CURE PARKINSON'S

Cure Parkinson's Research Strategy

Slow, stop, or reverse the progression of Parkinson's

Our mission

To identify treatments that will slow, stop or reverse Parkinson's, with urgency for people living with the condition.

Cure Parkinson's is a medical research charity that was established in 2005, by four people living with Parkinson's. They were frustrated by the lack of research that was focused on curing the condition. They wanted to find treatments that would modify Parkinson's progression by slowing or stopping or even reversing the condition to give them back their lives. They wanted a cure.

Key among the founding four was Tom Isaacs. Diagnosed in 1995 at 26 years of age, Tom walked 4,500 miles of the UK coastline to raise awareness and funding for Parkinson's research, and became a tireless advocate for research focused on disease modification for Parkinson's.

" It is humbling to know that so many fantastic people are out there and that their sole mission is to rid the world of Parkinson's.
Tom Isaacs (late co-founder)

Over the last 20 years, Cure Parkinson's has directly committed more than £25 million of funding into both preclinical and clinical research projects around the world focused on slowing, stopping and reversing Parkinson's. We have also leveraged more than £100 million in indirect funding from government, industry and charitable organisations to support clinical trial programmes that we have championed. We have been at the forefront of international efforts seeking curative therapies for this progressive condition. Here, we outline our research strategy explaining how we are accelerating the development of disease-modifying treatments for Parkinson's.

" Staying true to the vision of the charity's co-founders, Cure Parkinson's single-focused mission remains the same now as it did 20 years ago. However, the number of Parkinson's breakthroughs in recent years has aided our understanding of the biology of Parkinson's, enabling us to target therapeutics with the potential to affect the progression of the condition. With more disease-modifying therapies in trial than ever before, there is real hope that we will cure Parkinson's.

Helen Matthews
CEO, Cure Parkinson's

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Cure Parkinson's research strategy was published in 2025 based on data from our 2024/25 financial year

Executive summary

At Cure Parkinson's we have a single goal: to identify curative therapies for Parkinson's. This narrow remit helps to keep our attention focused.

Our research strategy presented below (pages 12-22) has been developed with help from individuals within the research and the Parkinson's patient community. It has been a collaborative process that has provided us with a clear roadmap for the next few years. The plan involves four key objectives that build on what we have done so far and drive us closer to the identification of disease-modifying therapies for Parkinson's.

> "Our clear focus means we are relentless in our pursuit of these objectives and the ultimate goal of disease modification for Parkinson's. We will bring together those who share this ambition and work collaboratively with them as we all strive for a world without Parkinson's.
>
> **Dr Simon Stott**
> **Director of Research, Cure Parkinson's**

1. Grow our treatment selection programme - the International Linked Clinical Trials (iLCT) initiative developed in partnership with Van Andel Institute.

2. Accelerate the clinical testing of new therapies - with the development of novel clinical trial platforms for Parkinson's.

3. Champion the development of combination therapies - seeking to maximise any synergistic effects to generate a greater impact in slowing Parkinson's.

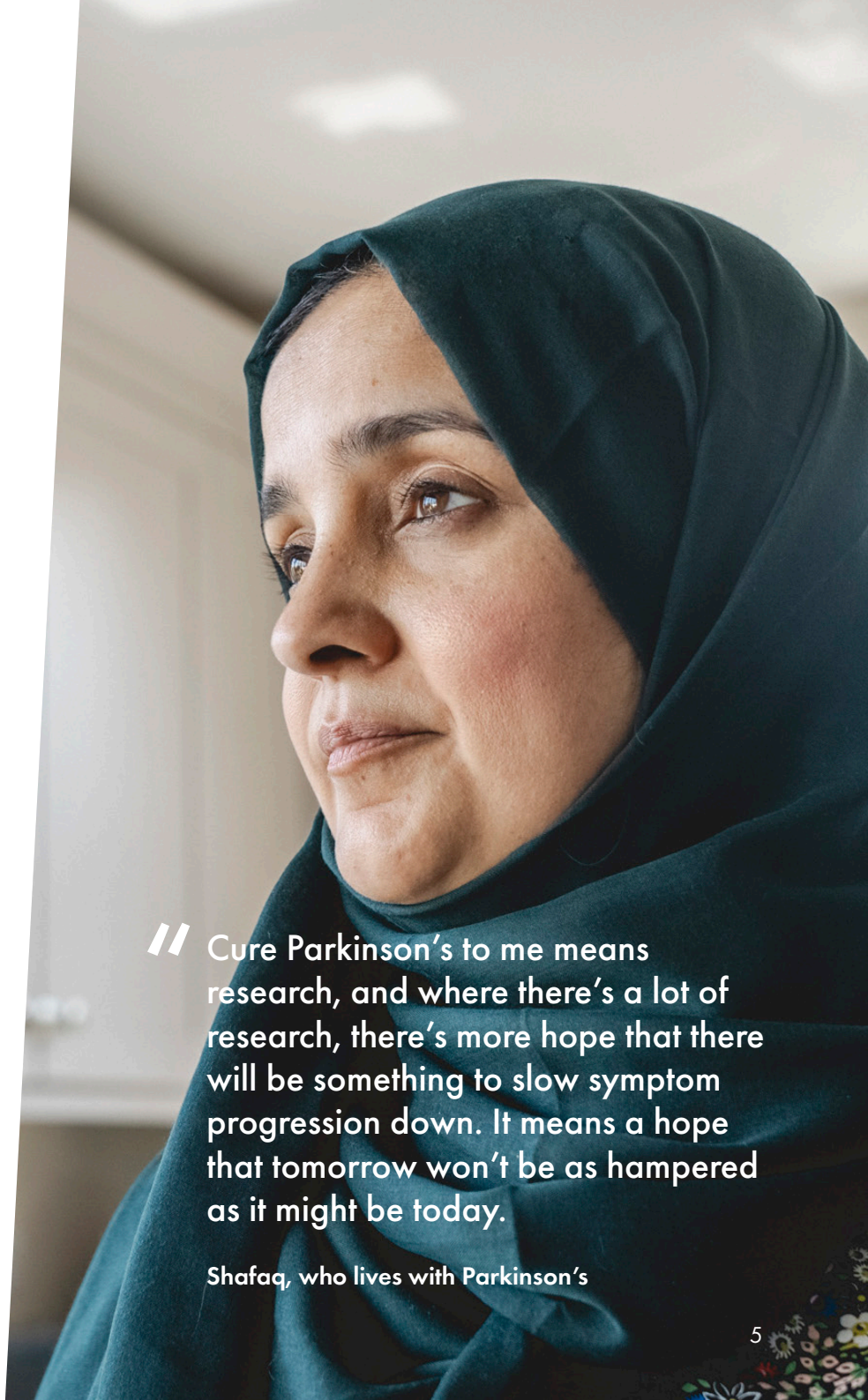
4. Make disease modification more personalised - targeting particular agents towards specific types of Parkinson's.

What is Parkinson's

Parkinson's is the second most common neurodegenerative condition after Alzheimer's, affecting 166,000 people in the UK and an estimated 12 million people worldwide. It is one of the most rapidly growing degenerative neurological conditions, with the incidence growing faster than normal demographic rates of population growth. Furthermore, as many countries have a growing elderly population, Parkinson's threatens to become a major burden on public healthcare systems.

Parkinson's is characterised by three main motor symptoms: slowness of movement, rigidity and a resting tremor. There are also a range of non-motor symptoms associated with Parkinson's including, but not limited to, loss of sense of smell, sleep disruption, constipation, and mood/cognitive changes. Parkinson's affects each person differently and symptoms can vary greatly from one individual to another, meaning that every person's experience with the condition is unique.

While there are medications that can help with managing the symptoms of Parkinson's, there are currently no treatments that slow or stop its progression. In addition, the symptomatic treatments lose their effectiveness over time. This highlights the need to urgently find disease-modifying therapies - treatments that will slow, stop or reverse the condition.



"Cure Parkinson's to me means research, and where there's a lot of research, there's more hope that there will be something to slow symptom progression down. It means a hope that tomorrow won't be as hampered as it might be today.

Shafaq, who lives with Parkinson's

What we do

At Cure Parkinson's, we focus on funding and facilitating research on disease modification for Parkinson's, with a strong emphasis on urgency for people living with the condition.

RESEARCH FUNDING – AN ACCELERATOR OF TRANSLATION

We fund both preclinical and clinical projects focused on slowing, stopping or reversing Parkinson's. Through our grant funding programme, we have supported research at more than 41 institutions across 12 countries.

The impact of this funding can be seen in the number of research reports being published each year in which Cure Parkinson's is cited as a funder.

Over the last five years, Cure Parkinson's has supported a number of high-profile clinical trials exploring disease modification in Parkinson's, which have concluded, including:

Two phase 3 trials

- The Exenatide-PD3 study: a phase 3 trial of exenatide in Parkinson's
- The ASPro-PD study: a phase 3 trial of ambroxol in Parkinson's

Multiple phase 2 trials

- The UP Study: a phase 2 trial of UDCA in Parkinson's
- The LixiPark Study: a phase 2 trial of lixisenatide in early Parkinson's
- The TRANSEURO study: a phase 2 trial of cell transplantation in Parkinson's
- The AZA-PD study: a phase 2 trial evaluating azathioprine in Parkinson's

Prof. Heather Mortiboys
Screening iLCT-evaluated drugs
University of Sheffield
Sheffield, England, UK

Prof. Aideen Sullivan & Prof. Gerard O'Keefe
GDF5
University College Cork
Cork, Ireland

Dr Katharina Klinger, Dr Anushka Takhi, & Dr Sinead O'Sullivan
iLCT Pipeline Project: Carnosic acid
German Center for Neurodegenerative Diseases
Bonn, Germany

Prof. Anthony Schapira
ASPro-PD
University College London
London, England, UK

Dr Joseph Mazzulli
Lonafarnib for Parkinson's
Northwestern University
Evanston, Illinois, US

Dr Poonam Thakur
iLCT Pipeline Project: Probucol and chlorogenic acid
Indian Institute of Science Education and Research (IISER)
Thiruvananthapuram, India

Our funded research projects

Cure Parkinson's has supported research at more than 41 institutions across 12 countries. This map highlights these countries and gives a look at some of the researchers carrying out this exciting work. Learn more about our projects by scanning the QR code or visiting our website at **cureparkinsons.org.uk/research-projects**

SCAN TO LEARN MORE

HOW CURE PARKINSON'S FUNDS RESEARCH

Four times per year, we have an open call for research grant applications. The projects proposed can be preclinical or clinical, but they must be of a potentially disease-modifying nature. In addition, preclinical projects must be within five years of clinical testing. This narrow funding remit helps to keep Cure Parkinson's focused on urgency, supporting projects with the potential to find a disease-modifying therapy quickly.

The applications are evaluated by an independent committee made up of research scientists, clinicians, regulatory and industry experts, and people living with Parkinson's. The committee firstly determine whether each application falls within our funding remit and, if it does, whether it is of interest. If the committee agree that it is of interest, they invite applicants to submit a more detailed, stage 2 application which is sent out for expert peer review.

At the next meeting with the peer reviewer feedback in hand, the committee will decide whether to recommend funding to the Cure Parkinson's trustees. These activities are in accordance with guidelines provided by the Association of Medical Research Charities (AMRC). If you would like to learn more about our grant application process, please see our website at cureparkinsons.org.uk/apply-for-funding

During the next three to five years, Cure Parkinson's will also consider introducing additional funding mechanisms such as calls for proposals in specific areas (including combination therapies) and strategic funding decisions to build momentum and partnerships in pursuit of our four key objectives.

HOW CURE PARKINSON'S INVESTS IN EARLY CAREER RESEARCHERS

In order to support the professional development of early career researchers, in 2023 Cure Parkinson's set up a programme that invited either PhD students or recent postdoctoral researchers to apply to join the Cure Parkinson's Research Committee. This is for a one-year term as Research Committee Interns, allowing them to gain experience in the grant evaluation process.

Over the year, the interns attend every committee meeting, observing the first meeting before being invited to comment on applications in their second meeting. For the third meeting, the interns act as a secondary presenter of a grant application before being the primary presenter at their final meeting. The Research Committee Intern programme is just one way Cure Parkinson's is supporting early researchers and encouraging them to have a career in Parkinson's research.

> **"I found the experience super enlightening. You very rarely see the backstage of how academia is run, and, generally, it is done through funding from charities and grant applications. Being an equal part in the committee was quite empowering.**
>
> **Dr Andrew Chai**
> **Research Committee Intern 2024,**
> **Cure Parkinson's**

COMMUNICATING RESEARCH – KEEPING PEOPLE LIVING WITH PARKINSON'S INFORMED

Cure Parkinson's shares key research findings on our website and on social media. These reports include both research that we have funded, but also important new developments in the area of disease modification for Parkinson's.

We are committed to keeping our supporters updated on each of our grant projects. We include information about the study and researcher, objectives, and related content and news reports. These are maintained and updated as projects progress and new grants are awarded.

We hold multiple in-person, hybrid and digital events throughout the year to keep the wider community updated on important developments in Parkinson's research. We host quarterly webinars in collaboration with the University of Edinburgh and the Journal of Parkinson's Disease. These one-hour sessions involve a panel of experts and people with Parkinson's to discuss the latest innovations in Parkinson's research. These webinars are designed for a lay audience and offer attendees the opportunity to ask the panel questions through a Q&A. All our webinars can be watched on our website: cureparkinsons.org.uk/webinars

In addition to online events, we hold in-person meetings. Every year in collaboration with Van Andel Institute, we hold a multi-day patient conference called 'Rallying to the Challenge' in Grand Rapids, Michigan, US. This meeting runs in parallel to the 'Grand Challenges in Parkinson's' conference, which is an academic conference for Parkinson's researchers. We invite presenters at Grand Challenges and others to give lay presentations at Rallying for people with Parkinson's.

Cure Parkinson's also holds bi-annual Research Update Meetings. We invite a selection of our funded researchers to present the results of their projects or clinical trials. Alongside our keynote presenters, we also invite early career researchers from funded labs to present academic posters for attendees. This is an initiative to give young professionals the opportunity to speak with people with Parkinson's directly and practice effective science communication. These events are livestreamed for those who cannot attend in person, and the recordings are posted on our website.

> **"Cure Parkinson's was established twenty years ago, on the backbone of teamwork with the Parkinson's community. Sharing our research provides our supporters and the wider Parkinson's community with up-to-date, valid, and verified information on potential life changing treatments. Money may be crucial to enable progress; teamwork will be the thing that will realise it.**
>
> **Lyndsey Isaacs**
> **Trustee, Cure Parkinson's**

BEYOND FUNDING AND COMMUNICATING ABOUT RESEARCH

Convenor – bringing the researchers together

At Cure Parkinson's we take our role very seriously as a convener of stakeholder meetings and workshops focused on topics of mutual interest for the field of disease modification in Parkinson's. We encourage the sharing of new data and information about projects in the precompetitive space, by holding workshops and conferences on topics that all stakeholders in Parkinson's research consider important. Following the meeting we disseminate reports of the discussions to the research community to share the progress and decisions being made by the attendees.

Conductor of research – adding value for the research community

In addition to funding and supporting research, Cure Parkinson's conducts and publishes research that we believe will be of interest and use to the broader scientific community. Each year, in collaboration with Parkinson's research advocates and members of The Michael J. Fox Foundation's research team, we produce a report on the clinical trial landscape for the development of new drug therapies for Parkinson's. This report is published in the Journal of Parkinson's Disease and represents an important reference for the Parkinson's community.

Involving people with Parkinson's and prioritising the patient voice

Our charity was founded by four people living with Parkinson's and the patient voice is important to everything we do. We aim to involve people living with the condition in all aspects of our work. This has taken the form of panels and workshops on topics of importance to the research being conducted, such as the use of lumbar punctures. People with Parkinson's sit on our research grant evaluation committee as reviewers of our grant applications, and to provide feedback on many of our research publications. Crucially, people with Parkinson's play a key role in the discussions that are held at our International Linked Clinical Trials meetings, commenting on the practicalities and risks associated with the agents being discussed.

RESEARCH ADVOCATE COUNCIL

We believe that research grounded in the lived experiences of those it aims to help is more likely to be relevant, inclusive, and impactful. That is why we embed Patient and Public Involvement and Engagement (PPIE) throughout our work. This ranges from influencing research priorities to improving how studies are communicated and delivered. By partnering with the Parkinson's community, we aim to promote research that reflects real-world needs and enables people to play an active role in the search for a cure.

To guide this work, we have established a Research Advocate Council of people with Parkinson's to bring diverse experiences, backgrounds, and perspectives. The council provides insights and feedback to strengthen our approach to research involvement. This ensures that the voices of people with lived experience are considered throughout our activities. The council plays a valuable role in shaping how we engage with the community, develop resources, and support inclusive, person-centred research practices. We also host regular patient-focused events, such as our Research Update Meetings and webinars, which create accessible opportunities for people with Parkinson's to learn about and contribute to ongoing research efforts.

EQUALITY, DIVERSITY AND INCLUSION (EDI)

Promoting and delivering EDI in our organisation and the research that we fund is essential. Parkinson's can affect anyone and everyone's experience of the condition is unique - we must reflect and build this diversity in everything we do.

We seek to ensure diversity across our team, our committees, and in our panels and workshops in order to ensure that all perspectives are being considered. We try to encourage inclusivity in research funding decisions we make, in how our funded research is designed, and the people with Parkinson's it involves.

Over the next three to five years we will publish our EDI strategy. We will be reviewing our approach for collecting data to determine how diverse our community of grant applicants, independent reviewers, research advocates, research committee and panel members are.

Research strategy

Cure Parkinson's is focused on supporting research targeting disease modification for Parkinson's.

OUR GOAL

Slow, stop or reverse Parkinson's with urgency for people living with the condition. To achieve this goal we facilitate, fund and promote research focused on new potentially disease-modifying treatments. Over the next five years, our research objectives are:

FOUR KEY OBJECTIVES:

1. Grow our treatment selection programme - the International Linked Clinical Trials (iLCT) initiative developed in partnership with Van Andel Institute.

2. Accelerate the clinical testing of new therapies - with the development of novel clinical trial platforms for Parkinson's.

3. Champion the development of combination therapies - seeking to maximise any synergistic effects to generate a greater impact in slowing Parkinson's.

4. Make disease modification more personalised - targeting particular agents towards specific types of Parkinson's.

1. Grow our treatment selection programme - the International Linked Clinical Trials (iLCT) initiative:

A panel of global Parkinson's experts annually charged with selecting potentially disease-modifying therapies for clinical testing.

In 2011 one of our co-founders, Tom Isaacs, and the Director of Research at the time, Dr Richard Wyse, asked each other if there was a proactive way that a small charity could speed up the development of new disease-modifying treatments for Parkinson's. Their answer to this question was the iLCT initiative.

iLCT is our flagship programme focused on selecting agents with the potential for disease modification in Parkinson's and supporting their clinical testing. Cure Parkinson's coordinates the iLCT initiative with our strategic partners at Van Andel Institute in Michigan, US.

> For more than a decade, Van Andel Institute and Cure Parkinson's have partnered to support the iLCT programme. Together with a growing list of collaborators, we are harnessing the power of teamwork and our collective expertise to pursue therapies that slow or stop Parkinson's progression and improve quality of life.
>
> **Professor Darren Moore, PhD**
> **Jay Van Andel Endowed Chair in Parkinson's Disease Research**
> **Chair, Department of Neurodegenerative Science Van Andel Institute**

Each year, the Cure Parkinson's research team generate a set of drug dossiers for which there is evidence of potential for disease modification in Parkinson's. These drugs can either be those with repurposing potential (agents that are already available on the market for the treatment of another condition) or experimental new molecules. Candidate drugs are identified by monitoring the literature, talking with biotech companies, and taking recommendations from academic researchers and people living with Parkinson's.

Each dossier contains everything that we know about a particular agent, from the scientific background and rationale, to preclinical evidence and any clinical data that is available. Every year, 15-20 of these dossiers are given to the iLCT committee to evaluate, score and rank. The top ranked drugs are considered 'prioritised' for clinical development and Cure Parkinson's then speaks to the stakeholders or owners of those prioritised agents about getting them into clinical trials with support from our iLCT funding partners. In 2024 we published a review of the iLCT programme, which at the time marked 12 years of activities. As of 31 March 2025, 256 dossiers have been evaluated by the iLCT committee, and the programme has been associated with 28 completed trials and 19 ongoing studies, involving over 6,800 people with Parkinson's, including the phase 3 trial of ambroxol in 330 people with Parkinson's.

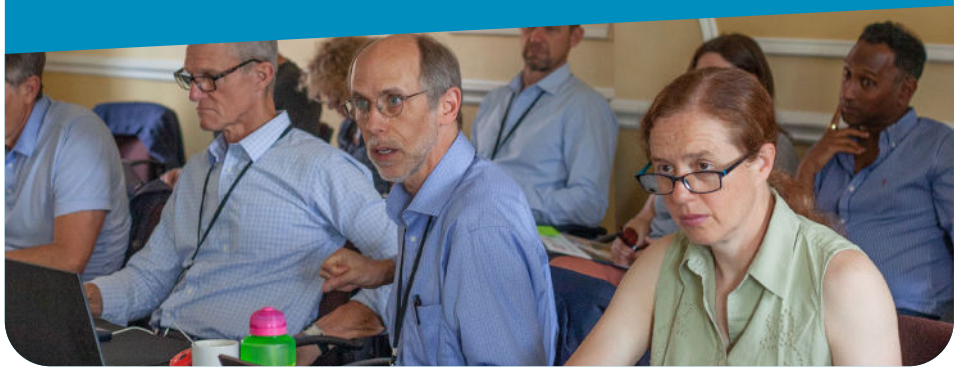
READ OUR ILCT REVIEW

"Since its creation 12 years ago by Cure Parkinson's and Van Andel Institute, the multinational achievements of the iLCT committee have been outstanding. These include the launch of more than 30 neuroprotective clinical trials involving thousands of Parkinson's patients, and the subsequent publication of results in leading journals, all of which has been transformational throughout the entire field of Parkinson's as we directly address the vital imperative for the development of new therapeutics to slow or stop disease progression.

Dr Richard Wyse
Director of Clinical Development
Cure Parkinson's

"There are numerous agents that seem quite promising for potential disease modification in Parkinson's, and so it's important to consider the strengths and weaknesses of each agent in the context of others when choosing which should be prioritised for moving forward in clinical trials in Parkinson's. The iLCT committee has done an outstanding job with this difficult task. I'm honoured to be part of this remarkable team.

Dr David Simon
Co-Chair, iLCT Committee



THE ILCT RESEARCH PIPELINE ACCELERATION PROGRAMME

Every year there are agents in the iLCT process that the committee believe are of interest but require further preclinical research. In order to help speed up the generation of this data, Cure Parkinson's set up the iLCT Research Pipeline Acceleration Programme, allowing us to commission research on these therapies. The aim of this programme is to rapidly fill the gaps in our knowledge around these agents, aiding in Cure Parkinson's sense of urgency to get the most promising compounds into clinical testing with people with Parkinson's.

> **"By working together with Cure Parkinson's, we're working faster and smarter to pinpoint these drugs and accelerate the development of the next treatments that will help not only people with dementia, but also Parkinson's.**
>
> **Dr Sheona Scales**
> **Director of Research, Alzheimer's Research UK**

Cure Parkinson's will leverage the success of the iLCT programme and further accelerate our efforts to identify new potentially disease-modifying therapies for the Parkinson's community.

This will involve broadening the initiative through several avenues.

Exploring cross-disease collaborations

Many neurological diseases share common features. For example, neuroinflammation is a biological feature of both Parkinson's and multiple sclerosis. This begs the question: should there be greater collaboration between charities focused on these conditions? In 2024, Cure Parkinson's signed a collaborative agreement with Alzheimer's Research UK (ARUK) to explore overlapping biology between the respective conditions. We have conducted treatment selection sessions at our iLCT meetings that evaluated agents that modulate shared biology and may have disease-modifying potential for both conditions. Over the next five years, we will endeavour to set up similar cross-disease collaborations with other disease indications.

Making iLCT dossiers available to clinical trialists

With over 260 dossiers written during the 13 years of the iLCT initiative, there is strong demand for access to the dossiers from Parkinson's clinical trialists (as well as groups focused on other disease indications). As part of our effort to accelerate the identification of new therapies, over the next five years Cure Parkinson's will be making non-confidential drug dossiers available to researchers and other charities. This will provide access and stimulate further research, as well as giving an opportunity to contribute new information to the dossiers.

More international collaborations

From humble beginnings, Cure Parkinson's has grown to become an international funder of preclinical and clinical research focused on disease modification for Parkinson's. As part of expanding our treatment selection programme, over the next five years we will be seeking to connect with more organisations around the world and collaborate with them to generate a more diverse pool of experimental agents to choose from and help move them into clinical testing.

De-risking of early stage agents

The iLCT programme started life as a drug repurposing effort, focusing on clinically available agents that could be rapidly tested in Parkinson's. There are, however, only so many drugs that can be repurposed and we have experienced enormous demand from biotech companies seeking to accelerate the development of their novel agents. Thus, the initiative is increasingly shifting from drug repurposing to de-risking new chemical entities and helping industry prepare their innovative therapies for clinical testing in Parkinson's. Cure Parkinson's is supporting this de-risking effort by funding multi-arm clinical trial platforms that will conduct rapid, short-term studies exploring the safety, dosing and target engagement of agents (read more on page 17). Over the next five years, we will seek to get more agents into clinical testing.

2. Accelerate the clinical testing of new therapies with the development of novel clinical trial platforms for Parkinson's:

The identification of promising experimental therapies is not enough, we need to speed up the clinical testing of these agents in parallel.

With a powerful treatment selection process like the iLCT programme, Cure Parkinson's focuses a lot of its attention on processes that can speed up the clinical testing of potentially disease-modifying therapies. Currently, the standard practice for testing of new therapies is to set up a clinical trial, test an agent for a certain period of time, and then analyse the results after the study has completed. It is an expensive, time-consuming process that is comparable to building a football stadium, playing a single game, and then dismantling the stadium before proposing to construct another for a new match.

One proposal for remedying this situation is the use of multi-arm, multi-stage (MAMS) clinical trial platforms. MAMS platforms are like giant conveyor belts for testing new treatments. They involve multiple treatment arms being compared to a single common placebo. In this fashion, three or more drugs can be tested simultaneously, in the same amount of time that it would normally take to test one drug. In addition to having multiple arms, MAMS trials offer a seamless transition between phases of clinical testing - this is the multi-stage part of the name. Rather than waiting until the end of a clinical trial to analyse the results (which is standard practice), MAMS trials incorporate regular, interim analysis checkpoints throughout the trial. This practice allows researchers to determine much earlier if a treatment is having an impact or not and, in doing so, experimental therapies that are not giving a positive signal of efficacy can be removed and replaced with an alternative treatment.

In 2018, Cure Parkinson's funded Professor Camille Carroll at Plymouth University to conduct a scoping study, which involved asking clinical trial experts, industry, regulators and people with Parkinson's for their views on aspects of setting up MAMS platforms to help accelerate the clinical development of new disease-modifying therapies. In 2024, Cure Parkinson's trustees went a step further and approved cornerstone funding for UK-based Edmund J Safra Accelerating Clinical Trials in Parkinson's Disease (EJS ACT-PD) MAMS platform. This clinical trial is led by University College London and is funded by a Medical Research Council (MRC) and National Institute for Health and Care Research (NIHR) partnership, Cure Parkinson's, The Michael J Fox Foundation, Parkinson's UK, The John Black Charitable Foundation, The Gatsby Charitable Foundation and Van Andel Institute.

The study will initially have three drug arms and one placebo group, and the plan for this huge project is to recruit 1,600 participants and randomly assign them to one of the study arms. The three agents being tested have been prioritised by our iLCT process and with support from government and funding partners, they will be able to transition smoothly and rapidly to the more definitive test of efficacy typical of a phase 3 trial, but with the option to discard those showing no promise at an early stage. Other promising drugs can then immediately be added for testing.

"EJS ACT-PD represents a major change in our approach to identifying disease-modifying treatments for Parkinson's. By improving all aspects of the efficiency of trial conduct through testing multiple treatments in parallel and incorporating interim analyses to quickly assess for signals of benefit, the trial will undoubtedly greatly increase our chances of finding treatments which slow down the rate of progression of Parkinson's, among a representative population of people with the condition.

Professor Tom Foltynie
Co-Principal Investigator of the EJS ACT-PD platform

DE-RISKING PLATFORMS: RAPIDLY PREPARING AGENTS FOR 'PRIME TIME'

In 2025, Cure Parkinson's announced funding for an innovative clinical trial platform called SLEIPNIR. Named after the Norse god Odin's eight-legged horse, SLEIPNIR is a multi-arm clinical trial that will conduct rapid, short-term studies exploring the safety, dosing and target engagement of agents being proposed for late-stage clinical testing. Dosing involves ensuring that the right amount of drug has been identified to have the desired effect, while target engagement allows investigators to know that the drug is doing what it is supposed to be doing. SLEIPNIR will also determine whether an agent is accessing the brain (if that is required).

With all of this data in hand for each new drug, investigators will be able to proceed to larger clinical trials with more confidence, knowing that they will be able to better determine if a drug is having the desired effect. These platforms also represent an important resource for the larger MAMS platforms like EJS ACT-PD, which will require a constant supply of new drugs that are 'trial ready' for testing.

> **"I believe SLEIPNIR is a critical stepping stone toward developing effective disease-modifying therapies for Parkinson's and, by extension, other neurodegenerative disorders with shared mechanisms. We are deeply grateful to Cure Parkinson's for their essential funding support of this groundbreaking platform.**
>
> **Professor Charalampos Tzoulis**
> **Principal Investigator, SLEIPNIR, University of Bergen, Norway**

THE GLOBAL PLATFORM TRIAL CONSORTIUM

In November 2024, Cure Parkinson's with France Parkinson convened a meeting of international research groups each seeking to set up and run a platform trial for Parkinson's. At the meeting, representatives from the US, France, Norway, the UK, and Australia provided updates on their progress and discussed the challenges that they have faced. The meeting was a great success with collaborative sharing of resources and the setting up of a consortium that will meet every year in order to accelerate the progress of these important projects. Networking between these platforms and alignment of activities will be important for the future of the projects, allowing for cross platform comparisons of results.

> **"By joining forces across borders, we are not just sharing knowledge, we are sparking hope and accelerating the journey towards groundbreaking advancements in Parkinson's research. Together, we stand stronger in our commitment to transform lives and pave the way to find a cure for Parkinson's.**
>
> **Dr Marie Fuzzati**
> **Scientific Director, France Parkinson**

3. Champion the development of combination therapies, seeking to maximise any synergistic effects in slowing Parkinson's.

A single agent may not be enough to slow the progression of Parkinson's, so we will expand our efforts focusing on testing drug combinations.

To date, most experimental treatments are clinically tested as monotherapies, which involves assessing a single drug to determine if it has an effect on the progression of Parkinson's. Monotherapies are very useful where a single factor causes a disease state. A good example of a monotherapy is a vaccine, which attempts to block a specific viral infection, and where the target is understood and the cause of the condition is well characterised.

However, for more complex conditions like Parkinson's where multiple biological pathways are believed to be affected, or where medical intervention may come too late for prevention, a potentially more impactful approach to treatment could be a combination of agents that target different aspects of the condition, having synergistic or additive beneficial effects. Tested alone, the components of a combination therapy may demonstrate limited efficacy, but when presented together they represent a sensible strategy to optimise potential therapeutic benefits, to reduce the risk of trial failure, and hopefully improve quality of life for the patient.

The challenge of all trials for Parkinson's is that a subtle effect on delaying progression is very difficult to detect within a reasonable time span (people with Parkinson's indicate three years is the maximum period acceptable for clinical trials) and without deploying huge numbers within groups. For those who live with the condition, however, a very subtle effect over their life span could be very significant in terms of quality of life. Study designs struggle to balance these factors, but where combinations are concerned synergistic effects may be detected where the effect of one drug alone may not.

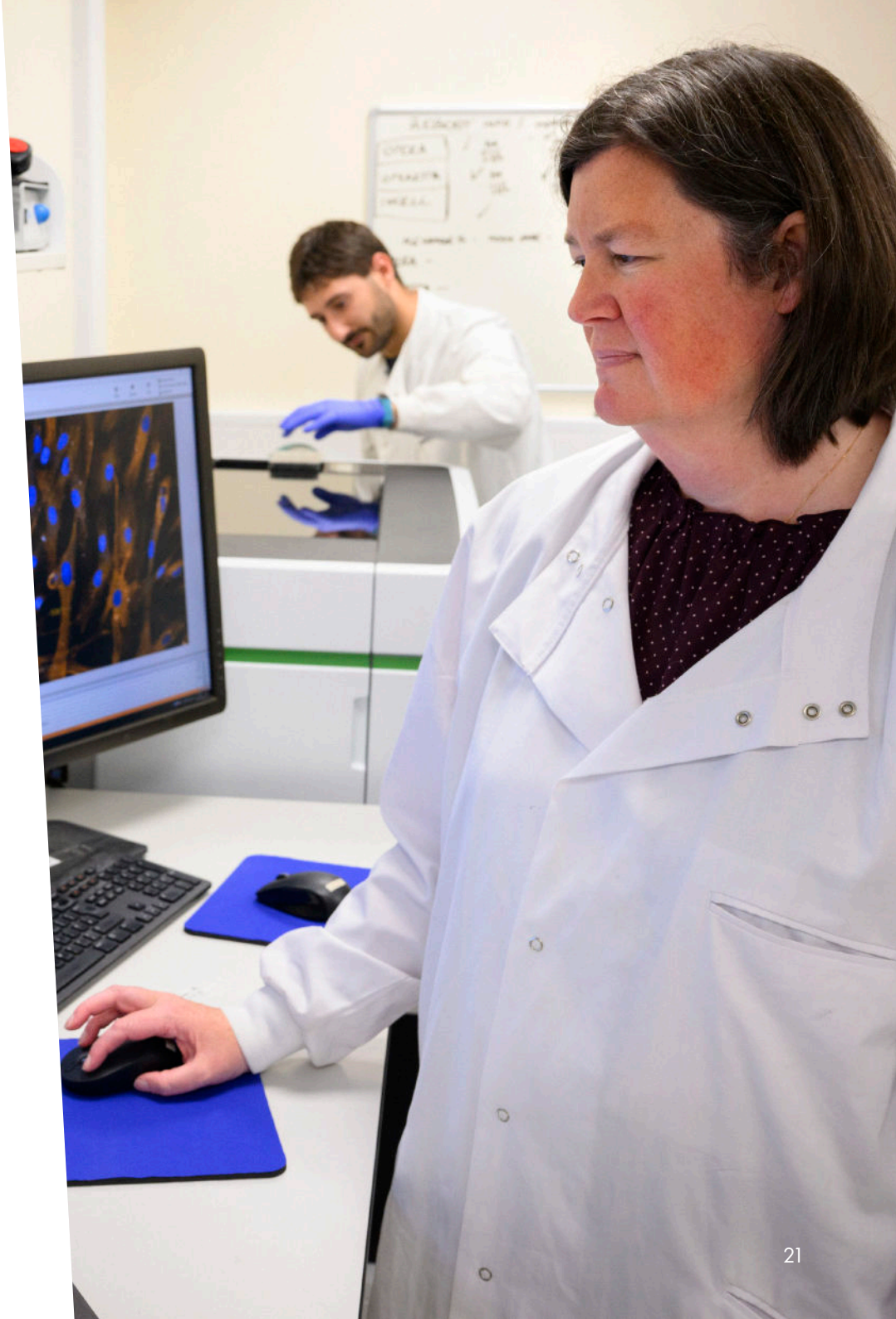
Combination therapies are now being readily employed across other medical fields (particularly oncology and antibiotics), and over the next five years Cure Parkinson's is planning to focus attention on combinatorial approaches to disease modification for Parkinson's. This began with a workshop of experts to determine how best we should approach combination therapies for Parkinson's. Next, we will have a dedicated funding call for rationally designed combinations that have disease-modifying potential in Parkinson's. These proposals can be for preclinical as well as clinical studies.

> **"Cure Parkinson's aim to encourage researchers to consider combination therapies earlier in the drug discovery process. We hope that by tackling the condition from multiple angles, we will increase the chances of uncovering a disease-modifying therapy for people living with Parkinson's now.**
>
> **Rachel Hughes, PhD**
> **Preclinical Research Manager, Cure Parkinson's**

COMBINATIONS OF ILCT AGENTS

Cure Parkinson's is already funding some exploratory investigations into combination therapies. This research is being conducted by Professor Heather Mortiboys at the University of Sheffield, and is looking for beneficial effects from combining iLCT evaluated drugs in a patient-derived cell model of Parkinson's. Leveraging the strength of our iLCT process - which has selected individual agents of interest - we are now seeking to determine whether synergistic benefits can be gained by rationally combining some of these drugs.

> "Parkinson's is a complex condition. As our understanding grows, it becomes increasingly clear that multiple cellular mechanisms should be targeted to have the best chance of restoring cellular health. This means exploring and testing combination therapies is a critical next step in drug discovery and highlights an important step to getting new therapies to the clinic.
>
> **Professor Heather Mortiboys**
> **Principal Investigator, University of Sheffield**



4. Make disease modification more personalised by targeting particular agents towards specific types of Parkinson's.

Developing better methods of patient stratification will allow for improved targeting of new therapies.

When Cure Parkinson's first started funding clinical trials in the late 2000s, the studies involved recruiting anyone with Parkinson's. However, as everyone in the patient community knows, there is a lot of variability between people affected by the condition. In addition, over time, research has accumulated indicating that there are specific subtypes of Parkinson's based on genetics and biomarkers. The iLCT programme is increasingly targeting drugs towards specific cohorts within the diagnosed population.

A good example of this is the clinical trial programme on ambroxol, a cough medication that has been identified to elevate levels of an enzyme called glucocerebrosidase (GCase). This is involved in the waste disposal system of cells. The region of DNA that provides the instructions for making GCase is called the GBA1 gene. Tiny variations in the GBA1 gene are associated with an increased risk of developing Parkinson's. People with Parkinson's have reduced levels of effective GCase activity, and this is believed to be involved with the progression of the condition.

In the phase 3 clinical trial Ambroxol for Slowing the Progression of Parkinson's Disease (ASPro-PD), for which Cure Parkinson's is part of a funding consortium, ambroxol will be tested in people with Parkinson's who carry genetic variants in their GBA1 gene as well as in people without this genetic risk factor. The process of identifying people with and without GBA1 variants has involved funding from Cure Parkinson's to set up and maintain a DNA sequencing platform called PD Frontline.

Over the next three to five years, more patient stratification will be employed in iLCT clinical trials and Cure Parkinson's will be supporting further efforts to provide more personalised therapies. These approaches to subtyping the patient community will include genetic and proteomic strategies, each of which will offer key insights into how and why a patient's Parkinson's may have started, and how each patient individually responds to the therapeutic approaches we are testing in our clinical trial programmes. This will then help indicate which disease-modifying therapeutics they should ideally receive in their long-term management in order to slow, stop or reverse their condition.

ASPro-PD is being funded by Cure Parkinson's alongside its strategic partners Van Andel Institute and the John Black Charitable Foundation, and by the Parkinson's Virtual Biotech, the drug discovery and development arm of Parkinson's UK. We would also like to thank the early supporters of this trial including Pears Foundation, Rosetrees Trust, The TJH Foundation and Frank Brake Charitable Trust.

Cure Parkinson's in 2030

Our hope is that a greatly expanded iLCT programme - involving cross-disease collaborations and the evaluation of combination therapies - will be feeding a robust pipeline of new disease-modifying therapeutic candidates. These experimental therapies will be evaluated in rapid de-risking studies or multi-arm, multi-stage clinical trial platforms to accelerate the Parkinson's community towards novel therapies that can reverse the progression of the condition. And importantly, the testing of these agents will be targeted at specific, defined cohorts of individuals so that the right patient is taking the right disease-modifying treatments.

This is our roadmap for slowing, stopping or reversing Parkinson's.

We will be unrelenting in our pursuit of this goal.

It is only a matter of time.

A message of thanks

Thank you to all of our funders, collaborators and supporters, and everyone in the Parkinson's community. We can only do this with your help and support. It's your generosity, and your fundraising ideas and energy, that power all of our research.

To help us deliver the plans in this strategy, and drive us faster towards the cure, we are aiming to raise £20 million in three years or less. The pace of the research will depend on how quickly we can reach that target.

If you can help us, or if you would like to get involved in our shared mission, please call us on +(0)20 7487 3892, visit our website at cureparkinsons.org.uk/donate or scan the QR code below.

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