PARKINSON'S UK
CHANGE ATTITUDES. FIND A CURE. JOIN US.

EAST MIDLANDS PARKINSON'S RESEARCH SUPPORT NETWORK

Monsters, mucus, and more

Parkinson's clinical research in 2020/2021

Simon Stott
The Cure Parkinson's Trust

The Cure Parkinson's Trust

THE SCIENCE OF PARKINSON'S

A UK-registered charity

Funds international research projects focused on disease modification in Parkinson’s

The Trust was founded in 2005 by four individuals with Parkinson‘s

Air Vice Marshal Michael Dicken | Tom Isaacs | Sir Richard Nichols | Sir David Jones

They were frustrated by the lack of research on ‘cure’


Tom Isaacs


LANDS END
NEW YORK 3147
JOHN O'GROATS 874
ISLES OF SCILLY 28
LONGSHIPS LIGHTHOUSE 1½
COASTIN' 4500 MILES
4TH FEBRUARY

The Cure Parkinson's Trust is focused on slowing, stopping and reversing Parkinson's

The Trust is a major funder of research focused on novel treatments for disease modification in Parkinson's

The Linked Clinical Trial initiative is a collaborative disease modification program

They evaluate 20+ compounds which have exhibited potential for disease modification in Parkinson’s.

They evaluate 20+ compounds which have exhibited potential for disease modification in Parkinson's.

Garvan Institute of Medical Research

P.R.A.G. Parkinson's Research Advocacy Group www.prag.site

THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH

SHAKE IT UP AUSTRALIA FOUNDATION

Parkinson's Foundation

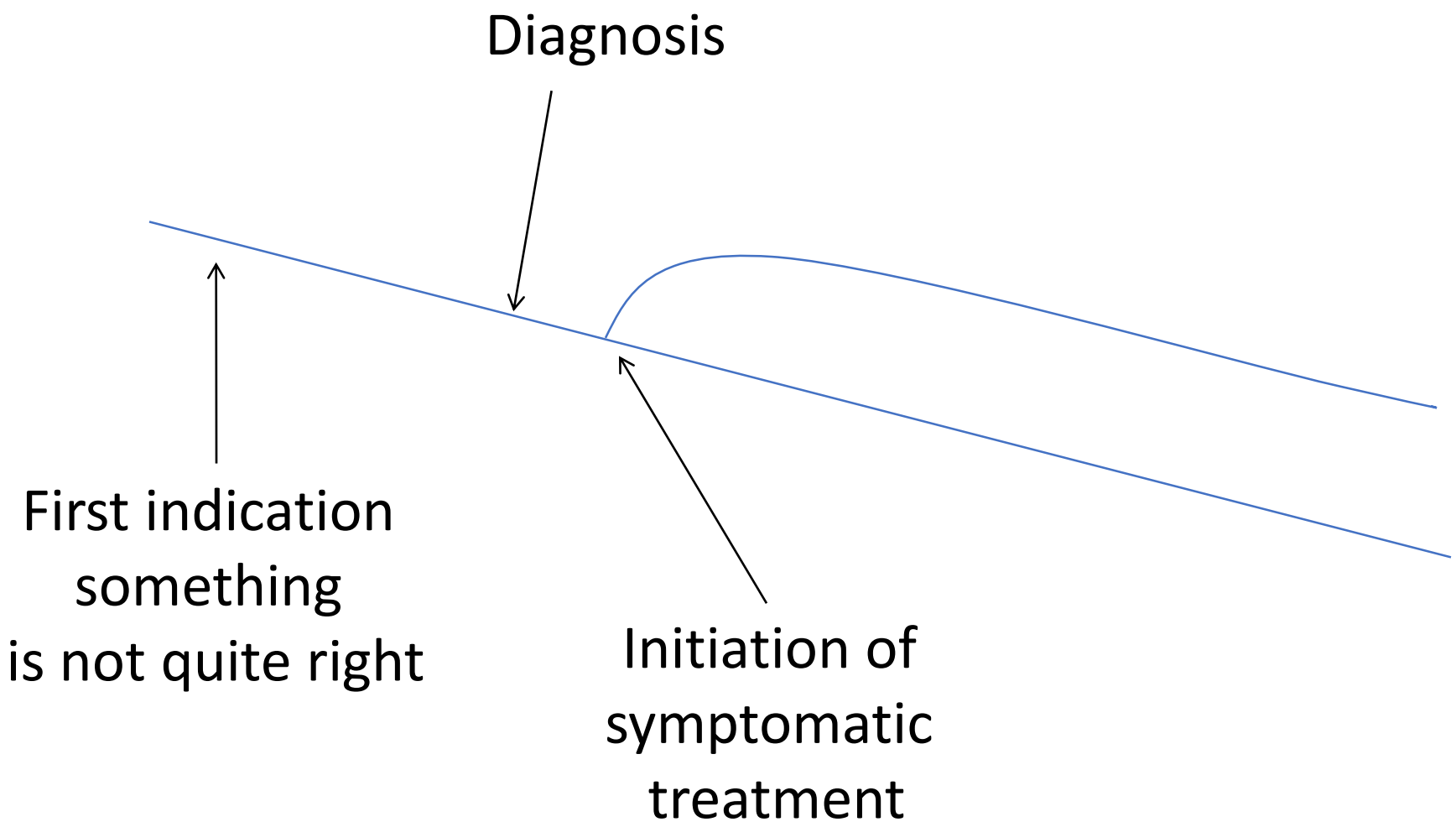
NIH National Institutes of Health

National Institute of Neurological Disorders and Stroke

THE SILVERSTEIN FOUNDATION FOR PARKINSON'S WITH GBA

PARKINSON'S UK

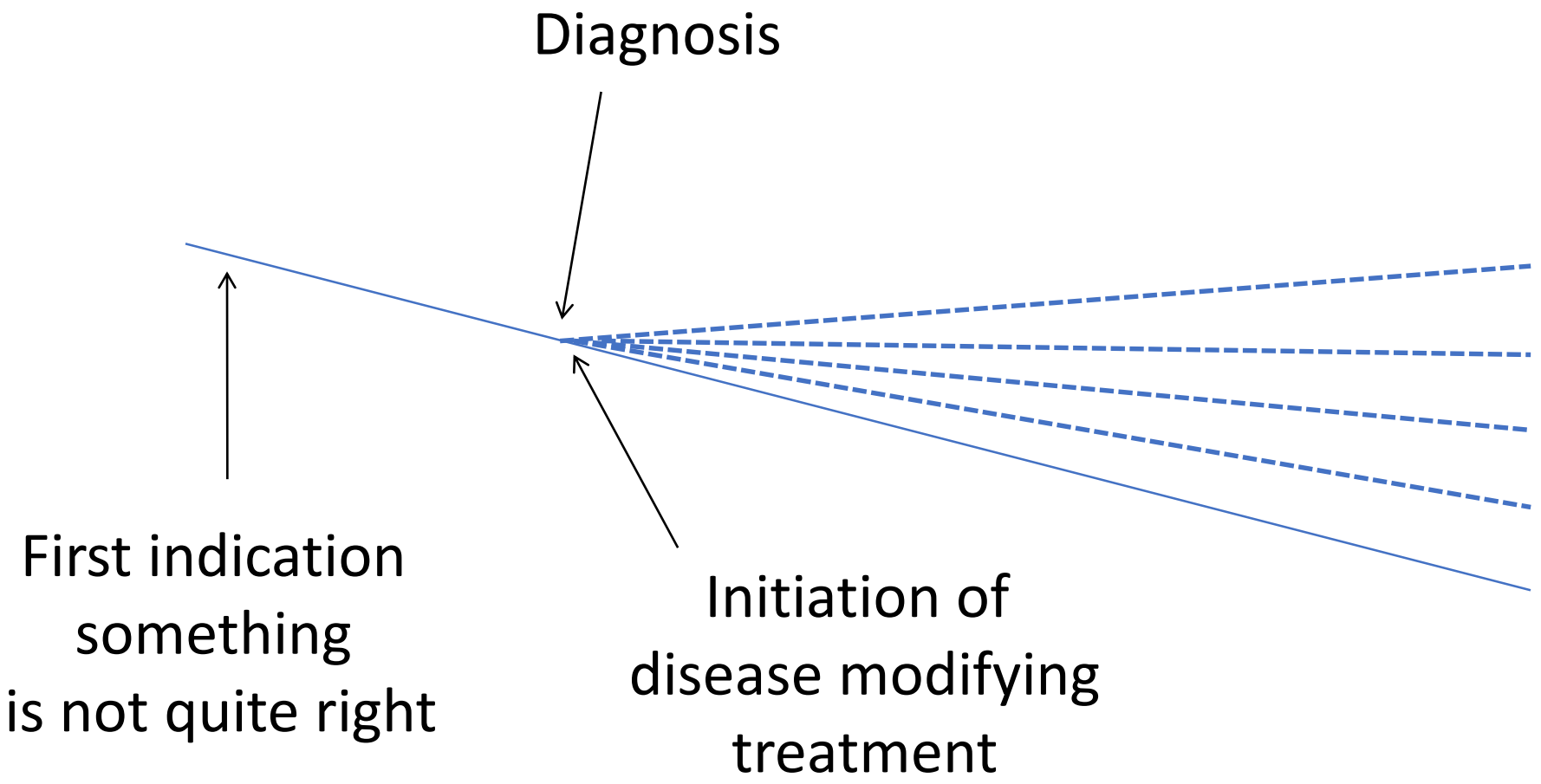
The normal trajectory of Parkinson's

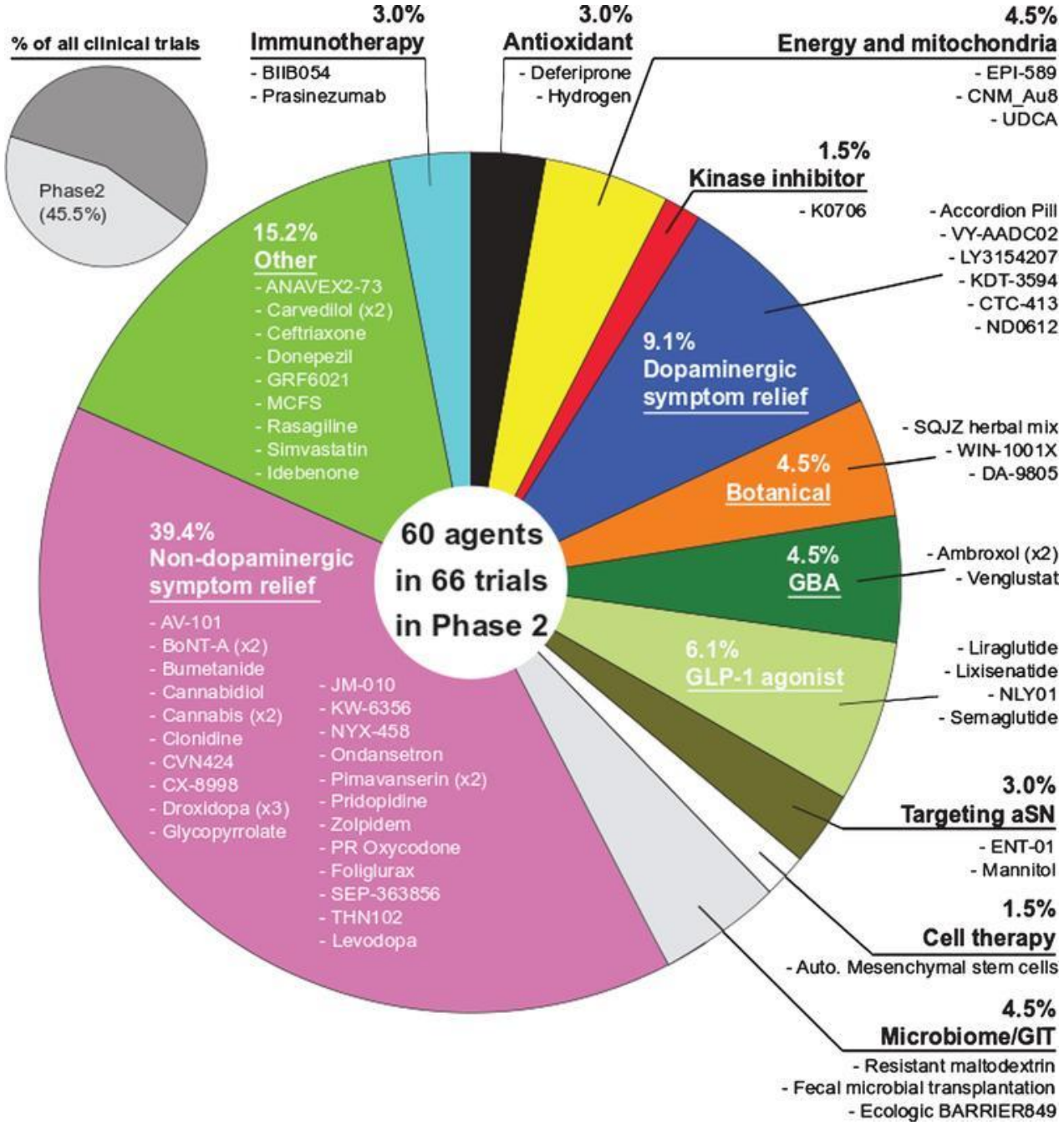


Disease modification:
“Any medical treatment of a disease that changes the trajectory of the condition”

A therapy that slows, stops or reverses the disease.

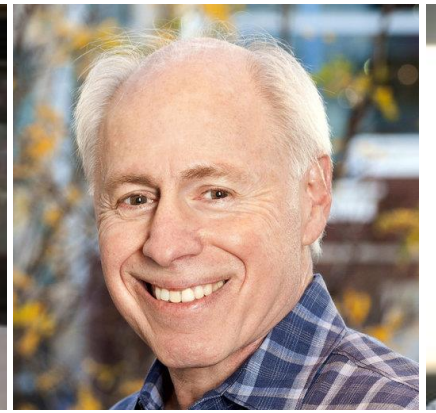
An altered trajectory for Parkinson's

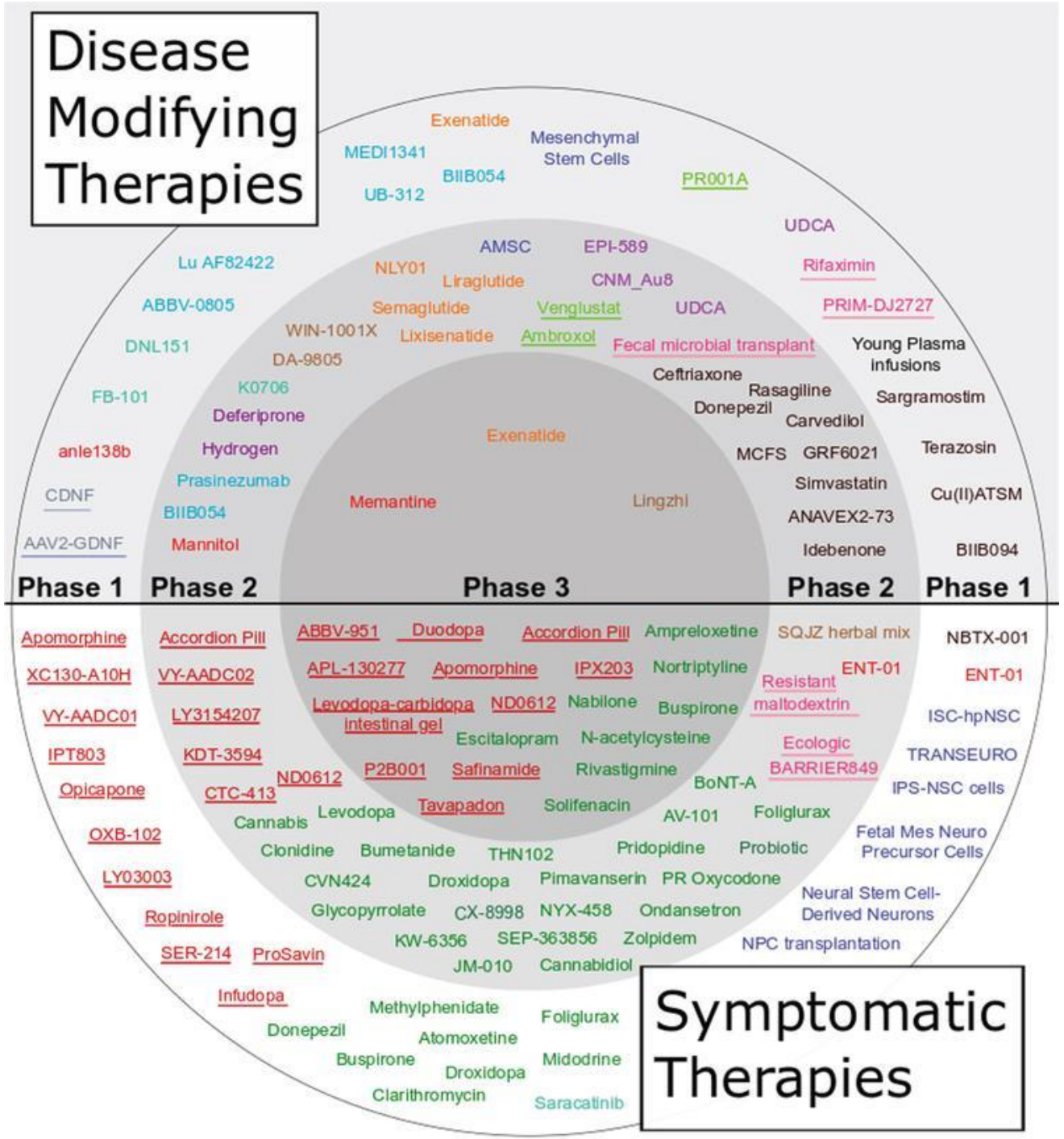




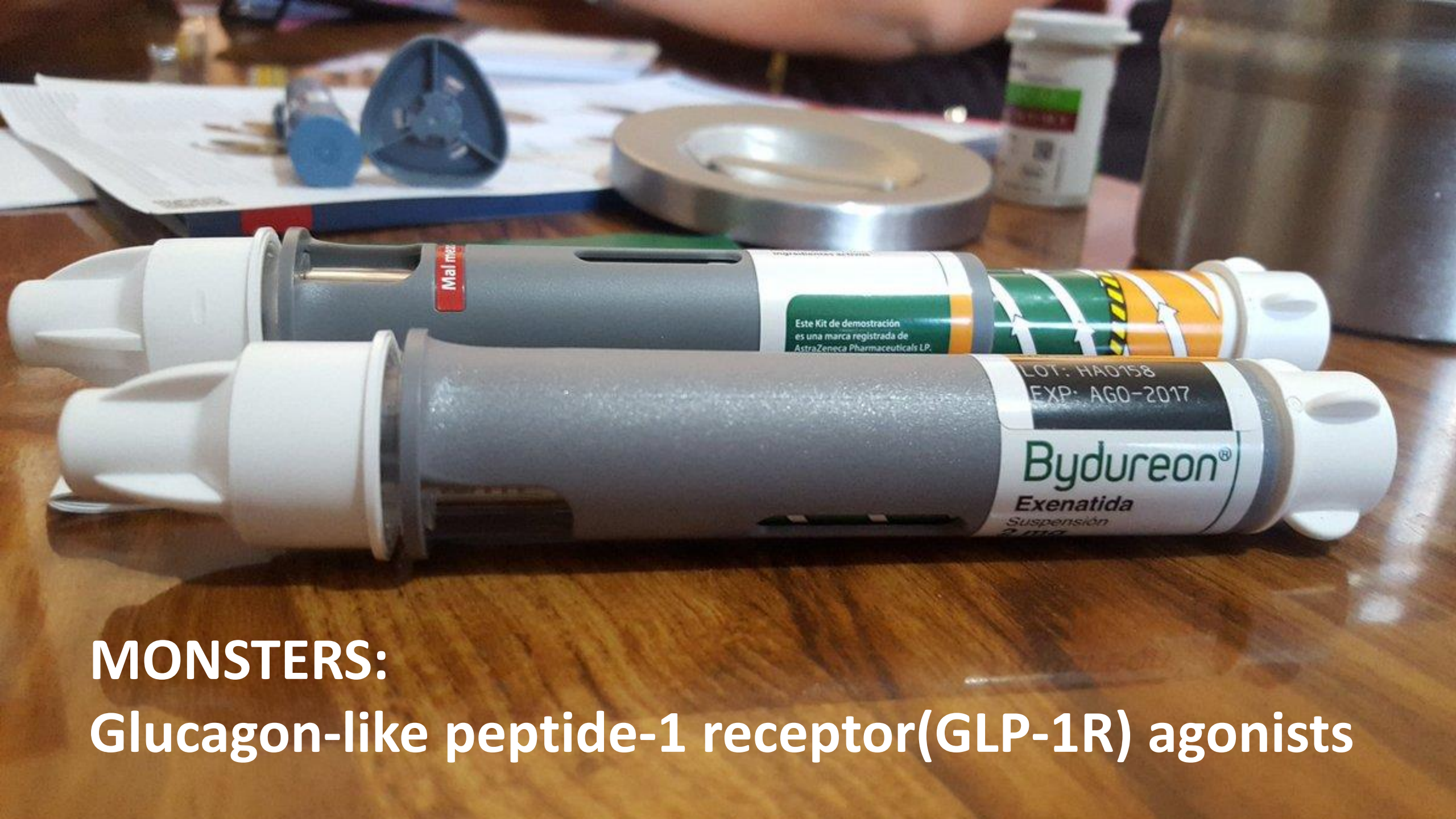
An overview of clinical trials for Parkinson's in 2019-2020:

https://content.iospress.com/articles/journal-of-parkinsons-disease/jpd202128

- Total = 145 clinical trials
- 57 trials (39%) focused on disease modification
- 12% of disease modifying trials supported by The Cure Parkinson's Trust

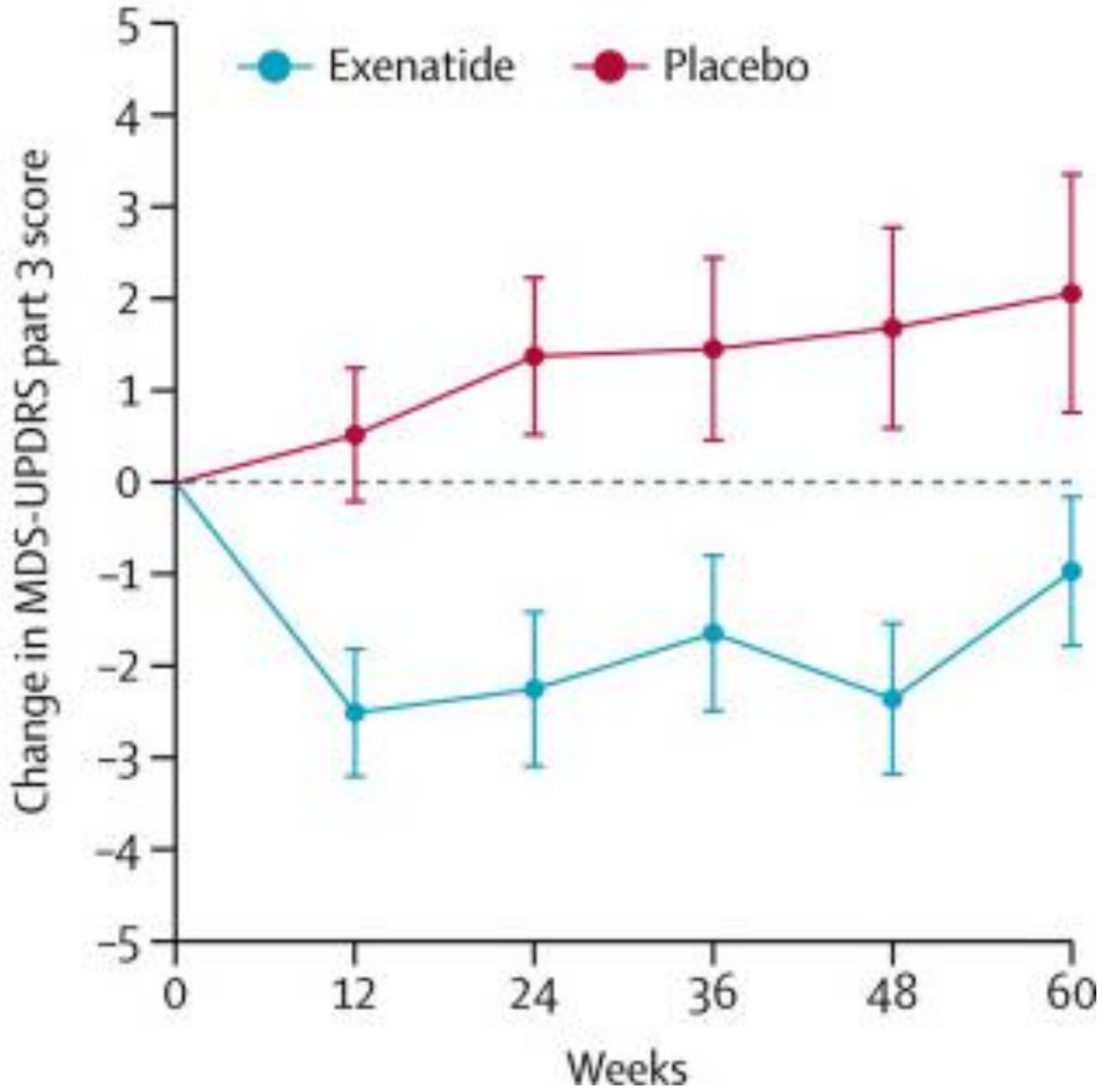


MONSTERS:
Glucagon-like peptide-1 receptor(GLP-1R) agonists

The Gila monster


Prof Tom Foltynie
…and a different Tom

Exenatide



Phase II clinical trial results provided very interesting results – a slowing of motor symptom progression over the 48-week study.

Athauda et al 2017 (The Lancet) https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(17)31585-4.pdf


doi:10.1093/brain/awaa262 BRAIN 2020: Page 1 of 10 | 1

BRAIN
A JOURNAL OF NEUROLOGY

Diabetes medications and risk of Parkinson's disease: a cohort study of patients with diabetes

Ruth Brauer,[1] Li Wei,[1] Tiantian Ma,[1] Dilan Athauda,[2] Christine Girges,[2] Nirosen Vijiaratnam,[2] Grace Auld,[2] Cate Whittlesea,[1] Ian Wong[1,3] and Tom Foltynie[2]

The results of a new study indicated that of the 100,288 cases of diabetes analysed, users of GLP-1 agonists (like exenatide) had a reduced risk of developing Parkinson's.

Exenatide

A Phase III clinical trial is now underway with the goal of recruiting 200 participants who will be assessed for two years.

Liraglutide

A Phase 2 clinical trial taking place at the Cedars-Sinai Medical Center, Los Angeles. It involves daily self-administered injections of liraglutide or placebo for 54 weeks.

The study is nearly fully recruited. Results are expected in 2021.

Lixisenatide

A Phase 2 multi-centre clinical trial being conducted in France. 158 patients will be recruited for 12 months of treatment. Results expected in 2021 – current recruitment is on track.

Additional GLP-1 clinical trials

A Phase II trials in Sweden for Exenatide

Semaglutide - Phase II trial in Norway

NLY01 - Initiation of a Phase II trial

NEURALY

Mucus: Ambroxol

Ambroxol is a drug which has been commonly used as an anti-mucolytic respiratory medicine since the 1980’s.

RESEARCH ARTICLE

Ambroxol Effects in Glucocerebrosidase and α-Synuclein Transgenic Mice

Anna Migdalska-Richards, PhD,[1] Liam Daly, MSci,[1] Erwan Bezard, PhD,[2,3] and Anthony H. V. Schapira, MD, DSc, FRCP, FMedSci[1]

SHORT COMMUNICATION

WILEY SYNAPSE

Oral ambroxol increases brain glucocerebrosidase activity in a nonhuman primate

Anna Migdalska-Richards[1] | Wai Kin D. Ko[2] | Qin Li[2,3] | Erwan Bezard[2,3,4,5] | Anthony H. V. Schapira[1]

More recently, ambroxol has been shown to boost the levels of activity in a protein (“GCase”) involved with waste disposal in cells.

Prof Anthony Schapira

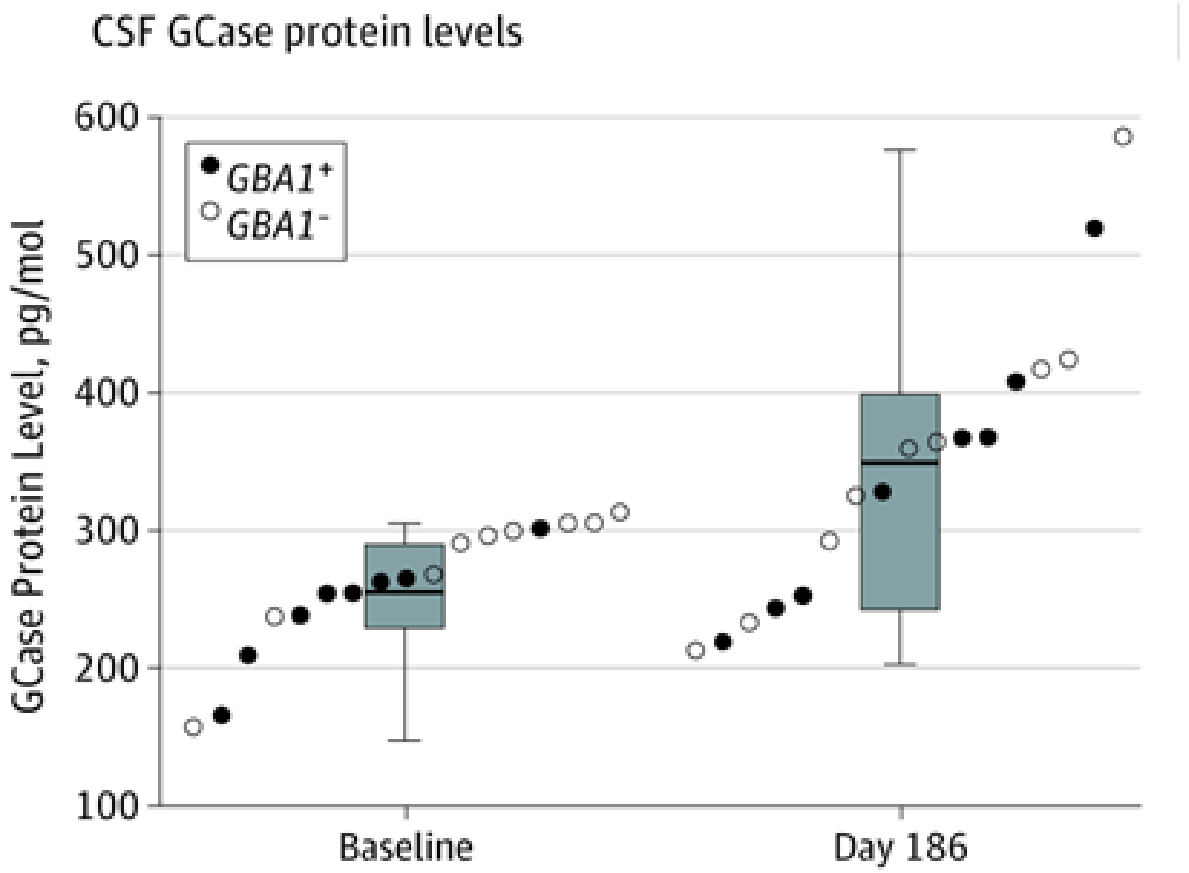
UCL

Queen Square Institute of Neurology

The “Ambroxol in Disease Modification in Parkinson Disease” (AiM-PD) study.

The study involved 18 participants, who were treated for 6 months with either ambroxol or a placebo.

The drug was well tolerated, and the results indicate that the drug was raising levels of GCase in the brain.



The next stage of this clinical program is now under development.

Part of the Rapsodi study

Welcome to PD-Frontline

PD Frontline aims to put people with Parkinson's at the forefront of research. This is an exciting new era for Parkinson's research. For the first time, drugs that protect against or slow down the progression of Parkinson's are a real possibility. Many of these drugs will be targeted at specific genes which we know influence the development of Parkinson's.

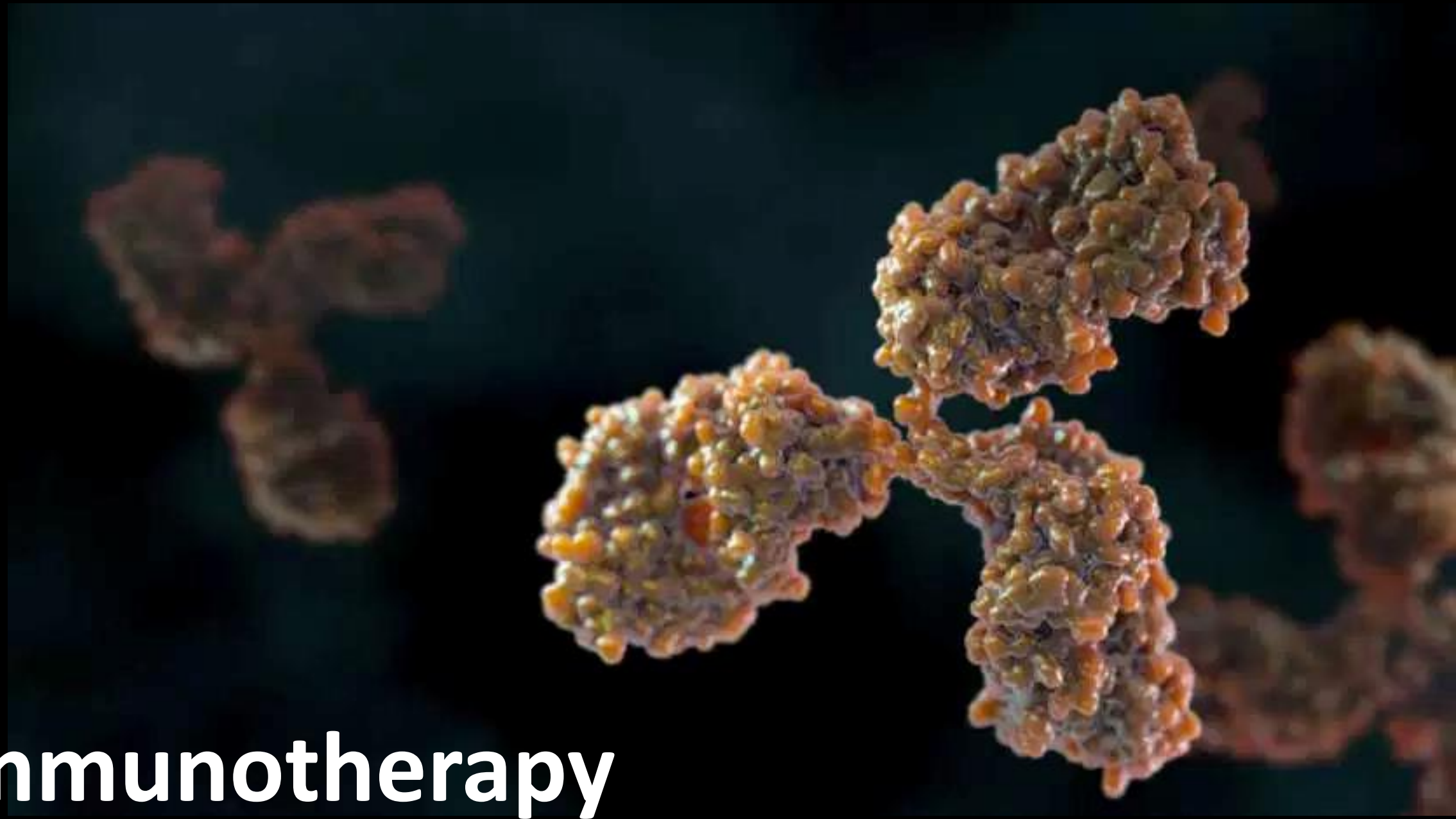
To test whether these drugs work, we will need to identify people with abnormalities in these genes who can be enrolled in clinical trials. PD Frontline enables you to be tested for two genetic risk factors for Parkinson's, called LRRK2 and GBA.

If you currently live in the UK and would like to #GetTrialReady, register for the study. It will take about 10 minutes.

Register for PD Frontline

If you have already registered login here

https://pdfrontline.com/en



Immunotherapy

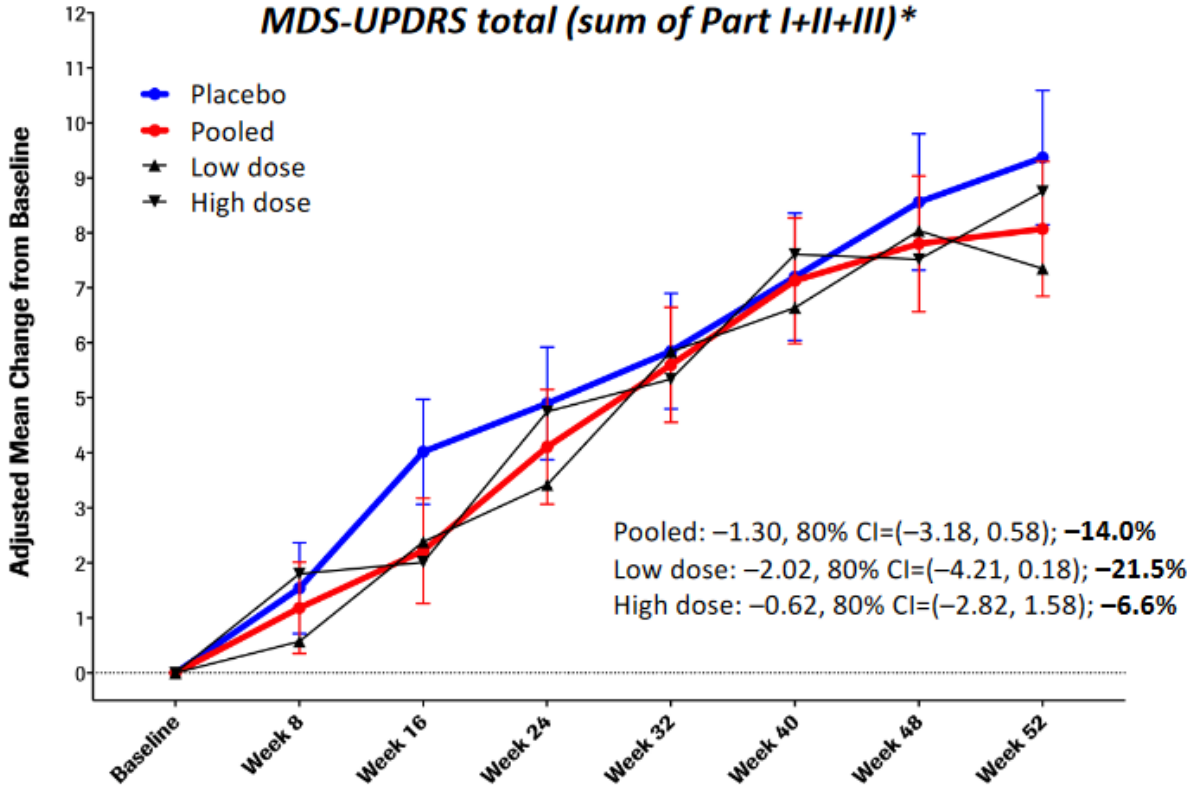
PASADENA

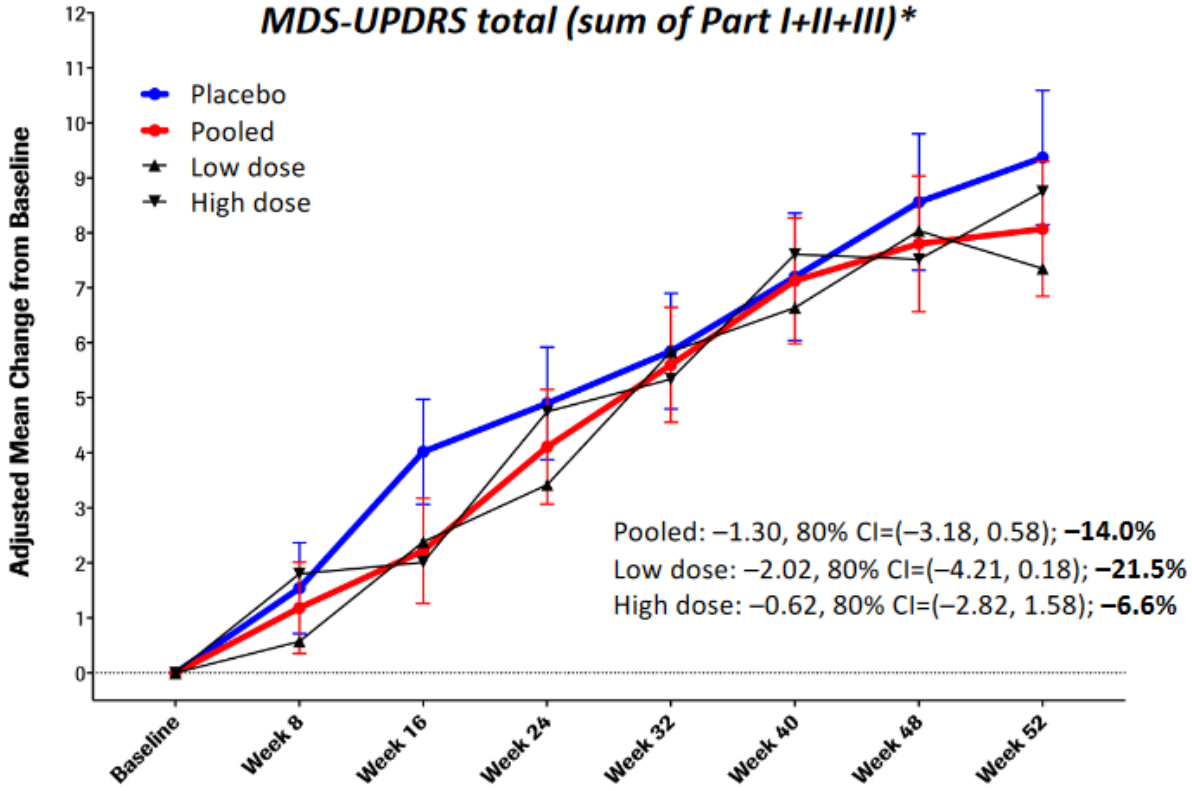
Prasinezumab – A phase II trial (300 people; 52 weeks)

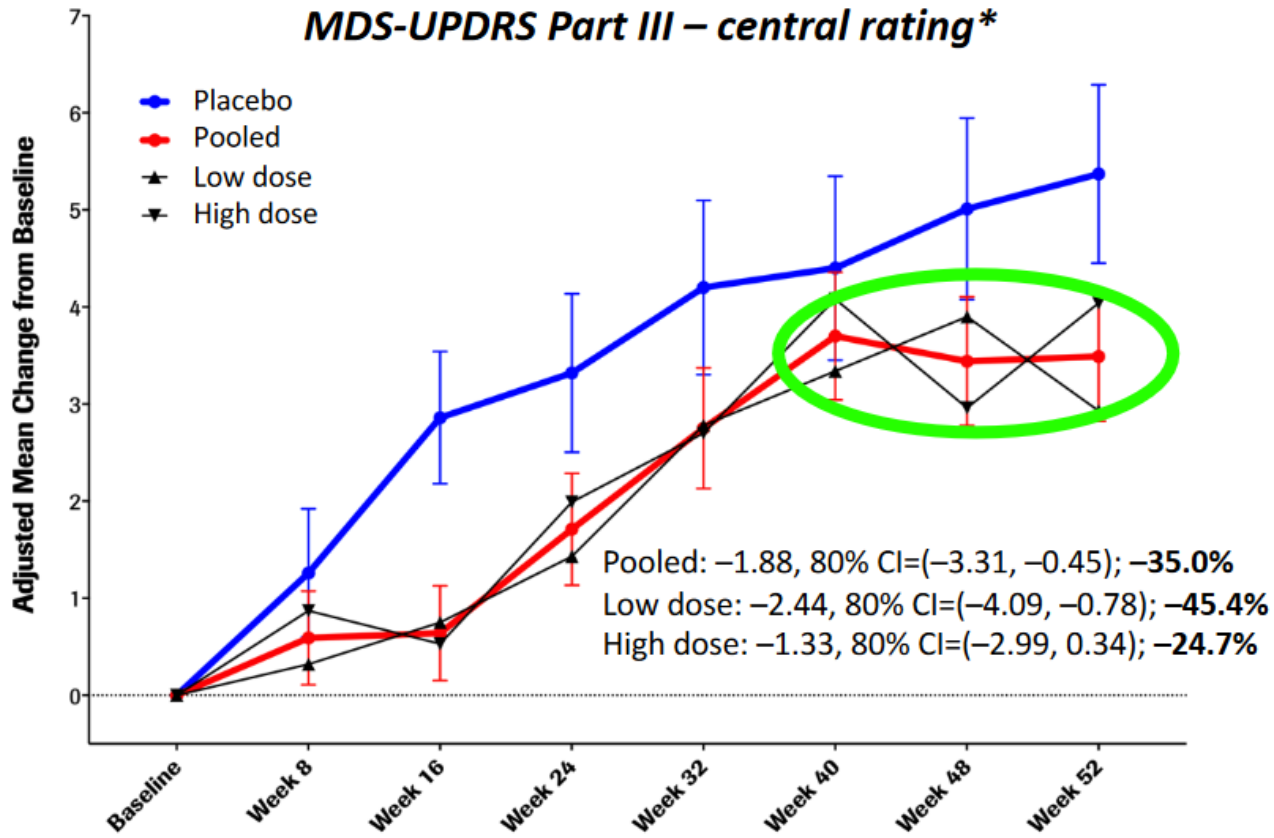
prothena

Roche

In April, the companies announced that the study had not met its primary endpoint but displayed signs of efficacy.


MDS-UPDRS total (sum of Part I+II+III)*
Adjusted Mean Change from Baseline
Placebo
Pooled
Low dose
High dose
Pooled: −1.30, 80% CI=(−3.18, 0.58); −14.0%
Low dose: −2.02, 80% CI=(−4.21, 0.18); −21.5%
High dose: −0.62, 80% CI=(−2.82, 1.58); −6.6%
Baseline
Week 8
Week 16
Week 24
Week 32
Week 40
Week 48
Week 52


MDS-UPDRS total (sum of Part I+II+III)*
Placebo
Pooled
Low dose
High dose
Adjusted Mean Change from Baseline
Pooled: –1.30, 80% CI=(–3.18, 0.58); –14.0%
Low dose: –2.02, 80% CI=(–4.21, 0.18); –21.5%
High dose: –0.62, 80% CI=(–2.82, 1.58); –6.6%
Baseline
Week 8
Week 16
Week 24
Week 32
Week 40
Week 48
Week 52


MDS-UPDRS Part III – central rating*
Placebo
Pooled
Low dose
High dose
Adjusted Mean Change from Baseline
Pooled: –1.88, 80% CI=(–3.31, –0.45); –35.0%
Low dose: –2.44, 80% CI=(–4.09, –0.78); –45.4%
High dose: –1.33, 80% CI=(–2.99, 0.34); –24.7%
Baseline
Week 8
Week 16
Week 24
Week 32
Week 40
Week 48
Week 52

BIIB054 – A Phase II study (300+ people; ends in 2022)

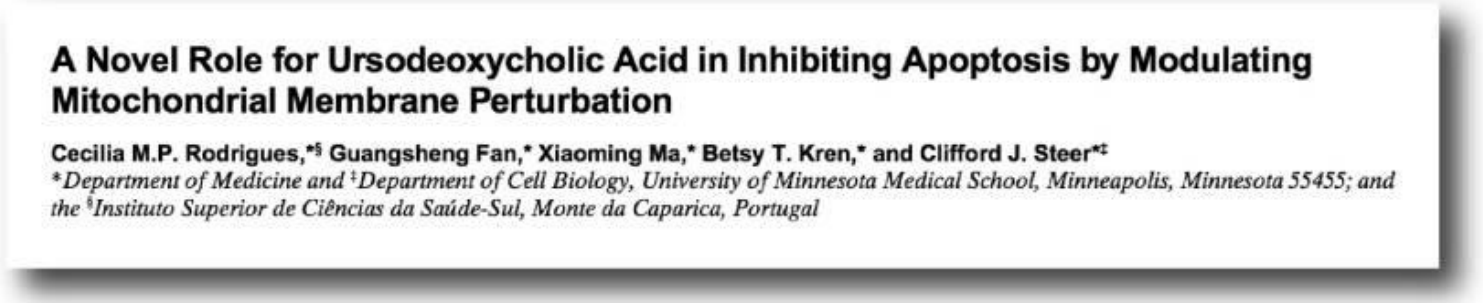
Biogen

PD01A – vaccine - Phase I results out to 4 years; Phase II starting in late 2020.


Supporting
Mitochondria

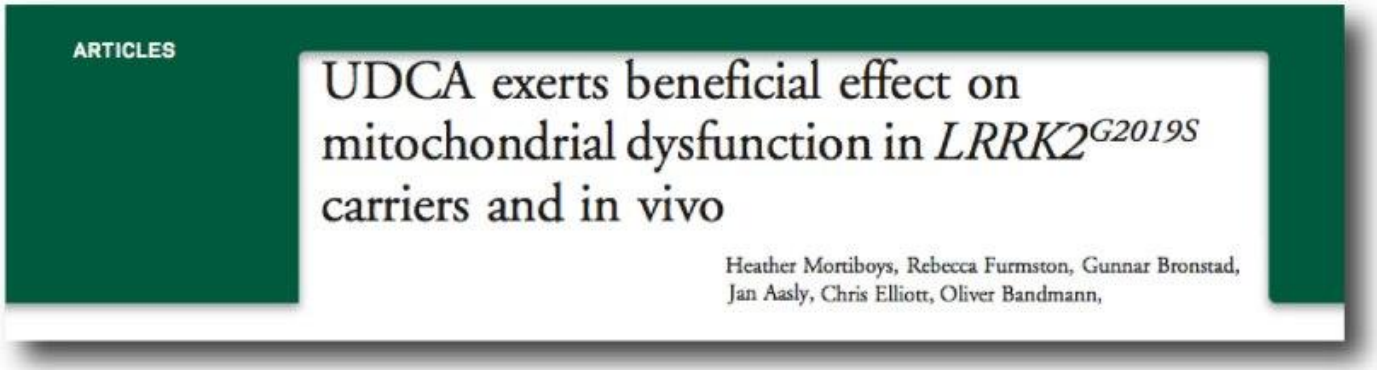
Ursodeoxycholic acid (UDCA)

UDCA is a bile acid which occurs naturally in the body and is used to dissolve gallstones.



A Novel Role for Ursodeoxycholic Acid in Inhibiting Apoptosis by Modulating Mitochondrial Membrane Perturbation

Cecilia M.P. Rodrigues,*§ Guangsheng Fan,* Xiaoming Ma,* Betsy T. Kren,* and Clifford J. Steer*‡
*Department of Medicine and ‡Department of Cell Biology, University of Minnesota Medical School, Minneapolis, Minnesota 55455; and the §Instituto Superior de Ciências da Saúde-Sul, Monte da Caparica, Portugal



ARTICLES

UDCA exerts beneficial effect on mitochondrial dysfunction in *LRRK2*^{G2019S} carriers and in vivo

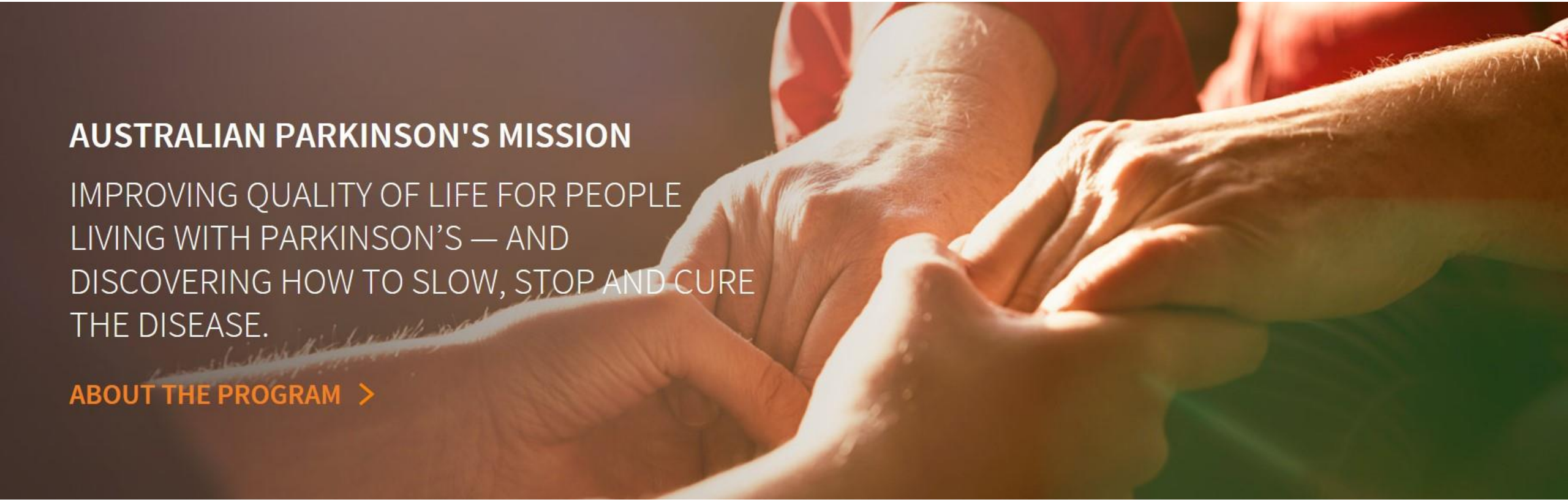
Heather Mortiboys, Rebecca Furmston, Gunnar Bronstad, Jan Aasly, Chris Elliott, Oliver Bandmann,

Recently UDCA has been reported to have beneficial effects on mitochondria in models of Parkinson's.

The 48-week UP Study ("UDCA in Parkinson's") is a Phase 2 clinical trial of UCDA in recently diagnosed Parkinson's involving 30 participants.

The results of this study will hopefully be available in late 2020.

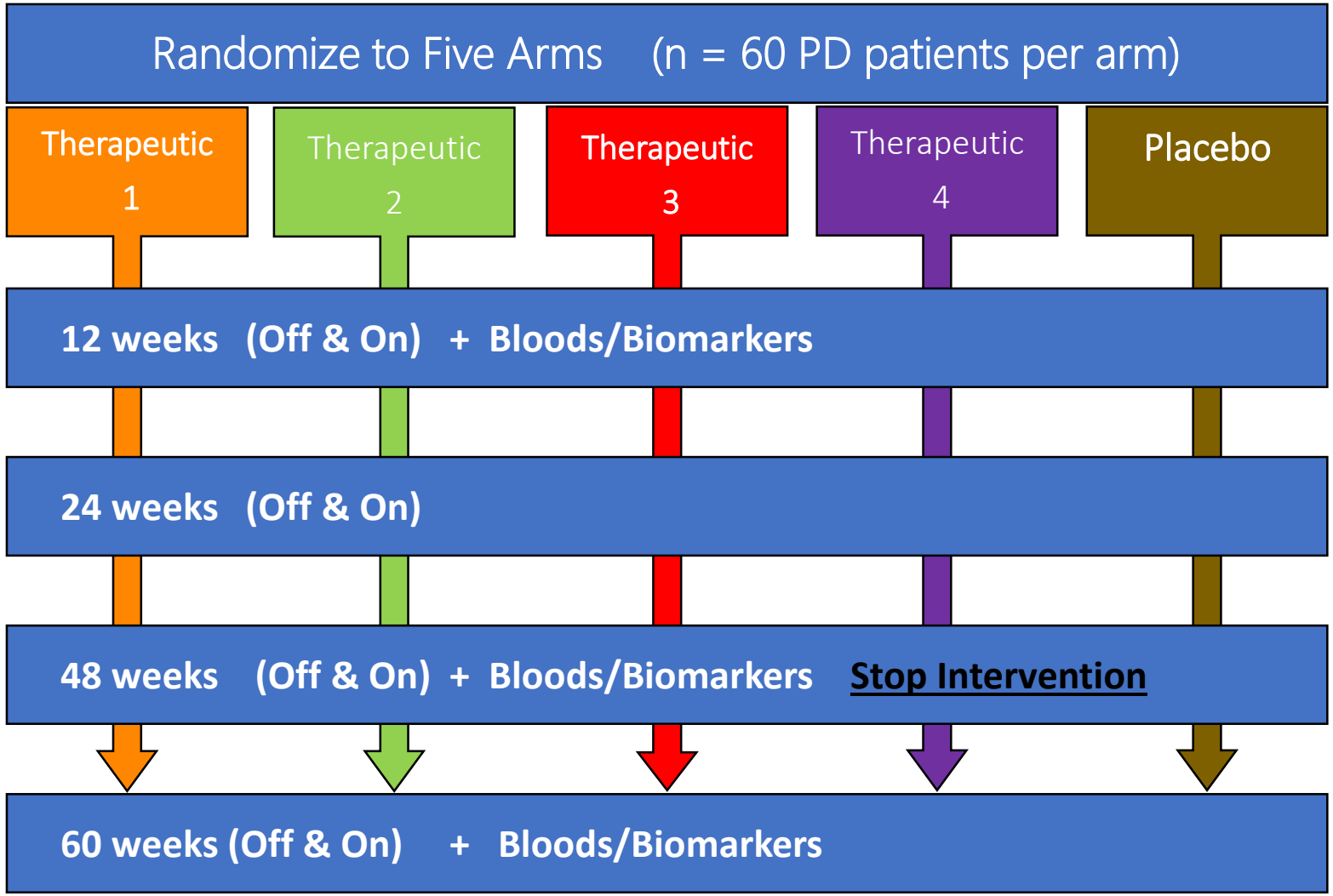
Australian Parkinson’s Mission



The Australian Govt committed $30M to clinical trial programme for PD

The first study is a multi-arm Phase 2 clinical trial evaluating 4 LCT prioritised drugs compared to a placebo over 60-weeks.

The first study has now started and a second study is now being planned.



Courtesy of Antony Cooper, Simon Lewis.

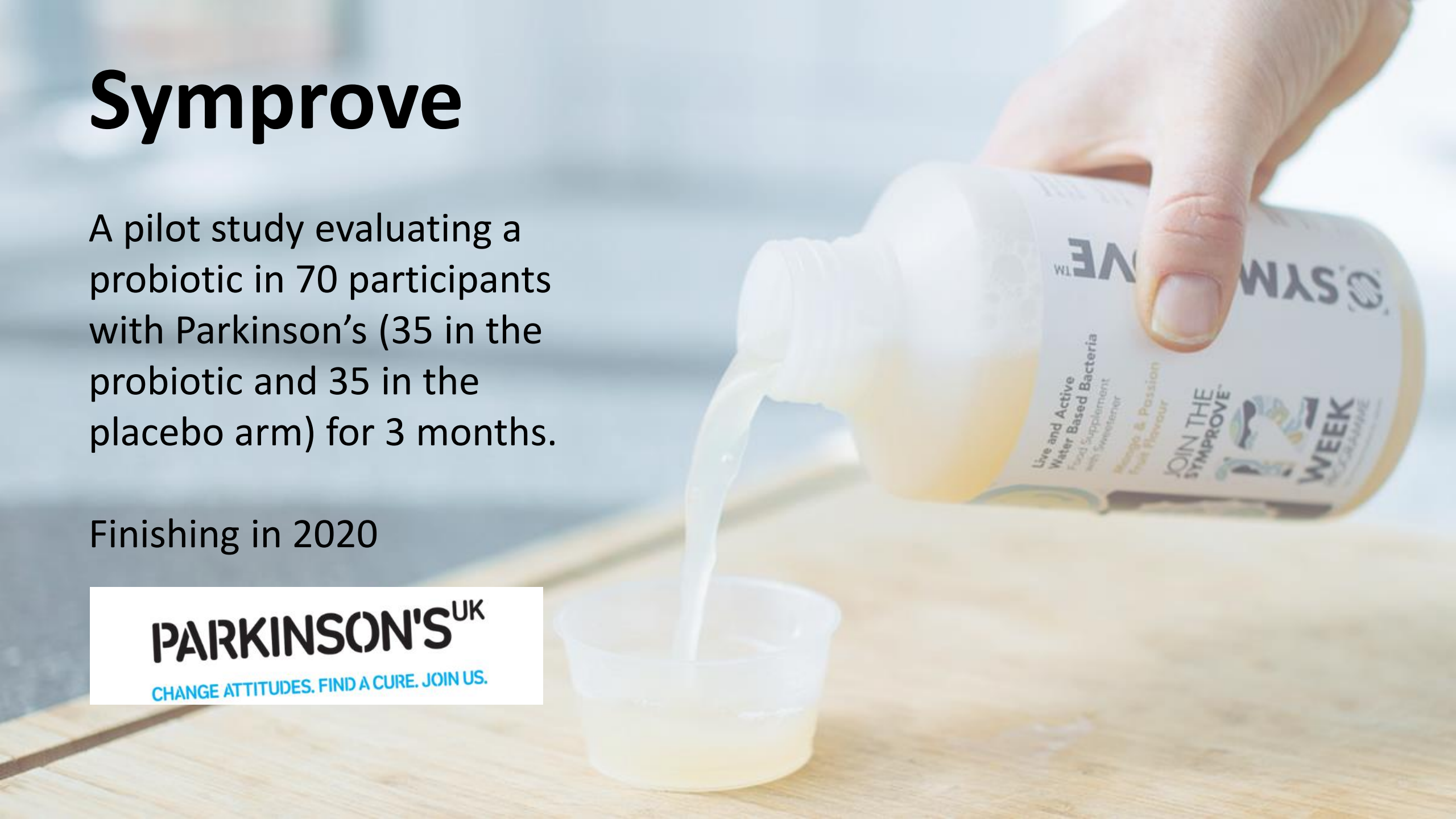
Symprove

A pilot study evaluating a probiotic in 70 participants with Parkinson's (35 in the probiotic and 35 in the placebo arm) for 3 months.

Finishing in 2020

PARKINSON'S UK

CHANGE ATTITUDES. FIND A CURE. JOIN US.



Nortriptyline

An antidepressant that has potentially disease modifying properties for Parkinson’s.

It is one of the drugs being evaluated in the Antidepressants Trial in Parkinson's Disease (or ADepT-PD) study.

ADepT-PD

Azathioprine

An immunosuppressive medication which is used in inflammatory conditions, like rheumatoid arthritis.

New study (AZA-PD) will be starting in Cambridge (UK) in 2020. It will involve 12 months treatment and a further 6-months follow-up of 60 participants.

Hey Simon, what do you think is going to work?

1. It depends on the type of Parkinson’s each individual has.

1. It depends on the type of Parkinson’s each individual has.

2. I do not expect any of these treatments to work.

KEEP CALM AND LOWER YOUR EXPECTATIONS

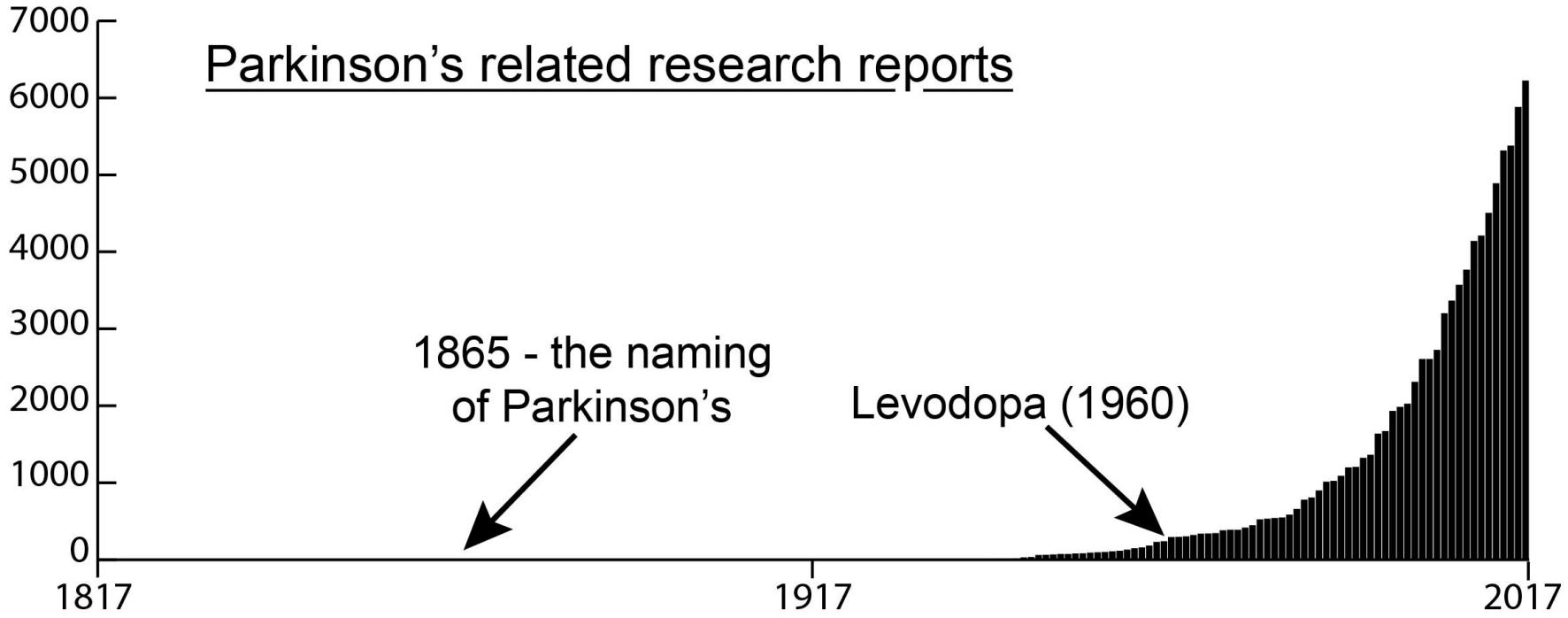
Martin Taylor

‘Positive realism’

Reasons for optimism?

PubMed

138,000 “Parkinson’s“
-related research reports

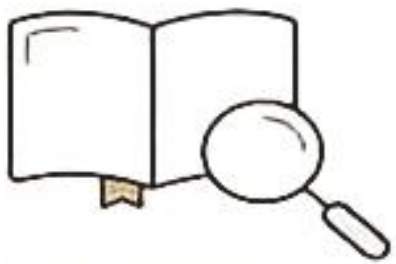


108,000 of them have been published
in the last 20 years

Framework of different roles

The activist

The mentor



The academic

The patient researcher

The communicator

The self-care expert

The hacker

The tracker

The healthcare partner

The innovator

The healthcare coordinator

The entrepreneur

“To me it's a celebration of what I can do”

- Mike Lloyd


Mike
New York Marathon
2018
GUIDE
Achilles
INTERNATIONAL
New Zealand

PARKINSON'S UK
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EAST MIDLANDS PARKINSON'S RESEARCH SUPPORT NETWORK

Thank you very much

Simon Stott
Cure Parkinson's Trust

simon@cureparkinsons.org.uk

The Cure Parkinson's Trust

THE SCIENCE OF PARKINSON'S