



**The** **BRAIN  
TUMOUR  
CHARITY**

Research | Awareness | Support

# Accelerating research to change lives

The Brain Tumour Charity's  
Research Impact Report 2018

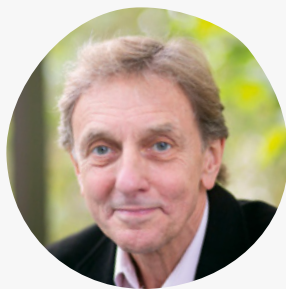






*I'm filled by hope knowing the difference research can make, and so was Natasha. Her final wish was to donate her brain to research. In doing so, she has given the gift of hope to so many others. As a family, we want to continue Natasha's legacy and believe wholeheartedly that the research funded by The Brain Tumour Charity will one day save families from the devastating experience we went through.*

**Graham and Shona Floyd, whose daughter Natasha died from a brain tumour.**



For too long, research on the causes and treatment of brain tumours has remained slow and hasn't produced the kinds of breakthroughs that we've seen for some other forms of cancer. The main reason has been chronic underfunding. Too few researchers were attracted into the field, and it was difficult to make rapid progress in understanding the causes of brain cancers, improving early diagnosis and developing new treatments. But with encouragement and support from The Brain Tumour Charity, the landscape of brain tumour research is beginning to change. More scientists are now working in the field and investment is slowly rising. Now, we need to take advantage of this momentum to accelerate the pace of discovery. Brain tumours are phenomenally complex and only research will help us to shed light on this cruel disease, to improve diagnostics and deliver better, safer treatments.

**Colin Blakemore**  
President, The Brain Tumour Charity



Quite simply, a cure can't wait. We are committed to defeating brain tumours; to improving survival and quality of life for everyone diagnosed with a brain tumour.

That's why, alongside our dedicated support services, we fund pioneering research around the world and we're not afraid to embrace new ideas to move us forward. We're proud of the research we fund, of everything it's achieved so far and we're proud that our approach to research puts the voice of those affected at the heart of decision making, as experts through experience. But above all, we're proud of and hugely grateful to our brilliant community of supporters.

Life-changing discoveries rely on exceptional research, but none of it would be possible without you. Thank you.

**Sarah Lindsell**  
Chief Executive, The Brain Tumour Charity



The Brain Tumour Charity is leading the fight against brain tumours. We're the largest dedicated funder of research into brain tumours in the world and research is always our biggest area of investment. That's because research is our hope for the future.

By investing in the best research today, we'll have a future where brain tumours aren't the killer they are now. They will no longer be one of the four least survivable cancers and will no longer result in life-altering disabilities for those that survive.

Our research strategy, *A Cure Can't Wait*, was developed for exactly this reason – to drive forward the very best research; research that will move us closer to our twin goals of doubling survival by 2025 and halving the harm caused by brain tumours by 2020.

We've achieved so much since The Charity was founded and our research portfolio is impressive. From research we funded at The University of Nottingham, we launched HeadSmart – our multi-award-winning, UK-wide awareness campaign, which has helped to halve diagnosis times in children. And, in our last report, we celebrated the development of new biomarker tests to improve the accuracy of diagnoses and

demonstrated that an existing drug had the potential to kill glioma cells. We also highlighted that prompt treatment in children does make a difference and we welcomed the development of an NHS-accredited clinical guide for early diagnosis. But we need to keep moving forward.

Thanks to your ongoing support, we've committed over £17 million to new, important research initiatives since the launch of our research strategy. In this report, we'll show you how we're building on previous discoveries to improve tumour characterisation, develop more targeted treatments, and integrate quality of life as a critical measure of successful treatment.

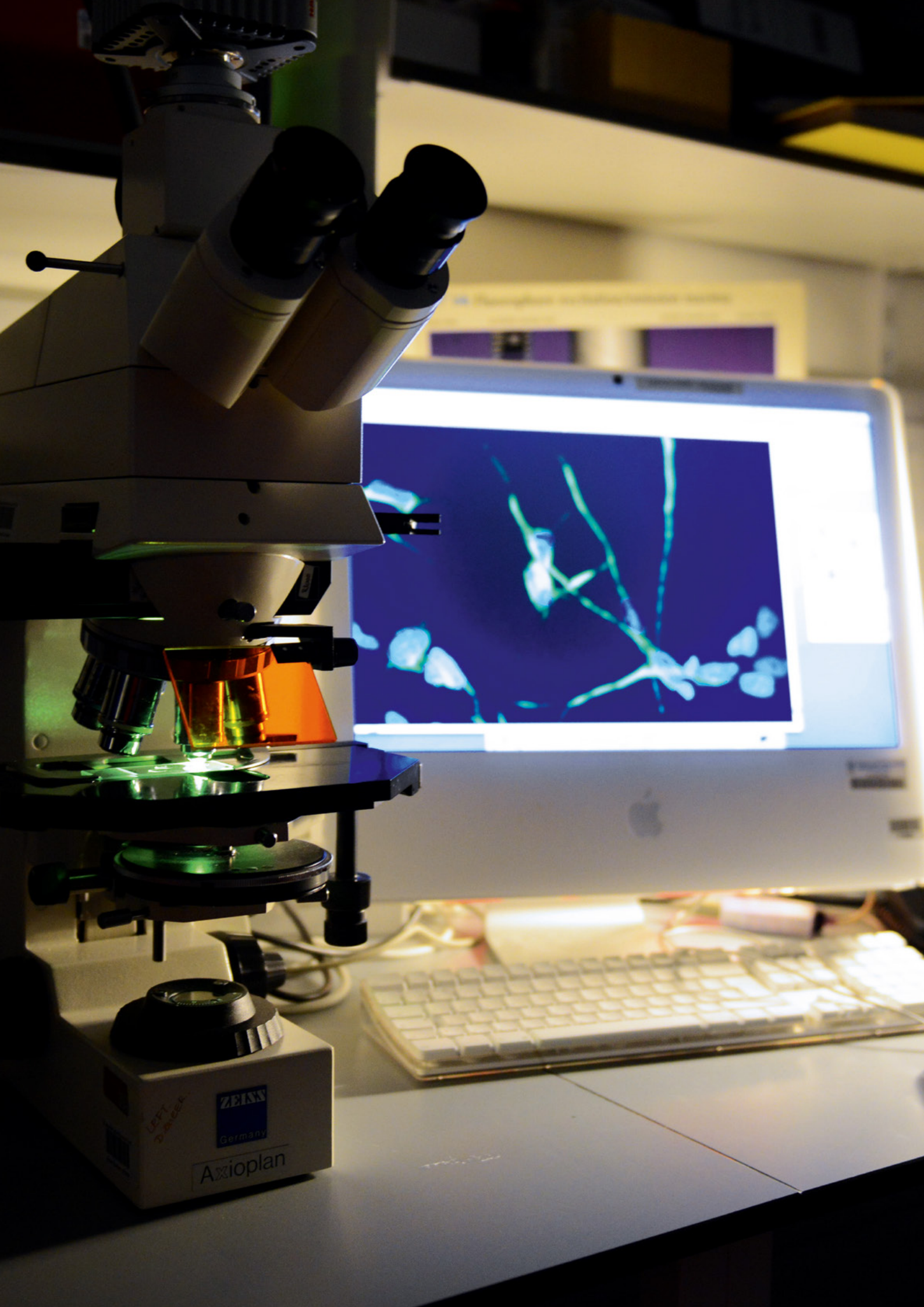
This is my 21<sup>st</sup> year in the fight against brain tumours and, as we enter 2018, I am more positive than ever that our research is making a real difference. We hope you're motivated and inspired by everything you read – change is happening.

Thank you for being part of a future with a cure. Together we can defeat this devastating disease.

**Neil Dickson**

Chair of the Research Subcommittee of Trustees, The Brain Tumour Charity





ZEISS  
Germany  
Axioplan

# Growing the field, accelerating progress

Brain tumours are the biggest cancer killer of children and adults under 40. But only 1.5% of cancer funding in the UK is spent on research into brain tumours.

In recent decades, we've witnessed significant progress in the treatment of other cancers – breast cancer survival has doubled in the last 40 years.<sup>1</sup> Whilst it's disappointing that we've not seen similar advances in brain tumour treatment, it's clear proof that, through excellent research, we can change lives.

That's why The Brain Tumour Charity is creating an environment where research into brain tumours can thrive.

We are committed to investing in and growing the field. We are committed to working collaboratively with leaders and organisations, worldwide, to accelerate discovery. And we're committed to bringing the most brilliant scientists and minds to the field.

Here's a taster of how we're doing that.

**We can't make progress without your help. A donation of £100 could pay for a test to detect the genetic changes associated with the development of a brain tumour. Thank you.**

## *Fostering a collaborative research process*

Our Quest for Cures grant award focuses on collaborative discovery – we insist upon a multidisciplinary team from at least two institutions. It drives a new and very different approach to research which is designed to bring fresh perspectives, complementary skill sets and strengthen the ties between basic and clinical research.

Discover the recent recipients of our Quest for Cures awards at [thebraintumourcharity.org/quest-for-cures](http://thebraintumourcharity.org/quest-for-cures)

## *Investing in future leaders*

It's vital that we encourage talent and breadth of knowledge in neuro-oncology research. Our award programme for Future Leaders is designed to attract the best scientists to the field. In this way, we can be confident in the quality and the ambition of the research we fund. With great researchers leading the field, we'll make breakthroughs sooner.

Read more on page 37 or at [thebraintumourcharity.org/funding-opportunities](http://thebraintumourcharity.org/funding-opportunities)

## *Removing barriers*

Supported by the voice of our community, we work with government organisations and influencing bodies to drive change. This includes identifying and mitigating barriers to research, such as biobanking infrastructure, so that resources can be used more effectively.

You can read more about the current barriers to research and what we're doing to help overcome them at [thebraintumourcharity.org/removing-barriers](http://thebraintumourcharity.org/removing-barriers)

# From lab to life

Research can lead to landmark discoveries but it's a slow and expensive process. In oncology, just five percent of the drugs that enter clinical testing are approved for patient use. In neuro-oncology specifically, it's even fewer.

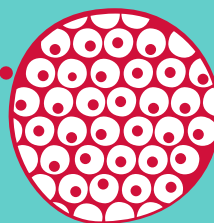
This graphic outlines the stages, time and cost of traditional drug development.

On average, the development of one new drug takes 10 years...



## Discovery

Knowing how the disease starts or develops, scientists identify compounds or molecules that could act to delay or stop this process. These are called drug candidates.



## Preclinical testing

A drug candidate goes through early testing in cells and animals to check how it works.



## Phase 1 clinical trial

The drug candidate is tested with a small group of patients for the first time, to make sure it's safe.

...and costs £1.15 billion



That's why, as well as investing in the best traditional research, we're doing things differently. Read about some of the ways we're starting a research revolution on page 39.



▲ **Phase 2 clinical trial**

The drug candidate is tested with a bigger group of people living with the disease – usually <100 for rare cancers.



▲ **Phase 3 clinical trial**

The drug candidate is tested with a larger cohort of people – usually >200.



▲ **Licensing approval**

Results from the studies are compiled and submitted to the regulatory agencies.



▼ **Medicine available**

After approval, the medicine is available to patients, subject to value and cost-effectiveness.

# A Cure Can't Wait

Our vision is for a world where brain tumours are defeated.  
We simply can't achieve that without more research.

In December 2014, we launched our five year research strategy, **A Cure Can't Wait**. It's our bold approach, influenced by world leaders in the field and patient voices, to break down the barriers to discovery and achieve our twin goals of doubling survival and halving the harm caused by brain tumours.

As part of **A Cure Can't Wait**, we've identified five key research priorities – Accelerate, Diagnose, Understand, Catalyse, Enhance – which are outlined in the graphic opposite. Every research project we fund can demonstrate a strong connection to these priorities. It's our smart and focused approach to make sure we have the biggest impact in the shortest time possible.



*I'm proud to say that, just half way through our strategy, we've already committed £17 million into research to address these key areas. Despite the challenging environment we face, we're thinking strategically and employing stringent peer-review processes to make smart research investments and we're taking care to ensure we span all phases of research and a wide variety of brain tumour types. In this way, we will get improved treatment to as many people as possible, as quickly as possible.*

**David Jenkinson, Chief Scientific Officer,  
The Brain Tumour Charity**

## DOUBLE SURVIVAL HALVE THE HARM

### ACCELERATE

Biobanking to accelerate research progress through centralised collection of, and access to, brain tumour tissue samples.

### DIAGNOSE

Diagnosing brain tumours earlier and more accurately for both children and adults.

### UNDERSTAND

Increasing understanding of the genetics and biology of tumour development to identify effective new treatments.

### CATALYSE

Translating laboratory discoveries into new and effective treatments that increase survival and quality of life.

### ENHANCE

Enhancing care and quality of life for everyone affected by a brain tumour, including patients and carers.

## AN INTERNATIONAL APPROACH

PIONEERING

PASSIONATE

COLLABORATIVE

SMART

**We always love to talk about our research! If you have any questions at all, please email [research@thebraintumourcharity.org](mailto:research@thebraintumourcharity.org)**



## Funding only the best

Exceptional breakthroughs come from exceptional research. That's why we're a member of the Association of Medical Research Charities (AMRC) and our research governance is so thorough; so that we're confident, and you can be too, that every project we fund is best-in-class and will drive us closer to a world where brain tumours are defeated.

Led by our strategic priorities, our grant allocation process combines international peer review with input from our independent Scientific Advisory Boards. In this way, every project is reviewed and shaped by scientific and clinical field-leaders, guaranteeing that new research builds on existing knowledge. It means that we invest our resources in the most effective way, committing to the projects that give the best chance of success and will lead to change.

### *Our research promise*

We promise that every project we fund is:

- Evidence-based
- Patient-led
- Outcomes-orientated
- Of exceptional quality
- Regularly reviewed

### *We're global, did you know?*

We're proud to say, without a shadow of a doubt, that the research we fund is world-class. That's because we encourage global collaboration – we don't just want the best scientists in the UK, we want the best in the world. As Dr David Jones speaks about on page 37, we can speed up the rate of discovery by bringing together multi-national teams with diverse skill sets. It's a promising and powerful approach to research that should bring clinical advances to those affected more quickly.

### *Evaluating our research*

We invest a lot in our research so it's vital that we keep track of how it's going. We expect all our grant recipients to update us regularly on the progress and outputs of the project and we like to keep our community updated too.

Scientific discoveries don't always follow an easy path but we want to make sure that progress is being made. If we feel it isn't, we instigate a rigorous assessment process that includes asking our scientific advisors to review the work. And, rest assured, if they aren't convinced of the ongoing merit of the research, we're not afraid to say 'stop' and reallocate the investment elsewhere.

**amrc**  
ASSOCIATION OF MEDICAL RESEARCH CHARITIES

## Guided by experts through experience

We recognise that patients and loved ones are experts on the impact of brain tumours, through their own experiences. In this way, their input is hugely valuable – it can help define what research is likely to have the biggest impact for those living with a diagnosis.

That's why the voices of those affected by a brain tumour are at the heart of our research selection process. We want to make sure that anyone affected by a diagnosis can help to shape research and contribute to the future of neuro-oncology.

### *Our Scientific Advisory Boards*

We have five lay representatives on our Biomedical and Quality of Life Scientific Advisory Boards (SABs) who provide valuable perspectives as experts by experience. Their input, alongside scientific and medical experts, is used to assess and prioritise the funding of research applications. It ensures that the research we choose to fund is important and relevant to those affected.

### *Our Research Involvement Network*

Over 100 people affected by a brain tumour are part of our Research Involvement Network, which improves collaboration between researchers and patients. Patients are given the opportunity to influence research as it's being designed and conducted, and share their experiences. Researchers benefit from new perspectives and can ensure their research genuinely reflects the needs of our community.

Since we launched our Research Involvement Network in October 2015, our community has shaped 67 different research projects.

# 6.2%

Only 6.2% of those diagnosed with a brain tumour are enrolled onto clinical trials compared to an average of 17.7% for all cancers.<sup>2,3</sup>

# Our research investment

Since the launch of *A Cure Can't Wait*, we've committed over £17 million to research. To date, that brings our total research commitments to over £35.6 million, making us the largest, dedicated funder of research into brain tumours in the world. But we won't stop until brain tumours are defeated.



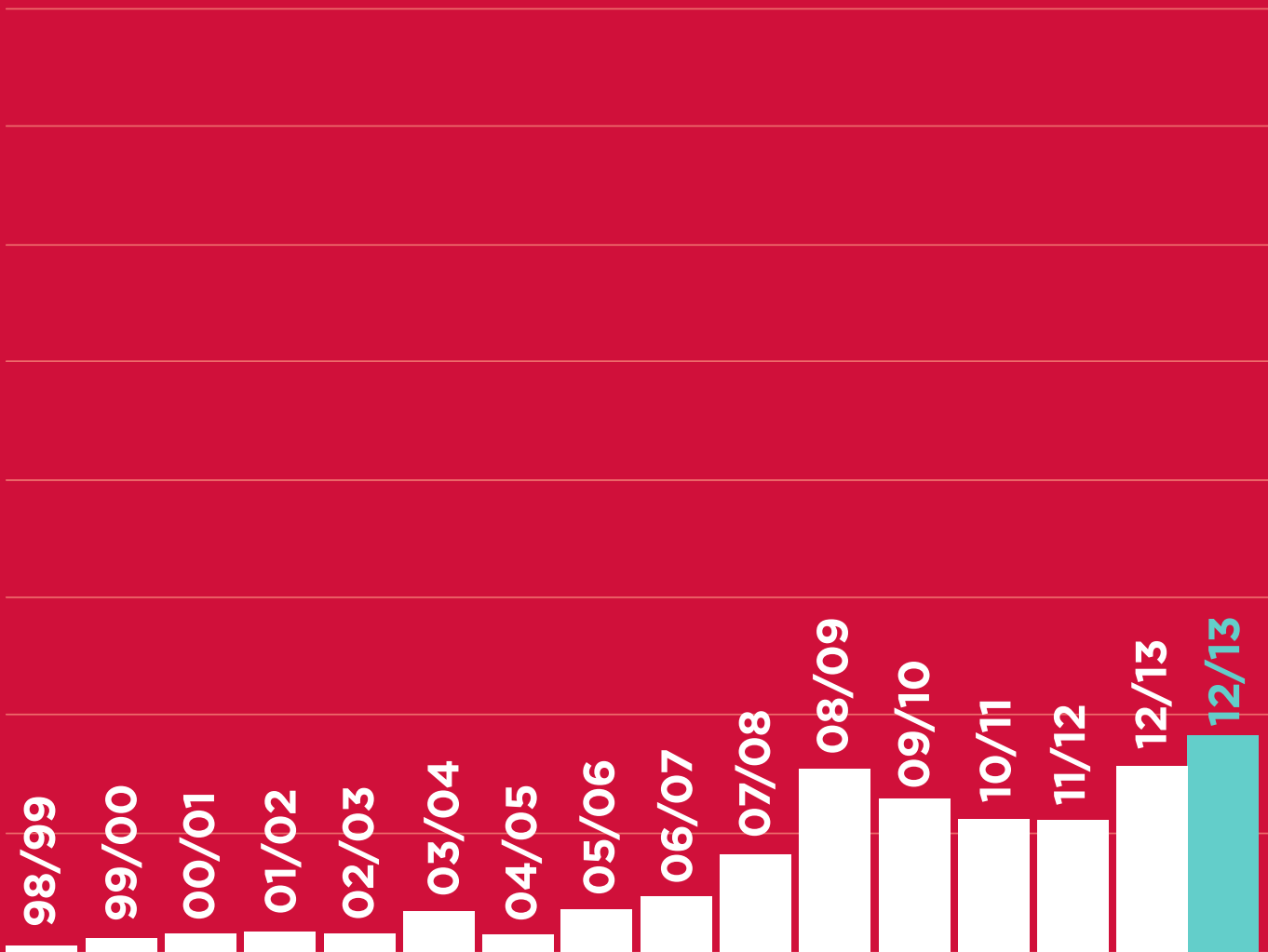
## Research spend

The amount of money The Charity spent on research and research costs.



## Research commitment

The amount of money The Charity committed to future research, including research due to happen beyond the year of commitment.





## Why did we invest less in 2014/15?

As you'll notice our research investment dropped in the 2014/15 financial year. That was the year we developed our research strategy – *A Cure Can't Wait*. To make the most impact, we had to make sure we were making smart investments and now, halfway through our strategy, we're investing more money each year and we're starting to see the early output of our research investments.



### *It doesn't stop there!*

As a result of the research we fund, scientists are often able to secure follow-on grants, increasing investment in the field.

Since our last report, 16 of our projects have secured further funding through other organisations, with a value of £7.5 million. It means that, in total, we've leveraged an additional £22.1 million for research into brain tumours.

# Our research in



**258 researchers**

**48 grants**



**8 programmes**



**26 projects**



**3 fellowships**



**1 studentship**



**10 clinical trials**



Numbers are based on research grants, funded by The Brain Tumour Charity, that were live in August 2017.

# numbers 2017



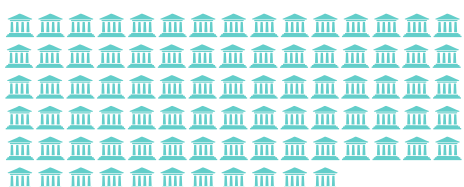
## 11 nations



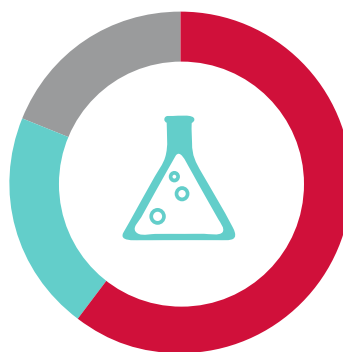
## 29 cities



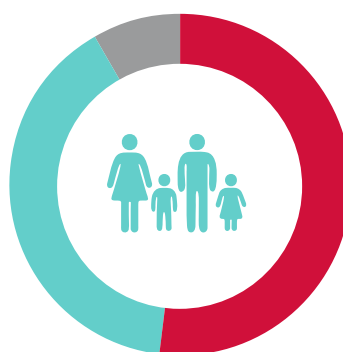
## 86 institutions



## Types of research



**Scientific** Clinical Quality of Life



**Adult** Paediatric Both

We're about to dive into just some of our world-class research projects. With the science comes some jargon, so check out our glossary at the back for anything you're not too sure on! You can read more about our complete research portfolio on page 32.



## Identifying new therapies and less invasive methods of delivery

Funded by The Brain Tumour Charity, Professor Susan Short is exploring new therapies and novel methods of treatment delivery. It is world-leading research to find better, safer treatments and the findings could be transformative. As Professor Short is active in both academic and clinical neuro-oncology, the team is in a strong position to catalyse lab discoveries into clinical treatments. It means we're better placed to get new treatments to patients more quickly.

Professor Short and her team have identified reovirus as a potential new therapy for glioblastoma. Reovirus is toxic to cells with an activated EGFR/Ras pathway, like brain tumour cells. When inside a tumour cell, reovirus replicates until the cell bursts. In this way, the tumour cell is destroyed and the virus is released, free to enter and destroy nearby tumour cells. In addition, the presence of reovirus stimulates the body's own immune system; activating local immune cells to attack the tumour. It's an extremely exciting discovery.

Importantly, Professor Short's research has proved that reovirus can cross the blood-brain barrier – a highly selective membrane that few substances can pass through. It means that reovirus, as a treatment, could be administered by injection into a blood vessel rather than directly into the tumour itself. From the bloodstream, reovirus can then pass through the blood-brain barrier to reach the tumour. This is a significantly less invasive and lower risk procedure for patients and is already being used to treat patients alongside standard chemotherapy and radiotherapy.

The team is also investigating the potential of haematopoietic stem cells (HSCs) to deliver other therapies directly to tumour cells. They've proved that HSCs pass the blood-brain barrier and that they 'home in' on brain tumour cells.



*Professor Susan Short,  
Professor of Clinical Oncology  
and Neuro-Oncology*

Leeds Institute of Cancer and Pathology

### PROGRAMME FACTS

- UNDERSTAND
- CATALYSE

£ Grant amount  
£1,416,000

🕒 Programme length  
Five years

👤 Age group  
Adults and Paediatrics

● Tumour type and grade  
Glioblastoma;  
high grade brain tumour



### Why we love this research

Professor Short's research has the potential to benefit a significant number of those diagnosed with a brain tumour as the research aims to identify new and better ways to deliver treatments, regardless of the tumour type.



“

Through my own journey, I have seen first-hand how current treatment options for glioblastoma are very dated and limited. I am thrilled to see that researchers are looking for new ways to deliver drugs to the brain and hope that soon patients will live for longer.

Steve White who was diagnosed with a glioblastoma in July 2016.

**25%**

Only 25% of those diagnosed with glioblastoma survive more than one year.<sup>4</sup>



## Using tumour biopsies to inform treatment

In the UK, Dr Darren Hargrave is leading BIOMEDE (BIOlogical MEDicine for Diffuse Intrinsic Pontine Glioma Eradication) – an international clinical drug trial. Until now, it's not been standard practice to take a biopsy from a child diagnosed with DIPG (Diffuse Intrinsic Pontine Glioma)\* – it was deemed risky and unnecessary as there were no treatments that could target any of the molecular characteristics identified. But now, through BIOMEDE, Dr Hargrave is driving new understanding and progress. The trial seeks to find better treatments based on tumour characteristics and therefore requires a biopsy from all participants. For the first time, we can test potential DIPG therapeutics in a structured way, based on the tumour's molecular structure.

Dr Hargrave has been instrumental in bringing many clinical trials to our shores, benefiting children with a variety of brain tumour types who might not otherwise have access to the latest treatments. The Charity is now supporting BIOMEDE alongside Cancer Research UK. Through this trial, Dr Hargrave will test the current standard of care against new, potentially better drugs.

Using the biopsies, the team will assess the level of two biomarkers in the tumour – EGFR and PTEN – and assign participants to one of three new drug treatments (everolimus, erlotinib or dasatinib). Importantly, the results will indicate whether personalising treatment, based on a better understanding of the individual's tumour, can improve outcomes.

The game-changing step to obtain biopsies from children with DIPG, following training for surgeons, means that we'll soon be in a much better position to understand the molecular changes driving DIPG tumours and accelerate treatment development for one of the most understudied, but deadly, childhood brain tumours.



*Dr Darren Hargrave, Consultant Paediatric Oncologist in Neuro-Oncology and Experimental Therapeutics*

Great Ormond Street Hospital and UCL Great Ormond Street Institute of Child Health, London

### TRIAL FACTS

- UNDERSTAND
- CATALYSE
- ENHANCE

£ Grant amount  
£110,296

🕒 Trial length  
Six years and nine months

👤 Age group  
Paediatrics

● Tumour type and grade  
DIPG; high grade brain tumour



### Why we love this research

Flexible trial design! Clinical trials can take years to set up due to ethical approvals and stringent governance. But BIOMEDE has been smartly designed to be adaptive. Researchers can add new drugs and remove failing ones without restarting the trial – it's much more time effective.





“

We were told from the moment Jessica was diagnosed with DIPG that there was no cure. She died three years later. We set up The Jessica Green Fund to raise money for The Brain Tumour Charity because we know that research is the only way to change the future for families affected by DIPG.

Lisa McLoughlin, who lost her six-year-old daughter to DIPG.

**DIPG tumours are often inoperable due to their location in a part of the brain called the pons. The pons is responsible for critical functions like breathing and blood pressure.**

## Developing tailored and targeted treatments

The Brain Tumour Charity has a long and successful history with Professor Clifford who has dedicated his career to the study of medulloblastoma – the most common high grade tumour in children. Since 2001, when The Charity’s founders began funding his work, his laboratory discoveries have translated into clinical practice and he’s a world leader in the use of molecular diagnostics to improve the accuracy of diagnosis. Professor Clifford is now leading an important programme called INSTINCT (The Institute of Child Health – Newcastle University – Institute of Cancer Research High-Risk Childhood Brain Tumour Network), which seeks to further understand the biology of these aggressive brain tumours and develop treatments which target their specific characteristics.

In our 2014 Research Impact Report, we told you that Professor Clifford was one of the authors on a game-changing scientific paper that introduced a consensus of four subtypes of medulloblastoma. It was a clinically important discovery as different subtypes respond differently to treatments. The ability to identify the particular subtype at diagnosis can provide clinicians with invaluable knowledge when planning the best treatments for those diagnosed.

Building on this research, in 2017, Professor Clifford further distinguished tumour characteristics, identifying seven, not four, subtypes of medulloblastoma – each with different diagnostic features and prognosis. This classification is now being used in INSTINCT to improve survival, and quality of survival, through the development of more tailored and targeted treatments (page 34).

As a result of Professor Clifford’s dedication to the field, the UK will soon be the first country in the world to use molecular diagnostics as routine practice at diagnosis for medulloblastoma. The Brain Tumour Charity has recently committed to fund biomarker testing for all children diagnosed with a medulloblastoma, to determine the molecular profile and tumour subtype. It opens the door for more children to join PNET5, a Europe-wide clinical trial investigating new treatment regimens, which are delivered based on the biological characteristics of each patient’s tumour.



*Professor Steve Clifford, Professor of Molecular Paediatric Oncology*

Wolfson Childhood Cancer Research Centre, Newcastle

### PROGRAMME FACTS

- ACCELERATE
- UNDERSTAND
- CATALYSE

**£ Grant amount**  
£3,200,261 (co-funded with Children with Cancer UK and Great Ormond Street Hospital Children’s Charity)

**🕒 Programme length**  
Six years and three months

**👤 Age group**  
Paediatrics

**● Tumour type and grade**  
Medulloblastoma;  
high grade brain tumour



### Why we love this research

Professor Clifford’s research has significantly improved our understanding of medulloblastoma subtypes. As well as using this to develop new treatments, it’s also led to clinical trials that aim to decrease treatment for less aggressive subtypes, for example the WNT subtype, sparing children from over-treatment and its unnecessary adverse effects.





“

Since Brooke's diagnosis, she has had to go through several surgeries and rounds of chemotherapy and radiotherapy. There is so much more to learn about medulloblastoma and it's great to see that researchers are looking at new and more targeted ways of treating this devastating disease.

Kayley Baker, whose nine-year-old daughter Brooke was diagnosed with an anaplastic medulloblastoma in 2015.

**1.5%**

Only 1.5% of the £580 million invested in national cancer research funding in the UK in 2016 was spent on brain tumours.<sup>5</sup>



# Our research history with Professor Clifford

## Grant

### award date

### Details

**13 July 2001**

Analysed gene variants in medulloblastoma

**7 May 2004**

Studied RASSF1A in childhood medulloblastoma – a gene that acts to suppress tumour growth

**6 Feb 2007**

Investigated the molecular basis of childhood medulloblastoma: from genomics to improved therapies

**20 Sept 2008**

Ran a feasibility study for real-time biological characterisation of medulloblastoma

**15 Dec 2008**

Identified the molecular characteristics of supratentorial primitive neuroectodermal tumour (sPNET) II

**10 Feb 2010**

Funded a biomedical scientist to support clinical trials

**17 May 2010**

Investigated biomarkers for improved disease risk assessment and therapy of childhood medulloblastoma

**17 May 2010**

Studied the role of MYCN – an oncogene – in the formation and progression of high grade medulloblastoma

**16 April 2013**

Identified initiator events and therapeutic targets in Group 3 medulloblastoma

**26 Mar 2014**

Established the INSTINCT programme for more tailored treatments of high grade brain tumours



# Our research history with Professor Kennedy

*Grant*

*award date*

*Details*

**1 April 2001**

Assessed quality of survival for children with medulloblastoma (alongside the PNET3 clinical trial)

**12 July 2004**

Studied, over time, the effect of child and parent factors on perceived quality of life of children treated for a brain tumour

**1 August 2006**

Developed, introduced and evaluated guidance to shorten symptom interval and enhance access to diagnostic pathways

**18 May 2016**

Studied the neuroanatomical indicators of cognitive dysfunction in short and long term survivors of childhood medulloblastoma

**18 May 2016**

Started the PROMOTE study: **Patient Reported Outcome Measures Online To Enhance** communication and quality of life after childhood brain tumour

**2 June 2017**

Measuring and evaluating the quality of survival in children recruited to the SIOP-PNET5-MB clinical trial

## Enhancing quality of life after diagnosis

Since 2001, Professor Colin Kennedy and his team have been using quality of life and quality of survival assessments to make sure that new brain tumour treatments for children are not only increasing survival, but that the treatments themselves aren't causing preventable harm. The Brain Tumour Charity's long term support of his work has allowed Professor Kennedy to take a longer view of the effects of treatment, giving a truer assessment of treatment impact on the developing brain.

Our support of Professor Kennedy's work has two strands. First, with funding from The Charity, Professor Kennedy's team has developed the first successful systematic assessment of quality of life for children with medulloblastoma who are participating in clinical trials. The information gathered through the assessment provides vital evidence of the long-term, day-to-day impact of treatment, which will help determine the best and safest treatments.

The quality of life of children with brain tumours is often significantly affected. Children can experience cognitive and visual impairments, mobility issues and fatigue, in addition to behavioural and emotional effects. Yet the discussion of issues like these, which impact a child's quality of life after treatment, does not routinely take place in consultations.

To address this, The Brain Tumour Charity is now supporting a second strand of Professor Kennedy's work – the PROMOTE research project (Patient Reported Outcome Measures Online To Enhance communication and quality of life). His team has set up and is assessing the use of an online feedback system to aid communication between the affected family and their doctor.

Using the platform, the team aims to understand the types of issues that should be discussed in consultations. The online set-up should enable timely feedback on symptoms, allowing clinical staff to focus care on the issues that are most relevant and important to families.

This simple, patient-led system has the potential to prevent unnecessary long term harm to a child's quality of life by allowing effective planning of the most appropriate help and services.



*Professor Colin Kennedy,  
Professor in Neurology  
and Paediatrics*

University of Southampton and  
Southampton General Hospital,  
Southampton

### PROJECT FACTS

● ENHANCE

£ Grant amount  
£298,114

🕒 Project length  
Three years

👤 Age group  
Paediatrics

● Tumour type and grade  
All childhood brain tumours



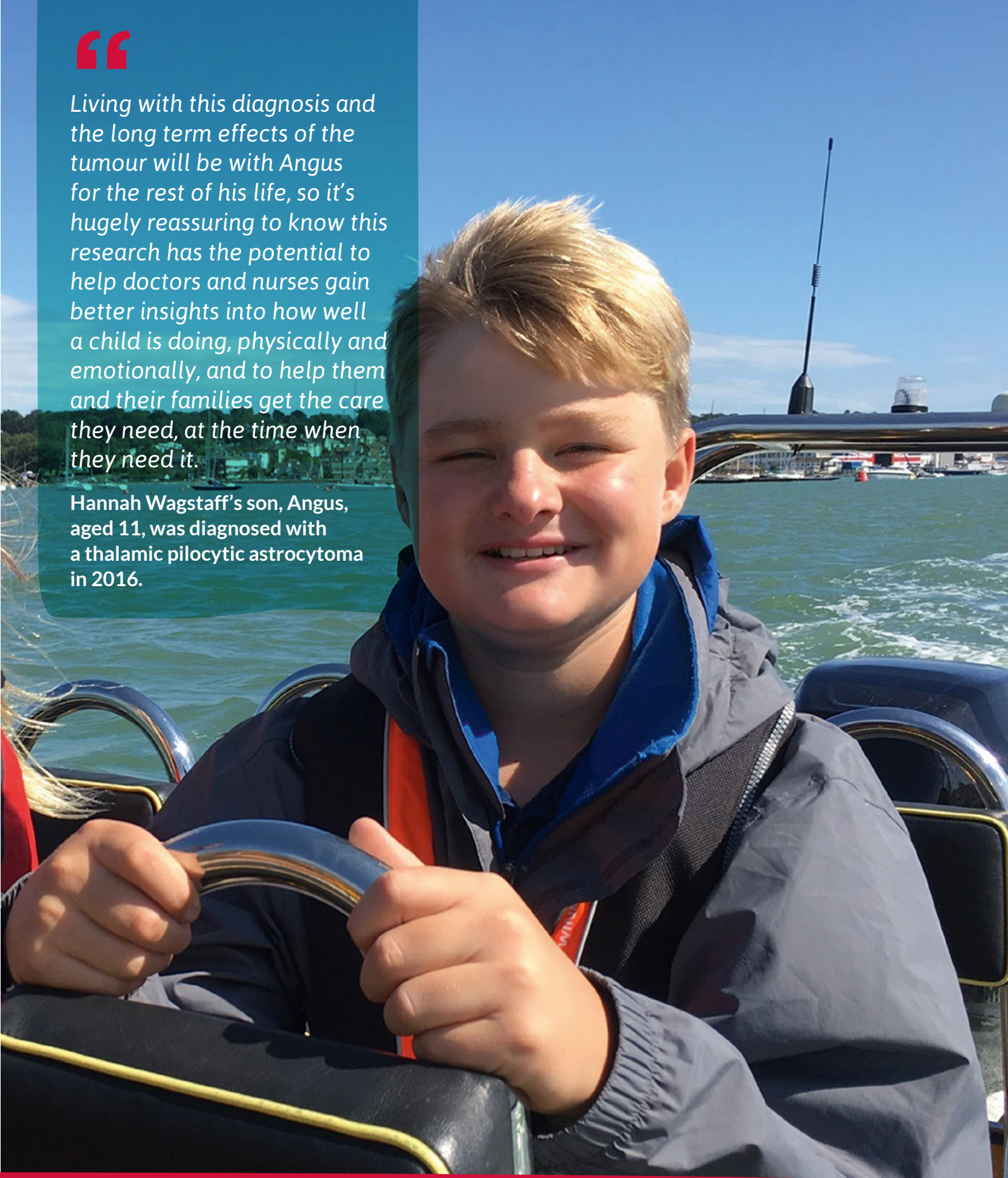
### Why we love this research

Professor Kennedy's 'quality of survival' assessment has been used in the PNET3, PNET4 and PNET5 clinical trials run by the European Society for Paediatric Oncology (SIOPE). Measuring quality of life as an outcome measure for brain tumour survivors has been recognised as a significant development in the field.

“

*Living with this diagnosis and the long term effects of the tumour will be with Angus for the rest of his life, so it's hugely reassuring to know this research has the potential to help doctors and nurses gain better insights into how well a child is doing, physically and emotionally, and to help them and their families get the care they need, at the time when they need it.*

**Hannah Wagstaff's son, Angus, aged 11, was diagnosed with a thalamic pilocytic astrocytoma in 2016.**



**62%**

Currently 62% of children who survive a brain tumour are left with life-altering disabilities.<sup>6</sup>



# International collaboration to develop better, safer treatments

Bringing together a multi-disciplinary team of experts from across Europe, The Everest Centre for Research into Paediatric Low Grade Brain Tumours was launched in June 2017. Over the next five years, it aims to improve understanding of low grade brain tumours, and develop and test new treatments that are significantly less harmful to children's quality of life.

Through four interrelated streams of research, the team – led from Heidelberg, Germany – will work together to get more effective, safer treatments to children as quickly as possible.

## 1. Determining the origin of low grade tumour types

Using molecular diagnostics and tumour genomics, the research will trace the tumour's 'cell of origin'. It will improve our understanding of why the cell behaves abnormally, thereby improving our chances of treating the tumour.

## 2. Identifying factors that affect tumour growth

Slow growing tumours can switch to become faster growing. This research will study what factors affect the speed of tumour growth so that they can be targeted as a way to stop or delay progression.

## 3. Developing low grade brain tumour models and pre-clinical screening

Low grade tumours have been notoriously difficult to model in the lab because of their slow growing nature. Expertise in Heidelberg and London will develop new, more accurate models to test new drugs and drug combinations.

## 4. Enabling an international clinical trial

The **LOW** Grade **G**lioma In Children (LOGGIC) clinical trial will assess how the specific molecular traits of a child's tumour influences the way it behaves, and will compare the efficacy of new, targeted therapies with the current standard treatments. It's an important step towards tailored treatments and will assess survival and quality of survival. This stream will fund important set-up costs, so the trial can start sooner.



*Dr David Jones, Group Leader for Paediatric Glioma Research*

German Cancer Research Centre (DKFZ), Heidelberg, Germany

### PROGRAMME FACTS

- ACCELERATE
- DIAGNOSE
- UNDERSTAND
- CATALYSE
- ENHANCE

£ Grant amount  
£4,999,107

🕒 Programme length  
Five years

👤 Age group  
Paediatrics

● Tumour type and grade  
Particular focus on gliomas; low grade brain tumours



## Why we love this research

While The Everest Centre was only launched recently, the research it's driving has significant potential to change the lives of children with a low grade brain tumour. It's a landmark initiative in worldwide research collaboration and the first centre of its kind in Europe to focus on low grade tumours.





Toby's diagnosis changed his life and ours. The Everest Centre has brought together international experts to accelerate progress towards more effective and less harmful treatments for slower growing brain tumours, which can have a devastating long term impact.

Rob Ritchie, whose son Toby was diagnosed with a low grade brain tumour on his brain stem at the age of five.

**26,870**

Globally, it's estimated that over 26,870 children and young adults have a paediatric low grade brain tumour.<sup>7-9\*\*</sup>



## Investigating the triggers that cause malignant transformation

For unknown reasons, adult low grade brain tumours usually undergo 'malignant transformation' to become a more aggressive high grade tumour, worsening prognosis. The Brain Tumour Charity is funding Dr Paul Brennan to study why these tumours change, and how the transformation could be predicted and stopped.

Earlier in his career, Dr Brennan successfully grew low grade brain tumour samples in the lab – a notoriously difficult feat because of the complicated and slow growing nature of low grade brain tumours. Through this, he was able to identify some of the molecular characteristics that differ between high grade and low grade brain tumours.

Now, using this knowledge and a technique that is relatively new in brain tumour research – CRISPR/Cas9 – Dr Brennan is inserting genes that are frequently found in high grade tumours, but missing from low grade tumours, into low grade tumour cells. If these genetic changes cause the cells to act like high grade tumour cells, we will have our first indication, from actual tumour cells, of the molecular changes that cause malignant transformation.

Dr Brennan will also investigate the epigenetics of the tumour cells and whether epigenetic changes can trigger low grade cells to act like high grade cells.

This research will reveal new targets for drugs that could delay or stop malignant transformation altogether, significantly improving life expectancy for those affected.



*Dr Paul Brennan, Senior Clinical Lecturer and Honorary Consultant Neurosurgeon*

University of Edinburgh  
and NHS Lothian, Edinburgh

### PROJECT FACTS

● UNDERSTAND

£ Grant amount  
£87,710

🕒 Project length  
One year

👤 Age group  
Adults

● Tumour type and grade  
Gliomas; low and high grade brain tumours



### Why we love this research

With improved understanding of what drives malignant transformation, Dr Brennan's research could identify new options for treating brain tumours. And, as a neurosurgeon with access to a large number of brain tumour samples, Dr Brennan is in a strong position to speed up this process, catalysing lab discoveries into clinical treatments.



“

Stopping tumours in their tracks – before they become malignant – should be a real priority in cancer research and I'm delighted it's taking centre stage in Dr Paul Brennan's work. The results will make a practical difference to hundreds, if not thousands of families like mine, for who transition has always been our biggest fear.

Gideon Burrows, whose low grade diagnosis progressed to high grade in 2016.



130

There are over 130 different types of primary brain and spinal tumour.<sup>10</sup>



## Using brain stimulation to prevent impairment during surgery

Diffuse low grade gliomas are a type of tumour that slowly spread through the brain. Surgery is often the first-line treatment for those diagnosed but because of the way the tumour infiltrates the tissue, surgery is difficult and poses a high risk to healthy areas of the brain. Mr Hart's research will expand our understanding of 'awake brain stimulation' which can be used during surgery to test areas of higher cognitive function and therefore prevent impairment.

During surgery it's critical to protect areas of the brain responsible for important cognitive functions. While we know broadly where these areas are in the brain, it varies slightly between individuals particularly in the presence of a tumour. During surgery a technique called 'awake brain stimulation' can help to identify important areas of brain function. The process involves applying an electrical stimulus to the brain while the patient is performing a task. It is well established for simpler functions like completing sentences or naming objects but not for more complex brain functions such as multi-tasking.

Mr Hart's research will help us better understand how we can test these more complex brain functions during surgery, so surgeons are better able to protect these areas of the brain. It will reduce the risk of long-term disabilities and improve quality of life for patients.



Mr Mike Hart PhD,  
Neurosurgery Registrar  
Addenbrookes Hospital, Cambridge

### PROJECT FACTS

- CATALYSE
- ENHANCE

£ Grant amount  
£50,000

🕒 Project length  
Two years and three months

👤 Age group  
Adults

● Tumour type and grade  
Diffuse tumours like oligodendroglioma;  
low grade tumours



### Why we love this research

The research we fund isn't just about improving survival rates, it's about improving quality of survival. Mr Hart's research should, in a relatively short space of time, give us something practical to apply during surgery that will make a significant difference to the quality of life after surgery.



“

My brain tumour affects my life every day. I'm learning to cope with it, but it's great to know that researchers are looking for ways to take out more tumour cells without damaging vital parts of the brain.

Jen McCrea, Young Ambassador for The Brain Tumour Charity, who is living with a Grade 2 oligodendroglioma.

**89%**

of people with a brain tumour experience ongoing symptoms including personality changes, and memory and cognitive problems.<sup>11</sup>

# The global picture

We could talk for hours about our research and the scientists we fund. There's so much exciting science happening and the research community is positive we're on the edge of a new era for accurate diagnoses and improved treatments.

For now, here's a snapshot of the 48 grants we're currently funding worldwide.

For more information about any of these projects, please go to [thebraintumourcharity.org/research](https://thebraintumourcharity.org/research) or call our research team on 01252 418190.







It's a pretty picture but we need your help to get more research underway – it's the only way we'll defeat brain tumours.

Donate online at [thebraintumourcharity.org/donate](https://thebraintumourcharity.org/donate) or call us today on 01252 237792. Thank you.

## Partnering with others

We know we can't do it alone. That's why we partner with other organisations and charities to make sure that we're driving progress as quickly as possible.

**By pooling expertise and maximising resources we're able to support large-scale research and fund more research into brain tumours, like the INSTINCT project led by Professor Steven Clifford at Newcastle University, highlighted below.**

With partners, Children with Cancer UK and Great Ormond Street Hospital Children's Charity, we have funded INSTINCT: The Institute of Child Health – Newcastle University – Institute of Cancer Research High-Risk Childhood Brain Tumour Network.

Researchers based at the major brain tumour research centres at Newcastle University, the University College London Institute of Child Health (ICH) and the Institute of Cancer Research (ICR) are exploring new ways to treat some of the most lethal childhood brain tumours. The team aims to save lives by developing tailored and targeted treatments.

The study will use the latest screening techniques to identify the genetic and biochemical profiles of aggressive brain tumours in children. The team will then link the tumour profile with the progress of each patient to identify links between tumour characteristics and prognosis. A better understanding of the biological mechanisms that drive brain tumours means that the researchers can develop drugs that target specific tumour characteristics.

Researchers hope that screening brain tumours will give patients a more accurate diagnosis and lead to personalised treatment that specifically targets the biological mechanism responsible for tumour development. It is hoped that this research programme will greatly enhance our understanding of these aggressive tumours and that this new understanding can be rapidly translated into new and effective treatments.

### **Our current co-funding partners:**

- Action Medical Research
- Cancer Research UK
- Children with Cancer UK
- Great Ormond Street Hospital Children's Charity
- Katy Holmes Trust
- OSCAR's Paediatric Brain Tumour Charity
- Stay Strong Stu
- The Medical Research Council

## Enabling future research

Every year, we receive many funding applications for innovative research. And if the science meets our stringent quality review and we believe it will make a difference, then it's research we want to fund.

That's why your support counts. It will help us say 'yes' to more research.

**Professor Karen Kirkby's path crossed with Professor Neil Burnet (Professor in Radiation Oncology) when her husband, Norman, spent a year working with him at Addenbrooke's. As a result, Karen was inspired to leave us a gift in her Will.**

"A vast amount of innovative research came out of that year and Norman, having attended clinics for patients diagnosed with a brain tumour, was struck by the need to improve outcomes. It's clear that research into brain tumours is an area of unmet need.

As an academic researcher, I'm passionate that research will make a huge difference to outcomes and quality of life, but if I don't commit to this myself by leaving a legacy, how can I expect anyone else to realise the importance? We both feel that better outcomes can be achieved through research and that The Brain Tumour Charity is an excellent way to make sure this happens as soon as possible."



Photo credit: Chris Hanley Photography







## Creating future leaders

At The Brain Tumour Charity we want to attract the best scientists to the field and retain the phenomenal talent of those already working tirelessly to understand more about the disease and improve treatments. It's these incredible scientists and clinicians that make breakthroughs, and we're committed to supporting them.

**The Charity first funded Dr David Jones in 2005 and, since then, he has become a world-renowned leader in his field. While he may have entered the field largely due to serendipity, Dr Jones explains how his career has evolved through his relationship with The Brain Tumour Charity and its founders, and his view on the future of research into brain tumours.**

“My history with The Charity started when I received funding for my PhD – so they've been with me from the start! In fact, that funding led to some ground-breaking discoveries in childhood brain tumours, like the identification of a new drug target, which are still influencing the field today.

In the following decade, The Charity continued to support my research, culminating in the recent launch of The Everest Centre for Research into Paediatric Low Grade Brain Tumours. It's a huge honour to lead this landmark initiative.

Beyond this direct support, The Charity's other activities have been greatly beneficial. By providing networks to interact with patients, researchers can be more effective in their work and the different funding streams on offer means support is available for smaller, specific projects that are

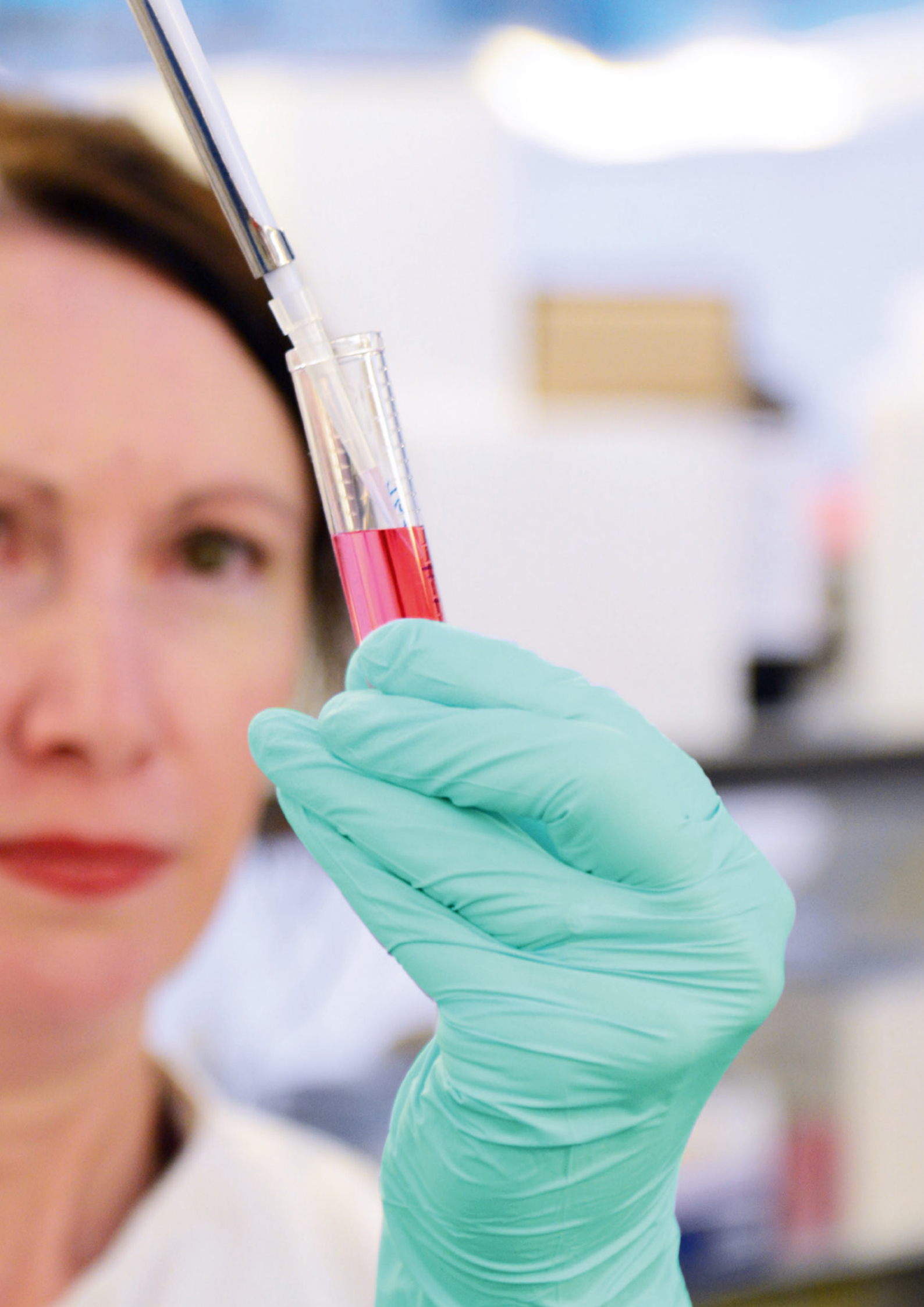
otherwise hard to fund. Another notable thing about The Brain Tumour Charity is their support of the best science globally. It's so important that support is available for international collaborations because the complexity of modern research means that no single centre can provide all of the knowledge, infrastructure and resources needed for truly transformative projects.

When it comes to the future of research into brain tumours, I think we have to acknowledge the scale of the challenge. The complexity and fragility of this special organ, and the diversity of tumour types, make brain tumours a unique, difficult foe.

However, I do now have genuine hope that we may start to see real progress. There have been numerous technical advances in recent years, which means that the research we do now would have been unimaginable even 10 years ago.

My main hope for the future of brain tumour research is that we continue to decrease the lag-time between scientific discoveries and patients seeing the benefits of this work in the clinic. We are now starting to see positive change in this area, which provides strong grounds for optimism.”

**If you're interested in our Future Leaders Grant Award, please go to [thebraintumourcharity.org/funding-opportunities](https://thebraintumourcharity.org/funding-opportunities)**



# We've started a revolution

At The Brain Tumour Charity, it's imperative that we fund the highest quality research, and we do. But it's also vital that we spot new opportunities and we're not held back by the status quo.

Here's a taster of some of the things we're doing to drive a revolution in research into brain tumours.

## *Patient-led databank*

If there's one thing that has the potential to change the research landscape, it's our patient-led databank – BRIAN (**B**rain tumou**R** Information and **A**nalysis **N**etwork).

For the first time, patients, clinicians and researchers will connect on a single platform so that we can better understand the clinical outcomes of treatment, alongside the patient's experience and wellbeing. In addition to clinical and medical data, those affected by a brain tumour will be able to upload real-time information about their diagnosis, the treatment they receive and the impact it has on their tumour and quality of life. The data will be made available to clinicians and scientists around the world.

The wealth of information and insight generated through this shared platform will inform new research and clinical developments to improve both survival and quality of life.

Dr Paul Brennan, senior clinical lecturer in neurosurgery at the University of Edinburgh, has described the databank as 'game-changing'. "With this project, researchers will for the first time have access to large amounts of data from lots of patients. This is game-changing for research into brain tumours, permitting researchers to ask questions and test hypotheses on a database that is more representative of the 'real-world' than ever before. The answers and insights generated will hopefully propel forward our search for new and effective treatments."

## *Expanding Theories Awards*

All great things start somewhere, so we're open to new avenues of investigation. These awards support scientists wanting to explore novel concepts and innovative research approaches that could fundamentally change our understanding or lead to significant developments in clinical practice.

## *Research into adult symptoms*

For one third of those diagnosed, it takes more than five visits to a medical professional to receive a diagnosis. Our HeadSmart campaign has helped drive down diagnosis times in children and teenagers from 13 weeks to 6.5, but it remains a different story for adults. We're funding research that will help to reduce adult diagnosis times – making sure everyone gets the treatment they need, as quickly as possible.

## *Partnering with the Structural Genomics Consortium (SGC)*

We're one of just a handful of charities to have partnered with the SGC – a programme of 200 scientists studying the structure and function of proteins in humans. Knowing the shape of proteins with biomedical importance will help us develop drugs that target, lock onto and act more effectively.

## *Launching The Brain Tumour Fund*

With the support of international venture capital firm NeoMed Management, The Charity is launching the world's first specialist brain tumour investment fund. The Fund, which is targeting £40 million in capital commitments, will invest in companies with products or technologies that build on oncology discoveries to improve survival or halve the harm caused by brain tumours.





# Changing the future begins today



**We want a future where brain tumours are defeated. A future where those affected receive an accurate diagnosis quickly and where treatments are tailored and safe so that everyone goes on to lead a life free from the burden of a past diagnosis.**

**This future is achievable.  
But only if we act and invest in research today.**

Research is expensive and painstaking – individual projects can take years. But it underpins everything. Research improves our knowledge and it's this knowledge that can be truly transformative, leading to better diagnosis, better treatments, and better quality of life.

We've seen phenomenal advances in other cancers over the past 10 years, and it's time that brain tumours saw the same success. With your support, we'll invest in more research, support more scientists and celebrate breakthroughs sooner.

So, if there's one thing you take from this report, let it be that we can't change today, tomorrow or the future without you.

## How your money can help

**£25**

Could buy 100 glass slides for researchers to study brain tumour tissue under the microscope.

**£100**

Could pay for a test to investigate the genetic changes that occur in a brain tumour.

**£250**

Could pay for a whole day of leading research. That's £21 a month, for one year.

**Please help us to defeat brain tumours.  
You can donate in the way that works for you.**



**Online:**  
[thebraintumourcharity.org/donate](https://thebraintumourcharity.org/donate)



**By phone:**  
**01252 237792**



# Glossary

## Biomarker

A distinct biological characteristic or substance, like a protein, that indicates a particular biological process. It can be measured and evaluated to identify, characterise and predict disease.

## Blood-brain barrier

A membrane that separates circulating blood from the brain. It's a very selective membrane that, in order to protect the brain, is only permeable to certain molecules.

## Biobank

A repository storing biological samples for use in research.

## Basic research

Also known as fundamental research, basic research grows our knowledge and understanding of a subject, like a disease.

## Clinical research

A branch of research that determines the safety and effectiveness of drugs, treatments and devices that are intended for human use.

## Epigenetics

Epigenetics are the traits that cannot be explained by the DNA code. For example a caterpillar and the resulting butterfly have the same genetic code, the same genotype, but look very different – they have a different phenotype. This is caused by variations in how the genes are expressed – the epigenetics.

## High grade brain tumour

Brain tumours classified as Grade 3 or 4 that display fast-growth characteristics.

## Low grade brain tumour

Brain tumours classified as Grade 1 or 2 that display slow-growth characteristics. Low grade tumours can transform to become a high grade – faster growing – tumour.

## Translational research

Research that applies the findings from basic research and translates it into medical practice to enhance human health and wellbeing.

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\* Following the 2016 revisions to WHO classification, this tumour is now known clinically as 'Diffuse Midline Glioma – Pontine Location H3 K27M'.

\*\* The estimated incidence of paediatric low grade brain tumours has been extrapolated from the 2017 IICC report using previously published patterns of brain tumour incidence in the UK and US







### *Closing remarks*

I know how passionate The Brain Tumour Charity is; they won't stop until brain tumours are defeated.

The Charity, its people, and the active community around it, drive change in everything they do - from promoting a better understanding of the symptoms and reducing diagnosis times, to improving access to specialist nurses and providing support to families just like mine. It is a true advocate for everyone affected, bringing the brain tumour community together with policy makers, expert clinicians and world-class scientists to make ground-breaking investments.

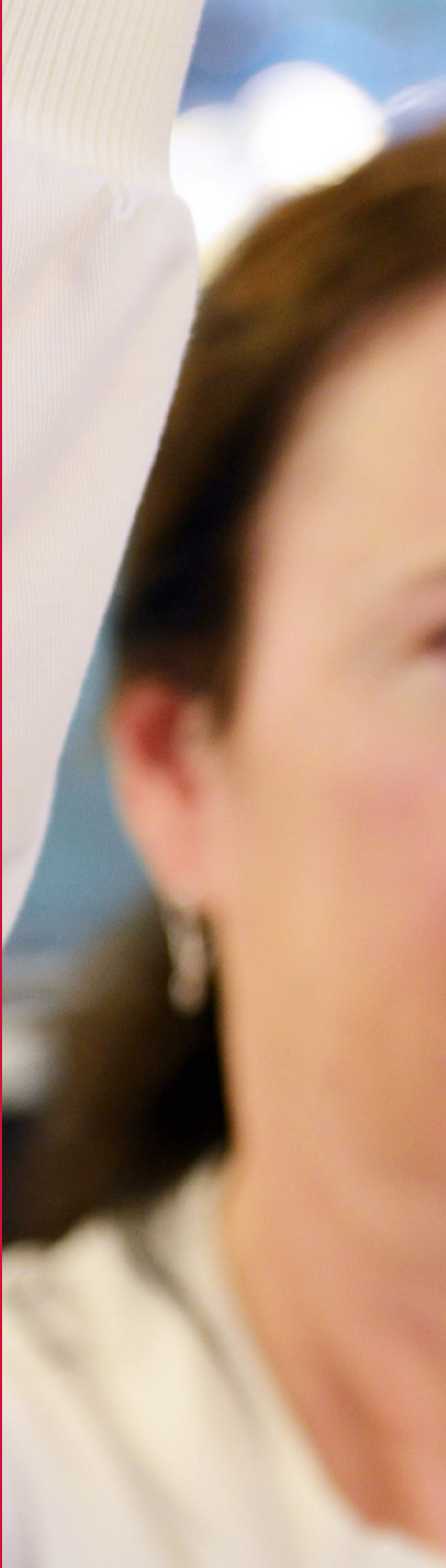
I draw enormous hope from the fact that research remains at the very heart of The Charity and I'm proud to support efforts that do, and will, make such a tangible difference for families and friends affected by this awful disease. I have no doubt The Brain Tumour Charity will continue to be at the forefront of change in its field and look forward to it achieving further breakthroughs and research success in the future alongside the rest of the brain tumour community.

**Jack Morris,**  
whose daughter Emily died  
from a brain tumour aged 31

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To find out more about any of the information or the research featured in this report, please don't hesitate to get in touch:

*research@thebraintumourcharity.org*  
*thebraintumourcharity.org/research*  
01252 418190



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