment of our patient community and their supporters. This is even more extraordinary when we recognise that EHE patient numbers will always be tiny due to the extreme rarity of the disease. That makes their achievements all the more amazing. As always, therefore, we want to recognise every single person who provided their support, in whatever form, to the Charity in 2022 by saying a simple but profound "Thank You"!

## Thank you!

**Left to right:**

Hugh Leonard (Chair of Trustees),  
Jeff Collins (Trustee),  
Kate Hooper (Trustee),  
Sally Baker (Trustee),  
Dr Oliver Pearce (Trustee).





## 01 Patient Support and Advocacy

2022 was another year in which the Charity and our EHE patient community continued to engage with all stake holders to increase understanding and awareness of EHE. Speaking opportunities are particularly valuable and we were delighted when **Hugh Leonard** was invited to speak at the prestigious **ESMO (European Society of Medical Oncology) Congress in Paris in September**. **Hugh joined Dr Silvia Stacchiotti and other panel participants in a session entitled 'Ultra-rare sarcoma: Navigating an endless sea'.**

Smaller speaking opportunities are also valuable. Kelly Denton spoke at fundraising events she organised in support of the Charity and her daughter who is an EHE patient. Hugh Leonard travelled to Derby in the UK to participate in, and to speak at, a major fundraising event held in memory of Hazel Peak by her colleagues at Rolls Royce.

Early in the year, as part of our ongoing patient support programme, the Charity participated in the second annual EHE360 Scientific Symposium and Global EHE Patient Conference. This event, coordinated by The EHE Foundation in the USA, is now established as a key component of our EHE global advocacy programme, and provides our patient community with opportunities to hear about exciting EHE research developments and to engage with clinical experts.

Collaboration is also a key feature of the Charity's advocacy initiatives. Global collaboration between the different national EHE foundations has continued to provide a common approach across international EHE programmes and initiatives. This included the start of an important programme to seek a label extension for a drug called sirolimus, which is producing positive results for patients but is not approved for treatment of EHE and is only available off-label.

Ensuring engagement with the UK EHE patient community is also a core objective. The UK EHE WhatsApp group has proved to be particularly successful in this area, although we also regularly communicate with our members through multiple social media and other communication routes. Through these communications we have been able to promote the UK EHE Biobank and have seen excellent patient engagement.

**More information about these and other events can be found in this report.**

## 02 Research

The Charity continued to fund important EHE research projects through 2022, as well as signing a further research contract at the end of the year.

A key focus for our funded research has been the ongoing European collaboration involving Istituto Nazionale dei Tumori (INT), Milan, the Institute of Cancer Research (UK), and the Royal Marsden Hospital, London. This multi-faceted programme is researching a number of key aspects of EHE, including the identification and validation of novel circulating and tissue biomarkers, and the development of patient-derived xenograft (PDX) mouse models and subsequent cell lines.

The Charity is also helping to fund the establishment of the first ever EHE-dedicated, prospective observational registry, which involves both European and UK hospitals. This registry will be part of the European STARTER project, and is being built, managed and coordinated by a dedicated team also based at INT in Milan.

In the UK, our focus has been on the continued work we are funding at the Bateson Centre in Sheffield, where the team are seeking to generate a zebrafish model of EHE. This has required painstaking attention to detail as the team have faced and solved multiple challenges.

All technical work relating to the four-year PhD we have sponsored in Dr Valerie Kouskoff's laboratory at the University of Manchester was completed and at year end Emily Neil was finalising her PhD thesis. Dr Kouskoff was also successful in securing a further grant from the EHE Foundation to evaluate the effect of PARP inhibitors on EHE.

The National EHE Biobank, funded by the Charity and based at The Royal Marsden Hospital in London, continues to gather critical tissue and fluid samples. We are continuing to work with the Royal Marsden to promote awareness of the biobank with hospitals across the UK.

## 03 Fundraising

Fundraising is the life blood of all that we do at the Charity and in particular our ability to fund key research. As always, our fundraising is a combination of grass roots activity driven by our patient community and their supporters, and charity-driven fundraising.

The largest of our two charity-driven events is the London Landmarks Half Marathon. In 2022 we had the largest team yet taking part, with 42 runners registered for the run. We were particularly delighted that two runners from the USA flew over specifically to take part in the race, along with the usual great support and involvement of our UK members.

The RideLondon-Essex 100-mile-long cycling sportive was also well supported, with 20 riders taking on this major challenge. As Chair of Trustees, and having spent several years encouraging others to participate for the Charity, Hugh Leonard also wanted to take part and he rode in the event.

We were also thrilled in 2022 to learn that the Charity had been successful in securing a substantial grant from the Texel Foundation. This was the third time since inception that the Texel Foundation has supported the Charity and was the largest single donation received to date, for which we are hugely grateful.

Fundraising can be both inspiring and emotional when organised in memory of a loved one. Hugh Leonard attended the first annual Hazel Peak Quiz Night, organised by Hazel's colleagues at the Rolls Royce facilities in Derby. A walk-in coffee morning event, attended by friends and family, was held in Skegness in memory of Allana Parker who was an active volunteer for the Charity.

The Commando Boot Camp, comprising 25 women in Yate in the UK, completed their planned half marathon carrying a 70kg log. Running in support of their friend and EHE patient, Nicola Henderson, these women epitomise the extraordinary dedication and generosity of our supporters.

A number of other events were organised by groups or individuals through the year, including stalls at festivals, cake sales, coffee mornings, 100-mile walks and the sale of home-knitted headscarves.

All of these wonderful contributions, together with similar events in prior years, have combined to provide the amazing fundraising the Charity has enjoyed, and which allowed us to report in August that the total funds raised, since our inception, had exceeded £1 million.



# Objectives and Achievements for 2022

Every year we review our activities and achievement against the goals that we set for ourselves. We believe that this honest appraisal is important so that all our supporters and stakeholders can see how we are progressing. Below is the 2022 assessment; while on the opposite page you will see our objectives for 2023.

## What we said we would do... ...and what we achieved

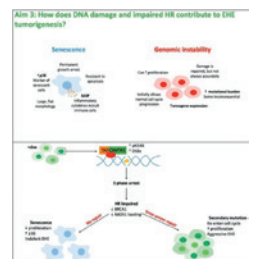
### 01 Patient Support and Advocacy

Review what is important to UK patients.	Patient engagement maintained through social media.
Launch UK biobank discussions with patient community.	Ongoing promotion of biobank continued successfully.
Progress regulatory discussion of IRE ablation.	Regulatory focus switched to repurposing (label-extension) of sirolimus for EHE.
Maintain sarcoma centre engagement	Communication maintained and copies of annual reports sent.
Re-launch pan-European patient engagement.	Pan-European engagement delayed awaiting start of pan-European patient registry.



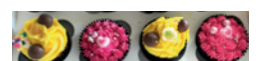
### 02 EHE Research

Engage and support existing projects.	Continued through the year.
Complete contracting of INT/ICR collaborative research projects.	Both projects contracted and initiated.
Evaluate new research, including immunotherapy.	Assisted with US grant cycle. Immunotherapy discussions initiated.
Continue to build/refine research coordination/strategy optimisation.	Ongoing, with close coordination with global EHE partners.
Initiate and coordinate review presentations.	First presentation held for Manchester PhD.



### 03 Fundraising and Finance

Support grassroots fundraising.	Continued to promote and support fundraising.
Revisit past fundraising post-COVID.	Past fundraising reviewed.
Initiate fundraising review.	Contracted with NOVA Fundraising for review.
Assess EU funding for EU projects.	Initiation on hold pending fundraising review.



### Charity Organisation

Review additions to charity bodies.	Reviewed but no changes made
Relaunch voluntary support.	Delayed pending fundraising review.
Re-establish social media.	Initiated and ongoing.
Continue to assess charity activities.	Continually reviewed by Trustees.





# Our Forward Focus for 2023

Because rare cancers are not rare to those who have them

## 01 Patient Support and Advocacy

- Continue sirolimus repurposing
- Assist patients with engagement with charity activities
- Launch new website
- Revitalise other social media
- Engage with European patient community

## 02 Research

- Support existing research
- Review and communicate results
- Engage with EHE partner foundations in research review
- Develop and promote coherent EHE research strategy
- Organise additional research review meetings

## 2023 AND BEYOND

## 03 Fundraising

- Support and encourage grassroots fundraising
- Coordinate key charity events (LLHM and RideLondon100)
- Continue to develop fundraising strategy with NOVA fundraising
- Coordinate review of research strategy and develop draft fundraising programme

## Charity Organisation

- Consider appropriate support for research strategy
- Implement fundraising strategy
- Establish structures for European engagement
- Evaluate need for additional structures and personnel for the above



# Foreword from the patient community

## **Jonathan Granek (Chair of EHE Rare Cancer Foundation Australia; Cancer Consumer Representative and Advocate; EHE Survivor and Research Subject; Husband, Father, Son, Brother, and Friend).**

My story began back in 2009 when I was an active, fit and healthy 26 year old who incidentally injured his back. Subsequent scans showed a suspicious lesion in one of my vertebra with a fracture. This led to more scans, a biopsy and an inconclusive diagnosis with four pathologists who had never seen anything like it before. I was then referred to Australia's most experienced sarcoma unit at the Peter MacCallum Cancer Centre in Melbourne, and four months after the fracture, I had a confirmed diagnosis of stage 4 EHE. Being relatively asymptomatic I was prescribed a 'watch and wait' palliative treatment strategy. Intervention would only be necessary if my disease progressed.

Patients with ultra-rare cancers face huge challenges because so little is known about these diseases. The paucity of research, especially in more advanced and complex cases like mine, results in very limited treatment options being available and no established treatment regime that could cure me. The clinical advice at the time was that systemic therapies available would only have a limited effect before the tumours become resistant and that I would almost certainly experience a shortened life span.

In short, the outlook was not great, but I knew that other EHE patients lived in constant pain, barely making it through the day. I saw myself as lucky and was determined to remain positive and hopeful that I could live in relatively good health even though I had an ultra-rare cancer. I also decided that I needed far greater knowledge of rare cancers and EHE to give myself the best fighting chance of surviving this horrible cancer.



Jonathan Granek

Following diagnosis, I spent much of my spare time over the next 5 years building my health literacy. I wanted to understand what it meant to have a rare cancer, and what was needed to improve outcomes. I read scientific publications; networked with prominent cancer researchers and clinicians; and connected with other EHE patients across the globe. I spent time learning more about the health system, how cancer research is conducted and new treatments are developed. And I joined Australia's oldest research institute, the Walter and Eliza Hall Institute of Medical Research (WEHI), as a consumer representative consultant.



## Cancer care is a monumental challenge

At the time of writing this, across the globe there are over 18M individuals being newly diagnosed with cancer annually and over 10M cancer deaths. By 2040, these diagnoses and deaths are expected to exceed 30M and 16M respectively. The impact is colossal.

While the number of deaths in the major common cancers have now decreased below that of population growth, the story is very different for patients diagnosed with one of the remaining 200+ rare and less common cancers. When we consider just rare cancers (those with an incidence of 6 per 100,000 cases or fewer) the outcomes are devastatingly poor, with the numbers of those newly diagnosed and dying outstripping population growth. Patients diagnosed today with rare cancers **have a very poor chance of survival**, almost entirely due to the **vacuum of research and development, and the funding to drive it**.

In addition to this research neglect, the management of rare cancers are more complex, requiring more people with less information available for decision-making. Complex multimodal tailored treatment approaches and multidisciplinary teams of experts are required to treat them. These factors have profound implications for health infrastructure and resources, imposing massive economic burden.

## Understanding where Rare Cancers Fall Short and How to Bridge the Gap

Research is key! Without it, no new evidence-based information is generated to instigate change and improvements. Challenges exist in every aspect of the care and management of rare cancers, without exception, but two critical areas can be singled out.

The first is the development of early detection and diagnostics. As for nearly all diseases, the earlier they are detected the greater the chance of successfully dealing with them. The second is prognostics and the development of effective treatments, but to progress with these, patient data, disease information and research of fundamental biology are all required.

## Support Groups as the Catalysts of Change

It became clear if the outcomes for rare cancers like EHE were to ever change for the better, these shortfalls would have to be addressed, and it needed to be organised, long-standing, far reaching and en-masse. In 2015, with the involvement of like-minded people also affected by EHE, I co-founded a registered not-for-profit charity called the EHE Rare Cancer Foundation Australia. Our sister Foundations in the US and UK were also founded that same year.

Today, we work in close partnership with each other, now with the additions of organisations in Canada and Italy too, and under the banner of the EHE Group. Together, we work to address the needs of people affected by EHE in over 75 countries across the globe, and support multiple research initiatives to bridge these gaps led by an impressive group of researchers and clinicians.

Our research initiatives to date for such a rare disease have been both world-first and world-class, but we are now at a pivotal juncture. The rate of progress is now very much in the hands of the growing international patient community who, by taking action and supporting multiple data-gathering initiatives, can meaningfully affect the necessary changes that will one day save lives. More than ever we must recognise that **“alone we are rare, but together we are strong”**.



# 01 Patient Support and Advocacy

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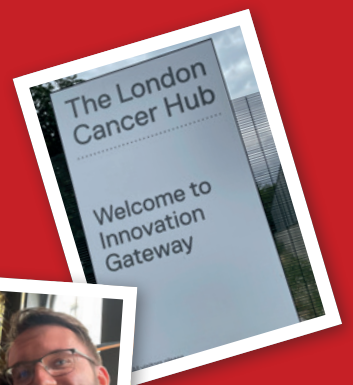
At the core of the Charity's patient support and advocacy activities are two simple objectives, both centred on our patient community. The first is outward looking, spreading awareness of EHE and the impact that an EHE diagnosis has on patients. The second, which is inward looking, is to try and ensure that individual patients and the community as a whole are as well informed as possible regarding any aspects of the disease that are important to them.

Receiving a diagnosis of EHE, an incurable, ultra-rare cancer, is devastating for every patient. EHE patients not only have to live with this fact, but also the realisation that EHE can turn aggressive at any time, when the disease becomes very destructive. Yet doctors cannot provide any prognosis or prediction of when this will happen as they don't know what triggers this change.

So we take every opportunity to bring these facts to the attention of others. Although social media is an important component of any messaging, we continue to believe that there is nothing better than speaking to actual audiences, ultimately hoping that it will result in growing support from all key groups (clinicians, researchers, regulators, governments, funders, and the general public) for our different activities. Over time we hoped to build momentum and see an increase in awareness of EHE, and we are delighted that this has indeed been the case.

Our inward-looking support of EHE patients is largely provided by the patient community itself, through both local and global EHE social media platforms, allowing the patient body to share experiences and provide valuable information on a range of topics. With EHE having both variable presentation and course, having access to others with similar disease presentation and facing similar challenges is important and comforting for those involved.

Sharing information about the charity and its activities is also the objective of the EHE Group quarterly global newsletter, The Pledge, edited and produced here in the UK for the EHE Community worldwide. In addition, we share this Charity Annual Report with as many people as we can as part of our awareness and patient support programme. We encourage anybody who is reading this report to share it with others, and so help us in spreading the word. And if you would like additional copies please contact us.



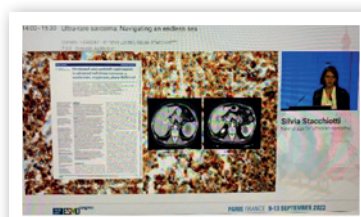


## Review by Sally Baker

**“2022 has been another good year with regard to our patient support and advocacy activities. We have taken advantage of several important speaking opportunities. We were also able to involve, and engage with, the EHE patient community at the EHE360 Scientific Symposium and Global EHE Patient Conference. Regulatory engagement involved initiating processes both in the UK and Europe to secure approval for sirolimus to be used in treating EHE. These and other activities are outlined below.”**

The speaking highlight of the year was Hugh Leonard participating in a panel discussion at the ESMO 2022 Congress, together with sarcoma/EHE specialists including Dr Silvia Stacchiotti. The session was entitled *‘Ultra-rare sarcoma: Navigating an endless sea’*. Hugh's presentation, entitled *‘Advocating for patients with ultra-rare cancer’* addressed the challenges ‘associated with ultra-rare cancers, and the importance of collaboration and partnership among patients, advocates, researchers, doctors, governments and pharma in the effort to find effective treatments for such rare diseases. Hugh took the opportunity to address particular areas of concern and how all parties together could help rare cancer patients.

Several other opportunities to talk about EHE were taken. Hugh Leonard spoke at Rolls Royce Submarines in Derby during a fundraising event in memory of Hazel Peak. Kelly Denton spoke at several events organised in South London, including the quiz night organised by Laptops & Lipstick, a local business group for women who are supporting the charity and Kelly, whose daughter has EHE.

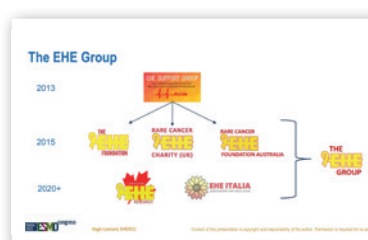


Under our advocacy objective, we were also delighted to engage with Dr Silvia Stacchiotti and the European-based AntiCancer Fund on seeking approval for the use of the mTOR inhibitor, sirolimus, in the treatment of EHE. There is now a growing body of evidence that this drug is beneficial to patients with progressive EHE. The challenge, however, is that the drug is not formally approved for the treatment of EHE and is therefore only available ‘off-label’. Having to be prescribed off-label means that for some patients the drug simply cannot be accessed (their doctor or hospital won't prescribe it) or cannot be afforded (available only at the patient's cost). We are therefore committed to addressing this inequality of access by securing the necessary approvals from the key regulatory bodies for use of the drug, with the relevant processes initiated at the end of the year.

Our engagement with, and support for, members of our patient community takes many forms, but the centre-piece of the year was the second annual EHE360 Scientific Symposium and Global EHE Patient Conference. This virtual event, organised by The EHE Foundation in the USA with input from the Charity and other EHE entities around the globe, provided the patient community with an update on key areas of research and clinical practice. Hugh Leonard was delighted to moderate and speak at a session focused on presenting and explaining the important ESMO paper *‘Epithelioid hemangioendothelioma, an ultra-rare cancer: a consensus paper from the community of experts’* published in late 2021. The event closed with the very popular **“Ask the Expert”** panel session, where four clinical experts experienced with EHE responded to tabled questions about the disease and its treatment.



2022 also saw an expansion in our ongoing collaboration with the different global EHE foundations. Our collaboration within Europe is particularly important as we progress the development of the EHE Prospective Clinical Registry across Europe and the UK, and also seek to establish a pan-European EHE patient network.



Collaboration is also critical for the simple fact that ultra-rare diseases cannot afford to waste funding through poor communication, duplication of effort, or missed opportunity. We will therefore always remain focused on ensuring that all elements of global EHE activity are as coordinated and optimised as possible. We owe this to our patient community, but also to our supporters and donors who provide us with funding and rightly expect it to be appropriately managed.

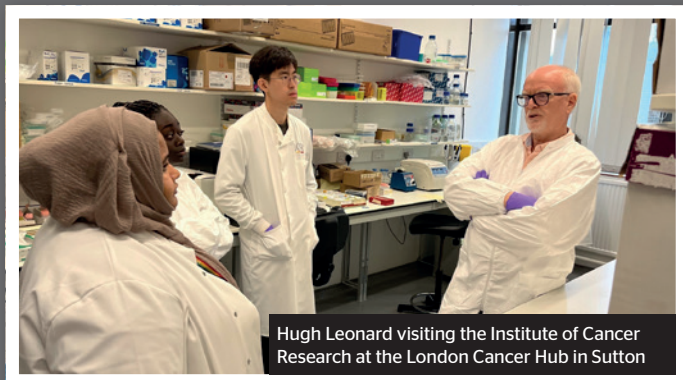


# 02 EHE Research

When the Charity was established in 2015, it was unclear how much interest there would be in EHE within the research community. We have been delighted therefore with the levels of engagement we have seen in the UK, Europe, north America and Australia since our inception. Here in the UK, all funds that we have received have either been spent or are allocated to research we have committed to, and which continues to produce exciting results.

We are also excited by the clear interest in both expanding our current projects and in establishing new research looking into different aspects of the disease. A continual challenge, of course, is raising the funds we need to drive that research, but we are confident that there is genuine appetite from established and respected centres of research to add to the ongoing global EHE research programme. That is why two of our core objectives for 2023 are to establish a clear strategic research framework for EHE and an associated fundraising strategy to support it.

While we are excited by the future potential and interest in EHE research, we are equally excited by the ongoing research we are currently funding. Summaries of these research programmes can be found on the following pages.



Hugh Leonard visiting the Institute of Cancer Research at the London Cancer Hub in Sutton

### EHE development

- EHE is a rare vascular sarcoma
- Heterogeneous disease
- Two fusion proteins unique to EHE
  - TAZ-CAMTA1 (TC) in <90% cases
  - YAP1-TFE3 (YT) in >10% cases
- Thought to be the only mutation in 45% cases
- Lack of *in vitro* endothelial cell models

Identification of a disease-defining gene fusion in epithelioid hemangioendothelioma

Novel YAP1-TFE3 fusion defines a distinct subset of epithelioid hemangioendothelioma

Emily Neil presenting her PhD results to the EHE research community

# Review by Dr Oliver Pearce and Dr Kate Hooper

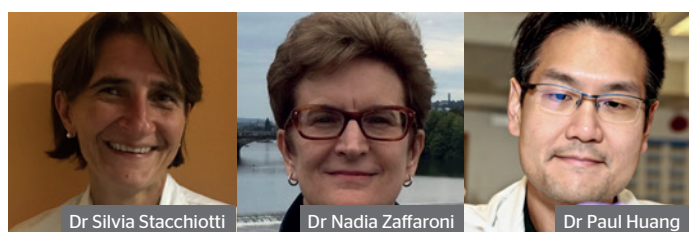
## European collaboration

The Charity, together with the EHE Foundation (USA), is funding this major European collaboration involving the Istituto Nazionale dei Tumori (INT), in Milan, the Institute of Cancer Research (ICR) in London, and the Royal Marsden Hospital in London.

The overall research program entitled '*Evaluation of Cytokines and Hormones as Biomarkers for EHE*' was initiated at the end of 2020 and extended and expanded at the end of 2022. The resultant overall research comprises a number of different objectives or projects as follows:

- i) the identification and validation of novel circulating and tissue biomarkers to inform patient management (prognosticators and predictors of response to medical agents) as well as potential therapeutic targets (**Project 1**)
- ii) the development of patient-derived xenograft (PDX) models (**Project 2**)
- iii) the assessment of the activity of drugs relevant for the disease (**Project 3**)
- iv) the generation of PDX-derived cell lines to investigate the cellular and molecular determinants of drug activity and to be submitted to a CRISPR whole-genome screen to identify new therapeutic targets (**Project 4**)
- v) the identification and evaluation of miRNAs (**Project 5**)
- vi) the description of the radiologic characteristics of EHE and their correlation with the clinical outcome (**Project 6**)

Dr Silvia Stacchiotti, one of Europe's leading sarcoma clinicians, and Dr Nadia Zaffaroni, one of our leading sarcoma researchers, are joint Principle Investigators (PIs) of the project in Milan; Dr Paul Huang is the PI at the ICR in London.



Updates as at the end of 2022 of the above projects are provided below:

### Project 1:

The assessment of circulating cytokines, hormones (and miRNAs), and ER $\alpha$ , Er $\beta$  and GPER expression and the identification of a novel biomarker for EHE.

Using a protein array able to simultaneously detect the expression of a hundred different cytokines in plasma samples of 15 EHE patients and healthy 6 individuals, a small panel of inflammatory cytokines was found to be

differentially expressed. Among them the researchers focused on Growth and Differentiation Factor-15 (GDF-15), a member of the TGF- $\beta$  super-family, which has multiple roles in a wide variety of cellular processes. Using a specific ELISA assay, they looked at the concentration of circulating GDF-15 in a retrospective series of 23 EHE patients and observed a statistically significant association of GDF-15 levels with EHE aggressiveness. This result was confirmed in a second cohort of 21 EHE patients prospectively collected within the currently ongoing observational study.

The assessment of circulating hormones and tissue expression of ER $\alpha$ , Er $\beta$  and GPER is ongoing.

The assessment of miRNAs is undertaken in Project 5.

### Project 2:

Development of additional PDX models.

At the end of 2022, the team had fully established one EHE PDX model, whose ability to reproduce the characteristics of the originating clinical tumor had been confirmed in terms of histo-morphology, presence of the *WWTR(TAZ):CAMTA1*, overall transcriptomic profile (as detected by RNA-seq) and presence of *CDKN2A* homozygous deletion. A cell line has also been established following disaggregation of the EHE PDX.

### Project 3:

Assessment of activity of drugs.

The PDX model was used to comparatively assess the activity of doxorubicin and sirolimus (at different doses). Doxorubicin showed almost negligible activity whereas sirolimus caused a dose-dependent tumor volume inhibition in treated mice and induced the down-regulation of mTOR signaling. At year end the PDX was being used to assess the activity of inhibitors of the Hippo pathway, such as the TEAD family of transcription factors.

This PDX and the corresponding cell line were exploited to provide further evidence supporting the value of GDF-15 in EHE. GDF-15 was detected in the medium of the EHE cell line as well as in the blood of EHE PDX but not in healthy mice or in mice carrying another sarcoma type, confirming that the cytokine was released by the EHE. Interestingly, the team also found that sirolimus decreased the abundance of GDF-15 in their *in vitro* and *in vivo* EHE models.

### Project 4:

Use of CRISPR in cell lines to help identify genes that confer drug resistance or sensitivity.

At the end of 2022 it was planned that the EHE cell lines would soon be provided to Dr Paul Huang (ICR, London) to start the CRISPR-based experiments.



## 02 EHE Research Continued

### Project 5:

Identification and evaluation of miRNAs.

The expression profiling of plasmatic miRNAs was initially carried out using OpenArray Technology (which evaluated the expression of 754 different miRNAs) in the retrospective series of 23 EHE patients. Six miRNAs were found differentially expressed between patients with indolent and aggressive EHE. In order to evaluate the overall miRNAome (global profile of expressed miRNAs), the research team repeated the analysis on both retrospective and prospective series of patients using miRNA-seq. At the end of 2022 results were being analyzed by a dedicated bioinformatician.

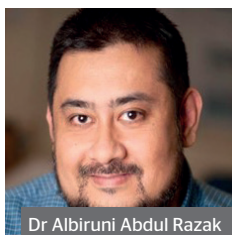
### Project 6:

Establishment and assessment of radiological data base.

The clinically-annotated radiologic scan collection on the study platform has been started. Response assessment is also collected by REDcap CRFs. The data analysis is planned to take place after the end of the study.

### Canada joins the collaboration

We are delighted to see this research collaboration continuing to produce positive results. We were also excited when the project was materially expanded with Canada joining the collaboration, following the same programme. The Canadian arm of the project is centered at the Princess Margaret Hospital (PMH)/Mount Sinai Hospital in Toronto and is being led by Dr Albiruni Abdul Razak, Medical Oncologist at PMH.



Dr Albiruni Abdul Razak

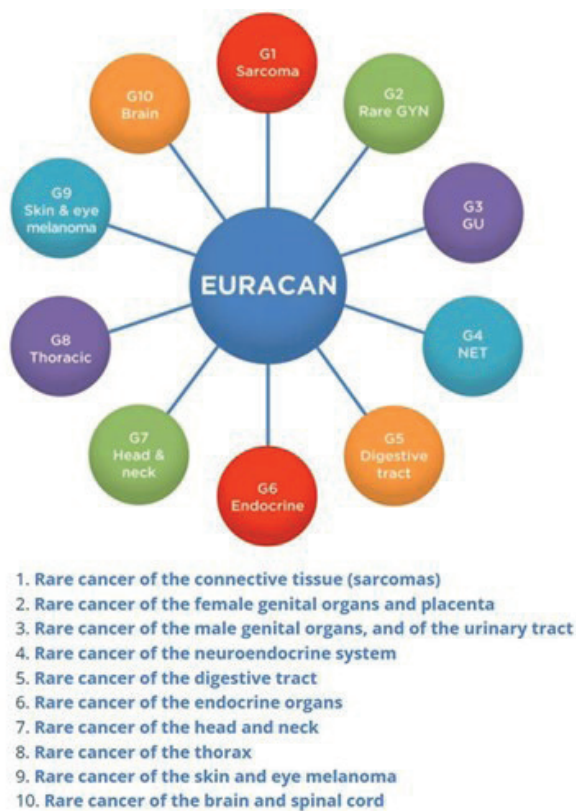
### EHE Prospective Observational Registry

A key challenge in understanding an ultra-rare disease such as EHE, with heterogeneous presentation, clinical course and variable response to the same treatment in different patients, is simply gathering patient data in a consistent and methodical manner to allow the disease to be studied and understanding to be gained. For ultra-rare diseases this is very difficult due to the lack of patient numbers in any one hospital, or indeed in any one country, leading to limited data and information being available.

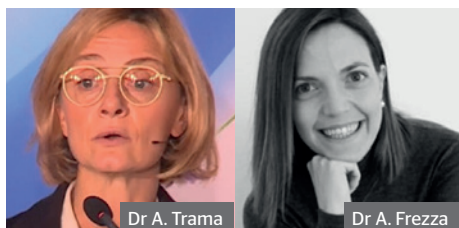
The Charity was therefore delighted when Dr Stacchiotti submitted a grant proposal to establish an EHE prospective observational registry to start to collect such data. Her proposal addressed the rarity and lack of patient numbers by making the registry pan-European, including the UK. The objective of the registry will be to collate data from participating hospitals across the European Union and the UK, providing key data and informational opportunities for clinicians and researchers who want to learn more about EHE, and support for those who suffer from it.

The original idea was to establish this as a stand-alone registry, centred at and managed from INT in Milan. However, early discussions in Milan led to the realisation that this registry could also be established within the STARTER (Starting an Adult Rare Tumour Registry) project, a new major initiative by EURACAN (The European Reference Network (ERN) on Rare Adult Solid Cancers) to establish registries for the ten recognised rare-cancer types across Europe. STARTER is also centred at INT in Milan, and is being led by Dr Annalisa Trama. The suggestion of using EHE as the first example of a sarcoma to be included in the registry was based on the core realisation that for such a rare disease, the establishment of a registry could be game-changing in terms of understanding and ultimately treating the disease.

The proposed study will aim to provide a description of the population affected by EHE, giving an insight into the natural history of the disease and its variants, leading to the possible identification of clinical and biochemical prognostic and predictive factors and answering some of the outstanding questions relating to the management and treatment of the disease.



Such an EHE registry will be the first of its type in the world, and offers a genuinely game-changing opportunity to the EHE community. The Charity was therefore delighted to help fund the three-year proposal with work starting in mid-2022. Agreeing and establishing the data collation protocol (CRF) for such a rare and heterogenous disease is itself a major challenge, but by the end of the year an appropriate CRF had been mapped out and the associated digital collection form had been generated and was being tested. The team, also led by Dr Trama and clinically assisted by Dr Anna Maria Frezza,

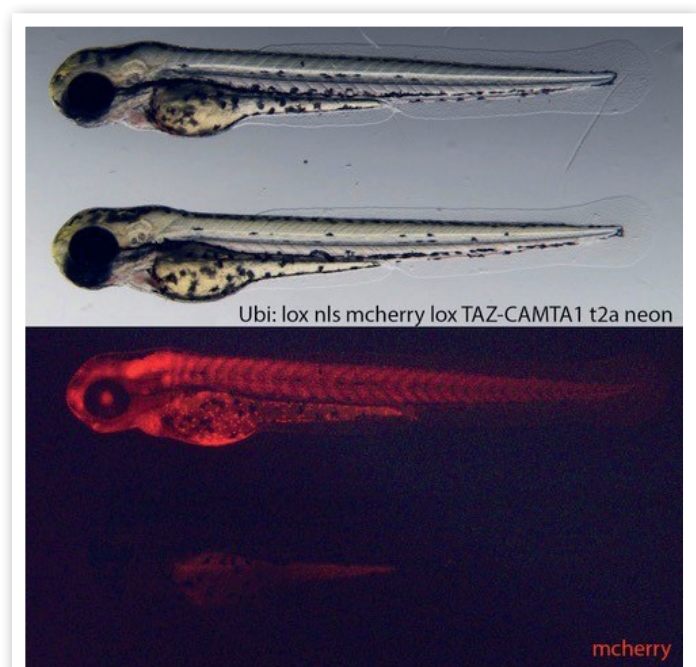


were hopeful that the testing process would be completed during the first half of 2023, allowing the enrolment of participating centres, and the introduction and launch of the project to be completed in the third quarter of the year.

## EHE zebrafish model development

The objective of this project is to develop a zebrafish model of EHE. The basic components of the project were to develop a zebrafish line with the TAZ-CAMTA1 gene translocation construct present in endothelial cells, and a second zebrafish line with a switchable mechanism to activate the TAZ-CAMTA1 when required. By then crossing these two lines, it was hoped to generate fish with the TAZ-CAMTA1 construct that could be activated at different times in the development of the fish. The switchable mechanism was required as the TAZ-CAMTA1 fusion protein is highly toxic and lethal to the zebrafish at the embryonic stage.

Several key challenges have been faced, and at the end of 2021, although the team had developed a fish line with the TAZ-CAMTA1 switch mechanism in the endothelial cells, they had still not been able to get the TAZ-CAMTA1 gene translocation construct to present in the endothelial cells of zebrafish. So the EHERCC team were excited to receive reports from Dr Van Eeden in early 2022 that Eleanor Markham, the MPhil graduate undertaking the work, had identified two independent transmitters of their 'switchable' transgenic where TAZ-CAMTA1 can be driven by a new promoter, 'ubi'. Photographs clearly showed the 'detection marker' in red. This marker is attached to the construct and so everywhere you see red, the construct is present. It appears everywhere in the fish including, for the first time, in the endothelial cells.



Dr Van Eeden, PI of the project at the Bateson Centre at the University of Manchester, was delighted as the construct presence in endothelial cells meant that the team were



## 02 EHE Research Continued

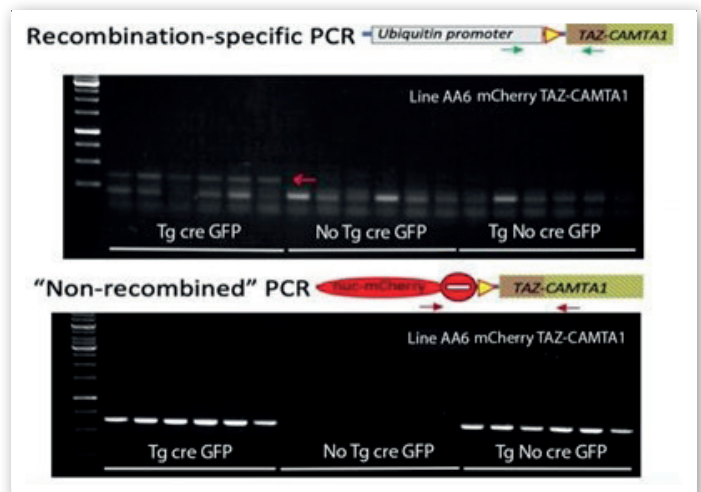
potentially just one step away from being able to express the TAZ-CAMTA1 fusion protein in zebrafish. The team needed to ensure that the first few fish coming from the injected parents with the 'switchable' transgenic in the endothelial cells were used to establish a stock, before starting to test if the switch was working.

The next challenge was to create a different line that would allow switching in the endothelial cells. For this, a fish was required where the Cre protein is expressed in the endothelial cells. The team were able to obtain a construct that contained a version of the Cre protein that is tagged with GFP, a florescent green indicator, which would allow them to see directly if that Cre protein is expressed in the right place.



Eleanor was subsequently pleased to be able to report that they had successfully developed a fish line transmitting the Cre protein as required, and attached a picture of the CreGFP switch transgenic that shows it is expressing the Cre protein in the blood vessels.

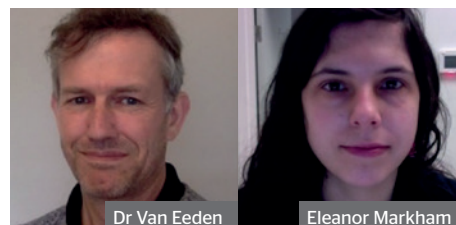
By the end of the year Eleanor had also been able to confirm that they had crossed both fish lines, namely the switchable TAZ-CAMTA (ubi:lox nls-mCherry lox TAZ-CAMTA1 fish (red) with the blood vessel switch line (flil:cre GFP fish (green). The team had then undertaken PCR tests on resultant embryos that contain both constructs and could see that the switch was happening by analysing the genomes of these fish. The team were clear that this did not yet show that the TAZ-CAMTA fusion protein was being expressed, but it did show that the switch system was doing what it was supposed to do.



Early in 2023, the team planned to start using antibodies and qPCRs to see if the TAZ-CAMTA1 RNA, and protein were actually produced.

Eleanor will also be doing further tests with the fish to check if it is doing what it is supposed to do. At the same time they will also be working hard to identify fish with the required characteristics and so increase the number of fish available for experiments.

This has clearly been a challenging project, but we are hugely impressed by Eleanor's tenacity and her attention to detail as she has progressed through the painstaking work required to create an EHE zebrafish model.



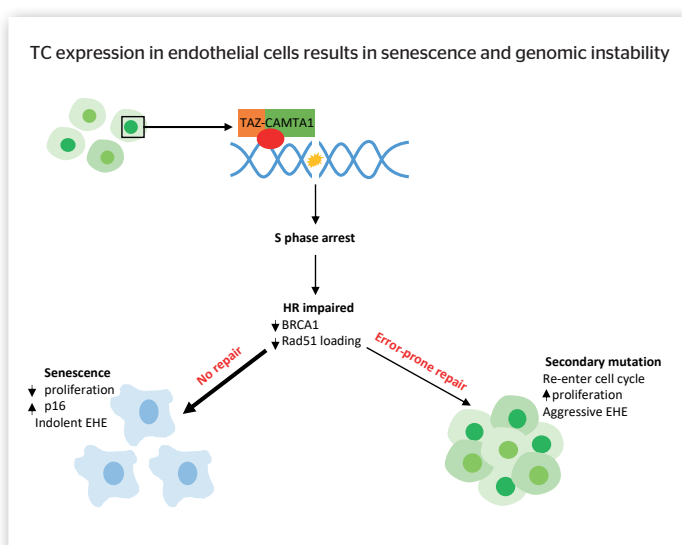
## Manchester-based research

### Emily Neil's PhD

2022 was the fourth and final year of our funding of the PhD being undertaken by Emily Neil in Dr Valerie Kouskoff's lab at the Division of Developmental Biology and Medicine, University of Manchester. Emily's work at the start of the year focused on confirming the results of some of her earlier experiments before starting to write up her thesis.



A key finding of Emily's work, reported in 2021, shows that EHE cells are captured in the S phase of the cell cycle. Her results also strongly suggested that these EHE cells captured in the cell cycle may ultimately become senescent, and may present as indolent disease. However, Emily also showed that homologous recombination (HR), the main DNA damage repair pathway in our cells, is impaired by the TAZ-CAMTA1 fusion protein. This in turn may lead to less reliable DNA repair mechanisms becoming active, with the resultant potential hypertranscription leading to secondary DNA mutations, some of which may allow the cells to avoid the S phase capture and so continue to proliferate. This is the first biological model we have seen that could explain the different levels of progression of EHE, from indolent to highly aggressive, and the unpredictable onset of more progressive disease from an initially indolent form.



### Additional grant to test PARP Inhibitors

With the identification of DNA damage as an important component of EHE biology, and interesting preliminary results on testing Olaparib, Dr Kouskoff submitted an application to the EHE Foundation in answer to its 2022 call for grant proposals.

Dr Kouskoff's proposed research was titled 'Understanding and Exploiting the Genomic Instability Promoted by TAZ-CAMTA1'. The research goal was to understand further how TAZ-CAMTA1 interferes with the DNA damage response and whether this interference represents a therapeutic vulnerability that can be exploited. Dr Kouskoff proposed to test the druggability of the DNA damage response interference by TAZ-CAMTA1.

Dr Kouskoff was duly awarded a grant in late 2022 to fund this work, initially focusing on PARP inhibitors.

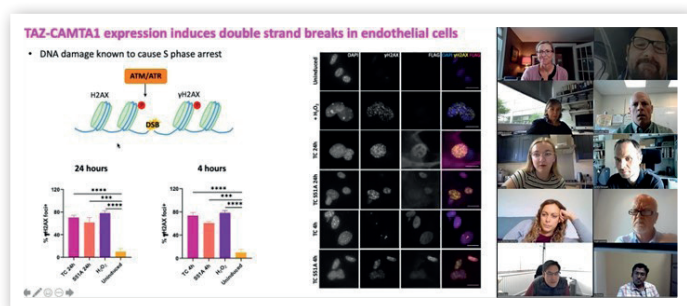
The final part of Emily's work was to therefore investigate whether PARP inhibitors are able to induce apoptosis (death) in TAZ-CAMTA1-expressing cells. PARP inhibitors, such as Olaparib, are commonly used to treat BRCA1-mutated cancers, where impairment of the HR DNA repair pathway causes genomic instability as error-prone pathways take over. Emily's assay revealed that TAZ-CAMTA1-expressing cells were more sensitive to Olaparib than TAZ-CAMTA1-negative cells and controls, as evidenced by a larger apoptotic population. This effect was particularly marked in the TAZ-CAMTA1-low populations, with TAZ-CAMTA1-high endothelial cells displaying a greater resistance to PARP inhibition. This may represent a mechanism by which cell death can be induced in these populations, with little effect on TAZ-CAMTA1-negative cells. This will require further experimentation to confirm. In 2023, Emily will be optimising a cell viability assay, which will allow calculation of the IC50 (half-maximal inhibitory concentration) of Olaparib in these cells, as well as allowing investigation of multiple drug concentrations and drug combinations at once.



## 02 EHE Research Continued

### Sharing our research results

One of the challenges of research programmes is ensuring the results and knowledge gained is shared with other researchers to maximise the chance of success, minimise the chance of missing something important, and avoid unnecessary duplication. To help achieve this target, and as part of the obligations of the researchers who accept EHE Group funding, researchers are asked to periodically present their results to a group of fellow EHE researchers so that the group can discuss the results, encourage brainstorming in an energised and creative environment, and think about how to use the research and what follow-on research may be justified.



The first of these online presentations was held in mid-2022. Emily Neil from the Manchester team presented the results of her work. A core group of EHE researchers took part. These included John Lamar from Albany Medical College in New York, Munir Tanas from the University of Iowa, Sandro Pasquali from INT in Milan, Paul Huang from the ICR in London, and Ajay Pobbati from Dr Rubin's lab at the Cleveland Clinic. The EHE Rare Cancer Charity was also pleased to welcome Dr Sorrel Bickley, Director of Research, Policy and Support at Sarcoma UK, and Denise Robinson, Director of Research at The EHE Foundation' in the US. Although this was the first such review session, participants were delighted by the discussion and pooling of ideas at the end of the presentation.

Dialogue was ongoing at the end of the year concerning further work using the Manchester EHE stem cell model system.

### Extending the sirolimus label

In late 2022, a group led by Dr Silvia Stacchiotti and comprising INT in Milan, the EHE Rare Cancer Charity UK, and the Brussels-based AntiCancer Fund, initiated a review process with the European Medicines Agency (EMA) seeking a label extension for the mTOR inhibitor 'sirolimus' so that this drug could be formally approved for the treatment of EHE in Europe. At the same time, the Charity and the AntiCancer Fund initiated a similar dialogue with the new NHS Drug Repurposing Programme in the UK

These initiatives are important because there is a growing body of compelling clinical evidence and experience demonstrating that sirolimus is having a noticeably positive effect for many EHE patients who have been prescribed the drug. Indeed, the drug is recognised as a potential first line treatment for EHE in the 2021 published ESMO paper *'Epithelioid hemangioendothelioma, an ultra-rare cancer: a consensus paper from the community of experts'*. Direct support for these label extension initiatives is being provided by doctors well known to our community through their participation, including Dr Silvia Stacchiotti from INT in Italy, Prof Robin Jones of the Royal Marsden in the UK, and Dr Bill Tap from Memorial Sloan Kettering in the USA.

Although some patients will be offered sirolimus 'off label', many will be denied access to the drug as it is not formally approved for EHE treatment and therefore their doctors and/or hospitals will not prescribe the drug. In addition, national health systems, funding entities and insurance companies may also refuse to fund the drug for the same reason, leaving patients with the option of funding themselves or not receiving this treatment. These circumstances result in a gross inequality of access across different countries in Europe, and even across different hospitals and health authorities within a single country.

#### An excerpt from the ESMO Consensus of Experts

"Among them, the highest clinical activity has been reported for mTOR inhibitors, with a progression-free survival (PFS) and overall survival in the range of 1 year and 2 years, respectively, and 10% of patients having even longer PFS. The panel agrees that these represent the preferred treatment options for patients with advanced and moderately progressive disease."

Dialogue and applications to the different regulatory bodies will continue in 2023, where the Charity will be fighting to achieve the appropriate label extensions and so secure access to this important drug for all EHE patients.

## The importance of biobanking

The collecting of biological samples is critical for future research into any disease. With common cancers, tissue and fluid samples are abundant and collecting these samples is less important. For a disease as rare as EHE, however, banking biological samples is absolutely critical. With so few patients, and many of these not undergoing surgery, tissue samples in particular are ultra-rare. It is in fact hard to over-state how important tissue donation is for moving EHE research forward.

For these reasons the Charity funded the establishment of the National UK EHE Biobank at the Royal Marsden Hospital, and continues to fund the annual costs for collecting the samples. We also continue to promote the EHE Biobank through our patient community, and encourage all patients who have surgery coming up, including biopsies, to contact their primary care team or the Charity using the contact details below so that plans can be made to ensure their samples are captured and stored. The message is relative simple, but so important ... "Your tissue can help researchers learn more about EHE, and ultimately help deliver a cure for the disease. It really is that important."

If you have any questions regarding the National UK EHE Biobank, then here are some important contacts:

Contact the EHE Tissue Coordinator at the National UK EHE Biobank at the Royal Marsden Hospital, at [rmh-trehebiobank@nhs.net](mailto:rmh-trehebiobank@nhs.net); or

Hugh Leonard at the EHE Rare Cancer Charity (UK) at [hleonard@ehercc.co.uk](mailto:hleonard@ehercc.co.uk)





# 03 Fundraising and Finance

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**2022 started positively, with the stress of the COVID pandemic largely behind us, and the fundraising landscape again looking positive. Sadly this picture would change through the year as the Ukraine situation led to turmoil in the energy and financial markets, rising inflation, and a severe cost-of-living squeeze for everybody.**

Despite this negative backdrop, the Charity enjoyed another positive year, largely due to the energy and enthusiasm of our members to continue to drive and support fundraising. Our patient community and their supporters have a huge, vested interest in seeing successful research deliver new treatments, and ultimately a cure for the disease. But as in the COVID crisis, we are also cognisant of the cost-of-living challenges now faced. We will therefore never take their inspiring enthusiasm, creativity and generosity for granted.

It was not just our individual members, their supporters and grassroots fundraising that led to such a positive year. We enjoyed record support for our London Landmarks Half Marathon event and the RideLondon-Essex 100 cycling sportive. We were also hugely grateful to the Texel Foundation for their award of the largest single grant we have ever received. Part of this unrestricted grant is now being used to allow us to engage with Fundraising experts as we seek to develop a broader fundraising strategy to drive a larger and more extensive research programme.



## Review by Jeff Collins

**At the end of 2021, we noted that we had seen a substantial recovery in fundraising post the COVID pandemic, and that the 2022 fundraising outlook was strong. I am pleased to be able to say that the enthusiasm of our supporters continued and we enjoyed great engagement from our patient community. That support ultimately enabled us to report in August that we had exceeded £1 million raised since our inception in 2015.**

2022 was another positive year. Our grassroots fundraising was strong, with our patient community and their supporters again supporting the charity. We also saw record interest in our two major charity-organised events, where we had 42 runners in the London Landmarks Half Marathon, and 20 riders in the RideLondon-Essex 100 event.

The Boot Camp Commandos, a group of dedicated and motivated young women based in Yate ran a half marathon carrying a 70kg log, raising more than £7,000. Friends of Hazel Peake at Rolls Royce Submarines in Derby organised a major Quiz Night in memory of Hazel, and with donor-matching raised more than £10,000 for the charity.

Fundraising is of course not just about big events, as all fundraising, no matter what size, is so important. Kelly Denton coordinated several fundraising events. Wendy Cassidy organised a walk in coffee-and-chat morning in Skegness in memory of her sister, Allana Parker and raised more than £500. Jess Ralph ran in memory of her friend Al Mundy, who had passed away due to EHE, raising more than £1,000. Sue Dean, whose son Paul has EHE, set about knitting and selling headscarves for Christmas, and also raised well over £1,000 for charity. Kelly Davis meanwhile completed a 100 mile trek along the South Downs raising nearly £4,000 in support of her brother, Tyler.

We were also delighted when the Texel Foundation awarded the Charity the largest single donation it has yet received. The £25,500 was granted as unrestricted funds, which also provides us with maximum flexibility to best serve the needs of the charity and our members. This was the third time that the Texel Foundation had donated funds to the Charity. We could not be more grateful to them for their fantastic support.

### Key objectives

In the 2022 calendar year our supporters including the Texel Foundation raised a total of £95,800 for the charity's key objectives. The sources of these funds are summarised on the pie chart above.

During 2022 we provided funding of £155,200 for our UK research projects at the Universities of Manchester and Sheffield, funding for the EHE National Biobank and Tissue Manager at the Royal Marsden and funded (jointly with the US EHE Foundation) the collaborative research project between INT in Milan and the ICR in London.

### Source of funds



### Administration/business running costs

In 2022, we once again received the generous support of a single donor who funded 100% of the charity running costs. As in all previous years, we segregated these funds, donated for administration purposes, from those received from all other sources, which can therefore be allocated to fund our key objectives, in particular, EHE research. It is the intention of the Trustees that the same will be true in 2023.

The charity received funding of £10,750 for its administration and business running costs account. During 2022, £6,600 of expenses had been incurred, which included an accrual of £1,200 for the independent examiner's fee. The remaining £4,150 related to fundraising events scheduled for 2023, with some funds remaining for future administration and business running costs.

The spend of £6,600 (excluding the £1,200 independent examiner's fee) included the fees associated with fundraising events conducted in 2022, and publishing costs, in addition to ongoing website maintenance.

*"We are once again so grateful to our patient community, their supporters, and the corporate groups and foundations who supported us through the year. A particular and huge thanks must go to the Texel Foundation for their wonderful grant. We are also grateful to all those who helped us and volunteered so that we could keep our charity running costs as low as possible. I also want to thank all the companies and service providers who have supported us with their services, often provided at no or reduced cost.*

*Although 2022 has been another positive year, we must recognise that the current financial climate means that 2023 and years beyond may continue to be financially challenging, impacting our supporters and restricting their ability to donate funds, no matter how much they want to. We will therefore continue to ensure that we already hold the funds for any funding commitments we enter into. We will also continue to manage all funds with the utmost care to ensure that we get the maximum benefit from every pound that we have so generously received."*

**Jeff Collins**



# Wonderful support for EHE in 2022

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The following pages highlight some of the amazing fundraising events that raised funds for EHERCC in 2022.

## EHERCC fundraising passes £1 million

The Charity was delighted in August to announce that the total funds it had raised since its inception in 2015 had exceeded £1 million. Jeff Collins, Trustee of the Charity, commented:

*"We are in reality a tiny charity with a tiny support base, due to the rarity of EHE, so it's pretty amazing that we have reached £1 million. To everybody who donated, ran, rode, swam, sold cakes, put on shows, quiz nights, race nights, rowed the Atlantic, sky dived, raffled, auctioned, and in any other way contributed to that total, including providing just encouragement and support, we just want to say a huge **THANK YOU.**"*

*But although we have been able to make a material contribution to global EHE research, we know that there is still a huge amount still to do. So while we thank all our supporters for all they have done in the past 7 years, we at the same time encourage them to plan for the next fundraiser. That second million needs to be raised!"*

## Texel Foundation grant awarded

The EHE Rare Cancer Charity were delighted to announce in June that they had received a grant award from the Texel Foundation, the philanthropic arm of the Texel Group. The Texel Foundation, established by the Texel Group in 2015, first supported us in that same year, shortly after the charity was started, providing the charity with its first corporate donation. The Foundation supported the Charity again in 2019 which was wonderful, and we were therefore delighted when at the start of 2022, we were invited to participate in their 2022 grant application round.



The application round was organised by Texel in compliance with IVAR's Open and Trusting Grant Making programme, promoting flexible funding, and designed to make the process of grant application easier, more open, and appropriate for those taking part, and to avoid unnecessary restrictions on the use of grants made. The application process was excellent as it was indeed very focused, with an initial short written application followed up by a meeting at which we were able to answer any questions that the Texel team had, and also describe in more detail what the charity was doing.

The Charity was then thrilled when we received the news that we had been successful in securing a grant award of £25,500. The focus of the grant application had been: (i) to allow the charity to increase participation in the pan-European EHE prospective study that is currently being finalised by the team at INT in Milan; and (ii) engagement with fundraising specialists.

The Texel Foundation grant is the largest single donation the Charity has yet received, and it is the largest donation from a corporate/foundation group. The funds will help us expand our activities and advance research into this terrible disease. The EHERCC could not be more grateful for this wonderful award.

**Thank you Texel Foundation!**

## London Landmarks Half Marathon – a brilliant day

The second quarter of 2022 started with the running of the London Landmarks Half Marathon. The EHE Rare Cancer Charity had 42 brilliant supporters who were all running for the charity and raising funds for EHE research. The Charity were also delighted when Denise Robinson, Director of Research at The EHE Foundation in the USA, and her close friend Ann Campbell, whose husband Steve passed away due to EHE, both flew over from America specifically to run and raise critical EHE funds for research.

We are so grateful to everybody who took part in the run for us. These people go out and train hard all through the winter to raise money for EHE research. They are awesome. We also want to thank Denise and Ann for flying over – that was very special. We loved having Ann here who was also running in memory of her husband, Steve, who died from EHE five years ago. It was a poignant reminder of why we are fighting so hard to beat this cancer.

The Charity team raised more than £17,500 for EHE research. We think that is a wonderful achievement and extend our thanks and congratulations to all who took part.

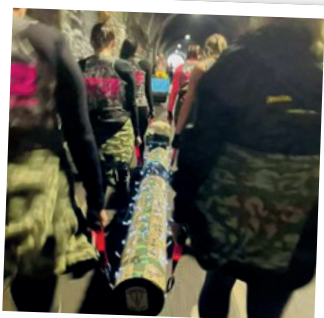




## 03 Fundraising and Finance Continued

### Superwomen run half marathon for Nicola

Many people will run a half marathon to raise funds for charity, but very few will want to do that while taking it in turns to carry a 70kg (154lbs) log for the 13+ miles. But that is exactly what Nicola Henderson's friends did in late January in Yate in South Gloucestershire.



Running from Bristol to Chipping Sodbury under their slogan "Normal is Boring", the 25 women known as Commando Boot Camp, and trained and supported by fireman and ex-Marine Lee Ralph, smashed their initial target of £500 and raised a staggering more than £7,000 for EHE research.

Nicola, an inspiring patient who underwent a liver transplant due to her progressive EHE could not have been more grateful:

*"So these are my friends... my lovely, crazy friends, who ran a half marathon for our cause; not only that, they are running with a 70kg (154lb) log!! The team are INCREDIBLE with a legend of a leader. I can never adequately express my gratitude to them for the amount of money and awareness raised for THE EHE RARE CANCER CHARITY UK!"*



### In memory of a very special woman

Wendy Cassidy wanted to celebrate the 50th birthday of her wonderful sister, Allana, who was diagnosed with progressive EHE in August 2018, and left us in 2020. This was a fundraising event that was very special for Wendy, but one she dearly wished was not necessary.

*"My brilliant, wonderful, funny and simply gorgeous sister, "our Larney", left us far too early last year after her battle with an ultra-rare cancer called EHE. Allana would have been 50 on the 13th June, so I am organising an event the day after in remembrance of her, and to celebrate her 50th, because I know that is what she would want us to do."*



Wendy's event, held in the Embassy Theatre Foyer in Skegness, gave those who knew Allana a chance to drop in and remember her and to share lovely stories about Allana. They also sold cakes, biscuits, tea and coffee to raise funds for EHE research, and set up a fundraising page so that people who could not make it were still able to contribute.

The event was a huge success, and many stories about Allana were indeed shared. Allana would have also been delighted and proud as Wendy raised more than £500 for EHE research on the day.



## Vibrant Headbands to raise research funds

Over the past seven years we have seen a lot of different ways that people have found to raise funds for EHE research, but Sue Dean, Paul Dean's mother came up with a new product, working with friends in the Women's Institute. They decided to knit vibrant headbands for the winter which they are selling to raise funds for EHE research. Sue explained:

*"With Christmas coming up and the icy cold winds forecast I thought why not put the headbands online so people can buy them. So I've set it up so that they are £10 each. With 80% of that going directly to The EHE Rare Cancer Charity UK and the other 20% covering the fees, postage and packaging. There are many colours just drop a message with the colour you'd like when you order!"*

What a fantastic idea, and by the end of the year Sue and her team of helpers had sold an amazing 170 headbands. That's £1,360 for EHE research. Totally brilliant Sue. Huge thanks for such an inspired idea. We love them.

## Running in memory of a dear colleague

Jess Ralph contacted the EHE Rare Cancer Charity in late September asking if we had any EHE running tops as she was running to raise funds for EHE research. The EHERCC are always delighted to provide running tops, both to support the runner, but also to spread further awareness of EHE. So we were thrilled that we did indeed have the right size top for Jess, for her run on 16th October.

Jess was running for her friend and colleague, Al Munday, who passed away in 2021 from EHE. Jess gathered donations when her friend passed away and then again in 2022 when it was his birthday. She wasn't able to do anything more at that time so had decided she'd run for the charity when she signed up for the Great South Run.

We were delighted when Jess posted news that she had made it around in one piece on the day and had raised more than £1,000 for EHE research, a tremendous result. Thank you Jess for your great support.





## 03 Fundraising and Finance Continued

### EHERCC Team cycle 100 miles to raise funds for research

The EHERCC organises two larger scale fundraising events each year. The second of these is the 100 miles cycling sportive, that starts and finishes in London, and is called RideLondon. In previous years this event had taken place in the county of Surrey, south and west of London. This year, however, the event had moved to the county of Essex, north and east of the capital.

EHERCC had twenty riders in the event who collectively raised nearly £20,000 for EHE Research. Paul Dean, an EHE patient himself, completed the ride in just over 5 hours, an amazing achievement.

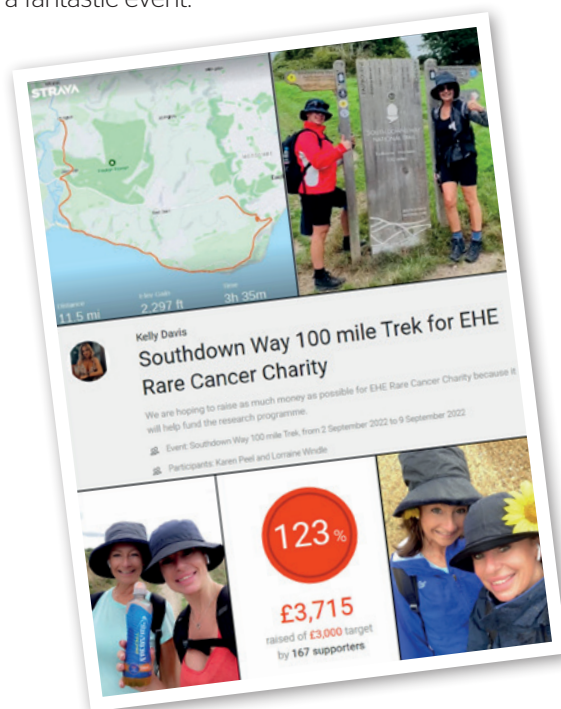
Hugh Leonard, Chair of Trustees, also took part. *"I have been encouraging people to take part in the London Landmarks Half Marathon and RideLondon events for the charity for 7 years now, and really felt it was time for me to take part. So I decided it had to be the RideLondon. It took me just over 7 hours, which I was very pleased with. It has been great training together as a group also, and of course we have raised a substantial sum for EHE research, which is wonderful."*

### "I will walk 100 miles..."

Kelly Davis's brother, who is on the front cover of this report, was diagnosed with EHE in early 2022. His diagnosis came "completely out of left field" as they say, and as for almost all of our members, was a shock. But also like nearly all of our other members, his family and friends are there to support him. Kelly decided she wanted to raise funds for EHE research and so we were delighted to see her post in August about her forthcoming campaign, an amazing 100-mile trek along the South Downs Way.

Then, on 13th September, Kelly posted news that they had completed the huge walk: *"So we made it! We completed the whole 100 Miles!!!! Back at home, slightly broken and completely drained, getting some well-deserved rest in! It's been a very challenging yet amazing journey for us! It's probably the hardest thing I've ever done in my life! The weather was against us, we had sun, wind, rain, hail and thunder storms! Literally didn't know what weather we were going to have thrown at us each day! It was so changeable! The terrain was a huge challenge! The hills and elevation were unreal most days! We were deliriously tired some days and so stiff from the day before. Each day seemed to roll into the next. A few days there was literally nothing to see, just following stony track after stony track, then climbing higher and higher! Relentless!! The last day at the Seven Sisters was by far the best day, what with the spectacular views. It was also the hardest with the elevation gain of 2,297ft."*

Kelly was super proud to be able to report that they had raised nearly £4,000 for The EHE Rare Cancer Charity to help fund EHE research. Kelly was rightly "over the moon" about their achievement and wanted to thank each and every person that had donated and had also helped with organisation or had supported them on their walk. We also want to say a huge thank you to Kelly and all her supporters for such a fantastic event.



## Kelly is fundraising again

Like many of our members who are affected by EHE, Kelly has thrown herself into raising funds for the EHE Rare Cancer Charity in the UK as Kelly's teenage daughter is an EHE patient.

Kelly has organised large work events and evening quiz nights, but she also never misses a chance to run a small stall in a local fair or market place. At the Penge October Fest Festival Kelly ran a bottle raffle stall, raising £261 for EHE research. That's £261 we did not have the day before. Thank you Kelly. Your drive and energy is wonderful. We are so grateful. And as always Max, her dog, joined in!



## In memory of Hazel Peake

It is always with mixed emotions that we publish news of fundraising events in memory of one of our EHE Warriors who is no longer with us in person. These events can however be very special indeed as people come together to celebrate the life of a loved one and dear friend. The quiz night held in Derby in memory of Hazel Peake was just such an event.

Hazel joined the EHE group in the UK in September 2021. She quickly became a regular voice in the UK WhatsApp group and maintained a real fighting spirit as she battled her aggressive EHE. Her branch of the Unite union supported the charity with a wonderful donation of £1,000, and Hazel was excited that her colleagues were also planning a quiz night for her early in 2022, to raise funds for EHE research.

Very sadly, Hazel's health deteriorated rapidly and she passed away in late January. Her colleagues, however, were determined to hold their quiz night to honour and celebrate their dear friend. And what a night it was. Organised by Paul Phillips, Lisa Neal and Katie Colbourne, a huge number of Hazel's friends and colleagues were there, together with Hazel's husband Andy and their daughter Emily.

The event, held at the Rolls Royce Leisure and Event Venue in Derby raised more than £10,000, thanks to the brilliant organisation and fantastic generosity of all who attended, and of all those who donated funds to the charity for EHE research. There was a lot of laughter, and just a few tears. But most of all there was a huge amount of love evident for a wonderful woman.

We also want to say a huge thank you to Paul, Lisa and Katie, and to Rolls Royce who provided the facilities and the evening meal. That allowed all the funds raised on the night to go to EHE research, something we are sure Hazel would have greatly appreciated.





EHE Rare Cancer Charity UK

# Financial Accounts for 2022

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# EHE Rare Cancer Charity (UK)

## Independent examiner's report

### Independent examiner's report to the trustees of EHE Rare Cancer Charity (UK)

I report to the charity trustees on my examination of the accounts of EHE Rare Cancer Charity (UK) (the Charity) for the year ended 31 December 2022.

### Responsibilities and basis of report

As the Trustees of the Charity you are responsible for the preparation of the accounts in accordance with the requirements of the Charities Act 2011 ('the Act').

I report in respect of my examination of the Charity's accounts carried out under section 145 of the Act and in carrying out my examination I have followed all applicable Directions given by the Charity Commission under section 145(5)(b) of the Act.

### Independent examiner's statement

I have completed my examination. I confirm that no material matters have come to my attention in connection with the examination giving me cause to believe that in any material respect:

- 1 accounting records were not kept in respect of the Charity required by section 130 of the Act; or
- 2 the accounts do not accord with those records; or
- 3 the accounts have not been prepared in accordance with the methods and principles of the Statement of Recommended Practice for accounting and reporting by charities [applicable to charities preparing their accounts in accordance with the Financial Reporting Standard applicable in the UK and Republic of Ireland (FRS 102)].

I have no concerns and have come across no other matters in connection with the examination to which attention should be drawn in this report in order to enable a proper understanding of the accounts to be reached.

*(signed) "RJP LLP"*

**Simon Paterson FCCA**

RJP LLP  
Ground Floor  
Egerton House  
68 Baker Street  
Weybridge  
Surrey  
KT13 8AL

Date: 23 October 2023



# EHE Rare Cancer Charity (UK)

## Statement of Financial Activities

for the period ended 31 December 2022

	Notes	Unrestricted funds £	Restricted funds £	<b>Total 2022 £</b>	Total 2021 £
<b>Incoming resources:</b>					
Donations	2	95,809	10,750	<b>106,559</b>	100,926
<b>Total incoming resources</b>		<b>95,809</b>	<b>10,750</b>	<b>106,559</b>	100,926
<b>Resources expended:</b>					
Costs of generating donations		1,812	562	<b>2,374</b>	12,201
Charitable activities		155,199	-	<b>155,199</b>	134,264
Governance costs		-	1,200	<b>1,200</b>	1,200
Other administrative costs		72	4,876	<b>4,948</b>	5,117
<b>Total resources expended</b>	3	<b>157,083</b>	<b>6,638</b>	<b>163,721</b>	152,782
<b>Net surplus for the year</b>		<b>(61,274)</b>	<b>4,112</b>	<b>(57,162)</b>	(51,856)
Transfer between funds		-	-	<b>-</b>	-
Balance brought forward		323,483	4,568	<b>328,051</b>	379,906
<b>Funds carried forward</b>	8	<b>262,209</b>	<b>8,680</b>	<b>270,889</b>	328,050

Funds carried  
forward for 2022  
£270,889

# EHE Rare Cancer Charity (UK)

## Balance Sheet

### as at 31 December 2022

	Notes	Unrestricted funds £	Restricted funds £	Total 2022 £	Total 2021 £
<b>Current assets</b>					
Debtors	5,9	208,391	3,780	212,171	153,748
Cash at bank and in hand		307,448	16,047	323,495	311,379
<b>Total current assets</b>		515,839	19,827	535,666	465,127
<b>Creditors: amounts falling due within one year</b>	6,9	(156,018)	(11,147)	(167,165)	(112,022)
<b>Net current assets (liabilities)</b>		359,821	8,680	368,501	353,105
<b>Creditors: amounts falling due after one year</b>	7,9	(97,612)	-	(97,612)	(25,055)
<b>Net assets (liabilities)</b>		262,209	8,680	270,889	328,050
<b>Funds carried forward</b>					
Unrestricted funds		262,209	-	262,209	323,482
Restricted funds		-	8,680	8,680	4,568
<b>Total funds</b>	8	262,209	8,680	270,889	328,050

The Charities Act 2011 requires the Trustees to prepare financial statements for each financial year which give a true and fair view of the state of affairs of the charity at the year end and of the surplus or deficit for the year then ended.

In preparing these financial statements, the Trustees are required to select suitable accounting policies, and then apply them on a consistent basis, making judgements and estimates that are prudent and reasonable. The Trustees must also prepare the financial statements on the going concern basis unless it is inappropriate to presume that the charity will continue in business.

The Trustees are responsible for keeping proper accounting records which disclose with reasonable accuracy at any time the financial position of the charity and to enable them to ensure the financial statements comply with the Charities Act 2011. The Trustees are also responsible for safeguarding the assets of the charity and hence taking reasonable steps for the prevention and detection of fraud and other irregularities.

These accounts were approved by the Trustees Committee on 22 October 2023 and signed on its behalf by:

(signed) "Hugh Leonard"

**Hugh Leonard**  
Chairperson



# EHE Rare Cancer Charity (UK)

## Notes to the Accounts

### for the period ended 31 December 2022

#### 1 Accounting Policies

**Basis of preparation:** The financial statements of the charity, which is a public benefit entity under FRS 102, have been prepared in accordance with the Charities SORP (FRS 102) 'Accounting and Reporting by Charities: Statement of Recommended Practice applicable to charities preparing their accounts in accordance with the Financial Reporting Standard applicable in the UK and Republic of Ireland (FRS 102) (effective 1 January 2019)', Financial Reporting Standard 102 'The Financial Reporting Standard applicable in the UK and Republic of Ireland' and the Charities Act 2011. The financial statements have been prepared under the historical cost convention.

#### Incoming resources

**Recognition of incoming resources:** These are included in the Statement of Financial Activities when:

- The charity becomes entitled to the resources;
- The trustees are virtually certain that they will receive the resources; and
- The monetary value can be measured with sufficient reliability.

**Deferred income:** Where grants are received in advance and specified by the donor as relating to specific accounting periods, these are deferred on an accruals basis to the period to which they relate.

**Tax reclaims on donations and gifts:** Incoming resources from tax reclaims are included in the Statement of Financial Activities at the same time as the gift to which they relate.

**Incoming resources with related expenditure:** Where incoming resources have related expenditure, the incoming resources and related expenditure are reported gross in the Statement of Financial Activities.

**Volunteer help:** The value of any volunteer help is not included in the accounts.

**Investment income:** Investment income is included in the accounts when receivable.

#### Expenditure and liabilities

Resources expended are inclusive of VAT where applicable which cannot be recovered.

**Liability recognition:** Liabilities are recognised as soon as there is a legal or constructive obligation committing the charity to pay out resources.

**Costs of charitable activities:** A research grant is recognised when the Charity formally notifies the recipient of the award following scientific review. The liability is measured as the total of expected payments for the award. Grant payments that are contingent on a successful outcome of and payable after a future scientific review are disclosed as commitments. Liabilities for awards payable more than one year after the balance sheet date are recorded at the value the Charity expects to settle the grant or award.

**Governance costs:** These include the costs of preparation and examination of statutory accounts, the costs of any general meetings and the costs of any legal advice to trustees on governance or constitutional matters.

#### Administrative fund

This fund has been established by the Trustees to fund all governance and administrative costs and is funded by a single donor for these restricted purposes.

## 2 Analysis of incoming resources

### Donation income:

	2022 £	2021 £
<b>Unrestricted funds:</b>		
Personal donations including fundraising events	62,593	76,125
Corporate and Foundation donations	33,216	3,901
	95,809	80,026
<b>Restricted funds:</b>		
Administration fund	10,750	20,900
	10,750	20,900

## 3 Analysis of resources expended

	Unrestricted funds £	Restricted funds £	Total 2022 £	Total 2021 £
<b>Costs of generating donations:</b>				
Just giving fees	478	562	1,040	1,101
Fundraising event entry and other fees	-	-	-	9,888
Credit card and other processing fees	1,334	-	1,334	1,212
	1,812	562	2,374	12,201
<b>Costs of charitable activities:</b>				
University of Manchester PhD Study	33,001	-	33,001	43,736
Royal Marsden Biobank	16,450	-	16,450	31,612
Zebrafish Study University of Sheffield	55,198	-	55,198	26,483
Fondazione IRCCS and ICR Biomarkers	36,608	-	36,608	32,433
Fondazione Prospective Study	13,942	-	13,942	-
	155,199	-	155,199	134,264
<b>Governance costs:</b>				
Independent examiners' fee	-	1,200	1,200	1,200
	-	1,200	1,200	1,200
<b>Other administrative costs:</b>				
Design and publishing	-	2,683	2,683	3,041
Website maintenance	-	2,088	2,088	1,883
Bank fees	72	105	177	193
	72	4,876	4,948	5,117

### Trustees' expenses

No expenses were incurred by Trustees during the period and reimbursed by the Charity (2021 - £6,293).

## 4 Taxation

The Charity is exempt from Corporation Tax on its charitable activities.

# EHE Rare Cancer Charity (UK)

## Notes to the Accounts (continued)

### for the period ended 31 December 2022

#### 5 Debtors

	Unrestricted funds £	Restricted funds £	<b>Total 2022 £</b>	Total 2021 £
Prepayment to the University of Manchester	-	-	-	50,533
Prepayment to Royal Marsden	60,685	-	<b>60,685</b>	32,805
Prepayment to Fondazione IRCSS Istituto Nazionale Dei Tumori	118,526	-	<b>118,526</b>	31,477
Prepayment to the University of Sheffield	28,715	-	<b>28,715</b>	26,483
Other debtors	465	3,780	<b>4,245</b>	12,450
	<b>208,391</b>	<b>3,780</b>	<b>212,171</b>	153,748

Included within the debtors figures above are amounts of £97,612 (2021 – £25,055) due after more than one year.

#### 6 Creditors: amounts falling due within one year

	Unrestricted funds £	Restricted funds £	<b>Total 2022 £</b>	Total 2021 £
University of Manchester	3,820	-	<b>3,820</b>	29,181
Royal Marsden	28,050	-	<b>28,050</b>	9,820
Fondazione IRCSS Istituto Nazionale Dei Tumori	95,433	-	<b>95,433</b>	37,005
University of Sheffield	2 28,715	-	<b>28,715</b>	26,483
Accrued independent examiners'	-	2,400	<b>2,400</b>	1,200
Other creditors	-	8,747	<b>8,747</b>	2,860
	<b>156,018</b>	<b>11,147</b>	<b>167,165</b>	112,022

#### 7 Creditors: amounts falling due after one year

	Unrestricted funds £	Restricted funds £	<b>Total 2022 £</b>	Total 2021 £
Fondazione IRCSS Istituto Nazionale Dei Tumori	54,207	-	<b>54,207</b>	-
Royal Marsden	43,405	-	<b>43,405</b>	25,055
	<b>97,612</b>	-	<b>97,612</b>	25,055

#### 8 Details of funds

##### Administrative Fund

This fund has been established by the Trustees to fund all governance and administrative costs and is funded by a single donor for these restricted purposes.



## 9 Commitments and contingencies

In July 2018, the Charity contracted with the **Bateson Centre at the University of Sheffield** to develop an EHE zebrafish model. In August 2019 and July 2021, a second and third phase of the project was agreed and in July 2022, the Charity contracted with the Bateson Centre to fund an additional one-year, full-time MPhil student to further assess the EHE zebrafish model that the Charity had funded in 2018 through 2021. The total cost of the project is £57,430 and commenced in July 2022. In 2022, £55,198 of payments were made and recorded as charitable activity cost (2021 – £26,483). The amounts committed to for 2023 have been included within Debtors and Creditors as appropriate.

In October 2018, the Charity contracted with the **Department of Developmental Biology and Medicine at the University of Manchester** for the carrying out of a four-year PhD study to research the impact of EHE on endothelial cells. The total cost of the contract was £173,237 to be incurred over four years from January 2019 as follows:

2019	£45,535
2020	£49,420
2021	£49,101
2022	£29,181

In 2022, £29,181 of payments were made and £33,001 recorded as charitable activity cost (2021 – payments of £49,101 and expense of £43,736). The amounts committed to for 2023 have been included within Debtors and Creditors as appropriate.

In March 2021, the Charity agreed to fund costs associated with the establishment and administration of an EHE Biobank and the provision of a Tissue Manager with the **Royal Marsden Cancer Charity and the Royal Marsden NHS Foundation Trust** with an estimated total cost of £85,150 over five years commencing in April 2021 (four years commencing April 2022 regarding the Tissue manager). In 2022, £7,750 of payments were made (2021 – £3,875) and £16,450 recorded as charitable activity cost (2021 – £5,945). The amounts committed to for future years have been included within Debtors and Creditors as appropriate.

In December 2020, the Charity contracted with the **Fondazione IRCCS Istituto Nazionale Dei Tumori in Italy and the Institute of Cancer Research: Royal Cancer Hospital, UK** to fund a project to assess the presence of novel biomarkers in EHE patient blood and tissue samples to inform patient management as well as potential therapeutic targets. The total cost of the project is €115,000 (£101,797) to be incurred over a maximum of 30 months and separately, the Charity agreed that the EHE Foundation based in the United States would fund €40,000 (£35,407) of the total costs. In 2022, payments of £24,965 were made and £21,634 was recorded as charitable activity cost (2021 – payments of £25,949 and £32,433 of charitable activity cost). The remaining amounts payable by the Charity have been included in Debtors and Creditors as appropriate.

In June 2022, the Charity agreed to expand the project contracted with the **Fondazione IRCCS Istituto Nazionale Dei Tumori in Italy and the Institute of Cancer Research: Royal Cancer Hospital, UK** to look in greater detail of the mRNA analysis and to develop additional PDX models of different variants of EHE. Total costs of the expansion over the two years of the project are estimated at £117,396 with costs funded 50% by the Charity and 50% by the EHE Foundation in the United States. In 2022, no payments were made and £14,975 was recorded as charitable activity cost (2021 – £nil). The remaining amounts payable by the Charity have been included in Debtors and Creditors as appropriate.

In December 2022, the Charity contracted with the **Fondazione IRCCS Istituto Nazionale Dei Tumori** in Italy to fund costs associated with a study aiming to provide a description of the population affected by EHE, giving an insight into the natural history of the disease and its variants, leading to the possible identification of clinical and biochemical prognostic and predictive factors. Total costs of the project are €91,500 (£80,995). In 2022, no payments were made and £13,942 was recorded as charitable activity cost (2021 – £nil). The remaining amounts payable by the Charity have been included in Debtors and Creditors as appropriate.

# Trustees' Declaration

As Trustees of the EHE Rare Cancer Charity (UK), the undersigned have fully reviewed the content of this Report of the Trustees and confirm that they each consider it to be a true and fair reflection of the Charity's activities and operations for the year ending 31st December 2022. They each confirm that there are, to the best of their knowledge, no exceptional or special events that have occurred or that should be reported.

The Trustees also confirm that they have undertaken their respective roles and responsibilities with due regard to the public benefit requirements of the charity, and have taken into account the Charity Commission's public benefit guidance when making any decision and producing any reports relating to EHERCC's charitable objects and its associated activities.

Signed this 25th day of October, 2023

*(signed) "Hugh Leonard"*  
**Hugh Leonard** Chair of Trustees

*(signed) "Jeff Collins"*  
**Jeff Collins** Trustee

*(signed) "Kate Hooper"*  
**Kate Hooper** Trustee

*(signed) "Oliver Pearce"*  
**Oliver Pearce** Trustee

*(signed) "Sally Baker"*  
**Sally Baker** Trustee

---

## Charity Information

### Charity Name:

The EHE Rare Cancer Charity (UK),  
A Charitable Incorporated Organisation (CIO)

### Also known as:

Also known by its acronym, EHERCC

### Charity number:

1162472

### Web address:

[www.ehercc.org.uk](http://www.ehercc.org.uk)

### Registered address:

23 Geneva Road, Kingston Upon Thames,  
Surrey, KT1 2TW

### Charity Trustees:

Mr Hugh Leonard (Chair)  
Mr Jeffery Collins  
Dr Katharine Hooper  
Dr Oliver Pearce  
Ms Sally Baker

Established in 2015.

Also working closely with EHE foundations in USA, Australia, Canada and Italy.

Managed and run by volunteers.

All running costs funded by single donor.

100% of all donations received therefore available to deliver core objectives.

# The Pledge

*The Pledge* is the quarterly newsletter of the EHE group of foundations. It is produced in London and provides details of the group's worldwide activities in their key areas of advocacy and patient support, research, fundraising, and any other stories of interest. If you would like to be added to the distribution list to receive a copy of *The Pledge* each quarter, please contact the Charity.







**EHE Rare Cancer Charity (UK)**

23 Geneva Road  
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Registered charity: 1162472



A huge thank you to [eightcreate.co.uk](http://eightcreate.co.uk)  
for the graphics and design work in  
producing this report



We would like to also thank  
Bennett Brookes Chartered  
Accountants for providing  
bookkeeping services to EHERCC



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**Cover images**

EHE patient Tyler Davis  
participating in  
immunotherapy trial.

and

Some of the EHE  
RideLondon Essex team.