A new gene therapy for Parkinson's disease has achieved promising results in its first human tests, involving 15 patients.

Professor Nicholas Mazarakis, the Lucas Lee Chair of Molecular Biomedicine at Imperial College London, devised the approach while working at biopharmaceutical company Oxford BioMedica in 1997. Sixteen years later, the results of the first tests in humans have been published in *The Lancet*.

“It's taken a long time to get to this point,” he says. “We've been fought all the way. People are hesitant to accept it as it's so dramatic.”

The treatment, called ProSavin, uses a modified virus to deliver three genes into the striatum, a part of the brain that controls movement. The genes are intended to boost the production of dopamine, a chemical that becomes deficient in patients with Parkinson's.

Current treatments can boost dopamine production temporarily, but the cells that produce dopamine continue to degenerate until the treatments are no longer effective.

I'm very pleased that it has appeared to work in the clinic. It has the potential to move to the next phase.

– Professor Nicholas Mazarakis

The new therapy aims to provide a long-term solution by stimulating dopamine to be produced in a different set of cells.

Other gene therapies have been tried in Parkinson's disease, but all employ a different approach. Professor Mazarakis's strategy is to deliver three genes that code for enzymes that produce dopamine. They are smuggled into the brain by a lentivirus, closely related to HIV, which incorporates its genetic material into the genome of the cells it infects, ensuring a long-lasting effect.
After first testing the treatment in rats, Oxford Biomedica worked with Professor Stéphane Palfi’s group at the University of Paris to carry out a study in macaques. While the study was ongoing in France, Professor Mazarakis received an unexpected phone call from his collaborator. “I can’t tell you what it is on the phone, but you’d better come over,” Professor Palfi said.

When he arrived in Paris, Professor Mazarakis saw monkeys that could barely move before the treatment climbing their cages.

“The surgeons couldn’t believe the effect,” he said. “Since then I knew that if the effect on movement in humans was as good as in primates, it would be something that can help people in late stage Parkinson’s disease, where they become very disabled.”

The team showed that the treatment corrected the movement deficits of the monkeys for up to three and a half years, without any visible adverse effects. Notably, it didn’t result in abnormal involuntary movements caused by treatments in use today.

Those results paved the way for the first tests in humans. Before beginning a double-blind, placebo-controlled trial straight away – the most rigorous type of trial – the team decided to test different doses on a small group of patients.

The trial participants, three in the UK and 12 in France, all in the advanced stages of the disease, underwent a single operation to inject the virus into the brain.

The treatment has been safe, with no serious adverse effects. The patients’ scores on movement tests have improved on average by 30 per cent, and they also report having a better quality of life. The first patients to have the surgery have now been followed up for four years, and the effect has been sustained. PET scans confirm that dopamine is being produced in the brain where it wasn’t before.

To find out about future clinical trials, please contact Oxford Biomedica or visit www.clinicaltrials.gov.