Cure Parkinson's 2022 Research Impact Report

The Association of Medical Research Charities (AMRC) recommends that member charities evaluate impact data to assess whether the research they fund is making a difference. As Cure Parkinson's (CP) facilitates a large amount of research through the international Linked Clinical Trials (iLCT) programme, we have taken this opportunity to reflect on the progress and potential areas for improvement for both CP-funded research and the iLCT programme.

This report measures research impact in the following ways:

1. The standard academic metrics of the number of publications and the number of citations (direct references) a publication receives associated with our awarded grants
2. The progression of individual therapeutics associated with CP funding through the different phases of study (and whether they are linked to iLCT)
3. The number of iLCT-related active and completed clinical trials involving people with Parkinson's in relation to the number of therapies evaluated

Contents

1. Overview of CP grant funding

CP's annual research grant funding approvals have continued to increase from 2005 to October 2022. Accumulated, this amounts to more than £16.3 million approved for research projects to date, with a further £347,553 of research project funding being approved but not contracted before the end of the 2022 (figure 1). On average (mean) 25% of research grant applications submitted to CP are successful in being recommended for funding each year.

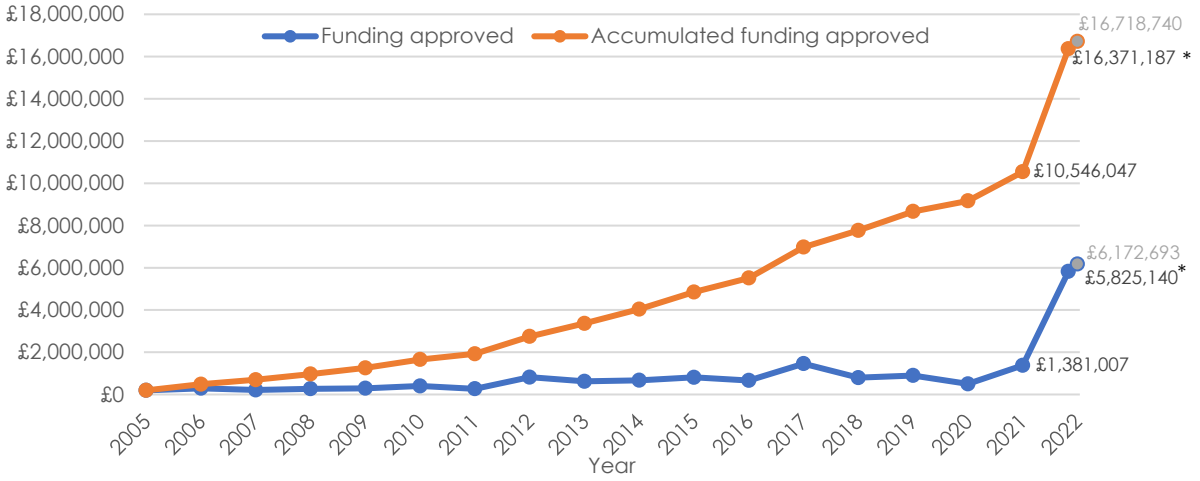


*Figure 1. Overall funding approved per year (blue) for research projects and cumulatively (orange) from 2005 to October 2022. *These figures include projects that were approved for funding by October 2022, when this report was written, however may not have been contracted at this point. Figures in grey show funding approved in November 2022.*

The current CP grant portfolio consists of research projects that can be categorized according to the stage and focus of research, as defined in table 1.

Stage	**Pre-Clinical**		Lab-based research evaluating potential therapies in models of Parkinson's
	Epidemiology		Research assessing risk factors, distribution, and determinants of Parkinson's in collective populations
	Clinical	Phase 1b:	Clinical assessment of intervention safety in people with Parkinson's
		Phase 2:	Clinical assessment of intervention tolerability and efficacy in people with Parkinson 's
		Phase 3:	Clinical assessment of intervention efficacy in a large group of people with Parkinson's
	Infrastructure		Projects supporting research logistics and efficiency, often facilitating collaboration
	Stratification		Projects identifying subtypes of Parkinson's to create cohorts for clinical studies
	Other		Research to support clinical development that does not fall into the previous categories
Focus	**Prevent**		Interventions aiming to prevent the onset of Parkinson's
	Slow/Stop		Interventions aiming to slow or stop Parkinson's progression
	Reverse		Interventions aiming to regenerate dopaminergic neurons and disease regression.
	Other		Projects including infrastructure, genetic stratification, and biomarkers

Table 1. Definitions of stage and focus of research used to categorise CP funded projects.

The majority (54%, 39/72) of CP-awarded research projects focus on slowing or stopping the progression of Parkinson's. The remainder focus on other areas to facilitate the advancement of therapeutics and clinical trials (25%, 18/72), specific strategies to reverse the progression of Parkinson's (18%, 13/72) and strategies to prevent the onset of Parkinson's (3%, 2/72) (figure 2A). The focus of all CP-awarded projects (active and completed grants) remains closely aligned with the strict funding remit of the charity.

The type of research has, however, shifted over time from mostly preclinical research to more clinical research. For projects completed before October 2022, the majority of research consisted of preclinical studies (62%, 29/47), phase 2 clinical trials (13%, 6/47) or other ways to facilitate the advancement clinical trials (e.g. focusing on outcome measures or learnings from trial participants) (19%, 9/47) (figure 2B).

Whereas, for active research, a larger proportion of the projects are clinical trials, phase 2 clinical trials (20%, 5/25) and phase 3 clinical trials (12%, 3/25), as well as infrastructure and stratification projects (12%, 3/25) to support clinical trials. Preclinical research accounts for only 32% (8/25) of our active projects (figure 2C).

A. Focus of research	Active	Complete	Total	% of all projects
Prevent	1	1	2	3%
Slow/Stop	13	23	36	50%
Reverse	5	8	13	18%
Slow/Stop/Reverse	0	3	3	4%
Other	6	12	18	25%
Total number of projects	25	47	72	

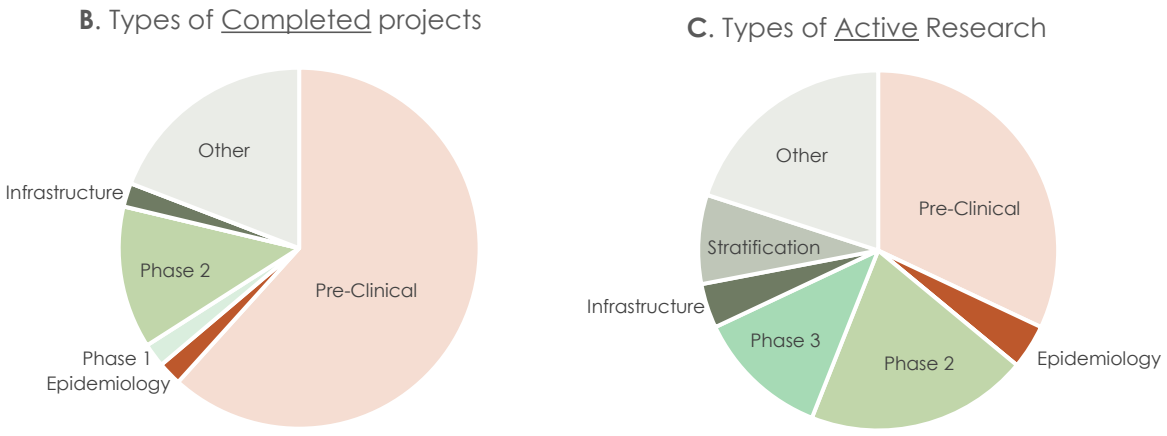


Figure 2. Overview of CP-awarded projects. A. Primary focus of the projects. B. Breakdown of completed projects by type of research. C. Breakdown of active projects by type of research.

CP has funded 35 different institutions in 9 countries (UK, USA, France, Canada, Sweden, Finland, Australia, Ireland, and Israel). More than half of all grants have been awarded to UK institutions (42/72) and this proportion rises to 70% (9/13) when focusing on institutions that have had more than one grant approved (figure 3).

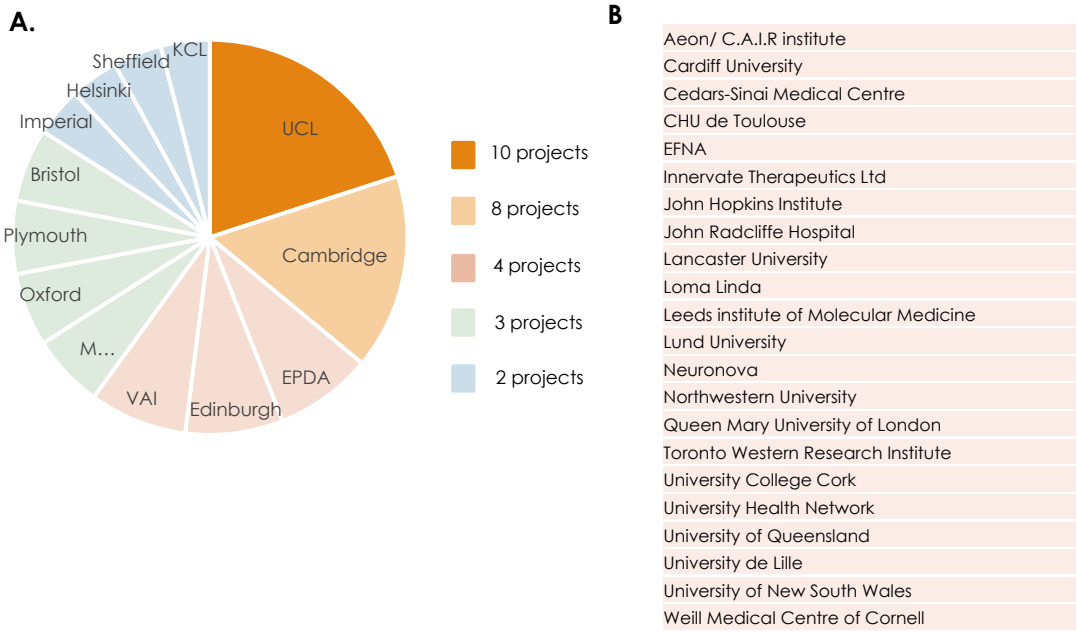


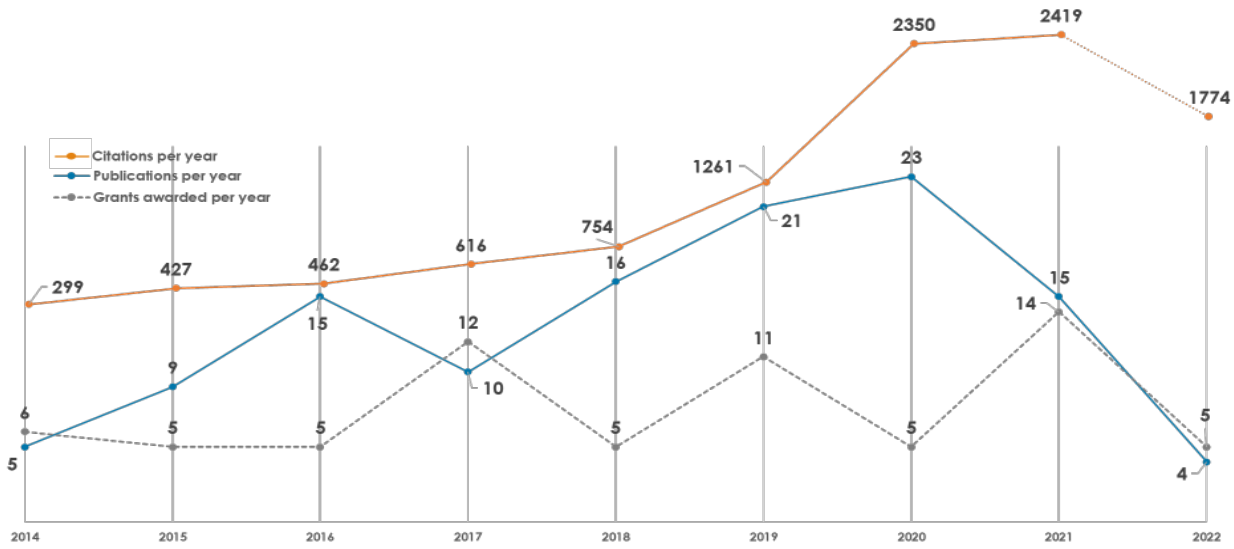
Figure 3. Number of grants awarded by institution. A. Institutions awarded more than one grant from CP. B. List of institutions awarded one grants from CP.

These figures highlight two key areas for improvement: 1) the geographic reach of our grant funding programme 2) inclusion and diversity within the research we fund.

2. Impact of CP-funded research: Publications and citations

Publishing work in peer-reviewed scientific journals can be used as a measure of research integrity and the number of times a paper is cited (directly referenced and acknowledged in a separate publication) can be used as an indication of research impact within the academic field. These are standard metrics that are used to assess the impact of academic research. Figure 4A shows the numbers of publications authored by CP funded researchers that have acknowledged CP as a funder in the years 2014-2022. This data shows 119 peer-reviewed publications have acknowledged CP funding during this time. Although this may seem like a modest number of publications, it is generally in line with the number of project grants (figure 4) awarded each year and these papers have accumulated almost 11,000 citations in this time, with this number increasing daily.

A.



B.

Type of access	No. of Publications	No. of Citations	Mean Citations	Definition
Gold	38	3578	94.16	All articles and related content immediately available, licensed for sharing
Bronze	12	1067	88.92	Free to read on publisher page but lack an identifiable license
Green	35	2158	60.23	Work also posted to an open repository, free to download
Hybrid	37	2158	58.32	Paid access or subscription to articles only
Closed	33	1919	58.15	Publisher provides pen access for articles which authors pay a publication fee

Figure 4. A. Publications (blue) citations (orange) of papers acknowledging CP funding and support in relation to the number of grants awarded each year (grey) (2014- October 2022) B. Accessibility of all publications acknowledging CP funding support (includes data prior to 2014). All data retrieved from Dimension on 12/10/22.

The dip in papers produced in 2021 reflects delays seen due to COVID-19; approximately 70% of CP's funded projects that were active in 2020 reported delays, increasing time for studies to complete and publish findings. The smaller increase in citations observed in 2021 fits with this assumption, however maintaining an increase over the year before suggests the lasting impact of these publications. Researchers listed as authors on these papers represent 20 different countries. Outside of the UK, researchers from the US and Canada are acknowledged most frequently (45 and 27 publications with at least one author from each of these countries, respectively). However, 112 of all 155 publications acknowledging CP have at least one author from the UK. Although our funding may be primarily based in the UK, these figures emphasise our efforts to promote international collaboration within our funded projects.

The publications and citations data has been retrieved from an online research platform called Dimensions and is reliant on Dimensions recognising CP as a funder of the research. This is dependent on how individual researchers acknowledge funding; discrepancies in the number of publications and citations occur based on where in the paper funding is cited and what name is used in the acknowledgment (variations

that have been used over the years include 'The Cure Parkinson's Trust', 'CPT', 'CP', 'Cure-PD'). To improve the accuracy of this, in recent years the CP research team have been actively requesting and reviewing pre-publication drafts from CP funded researchers to ensure consistent acknowledgement of funding. Additionally, the number of citations of CP-funded research may be limited because CP does not currently require results to be published as 'open access' (the ability to read a full publication without a fee) and figure 5B shows that the higher the level of open access (as defined in the table), the more citations a paper has received. Whilst CP promotes the use of the free AMRC open access platform, researchers and institutions prefer to publish in 'high impact' journals (e.g. Nature, Lancet, Cell, JAMA) which are most widely read by the academic field and often used in academia as a measure of success. Most journals offer open access options for a fee, but this is commonly in addition to the cost that researchers must pay to publish their work.

The reach, and therefore impact of our research, could be improved by asking for preprint access on servers such as MedRXiv or creating a small fund to cover open access publication fees for projects where there are no suitable alternative options or source of funds available, distributed on a case by case basis. As well as likely increasing the number of citations of CP-funded research, covering open access fees could also increase the amount of media attention our research receives (appendix 1 shows the top 5 current publications that have received the most citations and media attention).

3. Evaluating the progress of CP-funded research

Now turning to the impact of CP grant funding in terms of how our project results have influenced the progress of therapeutics through the various phases of study, figure 5 shows all the therapeutics that CP has approved funding for, whether they have been evaluated and/or prioritised by iLCT, whether they have moved into additional phases of research and which projects have been funded by CP or by others. It shows:

- 31 different therapeutics are associated with 50 CP funded projects
- 65% (20/31) of the CP-funded therapeutics have been evaluated by iLCT
- 71% (22/31) of all CP-funded therapeutics are still of interest as potential Parkinson's treatments
- 55% (12/22) of the therapeutics of interest are in active, due to start, or recently completed clinical trials
- 32% (7/22) of therapeutics of interest have moved into the next phase(s) of research since initial CP funding

4. Evaluating the impact of the iLCT programme

The previous section shows that a large proportion of CP funded projects relate to iLCT evaluated therapies, with many CP funded preclinical and pilot projects feeding into the iLCT process, and many clinical studies getting underway following the evaluation by the iLCT committee (figure 5).

63% of all CP funding (£10.4/£16.4 million) has been awarded for iLCT related projects. External investment for clinical trials of iLCT therapies is 10-fold this amount, which indicates the significant impact of the iLCT programme in progressing disease modifying trials for Parkinson's. Since the initiation of the iLCT programme in 2012, the CP research team has generated 205 dossiers on 159 different potentially disease modifying therapies for Parkinson's. This has resulted in 40 clinical trials testing 32 iLCT candidates across 17 different countries (UK, USA, Australia, Canada, Czech Republic, France, Germany, Hungary, India, Korea, Netherlands, Norway, Poland, Portugal, Slovakia, Spain, Sweden). This can be broken down to 20 completed trials of 15 evaluated iLCT drugs, involving 1,439 people with Parkinson's and 21 active or imminent trials of 17 evaluated iLCT drugs, involving 3,306 people with Parkinson's.

To put this in context, in 2021, nearly 40% of all potentially disease modifying therapies for Parkinson's reported by McFarthing et al (2022) to be in active clinical trial had been evaluated by the iLCT committee (Appendix 2).

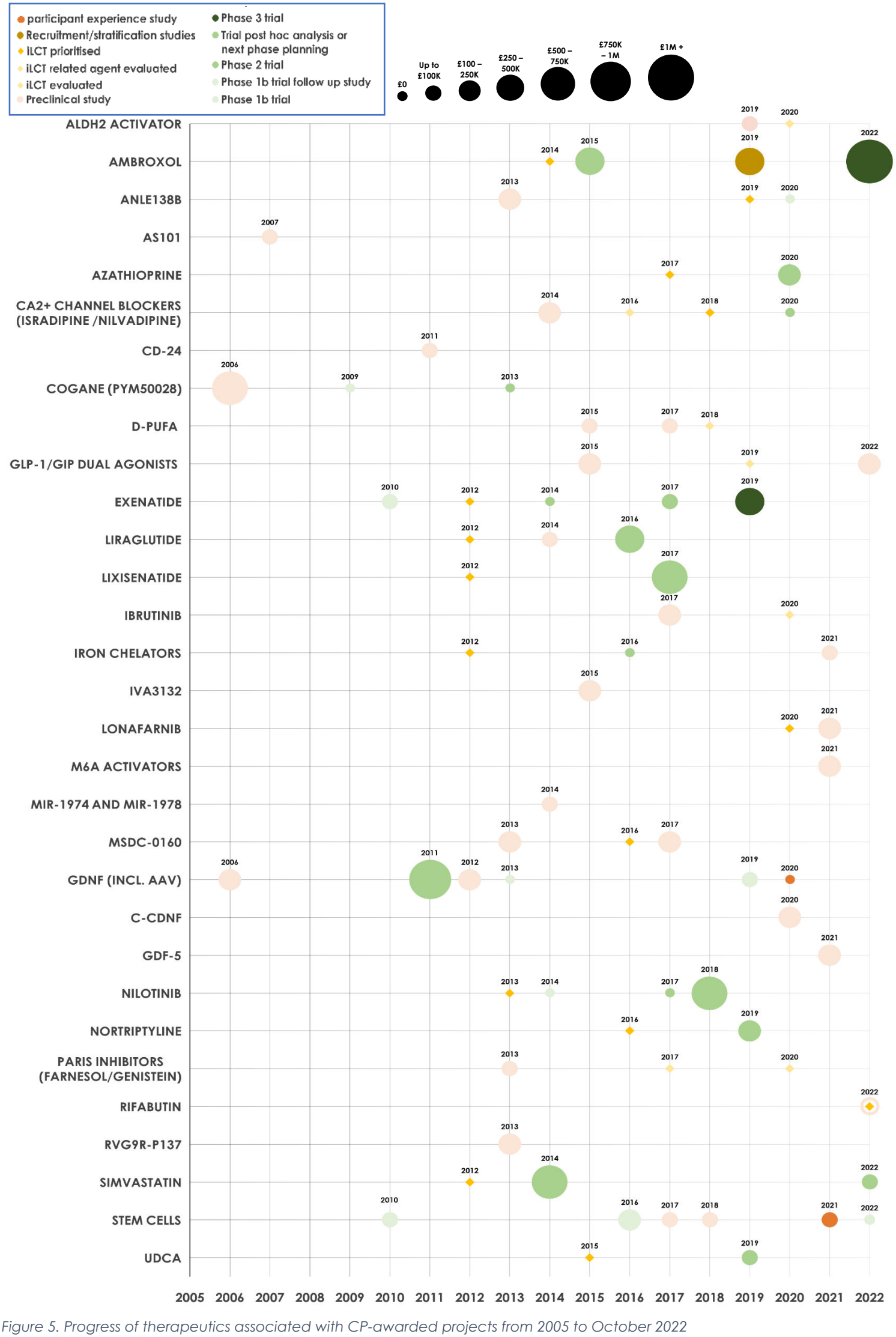


Figure 5. Progress of therapeutics associated with CP-awarded projects from 2005 to October 2022

5. Conclusion

CP supported research has had a significant impact in terms of publications and citations, progression of potentially disease modifying therapeutics through additional phases of study, and the number of disease-modifying trials available to people with Parkinson's. Looking forward there are three areas that should be explored further:

1. **How to expand the reach of our research funding opportunities**
2. **How to disseminate the findings of our funded projects more broadly**
3. **How to get more iLCT clinical trials underway**

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Cure Parkinson's

October 2022

Appendix 1. The top 5 publications of CP supported research by number of citations and media attention (using altmetric score)

Top 5 publications by **citations** (title hyperlinked)	**Focus**	**Citations**	Field Citation Ratio	Altmetric Score	Source of attention
Exenatide and the treatment of patients with Parkinson's disease. Aviles-Olmos et al, Journal of Clinical Investigation, 123(6), 2730-2736, 2013	**Exenatide**	**305**	69	60	News (4) Blogs (1) Twitter (19) Patents (7) Facebook (4) Reddit (1) Mendeley (311)
Human trials of stem cell-derived dopamine neurons for Parkinson's disease: dawn of a new era. Barker et al. Cell stem cell, 21(5), 569-573, 2017	**Stem Cells**	**229**	29	45	Blogs (3) Twitter (37) Patents (1) Facebook (2) Mendeley (398)
The glucagon-like peptide 1 (GLP) receptor as a therapeutic target in Parkinson's disease: mechanisms of action. Athauda and Foltynie, Drug Discovery Today, 21(5), 802-818, 2016	**Exenatide**	**202**	35	31	News (1) Blogs (1) Twitter (18) Patents (2) Mendeley (312)
a-Synuclein-induced down-regulation of Nurr1 disrupts GDNF signaling in Nigral Dopamine Neurons. Decressac et al, Science Translational Medicine, 4(613),263ra156, 2012	**GDNF**	**198**	43	38	News (3) Blogs (2) Twitter (3) Mendeley (180) CiteULike(1)
Randomised trial of intermittent intraputamenal glial cell line-derived neurotrophic factor in Parkinson's disease. Whone et al. Brain, 142(3), 512-525, 2019	**GDNF**	**159**	51	**225**	News (18) Blogs (7) Twitter (82) Facebook (2) Wikipedia (1) Reddit (2) F1000 (1) Mendeley (212)

N.B. The field citation ratio is the average number of citations a publication receives in comparison to the average number received by publications in the same year and field of research. All data retrieved from Dimensions 12/10/2022.

Top 5 publications by **altmetric score** (title hyperlinked)	**Focus**	Citations	Field Citation Ratio	**Altmetric Score**	Source of attention
Extended Treatment with Glial Cell Line-Derived Neurotrophic Factor in Parkinson's Disease. Whone et al. Journal of Parkinson's Disease, 9(2), 301-313, 2019	**GDNF**	84	39	**479**	News (57) Blogs (3) Tweets (27) Video Upload (1) Mendeley (109)
Mitochondrial pyruvate carrier regulates autophagy, inflammation, and neurodegeneration in experimental models of Parkinson's disease. Ghosh et al. Science Translational Medicine, 8(368), 368ra174, 2016	**MDSC-0160**	117	20	**356**	News (43) Blog (2) Twitter (40) Facebook (5) Google+ (1) Mendeley (182)
Randomised trial of intermittent intraputamenal glial cell line-derived neurotrophic factor in Parkinson's disease. Whone et al. Brain, 142(3), 512-525, 2019	**GDNF**	**159**	51	**225**	News (18) Blogs (7) Twitter (82) Facebook (2) Wikipedia (1) Reddit (2) F1000 (1) Mendeley (212)
PARIS farnesylation prevents neurodegeneration in models of Parkinson's disease.	**Farnesol**	9	n/a	**224**	News (27), Blogs (2)

Jo et al. Science Translational Medicine, 13(604), July 2021					Twitter (21) Wikipedia (1) Mendeley (19)
Parkinson's Disease Drug Therapies in the Clinical Trial Pipeline: 2020 McFarthing et al. Journal of Parkinson's Disease, 10(3), 757-774, July 2020	**Active Parkinson's clinical trials**	70	240	**180**	News (11) Blogs (1) Tweets (132) Patents (1) Facebook (3) Mendeley (147)

NB. Altmetric score is a measure of the volume of attention a paper has received in terms of social and traditional media e.g. News sources, Twitter, Wikipedia or others as given for each publication. These papers have created noise, and impact, outside of the research space. All data retrieved from Dimensions 12/10/2022.

Appendix 2. Therapeutics listed in active phase 1, phase 2 and phase 3 symptomatic and disease modifying Parkinson's clinical trials in 2021 taken from McFarthing et al (2022) - [Parkinson's Disease Drug Therapies in the Clinical Trial Pipeline: 2022 Update]

Those highlighted in blue = evaluated by iLCT at the time of the publication