BONE CANCER RESEARCH TRUST

STRIVING FOR PROGRESS THROUGH RESEARCH

OUR RESEARCH IMPACT REPORT 2023

THE BONE CANCER RESEARCH TRUST

In 2004, a group of families who had lost children and young people to primary bone cancer came together. At that time, there was virtually no accessible information and practically no funding for research into this disease. With guidance from Professor Ian Lewis, a consultant paediatrician and adolescent oncologist at St James's University Hospital, Leeds, the families registered the Bone Cancer Research Trust as a charity in 2006. Today, the Bone Cancer Research Trust is the leading charity dedicated to saving lives and fighting primary bone cancer.

OUR VISION

A world where primary bone cancer is cured.

OUR MISSION

To save lives and improve outcomes for people affected by primary bone cancer through research, information, awareness, and support.

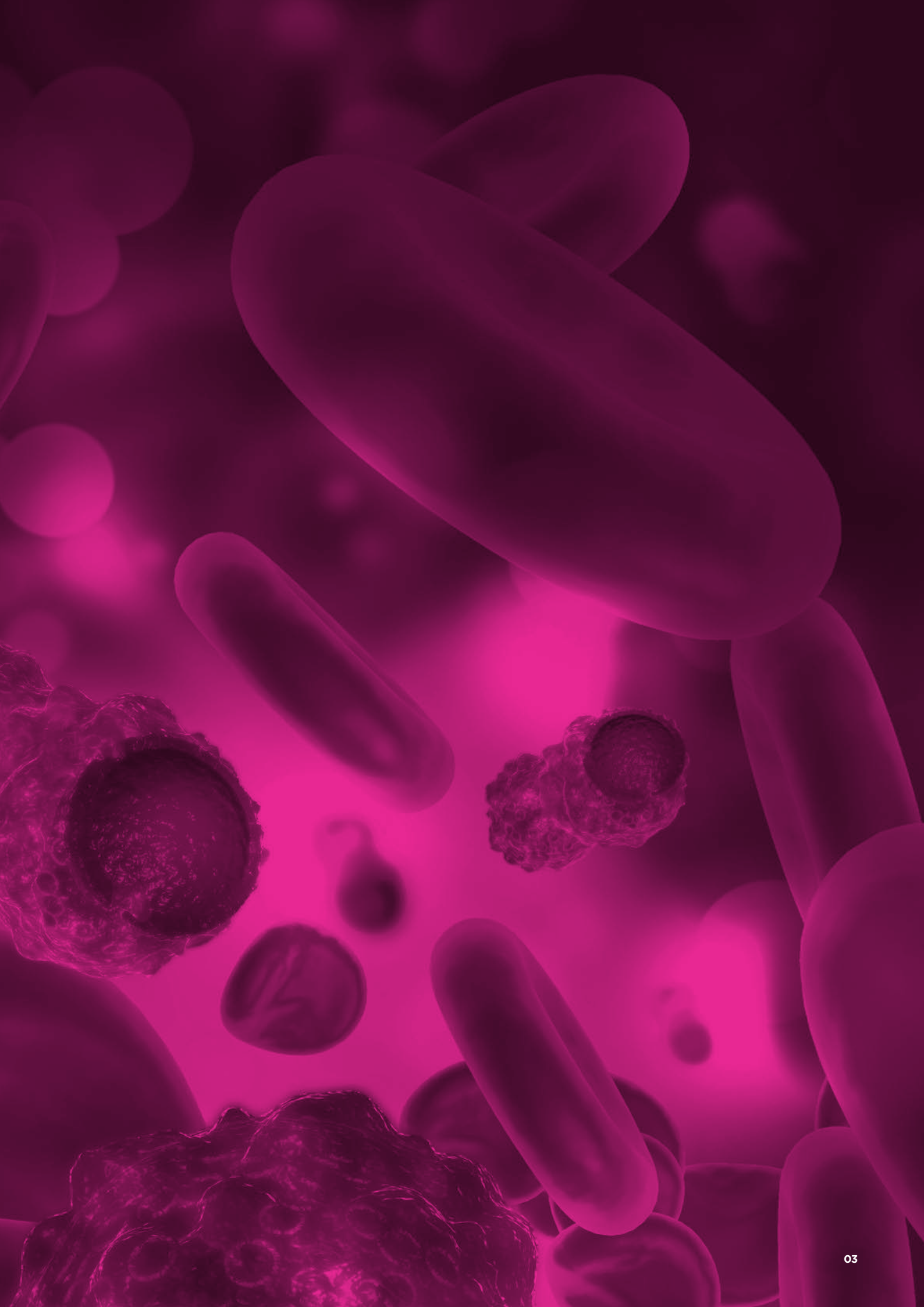
RESEARCH: As of August 2023, the Bone Cancer Research Trust has committed over £8.3 million to primary bone cancer research with the aims of achieving a better understanding of the disease, developing kinder and more effective treatments, and ultimately finding a cure.

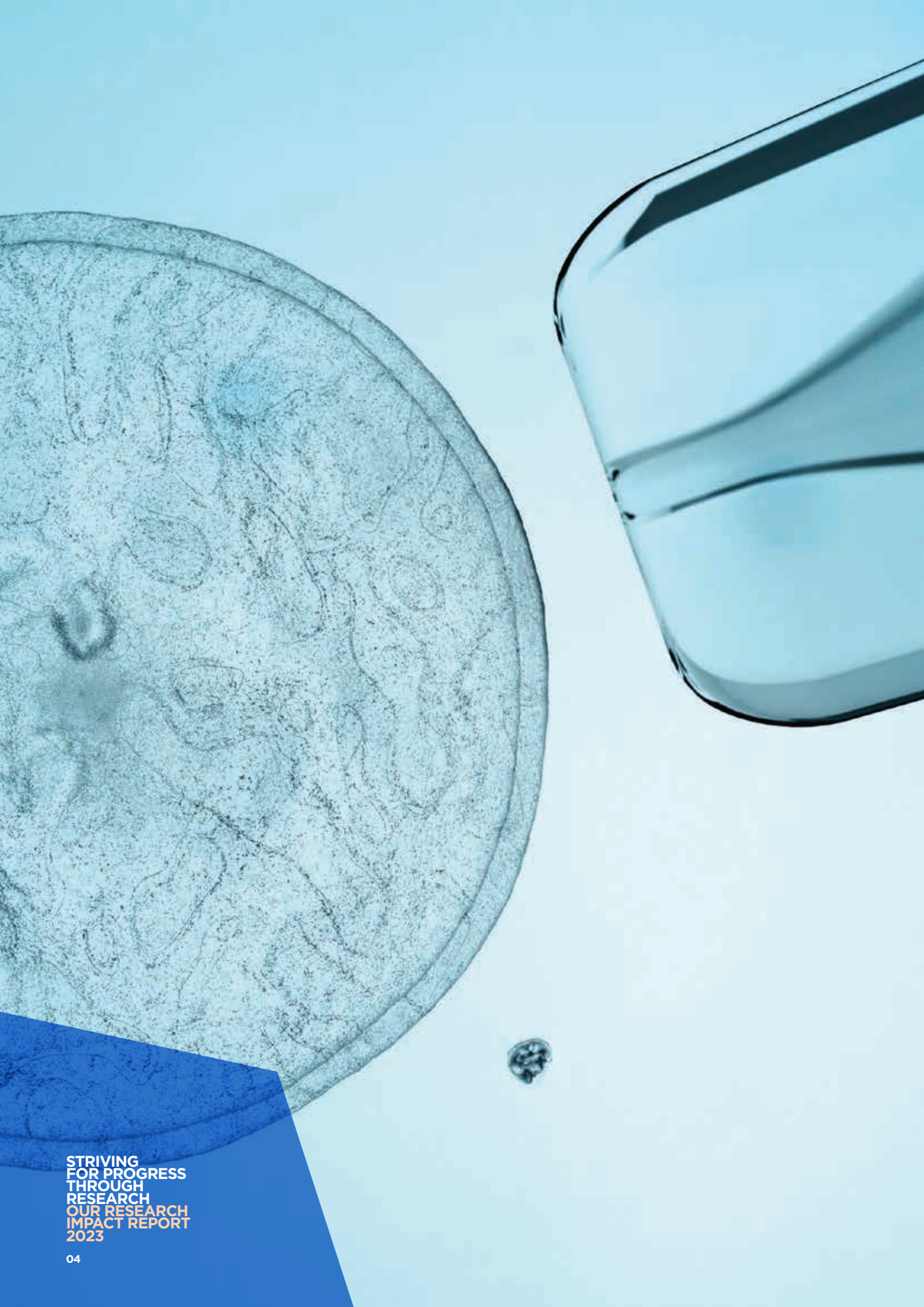
INFORMATION: Our portfolio of accredited information helps healthcare professionals, patients, their families, friends, and the public learn more about primary bone cancer and how it is diagnosed and treated.

AWARENESS: We are the voice of the primary bone cancer community, raising awareness amongst the public, healthcare professionals, researchers, and policy makers.

SUPPORT: We provide a dedicated Support & Information Service, which is freely available to anyone affected by primary bone cancer and tumours.

THE BONE CANCER RESEARCH TRUST RECEIVES NO REGULAR GOVERNMENT FUNDING FOR ITS LIFE-SAVING RESEARCH.





STRIVING FOR PROGRESS THROUGH RESEARCH

OUR RESEARCH IMPACT REPORT 2023

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WELCOME!

The effects of the COVID-19 pandemic and cost of living crisis continue to be felt by the primary bone cancer community. However, thanks to the continued efforts of our supporters, the Bone Cancer Research Trust remains more committed than ever to facilitate collaborative research aimed at accelerating the discovery of better and kinder treatments for our patients.

Since our last research impact report published in October 2021, and up to the completion of this report in August 2023, we have doubled our research commitment and have awarded over £4 million in grants to support innovative research.

We continue to fund researchers at all stages in their careers, with a particular emphasis on supporting early career investigators who will become the research leaders of the future. We are delighted to have awarded our first Early Career Fellowship, to decipher the causes of osteosarcoma resistance to chemotherapy and how to overcome them.

We endorsed the campaign #ResearchAtRisk, led by the Association of Medical Research Charities. This successful campaign resulted in the government providing additional financial support to research charities, with the specific purpose of ensuring that early career researchers were retained in the medical research field.

In 2021, we awarded our first international project. The grant is now completed, having achieved results that are already published in the scientific literature and may lead to further advances in finding new treatments for Ewing sarcoma.

Our 2022-2032 strategy has a particular focus on maximising the impact of clinical trials. We are thrilled that our new 'Clinical Trial Support' scheme has provided funding to facilitate the introduction of a new treatment to the rEECur clinical trial, for Ewing sarcoma patients suffering with recurrent or primary refractory disease.

With our first clinical study, ICONIC, coming to an end, we are excited to support Ad-ICONIC to continue the follow-up of patients, learning more from their response to treatment and utilising the samples collected to better understand the biology of osteosarcoma and discover new treatments.

Patients are at the heart of our research funding process. In the summer of 2021, we introduced our Patient and Public Involvement Panel (PPIP). Through PPI, lived experiences are brought to the forefront of research, ensuring that the questions we ask and the outcomes we achieve through our research projects align with the priorities of patients.

An enormous THANK YOU to all our supporters. As a result of your efforts and generosity, researchers, clinicians, and surgeons can continue to work tirelessly to improve the lives of primary bone cancer patients and their families.

Dr Zoe Davison,
Head of Research, Support & Information,
The Bone Cancer Research Trust.

Dr Kathleen Kane,
Research & Engagement Officer,
The Bone Cancer Research Trust.

Dr Victoria Vinader, Research Manager,
The Bone Cancer Research Trust.

WHAT DO WE MEASURE OURSELVES AGAINST?

2017-2022 RESEARCH OBJECTIVES

£2.8 MILLION

TO PRIMARY BONE CANCER RESEARCH

In 2017, the Bone Cancer Research Trust launched an ambitious strategic plan that pledged to commit over £2.8 million to pioneering research through an innovative grant programme. **We surpassed this target by 100% and committed £5.6million** to research between 2017-2022[1].

2022-2032 RESEARCH OBJECTIVES

Our 2022-2032 research strategy – *Accelerating Research to Help More Patients Survive and Thrive*[2] capitalises on the progress made, with seven ambitious objectives. To deliver these, we will commit **£10 million** of research funding over the next ten years and transform the landscape of primary bone cancer research.

OUR OBJECTIVES

1. Deliver a new and flexible grant programme supporting research on every form of primary bone cancer and tumour and facilitate the development of new clinical trials.
2. Involve patients through our Patient & Public Involvement Panel.
3. Ensure all patients can contribute to research through sample donation and participation in clinical trials and biological studies.
4. Bring all aspects of current primary bone cancer research together, harnessing data, technology, and skills to accelerate progress.
5. Facilitate and promote collaborative working.
6. Support the next generation of world class, primary bone cancer researchers.
7. Ensure all forms of primary bone cancer and tumour are represented in research.

"The Bone Cancer Research Trust's new research strategy 'Accelerating Research to Help More Patients Survive and Thrive' marks our strong commitment to continue funding pioneering research, embracing new technologies and facilitating collaborations among researchers to maximise progress for our patients. Overwhelmingly, the primary bone cancer community supported the need for finding better and kinder treatments, but also emphasised the need for those that survive to live better, fuller lives.

I am proud of everything we have achieved so far, and with the patients' voice at the centre of everything we do, the 2022-2032 research strategy focuses on improving survival for all primary bone cancer patients, including those diagnosed with rarer types, but also on improving the quality of life of all that live with and beyond a primary bone cancer diagnosis."

Dr Zoe Davison, Head of Research, Support & Information at the Bone Cancer Research Trust.

OUR RESEARCH IN NUMBERS

SINCE OUR LAST IMPACT REPORT...

WE HAVE **DOUBLED** THE RESEARCH INVESTMENT, COMMITTING £4 MILLION OVER THE LAST 2 YEARS, TAKING OUR TOTAL TO **OVER £8 MILLION.**

THE **INFRASTRUCTURE GRANTS** HAVE FACILITATED THE COLLECTION OF **12,438 PATIENT SAMPLES.**

OUR **FIRST CLINICAL STUDY, ICONIC** IS COMPLETED, **AD-ICONIC** CONTINUES AS THE LARGEST OSTEOSARCOMA COLLABORATION IN THE UK.

OUR **FIRST CLINICAL TRIAL SUPPORT GRANT** SUPPORTS THE INCLUSION OF **LENVATINIB** INTO THE **rEECur** TRIAL FOR RELAPSED OR RECURRENT EWING SARCOMA.

WE HAVE AWARDED **45 RESEARCH GRANTS,** TO SUPPORT EARLY CAREER RESEARCHERS, TOTALLING OVER **£2.6 MILLION** AND REPRESENTING **32% OF OUR RESEARCH COMMITMENT SPEND.**

RESEARCH FUNDED BY THE BONE CANCER RESEARCH TRUST HAS RESULTED IN **111 SCIENTIFIC PUBLICATIONS** WHICH HAVE BEEN **CITIED IN THE SCIENTIFIC LITERATURE 3910 TIMES.**

THE NUMBER OF CITATIONS BY OTHER RESEARCHERS IS HIGHLY INDICATIVE OF THE RELEVANCE OF THE KNOWLEDGE AND PRECEDENT GENERATED FROM THIS FUNDING.

148 GRANTS SINCE 2006. 148 GRANTS SUPPORT 93 PRINCIPAL INVESTIGATORS WITH SOME RECEIVING FUNDING ON SEVERAL OCCASIONS.

93 UNIQUE PRINCIPAL INVESTIGATORS	55 REPEAT FUNDING

360 CO-APPLICANTS AND COLLABORATORS SINCE 2006 SUPPORT PRINCIPAL INVESTIGATORS WITH SOME DOING SO ON SEVERAL OCCASIONS.

221 UNIQUE CO-APPLICANTS & COLLABORATORS	139 REPEAT COLLABORATIONS

488 ACADEMIC INSTITUTIONS SINCE 2006. 102 ACADEMIC INSTITUTIONS FUNDED, SUPPORTED BY MULTIPLE CO-APPLICANTS AND COLLABORATORS ON NUMEROUS OCCASIONS.

102 UNIQUE ACADEMIC INSTITUTIONS	386 REPEAT FUNDING OR COLLABORATIONS

FINDING NOVEL THERAPEUTIC OPTIONS

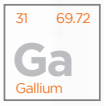
"I was diagnosed with metastatic Ewing sarcoma in 2010 at the age of 16. I underwent chemotherapy, a stem cell transplant, and radiotherapy. The treatment was tough, I received more blood transfusions than I can remember and was constantly in and out of hospital. The treatment left me feeling exhausted, sick, and unable to maintain the kind of life a normal 16-year-old should have. It was many years later that I learnt the drugs used in my treatment had changed little in the decades before and indeed after my diagnosis.

It is vital that work continues to find new treatment options, which can reduce the harrowing effects of treatment at the time, and the harmful long term side effects. Be it through reducing the amount of time spent in hospital, removing some of the side effects of treatment, or finding new options that allow a higher quality of life in the years post-treatment, the search for novel treatments is hugely important. Through the research funded by the Bone Cancer Research Trust, kinder and more effective treatment methods are being discovered, moving away from the dated treatment options of the past, and onto immunotherapy, targeted therapies, and improvements to chemotherapy and radiotherapy."

Nick Massey, Ewing sarcoma patient.

Responding to the Bone Cancer Research Trust's stakeholder consultation, our community ranked **finding new and more efficient treatments** as a top research priority. We have chosen some exciting examples of recent projects to illustrate this area.

Although most drugs are composed of hydrogen, carbon, or oxygen, researchers are trying to harness different physical and chemical properties from other elements to target and kill cancer cells. One example is the metal gallium.



BONE-SEEKING METAL-BASED DRUGS TO OVERCOME CHEMOTHERAPY RESISTANCE IN OSTEOSARCOMA

Dr Rama Suntharalingham from the University of Leicester was awarded an Idea Grant to investigate if molecules containing gallium could be used to target osteosarcoma cells that are resistant to chemotherapy.

The group successfully prepared compounds that, in the laboratory, displayed high potency against chemotherapy resistant osteosarcoma cells. They were also able to enclose these drugs into nanoparticles, so they could be delivered more efficiently inside cancer cells. Dr Suntharalingham is now looking to improve the delivery of these agents selectively to the bone tumour cells.

The research has taken significant steps towards identifying effective and targeted treatments able to overcome chemotherapy resistance in osteosarcoma, which have the potential to be translated from the laboratory to the clinical setting[3,4].

"The Bone Cancer Research Trust funding has enabled us to identify gallium-containing small molecules and nanoparticle systems that are highly potent towards a resistant sub-population of osteosarcoma cells linked to relapse and metastasis. Next, we will look to add 'osteosarcoma cell-targeting groups' onto our nanoparticle platforms to enable high selectivity toward osteosarcoma cells, prior to pursuing opportunities for translation.

As a direct result of the encouraging results obtained during the Bone Cancer Research Trust project, my research group were able to secure a 4 year-PhD studentship funded by the University of Leicester and the Chinese Scholarship Council. The PhD project will aim to develop multi-nuclear gallium-containing clusters with even higher potency towards osteosarcoma cells than the compounds we have developed thus far."

Dr Rama Suntharalingham, University of Leicester.

IMPROVING OUTCOMES THROUGH PERSONALISED TREATMENTS

It is becoming increasingly apparent that even within the same type of tumour, targeted treatments should be directed towards the specific population of patients that are most likely to benefit from them.

We awarded a research project grant to Professor Sibylle Mittnacht at University College London Cancer Institute, to investigate the potential of using PARP inhibitors to treat osteosarcoma patients that carry a mutation on the *RB1* gene. PARP inhibitors (inhibitors of poly adenosine diphosphate-ribose polymerase) prevent cancer cells from repairing the DNA breaks that naturally arise or are caused by chemotherapy and or radiotherapy and are currently being used successfully (alone or in combination with other therapies) to treat several cancers, particularly ovarian tumours.

Mutations that result in the loss-of-function of the Retinoblastoma tumour suppressor (*RB1*) gene affect the ability of cancer cells to repair DNA breaks. Professor Mittnacht has demonstrated in laboratory models that osteosarcoma cells containing this mutation are extremely sensitive to treatment with PARP inhibitors[5].

This grant will allow the research team to extend their work and undertake the necessary investigations to support the design of a clinical trial utilising PARP inhibitors to treat osteosarcoma patients, an approach that would be applicable to the 40-60% of osteosarcoma patients who present with the *RB1* mutation.

"The focus of our research has been for some time to understand how cancers develop. From this understanding, we now know that certain cancers present with vulnerabilities that relate to their specific molecular makeup. Our lab focuses on using this knowledge to design better treatments for osteosarcoma.

With funding from the Bone Cancer Research Trust, we are seeking to translate a discovery we made in basic conceptual research into clinical use. Some osteosarcomas are hypersensitive to drugs that have shown very strong impact on the outcomes for ovarian cancer patients.

We are trying to understand how we can identify osteosarcoma patients with hypersensitive cancers in the clinic and will seek an opportunity for a clinical trial to use these drugs, as they are currently used in ovarian cancer - up front to prevent metastasis, recurrence, and disease progression. To succeed, we need to collaborate with our clinical colleagues, and we need access to clinical data and samples, which are both made possible through the ICONIC study.

I am so impressed by the drive and inventiveness of the Bone Cancer Research Trust supporters! If we get to make a change in this disease, it is because of your unrelenting dedication.
Thank you to every one of you."

Professor Sibylle Mittnacht,
University College London.

DOES OESTROGEN HAVE A PROTECTIVE EFFECT IN CHONDROSARCOMA?

In 2019, the Bone Cancer Research Trust organised its first chondrosarcoma planning symposium. It brought together clinical and academic researchers, to discuss the progress being made in current trials and biological studies and to plan future projects.

We responded with the launch of our first Idea Grant call focused on chondrosarcoma research, which was awarded in 2020 to Professor Alison Gartland at The University of Sheffield to investigate if oestrogen has a protective effect in chondrosarcoma. This hypothesis derives from the fact that chondrosarcoma disproportionately affects men, with women having improved survival compared to men of similar age; an advantage that seems to diminish after the menopause[6].

With this funding, the Sheffield research group has confirmed that oestrogen decreases the growth of chondrosarcoma tumours in the laboratory[7]. With further funding newly awarded in 2023, they aim to elucidate the biological mechanisms by which these effects take place and if they can be exploited to identify new targeted therapeutics for chondrosarcoma.

This project highlights the need for achieving a better in depth understanding of the different populations affected by primary bone cancer and the effect certain characteristics (age, sex, anatomical location, type, and grade of primary bone tumour, etc.) have on the outcomes for patients. To achieve this, at the end of 2021, we embarked on a collaboration with Sarcoma UK to fund **"Improving outcomes in sarcoma through analysis and interrogation of national cancer data"**, a project based at University College London and NHS England (formerly NHS Digital) that interrogates the National Disease Registration Service (NDRS) for primary bone cancer patient data, with the aim of identifying specific areas of need and opportunities for research that can lead to improvements in patient care.

HARNESSING THE IMMUNE SYSTEM TO COMBAT EWING SARCOMA

There is great interest in boosting the ability of the immune system to control cancer. Despite the success in treating melanoma, lung and colorectal cancer, immune checkpoint inhibitor therapy has proven ineffective in Ewing sarcoma. At the start of our 2017-2022 strategy, the Bone Cancer Research Trust awarded a 4-year PhD studentship to Professor Graham Cook at the University of Leeds to investigate if a different immunotherapy approach could be applied to Ewing sarcoma.

Oncolytic viruses are naturally occurring viruses that selectively target and kill cancer cells whilst leaving healthy cells unharmed. After entering the tumour cell, an oncolytic virus replicates and causes it to 'burst', releasing immune stimulating proteins and shedding virus. This sends signals to immune cells, recruiting them to the surrounding area (the tumour micro-environment) and initiating anti-tumour responses. However, Ewing sarcoma tumours are referred to as 'cold', this means that they trigger a less powerful immune response when exposed to immunotherapies, compared to other 'hot' tumours.

PhD student Tyler Barr investigated the tumour cell killing effect of oncolytic viruses against standard laboratory Ewing sarcoma cells and those directly derived from patients[8]. In 2022, with her PhD now completed and through funding from other charities obtained because of the encouraging results achieved during this Bone Cancer Research Trust funded studentship, the research into oncolytic viruses continues not only for Ewing sarcoma, but also osteosarcoma.

"There is a desperate need for new treatment options for Ewing sarcoma patients. Our Bone Cancer Research Trust-funded work has centred on harnessing the immune system to fight cancer, a concept that has seen much success in a number of other cancer types. The 'cold' immune micro-environment in Ewing sarcoma tumours presents a barrier for immunotherapy, but the idea behind oncolytic virus therapy is that it can reverse the suppressive effects of the tumour, 'waking up' the immune system again. I am extremely hopeful for the future of oncolytic virus therapy, and indeed other immunotherapies, for the treatment of sarcoma."

Dr Tyler Barr, University of Leeds.

2ND GENERATION CLOFARABINE DERIVATIVES AS CD99 INHIBITORS FOR EWING SARCOMA

Our stakeholder consultation told us that to benefit patients, the primary bone cancer community wants us to fund the best research, regardless of where it takes place.

In 2021, the Bone Cancer Research Trust awarded its first project to an overseas institution.

Professor Aykut Üren at Georgetown University, USA has investigated the potential of inhibitors of a protein named CD99, present on the surface of Ewing sarcoma cells, to kill cancer cells whilst maintaining an acceptable side effect profile. The new compounds selectively recognise the Ewing sarcoma cells and inhibit CD99 without getting inside the cell. Based on this behaviour, we anticipate that the new compounds will cause fewer side effects in patients.

Results have already been published in the scientific literature. These findings provide a road map for the future development of selective CD99 inhibitors for targeted treatment of Ewing sarcoma[9].


BONE
CANCER
RESEARCH TRUST

PPIP
PATIENT AND PUBLIC INVOLVEMENT PANEL

ENSURING PATIENT AND PUBLIC NEEDS ARE AT THE HEART OF OUR RESEARCH

ESTABLISHING THE BONE CANCER RESEARCH TRUST'S PATIENT & PUBLIC INVOLVEMENT PANEL (PPIP)

The primary bone cancer community face a range of challenges, largely relating to the rarity and complexity of this disease, alongside the scarcity of research funding.

This means that they are uniquely placed to identify key research priorities and guide high-quality, patient-centred research. Within a recent survey of our stakeholders, 91% of respondents acknowledged the importance of patient and public involvement (PPI) in research.

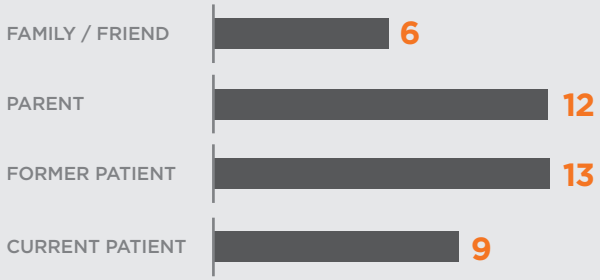
Despite this, opportunities for members of the primary bone cancer community to be meaningfully involved in research have historically been lacking.

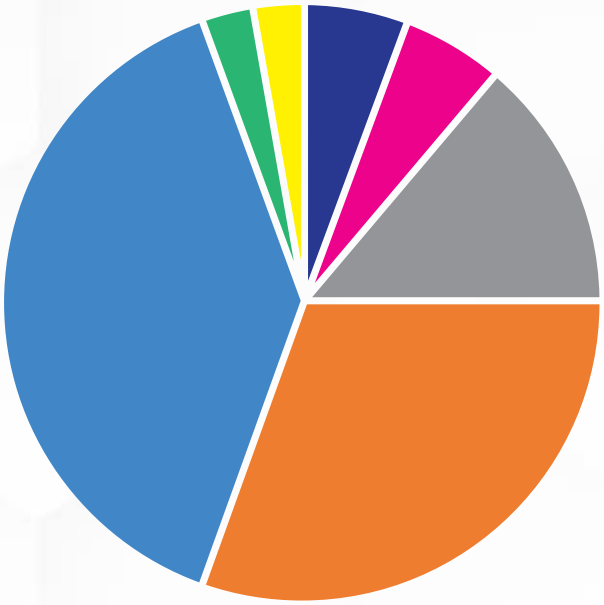
According to the National Institute of Health Research (NIHR), the aim of PPI is to ensure that research is carried out 'with' patients and members of the public, rather than 'to', 'about' or 'for' them.

For the Bone Cancer Research Trust, PPI means ensuring that patients and their support networks are at the very heart of our research funding processes and, ultimately, gives them a voice when it comes to shaping the research that matters to them.

In August 2021, we set out to establish a diverse and representative panel, encompassing lived experiences from right across the primary bone cancer community. Since then, the Patient & Public Involvement Panel (PPIP) has steadily grown, now comprising 40 members, including current and former patients, as well as parents, other family members and friends. Their lived experiences span a breadth of primary bone cancers and tumours, from the most common to some of the rarest.

PPIP MEMBERS' EXPERIENCE OF PRIMARY BONE CANCER





TYPES OF PRIMARY BONE CANCER AND TUMOUR REPRESENTED WITHIN PPIP

- 15 OSTEOSARCOMA
- 11 EWING SARCOMA
- 8 CHONDROSARCOMA
- 2 CHORDOMA
- 2 ADAMANTINOMA
- 1 AMELOBLASTOMA
- 1 GIANT CELL TUMOUR OF THE BONE

To date, members have been involved in a number of key activities, making important contributions to the development and review of research funding applications submitted to BCRT and to other funding bodies.

CONSULTATION MEETINGS:
A CHANCE FOR RESEARCHERS TO SHARE THEIR IDEAS WITH MEMBERS OF THE PRIMARY BONE CANCER COMMUNITY AND TO RECEIVE VITAL FEEDBACK AHEAD OF APPLICATION DEVELOPMENT.

APPLICATION DEVELOPMENT:
PANEL MEMBERS SUPPORT RESEARCHERS TO SUCCESSFULLY COMMUNICATE THEIR PROJECT TO A LAY AUDIENCE, PROVIDING INPUT ON THE LAY SECTIONS OF THE FUNDING APPLICATION AHEAD OF SUBMISSION.

LAY REVIEW:
PANEL MEMBERS BRING THEIR LIVED EXPERIENCES TO THE APPLICATION REVIEW PROCESS, PROVIDING THE INDEPENDENT SCIENTIFIC ADVISORY PANEL (ISAP) WITH FEEDBACK ON THE IMPORTANCE, RELEVANCE AND CLARITY OF THE PROPOSED RESEARCH.

EXPLORING THE IMPACT OF PPIP: 2021 – 2023

PPIP: IMPACT IN NUMBERS

25 MEMBERS HAVE TAKEN PART IN PROJECT CONSULTATION MEETINGS

22 MEMBERS HAVE COMPLETED LAY REVIEWS, CONTRIBUTING FEEDBACK TO ISAP

COLLECTIVELY, PPIP HAS SUPPORTED THE DEVELOPMENT & REVIEW OF 28 PROJECT APPLICATIONS

SUPPORTING THE INVESTMENT OF OVER £2.6 MILLION INTO PRIMARY BONE CANCER RESEARCH BY BCRT ALONE

PPIP: IMPACT THROUGH EXPERIENCE

A crucial measure of impact across all our PPI activities is the perceived benefit and value for our panel members, who generously share their time and expertise in support of primary bone cancer research. We endeavour to provide meaningful opportunities for involvement, tailoring to members' interests and experiences.

"*After our son's osteosarcoma diagnosis, I found myself applying the many techniques I'd used in my career. I wanted to learn all I could about osteosarcoma, treatments, outcomes, research, and medical terminology. I was confident in asking the 'professional' questions, saying if I didn't agree, making suggestions, trying to look 'outside the box'.*

Through PPIP I can make a contribution that might improve the outcome for others. I feel it is important that all those touched by primary bone cancer have a representative that will give them a voice, especially as outcomes have improved so little and for so many years. As members of PPIP, we can provide our perspective in the important quest to find and provide input to relevant research projects, to make this happen."

Chris Hassall, PPIP member,
and father of Adam.

Since its inception, the scope of PPIP has always been to facilitate open channels of communication between the primary bone cancer community and any researchers in this field, regardless of the source of funding they are seeking.

After supporting the development and review of many applications to the Bone Cancer Research Trust specifically, in 2023, we welcomed several requests from researchers applying for funding from elsewhere. This has allowed us to reach out to a wider community of primary bone cancer researchers, and for our panel members to influence a broader remit of research.

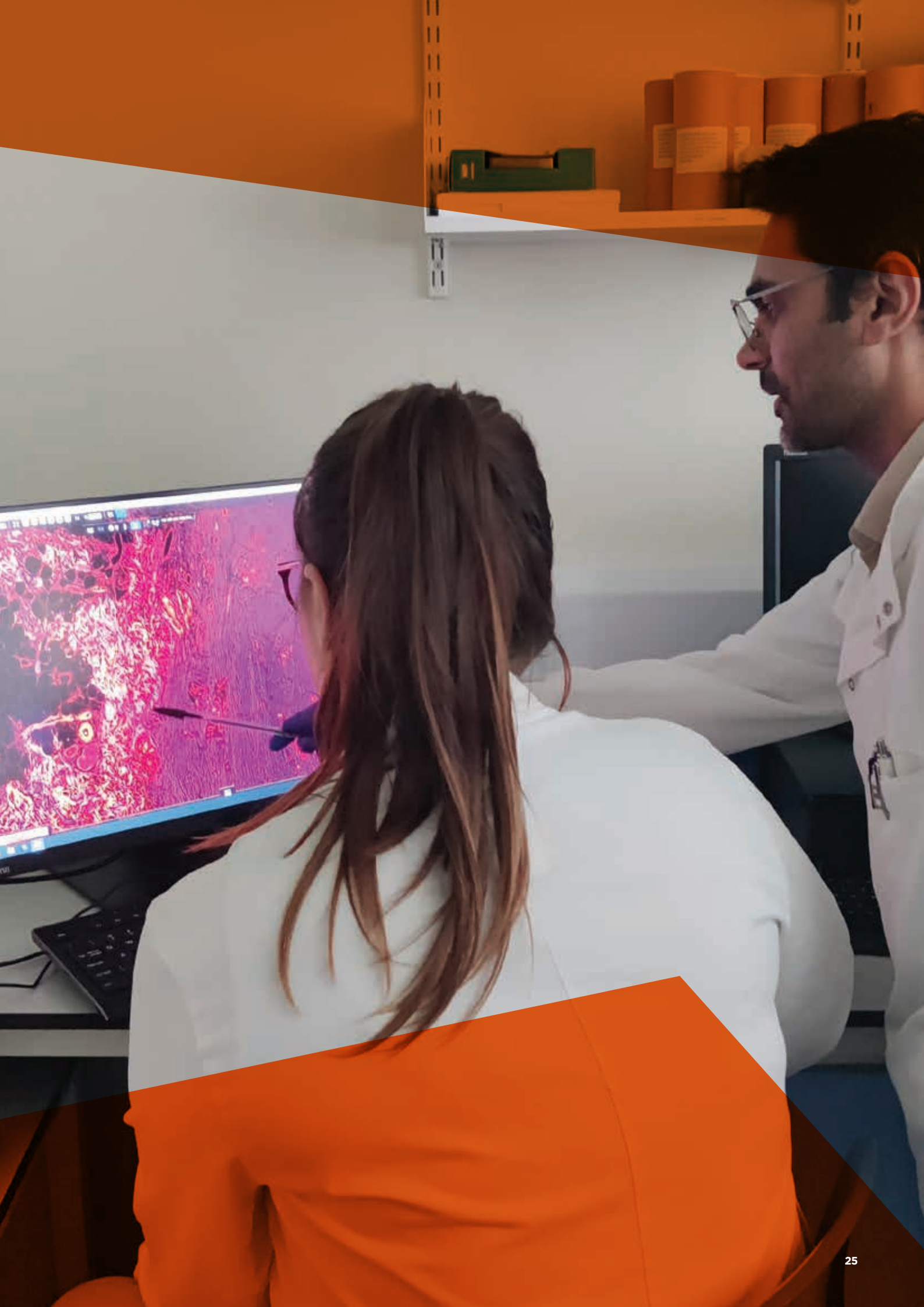
By gathering feedback from researchers, we are able to understand the knowledge gained and overall impact of the shared experiences of the primary bone cancer community.

"Engagement with PPIP has really helped us to confirm what our priorities should be in terms of our research proposal. Through both the verbal and written feedback, we have been able to adapt our interview questions and methods that will hopefully facilitate open and honest discussion in a safe environment for teenagers with primary bone cancer and their family members.

Discussion with panel members caused us to consider whether we should look at interviewing at different stages of treatment as well as involving patients off treatment. We also gained valuable feedback on the best approaches to interviewing teenagers.

Patients' and family members' lived experiences are fundamental to shaping research. The goal of our research is to improve the care, experience, and outcomes of people with primary bone cancer so it is vitally important that we use these experiences to guide what our research priorities should be."

Kate Gildersleve,
Senior Paediatric Physiotherapist
Alder Hey Children's Hospital.



FUNDING CLINICAL RESEARCH THAT DIRECTLY BENEFITS BONE CANCER PATIENTS

OUR FIRST CLINICAL TRIAL

ICONIC
IMPROVING OUTCOMES THROUGH COLLABORATION IN OSTEOSARCOMA
A BONE CANCER RESEARCH TRUST FUNDED PROJECT

There have been no significant advances in the treatment of osteosarcoma for the last 20 years. Currently, all patients are treated in the same way, making the promise of 'personalised treatments', which is changing care for other cancers, elusive for osteosarcoma patients.

We need to understand why some patients respond to treatment while others do not, and what drives some osteosarcoma tumours to become resistant to therapy, returning after initial response and spreading to other parts of the body.

ICONIC - Improving Outcomes Through Collaboration in Osteosarcoma - was the first clinical study funded by the Bone Cancer Research Trust; it aimed to recruit every newly diagnosed patient with osteosarcoma in the UK to produce the first fully annotated osteosarcoma patient register.

ICONIC (NCT04132895) is an observational clinical study involving patients, clinicians, researchers, surgeons, and healthcare professionals. They work together to ensure each patient's tumour is fully studied genetically and biologically, with associated clinical data (diagnosis, treatment, follow up +/- relapse) to understand the impact on the outcome of patients. The aim is to start making informed connections, to better understand the disease, so that new tailored treatments can be identified and better outcomes for patients can be achieved.

Recruitment began in November 2019. To date, 29 centres across the UK are involved. Even within the constraints of the COVID-19 pandemic, 250 patients of all ages and with tumours at all anatomical locations have been recruited, a rate of approximately 7 patients per month.

250 PATIENTS RECRUITED SINCE 2019

29 CENTRES INVOLVED SINCE 2019

All presentations at diagnosis (metastatic or localised) and all treatment options, including patients who have received mifamurtide (Mepact®) are represented.

Patients' tissue samples have been collected successfully and laboratory protocols have been improved for an in-depth analysis looking at changes in DNA, RNA and protein content that may help identify new therapeutic targets. Blood samples containing circulating tumour cells (CTCs) and circulating tumour DNA (ctDNA) that may serve as markers to monitor response to treatment or disease progression have also been collected and are now being analysed.

Patients have completed their patient reported outcome (PRO) questionnaires, and by correlating these with clinical data over time, factors that can improve the physical and emotional quality of life of osteosarcoma patients can be identified[10].

"When my 5-year-old daughter, Arianna, was diagnosed with osteosarcoma, I started looking into clinical guidelines and scientific literature about the therapy she was about to start. Using my academic background, I quickly came to realise that there was virtually no advancement in treating osteosarcoma in decades and the prognosis for Arianna was virtually unchanged since I was her age; a nearly 50/50 chance of a 5-year progress free survival. It is still hard for me to comprehend that the life of my daughter was a result of a flip of a coin or just a random outcome as we call it in economics. A feeling of desperation, but also disappointment of the limited progress in clinical research in osteosarcoma.

So, it was an immediate and big 'YES' from us when we were asked from Arianna's oncologist in Oxford to participate in the ICONIC study. Although I knew that this study would have no impact on Arianna's treatment, it was a relief for me to know that research on that scale was finally happening and a hope that children with osteosarcoma in the future will have a better chance in life than Arianna. Building large collaborations between clinical sites can provide us with an understanding of the tumour pathology in osteosarcoma as well as variation in the treatments and patient experience and response to them. This understanding lays the foundations for the research and clinical communities to build large randomised controlled trials and observational studies that could discover the next breakthrough treatment in osteosarcoma. Hopefully, a step away from platinum-based outdated treatment with dreadful side effects and towards promising immunotherapy treatments, similar to other cancers, that would improve patient survival, quality of life, and experience. I am delighted that Arianna's tissue samples and collected data used in the ICONIC study will provide a small but important contribution towards that direction."

Dr Apostolos Tsiachristas,
father of Arianna, University of Oxford.

WHAT IS NEXT FOR ICONIC?

A follow-on study, "Advancing ICONIC" (Ad-ICONIC) has been funded by the Bone Cancer Research Trust. Due to start in 2023, Ad-ICONIC builds on the success of ICONIC, making use of the data and samples already collected, while continuing to recruit new patients who will be followed for up to 5 years.

Ad-ICONIC is also aiming to investigate how to exploit immunotherapy in osteosarcoma and, through international collaboration, develop a new clinical trial that incorporates new therapies elucidated through a better understanding of the biology of osteosarcoma achieved by ICONIC and Ad-ICONIC.

"To identify new treatments and improve the survival of osteosarcoma patients, we need a co-ordinated approach, working together to address important research questions more efficiently and effectively. ICONIC garnered support from the osteosarcoma community across the UK and demonstrated that indeed it is possible to set up such a highly collaborative research network.

Ad-ICONIC now aims to drive forward this research, making the best use of the existing infrastructure, extending the study, and utilising the data and valuable blood and tissue samples generously donated by patients to improve the treatment and all aspects of care for osteosarcoma patients, so they may have better outcomes and experience a better quality of life."

Professor Sandra Strauss,
University College London Hospital,
London Sarcoma Service and Cancer
Institute, University College London.

NEW CLINICAL TRIAL SUPPORT FUNDING SCHEME

The Bone Cancer Research Trust wanted to fill a much-needed gap in the funding of additional studies associated with existing clinical trials, which could result in significant patient benefit but are not funded by the original trial design.

In 2022, we awarded our first Clinical Trial Support Grant to Dr Martin McCabe at the University of Manchester and The Christie NHS Foundation Trust, to facilitate the addition of multiple tyrosine kinase inhibitor (mTKI) **lenvatinib** in combination with high dose **ifosfamide** as a new treatment regime in **rEECur**, an ongoing international clinical trial examining chemotherapy options for Ewing sarcoma patients whose disease has either returned (relapsed) or does not respond to initial treatment (refractory).

This funding will help define the appropriate dosing, ensuring that the levels of lenvatinib in the blood when given in combination with ifosfamide are adequate. It will also help develop biomarkers to predict which patients are more likely to respond to lenvatinib and to compare tumour samples to detect the presence or absence of particular proteins that may be characteristic of relapse.

Recruitment on the lenvatinib/ ifosfamide combination started in the UK in June 2023 with multiple countries to follow in brief.

INFRASTRUCTURE GRANTS CONTINUE TO FACILITATE THE COLLECTION OF SAMPLES - AN ESSENTIAL RESOURCE FOR PRIMARY BONE CANCER RESEARCH

Ten years after the Bone Cancer Research Trust funded its first research projects, access to patient samples remained a barrier to research. Without them, researchers could not access the genes and proteins that could help them better understand the causes of primary bone cancer or that could be targeted to identify and evaluate potential new treatments. As a small charity, a national biobank, akin to those initiated by larger charities and organisations, was not feasible. An innovative approach was needed.

In 2016, we undertook a stakeholder consultation to assess the best way to support sample collection and established a new grant scheme providing funds to all five primary bone cancer surgical centres in England (Birmingham, Newcastle, Stanmore, Oswestry and Oxford) to facilitate patient consent and recruitment, and to collect and process tissue and blood samples for research. Coinciding with the launch of our 2017-2022 strategy, we awarded the first Infrastructure Grants in 2017.

Over the following five years, £443,535 has been invested across the five centres, facilitating the collection of **12,438** blood, paraffin embedded, snap frozen, and other samples, with **6288** being sent to active primary bone cancer research projects. Samples that are not used immediately are bio-banked for later use.

A further **6665** samples have been sent to researchers from banked archives facilitated by our infrastructure grants and other sources over this period.

All samples are fully documented with patients' clinical history and their collection has acted as a true catalyst for research; to date, these samples have supported 22 scientific publications.

SAMPLES BIO-BANKED THROUGH THE INFRASTRUCTURE GRANTS

TYPE OF PBC	BLOOD, PARAFFIN EMBEDDED AND FROZEN TISSUE SAMPLES BIO-BANKED
Osteosarcoma	1645
Ewing Sarcoma	585
Chondrosarcoma	2293
Chordoma	483
Spindle Cell Sarcoma of the Bone	89
Giant Cell Tumour of the Bone	720
Adamantinoma	48
Angiosarcoma of the bone	83
Other	204
Total	6150

Patients and their families are very supportive of this initiative; to date, an average of 85% of all patients that were approached consented to donate samples across all centres since 2017.

The remit of the Infrastructure Grants continues to expand. They played a key role in the inclusion of bone sarcoma samples in the 100,000 Genomes Project[11] and their involvement in facilitating the consent and collection of samples for whole genomic analysis remains key. As part of an agreement between the Royal Orthopaedic Hospital, Birmingham, Genomics England and the Bone Cancer Research Trust, we now fund a Research Genomics Nurse, to increase the number of patients undergoing whole genomic sequencing (WGS). Linking the amount of WGS data to samples requested by researchers is a very exciting prospect to accelerate the search for novel therapies.

12,438 SAMPLES COLLECTED SINCE 2017

6288 SAMPLES SENT FOR USE IN PROJECTS

85% OF PATIENTS CONSENTED TO DONATE SINCE 2017

"The Royal Orthopaedic Hospital is a specialist trust for orthopaedic oncology and as such we treat and care for a wide spectrum of patients of all ages and ethnicities. This diversity and specialism enable the Royal Orthopaedic Hospital to work with many research partners in the provision of tissue samples from very rare bone and soft tissue sarcomas that are essential to furthering their research into sarcoma. Without this vital resource, progress on future treatment or drug development to improve options for our patients would be restricted.

On behalf of The Royal Orthopaedic Hospital, we would like to say a big thank you to all those who have made donations to enable the Infrastructure Grant funding and help us continue with our work."

Dionne Wortley, Research Tissue Bank Co-ordinator, The Royal Orthopaedic Hospital NHS Foundation Trust.

BRINGING THE RESEARCH COMMUNITY TOGETHER TO ACCELERATE PROGRESS

We continue to bring together the best researchers in the field to encourage exchange of ideas and promote collaboration.

RESEARCH CONFERENCES

Following the success of the 1st International Ewing sarcoma Symposium in 2020, the Advances in Ewing sarcoma Research (AESR) international symposium is now established as a key meeting in the international Ewing sarcoma research community calendar.

The meeting was held virtually in 2021 and, for the first time, as an in person / hybrid event in 2022, attracting over 100 researchers from across the world. Keynote, short oral presentations and posters were followed by group discussions.

The 2022 conference was co-sponsored by Children with Cancer UK and co-hosted by the Bone Cancer Research Trust, Professor Sue Burchill from the University of Leeds and Professor Thomas Grünewald from the German Cancer Research Center (DKFZ) in Heidelberg, Germany.

The meeting concluded with the announcement of the £1 million Research Programme for Ewing sarcoma funding call in partnership with Children with Cancer UK that will be awarded in 2023.

AESR
ADVANCES IN EWING SARCOMA RESEARCH
A BONE CANCER RESEARCH TRUST AND UNIVERSITY OF LEEDS COLLABORATION

BONE CANCER RESEARCH TRUST
UNIVERSITY OF LEEDS

In 2022 we organised and sponsored a chondrosarcoma symposium that welcomed 28 delegates both in person and virtually. The meeting brought together those working on chondrosarcoma research in the UK to share progress and ideas. Important collaborations were forged, and the discussions helped us to understand where priorities lie in chondrosarcoma research. We responded to these needs with the launch of our **first dedicated research programme funding call focused on chondrosarcoma**, due to be awarded in early 2024.

RESEARCH CONSORTIA

To improve outcomes for primary bone cancer patients we must fund high impact, collaborative research. We recognise the importance of international collaboration in clinical and translational research and the need for allocating dedicated time and support to bring people together to facilitate a co-ordinated approach to this research. In 2022, we introduced a new funding scheme to support the setting up or continuation of primary bone cancer consortia.

We have funded the **EURO EWING Consortium**, a European collaboration working towards establishing international clinical trials for Ewing sarcoma. We have also funded a **Surgical Consortium**, a multi-national group led by orthopaedic surgeon Mr Kenneth Rankin, which is working towards the introduction of fluorescence guided surgery (FGS). This technique improves a surgeon's ability to successfully remove the entire tumour as a 'glowing' mass, decreasing the likelihood of any cancer cells remaining, whilst limiting the removal of too much healthy tissue.

The EURO EWING Consortium (EEC) was established in 2013 to improve outcomes in Ewing sarcoma. By bringing together clinicians and researchers across Europe it has facilitated the establishment of Euro Ewing 2012[12] and rEECur, two international clinical trials defining clinical practice for newly diagnosed patients and those with recurrent or refractory disease respectively. The INTER EWING-1 trial which builds upon the results from Euro Ewing 2012 will commence in 2023.

"The Bone Cancer Research Trust funding has enabled us to continue to support existing collaboration and projects in several ways:

- *Bringing together Ewing sarcoma experts from across Europe and further afield at virtual and face-to-face meetings to develop new and build on the existing relationships that are essential for progress in a rare cancer.*
- *Supporting patient and public involvement through our highly valued patient advocacy group of which members have been involved in grant applications, carrying out patient advocate-led research and being active members of working groups and committees.*
- *Enabling focussed working groups to be established so that research can be carried out in a collaborative and co-ordinated fashion in areas of unmet need such as surgery and radiation oncology.*
- *Supporting the Scientific Project Manager role which facilitates the activities of the EEC and has oversight over all the work that the Consortium carries out.*

We are very grateful for the continued support from the Bone Cancer Research Trust and for the recognition our efforts have received."

Dr Abigail Evans, Scientific Project Manager, EURO EWING Consortium, University College London.

"I have been involved as a Patient Advocate with the Euro Ewing Consortium (EEC) since the end of 2017 - beginning of 2018. I found out their details from the bottom of my daughter's trial paperwork. The EEC brings together biologists, researchers, oncologists, and orthopaedic surgeons. All very clever people in their field who are involved or have an interest in Ewing sarcoma (ES). ES is rare, the only way for trials to come to fruition and be large enough to have merit is to recruit into those trials from wider geographical areas. The EEC's most recent trial, Euro Ewing 2012 compared two different arms of treatment and now those results are what's widely used to treat ES. A consolidated treatment proved most effective; without the EEC this would not be saving lives across the world.

Patient Advocates (PA) involvement in the EEC is crucial, there are past patients and parents of treated children involved. PAs bring the human element back to discussions which can often be hard. You may be looking at slides of data, which is just numbers; however, it is always salient to bring those numbers back to human beings, often children, and the impact of the disease for families and communities.

In my experience, the EEC is a very powerful and amazing force in driving forward the treatment opportunities for the ES community."

Jane Wingrove, mother of Daisy and EEC Patient Advocate.

SUPPORTING THE NEXT GENERATION OF PRIMARY BONE CANCER RESEARCHERS

The Bone Cancer Research Trust is committed to growing the primary bone cancer research community and will continue to nurture and invest in the next generation of talented young researchers.

Since 2006, we have awarded 45 research grants amounting to over £2.6 million to support early career researchers in different ways; this represents 32% of our total research spend commitment. 31 of these grants - a commitment of £1.3 million, have been awarded since our last impact report in 2021.

To date, we have supported the training of **10 PhD Students**, 3 of them are now continuing their research as post-doctoral investigators and we appointed our first **Early Career Fellow** in 2022.

The Bone Cancer Research Trust is unique among other funders in allowing postdoctoral researchers to act as principal investigators in Idea Grants. This is an important step towards establishing their careers as independent researchers in the field.

Luke Farrow, PhD student, University College London.

The Early Career Fellowship is a personal award that aims to support talented primary bone cancer researchers in their transition from postdoctoral researchers or newly appointed faculty members to independent investigators in the field. Our hope is that this award will retain the brightest minds in primary bone cancer research, expanding our research community within the UK and bringing us one step closer to a cure.

Dr Lucia Cottone at the Cancer Institute, University College London, is our first Early Career Fellow. During the next 5 years, she will focus her research on understanding the molecular events that cause osteosarcoma cells to become resistant to chemotherapy and will try to identify novel ways to modify their behaviour, so they regain sensitivity to chemotherapy.

"Research is financially demanding and securing long term funding is fundamental to ensuring success and sustaining resilience and retention. This is particularly true for early career scientists as they build on their expertise, expand their network both nationally and internationally, and take their first steps towards becoming independent. Supporting these scientists in such a critical phase of their career is pivotal to progressing research into primary bone cancer."

Dr Lucia Cottone, University College London.

Also in 2022, we introduced our **Skills Development Grants**, a new funding scheme that allows early career researchers to travel to and present their results at national and international conferences or spend time at another laboratory to carry out a research project, to learn specific techniques or attend courses. These are fundamental skills in their training and will help them interact with other researchers, establishing essential networks of collaboration.

"The Bone Cancer Research Trust's Skills Development Grant provided me the opportunity to attend the Advances in Ewing sarcoma Research (AESR) Symposium in Leeds in 2022. The diversity in the research on Ewing sarcoma – ranging from basic understanding of the disease to new treatment approaches – fascinated me. As a young investigator, it was very helpful to get new insights into the latest research of sarcoma experts. It will support me in identifying putative gaps in the field that may lack attention of the research community, so far. After two years of only attending virtual meetings due to the pandemic, it was my first in-person meeting since the beginning of my PhD studies. Networking is an important part in the scientific career as co-operations can accelerate research immensely. I was able to meet many faces at the symposium that I had only read research articles from or even been in email contact with before. Furthermore, I was given the opportunity to present a poster about some of my own data to an expert audience. I am very grateful for the support by the Skills Development Grant that provided me this valuable experience. Thank you!"

Maximilian Kerkhoff, University Hospital Essen, Germany.

NUMBER OF GRANTS SUPPORTING EARLY CAREER RESEARCHERS SINCE 2006

- 9 EARLY CAREER RESEARCHER AS PI
- 10 PHD STUDENTSHIP
- 3 SUPPORTED AS POSTDOCTORAL RESEARCHER AFTER PHD
- 1 EARLY YEARS CAREER FELLOWSHIP
- 22 SKILLS DEVELOPMENT GRANT

32%

OF RESEARCH COMMITMENT SPEND SUPPORTING EARLY CAREER RESEARCHERS SINCE 2006

HIGHLIGHTS OF OUR RESEARCH 2021-2023

We have forged collaborations, introduced new funding schemes, and maintained our support of the primary bone cancer research community to find new and kinder treatments for patients. Here are some of the highlights since 2021 and up to the date of publication of this report in 2023.

2021

- Following the launch of the UK's first adamantinoma research programme in 2020, we award two Idea Grants to identify biomarkers for diagnosis & progression and signalling proteins that can be targeted as novel treatments for adamantinoma.
- We award 3 Idea Grants investigating the potential for RNA technology to target the *TP53* gene, extracellular vesicles that facilitate lung metastasis, and novel gallium containing drugs that seek and destroy chemotherapy resistant osteosarcoma cells.
- We begin to fund the Euro Ewing Consortium (EEC) in collaboration with Ewing's Sarcoma Research Trust (ESRT). EEC focuses on developing new international trials and co-ordinating data through international collaborations.
- We award our first International Explorer Grant. Findings have proven the validity of the hypothesis and support the future development of selective CD99 inhibitors for targeted treatment of Ewing sarcoma.
- Funding continues for the fourth year of our Infrastructure Grants, facilitating the collection of patient samples for research.
- We award funding to investigate innovative drug combinations that could make immunotherapy an effective treatment option for osteosarcoma.
- Following the success of the 1st International Ewing sarcoma Symposium in 2020, Advances in Ewing sarcoma Research (AESR) 2021 brought together over 100 researchers from across the world, to enhance collaboration in Ewing sarcoma research.
- An Explorer Grant aims to identify a prognostic blood test measuring microRNAs in connection with patients' clinical data to identify Ewing sarcoma patients at greater risk of early progression.
- 2 Idea Grants are funded, to investigate the potential of drugs that "wake up" dormant cancer cells as novel treatments for chordoma and to develop new materials that can kill cancer cells, help with bone repair after surgery and ultimately prevent recurrence for osteosarcoma and chordoma patients.
- A second Explorer Grant is dedicated to adjusting chemotherapy dosing regimens for teenagers and young adults with Ewing sarcoma, maximising effects while reducing unwanted effects.
- To mark our 15th anniversary, we launched our most ambitious research funding grant call yet for Idea Grants, large research projects and PhD studentships.
- We launch our Patient and Public Involvement Panel (PPIP) to ensure the views and experiences of the primary bone cancer community are central to our funding decisions and shape future research.

2022

- Chondrosarcoma Research Symposium brings together surgeons, clinicians and researchers to define priorities and establish collaborations in chondrosarcoma research.
- We maintain our commitment to grow and support the new generation of primary bone cancer researchers, appointing our first Early Career Fellow.
- Advances in Ewing sarcoma Research returns with its first in person meeting, attracting over 70 UK and international researchers. In partnership with Children with Cancer UK, we launch a £1 million funding call to fund translational research in Ewing sarcoma.
- Funding is awarded to advance the encouraging results obtained as part of our PhD project aiming to make Methotrexate a kinder treatment option.
- Our first Clinical Trial Support Grant allows the introduction of mTKI lenvatinib to the rEECUr trial for relapsed or refractory Ewing sarcoma.
- Our funded research identifies non invasive biomarkers (DNA-methylation) which could potentially help to identify osteosarcoma patients most at risk from disease progression or relapse.
- The Bone Cancer Research Trust announces its 2022-2032 Strategy - More patients surviving. More patients thriving.
- Funding looking into new drugs to treat osteosarcoma is awarded with the aim of studying a number of potential new treatments reaching the clinic.
- Results from the Euro Ewing 2012 trial redefine chemotherapy standard of care for Ewing sarcoma.
- We award funding for the continuation of our first clinical study ICONIC.

2023

- As part of our anniversary grant call, we award our 10th PhD studentship. Work commences to investigate how immune cells can be reprogrammed through genetic engineering (CAR T cell therapy) to identify and kill osteosarcoma cells.
- Our Patient and Public Involvement Panel is now supported by 40 volunteers with lived experience of primary bone cancer.
- Euro Ewing Consortium and Surgical Consortium receive funding to promote collaboration and to facilitate new international clinical trials for Ewing sarcoma and improve surgical margins for bone sarcoma patients.
- Research commences to identify biomarkers that could reduce the frequency of scans for chordoma patients.
- We launch our first chondrosarcoma research programme funding call, a multidisciplinary collaborative translational programme of work that will be awarded in 2024.
- A stakeholder consultation carried out in 2022 helps us define our research priorities. We launch our 2022-2032 Research Strategy.
- Infrastructure Grants continue making an invaluable contribution to primary bone cancer research projects, having collected over 12,000 patient samples to date.
- Skills Development Grants continue help the development of early career researchers, with 5 laboratory stays funded to expand their training.

CLOSING REMARKS

These are exciting times, advancing technologies in genomic analysis have the potential to be incorporated into clinical practice and we hope these will help discover new therapeutic targets that can bring the promise of personalised targeted treatments closer for primary bone cancer patients.

We enter our next strategic period with two ambitious objectives, *"More patients surviving. More patients thriving."*

We have heard from so many patients who had to visit their GP multiple times, were misdiagnosed with other conditions, and received delayed diagnosis.

Bone cancer patients are passionate about contributing to research through the donation of samples, participating in clinical trials and becoming involved in the research we fund through our PPI panel. On their behalf, the Bone Cancer Research Trust remains focused on finding better and kinder treatments and surgeries for initial treatment and to combat relapse and metastasis; we are also pushing for innovative technologies and pioneering data analysis being applied to achieve earlier, faster, and smoother diagnosis.

To all the researchers, clinicians, surgeons, and healthcare professionals, **THANK YOU** for your hard work and dedication.

To the bone cancer community, **THANK YOU**; with your continued support, we can fund more research, so ground-breaking discoveries and treatments can become a reality for patients.

"I have a profound admiration and respect for the Bone Cancer Research Trust's founders, that created something so beautiful from the most devastating pain of losing a child to this horrific and cruel disease. It shows their kindness and compassion for the ones that will be diagnosed in the future and want to improve their outcomes.

The Bone Cancer Research Trust is not only a charity, but also a lifeline and a big family for patients, carers, and their loved ones. It is very exciting to hear about the recent developments and collaborations with other charities, that are the key to success.

My own diagnosis was a difficult and long journey. By the time my osteosarcoma was confirmed I was on the verge of a pathological fracture and there was some regional spread.

The side effects of MAP chemotherapy made me question how far I was willing to go to survive. After surgery I lived isolated in a hospital room for many months; adjuvant chemotherapy was even harder on my body since the tumour was very resistant to the treatment, a more radical resection was needed, and I was profoundly neutropenic. I hope future patients receive better and kinder treatments, that their experience of diagnosis is improved, and they can access multidisciplinary care that considers the consequences of treatment and late effects like disabling chronic pain.

This is why the work of the Bone Cancer Research Trust is so important, not only because the research they fund searching for better treatments for primary bone cancer, but because of the support they provide, ensuring patients do not feel completely isolated and fearing being discharged at the end of their treatment, and the education campaigns they undertake to increase awareness of bone sarcoma among primary care professionals to improve diagnosis. THANK YOU"

Florencia Pistritto, osteosarcoma patient.

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Please scan the QR code to view the publications acknowledging funding from the Bone Cancer Research Trust since 2006 to August 2023.

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STRIVING FOR PROGRESS THROUGH RESEARCH
OUR RESEARCH IMPACT REPORT 2023

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