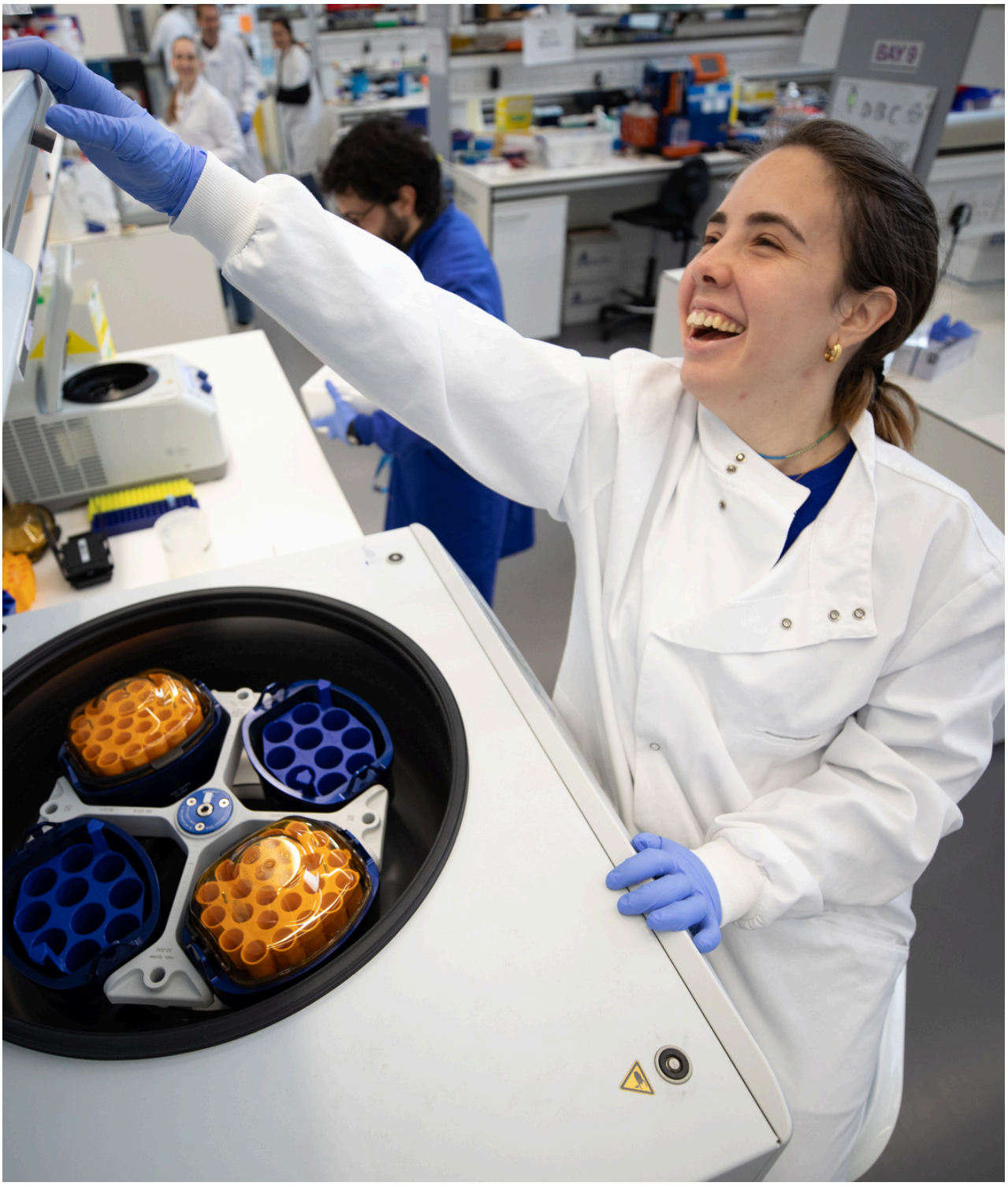
ZAYED CENTRE
FOR RESEARCH
INTO RARE DISEASE
IN CHILDREN

Annual Report 2024/25



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INTRODUCTION

The Zayed Centre for Research into Rare Disease in Children continues to transform outcomes for children with the rarest and most complex conditions. Since its opening in 2019, the centre has brought together world-leading clinical care, cutting-edge scientific research and advanced manufacturing capabilities to accelerate the journey from scientific discovery to patient treatment.

This year saw landmark achievements reflecting the expertise and collaboration fostered through the Zayed Centre for Research.

- In July 2024, researchers at the Zayed Centre for Research **became the first to use a groundbreaking HiP-CT, a new heart imagine technique to reveal the heart's structure** in extraordinary detail.
- Global collaborations delivering **faster diagnoses for children with epilepsy.**
- From **tissue engineering to growing miniature organs in the lab,** researchers at Zayed Centre for research is transforming how and when we can treat children born with serious conditions.
- **New partnerships** tackling the worldwide shortage of **viral vectors** (modified viruses used in cell therapies).

The impact of this work goes beyond clinical and scientific breakthroughs. It means children and families worldwide can benefit from earlier diagnoses, more targeted treatments and better outcomes in the long term.

This report shares the highlights of 2024/25 and the continued commitment to advancing research, care and hope for children everywhere.

RESEARCH IN NUMBERS

These research statistics cover the financial year 2024/25, which is a standardised annual reporting year for GOSH and the National Institute for Health and Care Research Great Ormond Street Hospital Biomedical Research Centre (NIHR GOSH BRC).

42 researchers based at the Zayed Centre for Research.

93 active projects with £41M of external funding to work in areas spanning gene, stem and cellular therapies, tissue engineering and regenerative medicine and accelerating new techniques in treating cancer.

116 patients recruited across these projects. The wide range of research includes innovations in diagnostics, advanced therapies, and patient-centred care.

16 new research projects launched by Research Investigators in 2024/25.

10 projects focused on gene and cell therapies.

22 active clinical trials involving cell and gene therapies.

122 peer-reviewed publications involved the Centre, including in high-impact journals such as *Nature Communications, The Lancet Neurology* and *The New England Journal of Medicine.*

PATIENT STORY: MEET GUNREET

Pioneering Gene Therapy Brings New Hope for Children with AADC Deficiency

Meet Gunreet, our first NHS patient to be treated with a new gene therapy for aromatic L-amino acid decarboxylase (AADC) deficiency.

When she was just nine months old, Gunreet was diagnosed with AADC deficiency, a very rare and serious condition that affects the brain and nervous system. Her mother, Sandeep, became worried when she noticed Gunreet wasn't meeting milestones like lifting her head or grasping objects. After several months of tests, Gunreet was admitted to hospital with a severe virus and a neurological episode. She was then referred to Great Ormond Street Hospital (GOSH), where specialist genetic testing confirmed the diagnosis.

AADC deficiency is caused by a fault in the gene that makes the AADC enzyme. This enzyme helps produce chemical messengers, including dopamine and serotonin, which allow the brain and body to communicate with each other. Without enough of these messengers, children struggle to control movement and vital functions like head and neck strength, facial expressions, blood pressure and heart rate. The condition is extremely rare, often life-limiting, and affects every aspect of a child's development.

In February 2024, Gunreet received a pioneering gene therapy at GOSH, becoming the youngest patient in the UK to be treated in this way on the NHS. Since then, her progress has been encouraging, with improvements in her movement, comfort and everyday quality of life. Professor Manju Kurian, consultant paediatric neurologist at GOSH, based at the Zayed Centre for Research, reflected on the broader impact of the therapy:

"AADC deficiency is a rare condition but often a cruel one that has such a profound impact on children and their carers and families. We know children with the condition have painful episodes that can last for hours and, as their condition progresses, their life becomes more and more difficult. It's incredible to me that I can now prescribe novel gene therapies just as I would prescribe paracetamol and antibiotics. The natural history of the condition is that most patients cannot fully hold their head up or make any developmental progress after that milestone. Gunreet's progress over the last year has been really impressive. We're hopeful that one day she will be able to talk or walk, as seen in some of the young patients treated in the clinical trial."

Professor Manju Kurian

OUTPATIENT VISITS AT FALCON WARD, 2024/25

In 2024/25, 19,069 outpatient appointments were attended at Falcon Ward — a 6.6% increase on the previous year, with Cardiology, Urology, and Immunology the busiest specialties.

Specialty	Attendeed appointments
Cardiology	12,398
Urology	1,442
Immunology	1,123
Cardiothoracic Transplantation	843
Endocrinology	452
Specialist Neonatal and Paediatric Surgery	441
Pulmonary Hypertension	424
Clinical Genetics	351
Dermatology	297
Infectious Diseases	259
Neurology	210
Neurosurgery	168
Neuromuscular	133
Respiratory Medicine	94
Nephrology	74
Epilepsy	66
Psychological Medicine	66
General Paediatrics	52
Pain Management	47
Craniofacial	30
Gastroenterology	21
Spinal Surgery	19
Rheumatology	18
Metabolic Medicine	12
Cardiac Surgery	10
Bone Marrow Transplant	7
Orthopaedics	5
Cystic Fibrosis	4
Chem Pathology	2
ECMO	1

INTERNATIONAL PATIENTS

GOSH cares for international patients from across the globe, offering specialist treatment for some of the most complex childhood conditions.

- Australia
- Poland
- Romania
- Russia
- Qatar
- Greece
- Portugal
- Cyprus
- Ireland
- Malta
- Norway
- UAE
- Spain
- Saudi Arabia

FAMILY FEEDBACK

"First time I attended this hospital with my daughters and had a fantastic experience, very friendly staff and receptionist. I arrived early but was seen straight away. A very clean and pleasant hospital."

"Very clean – amazing facilities – amazing staff– overall extremely happy."

"The new Zayed Centre was an excellent addition to the already amazing experience. GOSH is perfect."

"GOSH has always been a very good hospital. I haven't had any problems in the last five years. Super helpful, polite, clean. Good service all round. GOSH is always a great experience, very professional and polite helpful staff."

"The premises are great, clean, beautiful interior, well equipped. Very friendly staff introduced themselves, playful with our baby."

SPOTLIGHT: PROFESSOR PAOLO DE COPPI RECOGNISED ON TIME100 HEALTH LIST

In May 2024, Professor De Coppi was named on TIME's 100 Health list, recognising his global influence in paediatric surgery and regenerative medicine. His leadership in prenatal therapies and tissue engineering exemplifies the Zayed Centre for Research's mission to transform children's futures.

Based at the Zayed Centre for Research, Professor De Coppi is a global leader in his field. Professor De Coppi also serves as President of the European Paediatric Surgical Association and holds academic and clinical appointments in Belgium, the United States and Italy. His collaborative spirit and patient-centred approach underpin his research and clinical work, which have led to life-changing innovations.

Professor De Coppi leads ground-breaking research into prenatal and regenerative medicine that is transforming care for children with serious congenital conditions. In 2018, in a UK first, he was part of a team who pioneered foetal surgery to repair spina bifida inside the womb.

At the Zayed Centre for Research, Professor De Coppi's team worked with Dr Mattia Gerli's team to establish a safe method to derive organoids (small, simpler versions of organs) from amniotic fluid of ongoing pregnancies, paving the way to a safer approach to early diagnosis and personalised prenatal treatment of congenital malformations.

Professor de Coppi's team is also at the forefront of tissue engineering, using bio-printing and organoid technology to grow miniature versions of organs such as lungs and stomachs in the lab.

These models allow researchers to study organ development and test potential treatments in a way that is safer and more accurate than animal testing. This work is laying the foundations for a future where babies with life-threatening conditions could be diagnosed earlier and treated more precisely. It is a vision of medicine that begins at the very start of life, offering new hope for children and families around the world.

Additionally, engineered tissue developed in his lab has been applied to develop substitutes for missing organs, for example, an oesophagus for the treatment of Oesophageal Atresia. The first similar translational attempt had been previously safely demonstrated by Professor De Coppi in 2010 with a tissue-engineered trachea transplanted to a child born with a congenital tracheal stenosis (an extremely narrow windpipe). The child, now an adult, is well and did not require any further surgery.

Reflecting on the recognition of this pioneering work, Professor De Coppi credited the teams he works alongside and the hospital environment that enables close collaboration between lab and bedside teams.

"I feel very proud to work in an environment where we can continuously go from bench to bedside and back again, to improve treatment options for patients at GOSH and around the world. The Zayed Centre for Research offers excellent facilities that really helps make this possible. I am privileged to always be surrounded by people who are better to me and this recognition is testament to the spirit of teamwork that surrounds our endeavours."
Professor Paulo De Coppi

His most recent research advanced within the Zayed Centre for Research, co-led with Associate Professor Stavros Loukogeorgakis' group, is focused on developing an in-utero drug therapy for babies with congenital diaphragmatic hernia (CDH) to promote lung growth, helping to prevent the devastating effect of a missing diaphragm.

Professor De Coppi's leadership is helping to redefine what's possible for children facing some of the most complex conditions. His work embodies the mission of the Zayed Centre for Research: to develop kinder, more targeted treatments that transform children's lives, wherever they come from.

HIGHLIGHTS 2024/25

The following marks the highlights of the finanical year 2024/25, which is a standardised annual reporting for the year for GOSH and the NIHR GOS BRC

April 2024

Mahboubian Professor Claire Booth leads the pilot to make gene therapies more available around the world

In April 2024, GOSH, supported by Great Ormond Street Hospital Charity (GOSH Charity) and LifeArc, announced a pioneering plan to make life-changing gene therapies for rare diseases more widely accessible to children.

In a UK first, the plan would see GOSH, as an NHS Trust, hold the market authorisation for a gene therapy treatment. This means the hospital could licence and distribute a therapy directly, bypassing traditional commercial pathways that often limit access to rare disease therapies.

The pilot will focus on a lentiviral gene therapy for ADA-SCID, a rare genetic immune disorder. This therapy was co-developed by GOSH and the UCL Great Ormond Street Institute of Child Health (ICH), in collaboration with UCLA.

Professor Claire Booth, based at the Zayed Centre for Research, is leading this work. She explains:

"It's simply not good enough that we have treatments that we know work, but we can't get them to our patients. We must do something radical to tackle this."

Mahboubian Professor Claire Booth

The Zayed Centre for Research's unique combination of clinical, research and manufacturing facilities makes this innovation possible. If successful, it would create a model that would unlock access to proven therapies for rare and ultra-rare conditions worldwide, transforming the outlook for children and families who, right now, have few treatment options – or none at all.

To find out more, click here.

July 2024

Using cutting-edge imaging to transform understanding of heart defects

In July 2024, researchers at the Zayed Centre for Research became the first in the world to apply a new imaging technique called Hierarchical Phase-Contrast Tomography (HiP-CT) to study heart disease. Originally developed to scan entire adult organs at near-cellular resolution, HiP-CT offers detailed, 3D imaging that allows researchers to study both healthy and diseased hearts at multiple levels – from overall shape to microscopic structure.

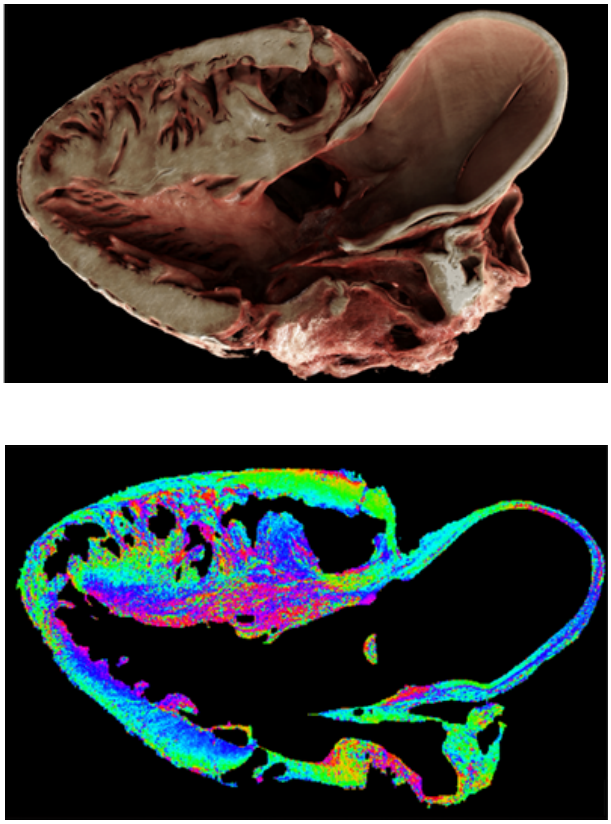
The research is being led by Professor Andrew Cook and his team at UCL, working with a multidisciplinary group including engineers at UCL and the European Synchrotron Radiation Facility (ESRF) in France. Their first paediatric study focused on tetralogy of Fallot – a complex congenital heart defect involving four structural abnormalities. Using more than 500 heart samples, in a collaboration with researchers from London, Leeds and Birmingham, a PhD student in the team is using HiP-CT to re-examine the anatomy of this condition in greater detail than ever before.

The next phase of the work, which is being prepared for publication, investigates the heart's conduction system – the electrical pathways that regulate rhythm – as well as changes in the organisation of the heart muscle, which is important for function. These are disrupted in children with tetralogy of Fallot. A second PhD student has begun using the same approach to study another condition called single ventricle disease, where one of the heart's chambers doesn't form properly. All this work is shedding new light on how these heart defects develop.

Recently, the team received funding of £500,000 from the Wellcome Trust to combine HiP-CT with spatial-omics and artificial intelligence, so researchers can link the high-resolution imaging with gene expression.

The work involves close collaboration with engineers and physicists at UCL and ESRF and experts in computational biology and mathematics at the University of Cambridge. The aim is to expand this work next year to find new treatment targets and open up possibilities for children around the world with life-threatening heart conditions.

To find out more, click here.



Three-dimensional 'cinematic' style rendering of a heart with tetralogy of Fallot together with a representative 'myomap' of the entire heart. The different colours show orientation changes in the muscle cells within the heart's wall. Image credits: Joseph Brunet, UCL (top); Vaish Sabarigirvasan, UCL (bottom).

October 2024

A world-first clinical trial for children with aggressive blood cancer

In autumn 2024, GOSH Charity announced funding for a £2.4million world-first clinical trial to test a novel CAR T-cell therapy in children with relapsed and drug-resistant T-cell acute lymphoblastic leukaemia (T-ALL).

T-ALL is an aggressive form of blood cancer. For some children, conventional treatments, including chemotherapy and bone marrow transplant, don't work. There's no standard of care for these children yet, and right now, long-term survival chances for these children are as low as 30%.

CAR T-cell therapy relies on using disarmed viruses to equip T-cells with the chimeric antigen receptor (CAR) that targets CCR9 – these are called viral vectors. Excitingly, the viruses for this trial will be made in GOSH's own Zayed Centre for Research. The state-of-the-art gene and cell therapy facilities at the centre have authorisation from the MHRA to manufacture viral vectors for use in clinical trials.

CAR T-cell therapy is a relatively new approach to cancer treatment that genetically modifies the body's own immune cells, called T-cells, so they recognise and kill cancer cells. So far though, it has proven difficult to use it as a treatment for T-ALL as it hasn't been possible to find a target in cancerous T-cells that sets it apart from healthy ones. But researchers at UCL have recently identified a target – a protein called CCR9. This clinical trial will test the effectiveness of a CAR T-cell therapy targeting cancer cells via CCR9.

Dedicated research projects for children's cancers are rare, with paediatric clinical trials traditionally starting later than adults and taking on average six and a half years longer to complete.

Dr Sara Ghorashian, Consultant Haematologist at GOSH, who is the lead clinician on this trial, says:

"Too often, children wait unacceptable amounts of time to access new cancer treatment, which could make all the difference. This study will pave the way for research to always include children and make it a matter of course that both paediatric and adult patients are incorporated within clinical trials at the same time. Our goal is to never have a situation where children are left behind. We hope that we can prove the benefit of this novel approach to influence a change in the law in the future."

Dr Sara Ghorashian

To find out more, click here.

November 2024

Pioneering therapy gains global approval

This year saw a landmark breakthrough with the regulatory approval of AUCATZYL, a next-generation CAR T-cell therapy for adult relapsed or refractory B-cell acute lymphoblastic leukaemia (B-ALL).The novel CD19 CAR used in AUCATZYL was developed and tested through a collaboration between clinicians based at the Zayed Centre for Research — Professor Persis Amrolia, Dr Sara Ghorashian, and UCL's Dr Martin Pule. The treatment was initially trialled in children through the CARPALL study, funded by GOSH Charity and Children with Cancer UK, and supported by the NIHR GOSH Biomedical Research Centre.

The clinical trial showed excellent results with an improved safety and engraftment profile compared to standard-of-care, Kymriah.

To find out more, click here.

February 2025

Global collaboration in epilepsy genomics

Dr Amy McTague, based at the Zayed Centre for Research, has played a pivotal role in the International Precision Child Health Partnership (IPCHiP), a global alliance of leading children's hospitals. Her research has transformed how genomic testing is used for children with unexplained seizures, particularly in severe forms of epilepsy that often begin in infancy.

By introducing rapid genome sequencing into routine clinical pathways, Dr McTague's work enables earlier and more accurate diagnoses. This speed can be life-changing, allowing clinicians to start the most effective treatment sooner, prevent unnecessary interventions and give families vital clarity. These advances are not only improving survival chances and quality of life for children but are also setting new international standards for precision medicine in paediatric neurology.

To find out more, click here.

March 2025

£5 million awarded to Zayed Centre for Research scientists in GOSH Charity's largest ever research funding scheme

Two pioneering scientists based at the Zayed Centre for Research have been awarded a combined £5million through GOSH Charity's most ambitious research funding scheme yet.

The awards will support transformational projects led by Professor Claire Booth and Professor Waseem Qasim, both internationally recognised for their work in gene and cell therapy. Their research is made possible by the cutting-edge facilities and collaborative environment of the Zayed Centre for Research, where scientists and clinicians work side by side to accelerate breakthroughs for children with the rarest and most complex conditions.

Professor Booth has received £2.6 million to develop safer, more effective gene therapies for children with inherited immune disorders.

Her programme will bring the latest gene-editing technologies into clinical use at GOSH, with the potential to extend these approaches to a broader range of genetic conditions. Professor Booth is also working on new ways to ensure children can access proven treatments more quickly.

Professor Qasim has been awarded £2.4m to explore how to make genome editing safer and more accessible for children with aggressive blood cancers. His team hopes to refine donor-derived CAR T-cell therapies so they can be used earlier and more widely. This work builds on the world-first use of base editing to treat a child with incurable leukaemia, led by Professor Qasim and his team at the Zayed Centre for Research.

These major awards form part of GOSH Charity's £70m research strategy and underline the Zayed Centre for Research's vital role in advancing global child health. Together, these programmes aim to make life-changing strides forward for seriously ill children in the UK and beyond.

To find out more, click here.

April 2025

Partnership accelerates next generation CAR T therapies

ViroCell Biologics produced the viral vectors needed for a new clinical trial (CARPALL) led by Professor Persis Amrolia at UCL GOSH ICH. This trial, which began enrolling patients in March 2025, represents the next generation of CAR T-cell therapies for children and young people with relapsed acute lymphoblastic leukaemia (ALL).

These specially engineered viral vectors are the essential starting point for manufacturing many gene therapies. Their availability can mean the difference between a clinical trial starting on time or facing long delays.

Over the last year, the first batches of ViroCell's gene therapy products were manufactured at the Zayed Centre for Research's Gene and Cell Therapy facility – the largest academic unit of its kind in the UK. By investing in new technology platforms and working closely with the Zayed Centre for Research, ViroCell is helping to address a global shortage of viral vectors, a challenge that affects hospitals and research centres worldwide.

To find out more, click here.

A VERY SPECIAL THANK YOU

The establishment of the Zayed Centre for Research into Rare Disease in Children was made possible by an extraordinary £60 million gift in 2014 from Her Highness Sheikha Fatima bint Mubarak, wife of the late Sheikh Zayed bin Sultan Al Nahyan, the founding father of the United Arab Emirates. We are also deeply thankful to Research England, the Wolfson Foundation, John Connolly & Odile Griffith, the Mead Family Foundation and the Rachel Charitable Trust, for their generous contributions towards the creation of the Zayed Centre for Research. The centre is a collaborative effort between Great Ormond Street Hospital, UCL, and Great Ormond Street Hospital Charity.

APPENDIX

Acronyms

BRC	Biomedical Research Centre
GOSH	Great Ormond Street Hospital
GOSH Charity	Great Ormond Street Hospital Children's Charity
MHRA	Medicines and Healthcare Products Regulatory Agency
NIHR	National Institute for Health and Care Research
PI	Principal Investigator
UCL GOS ICH	University College London Great Ormond Street Institute of Child Health

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