A World Premiere in Parkinson's Disease

With significant clinical results published in the Nature Medicine Journal, InBrain Pharma is about to durably modify the advanced Parkinson's disease management

A breakthrough therapeutic approach for Parkinson's disease:
Anaerobic dopamine brain infusion[1]

Lille, January 27, 2024 – InBrain Pharma, a clinical stage biotech specialized in therapeutic solution development against neurodegenerative diseases , is thrilled to announce the publication of the outstanding results of the Phase I/II DIVE-I monocentric study conducted at the Lille University Hospital in the *Nature Medicine Journal.* This article, titled *"Intracerebroventricular anaerobic dopamine in Parkinson's disease with L-dopa-related complications: a phase 1/2 randomized-controlled trial*[2]*,"* deals with a revolutionary therapeutic approach : A continuous and personalized brain infusion of dopamine thanks to an innovative galenical formulation & the invention of a new route of administration

A therapeutic breakthrough that will likely result in revisiting the today management guideline of advanced Parkinson's disease

For nearly 60 years, direct delivery of dopamine to the brain was deemed as impossible after the failures of Teams of Dr. Horn in Melbourne, Dr. Mark in Boston, and Dr. Fahn in New York during the 1980s. The rapid oxidation of the chemical entity had rendered the attempt unsuccessful.

InBrain Pharma has overcome two major technological hurdles: stabilizing the chemical entity of dopamine and ensuring its controlled, continuous delivery in situ near the striatum, the brain area becoming depleted in dopamine over time.

These two combined achievements made possible the brain infusion of a deficient neurotransmitter, correcting symptoms of a neurological disorder into which the neurotransmitter plays a central role.

This invention is that of Professors David Devos and Caroline Moreau, with the support of their teams at the University of Lille, the Lille University Hospital, INSERM and at InBrain Pharma, of which they are co-founders and scientific advisors. Direct access to the brain to introduce the missing neurotransmitter at the right dose in the right place - close to the striatum - marks a decisive turning point in the therapeutic management of Parkinson's disease and will most likely lead to a revision of the disease treatment guidelines as we learn more about how this new therapeutic approach can benefit Parkinson's patients.

This therapeutic breakthrough now enables a **pharmacological neuromodulation of dopaminergic receptors by a personalized, continuous and circadian delivery of deficient dopamine directly to the brain of patients suffering from advanced Parkinson's disease with severe and refractory late complications related to L-Dopa treatment**[3]**.**

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[1] Oxygen-free to prevent oxidation
[2] Nature Medecine's article :https://doi.org/10.1038/s41591-024-03428-2
[3] https://www.datapressepremium.com/rmdiff/2010520/InBrainPharma_PR_Publication_Journal_of_Parkinson_Disease_VDEF3.pdf

Professors Devos and Moreau, who were also nominated last summer for the European Inventor Award 2024, are writing a new chapter in the modern history of science, by introducing personalized medicine into the management of a neurodegenerative disease, and opening up a whole new field of exploration and hope in the fight against other diseases affecting the brain (other neurodegenerative, neurometabolic, neurooncological diseases, etc.).

An innovative therapy to compensate for dopamine deficiency with personalized titration

Parkinson's disease, which progressively destroys the dopaminergic neurons essential for the automatic control of movement, cognition and emotion, affects more than 9 million people worldwide. Its motor symptoms, such as akinesia, muscle rigidity and tremors, appear when more than 50-70% of dopaminergic neurons are destroyed.

Although L-Dopa remains the reference treatment today, its efficacy diminishes over time. Invasive treatment options - known as device-assisted therapies (DATs) - being either non-drug-based, such as electrodes for deep brain stimulation, or drug-based, with L-dopa or related drugs associated to external pumps for continuous subcutaneous or enteral infusion, are available to increase central bioavailability of L-dopa and greater conversion to dopamine.

However, the DAT's use remains limited. Only a third of advanced-stage patients has been treated with them. Therapeutic management at this stage of the disease therefore calls for new approaches to relieve the two-thirds of Parkinson's patients who are left without any solutions, and who remain on oral therapy with an inadequate motor symptom control.

InBrain Pharma's innovative therapy by restoring the dopamine brain level in Parkinson's patients by continuous cerebral perfusion will help meet this pressing need for new therapeutic offerings.

Promising results from the DIVE-I phase I/II study

The DIVE-I study comprising two phases, a phase I to assess feasibility and safety, and a phase II assessing the efficacy and the safety of A-dopamine[4] showed:

1. **An improved motor symptom control:**
    - Significant reduction in overdosing (dyskinesia) or underdosing (bradykinesia) compared to optimized oral Parkinson's treatment.
    - An average gain of 4.4 hours of "ON" time (perfect motor control) without dyskinesia.
    - An average gain of 6.6 hours of functional autonomy per 24-hour period.
2. **A reduction in oral dosage:**
    - A 60% decrease in daily L-Dopa equivalent dosage due to continuous A-dopamine administration.
3. **An Excellent safety profile:**
    - No serious adverse events related to A-dopamine.
    - Transient and expected side effects, such as nausea, similar to oral L-Dopa treatments.
    - Significant reduction in L-Dopa-related dyskinesia.

[4] https://www.datapressepremium.com/rmdiff/2010520/InBrainPharma_PR_Parkinson_congress_VDEF.pdf

4. **Patient satisfaction:**
    - All patients having completed Phase II chose to continue treatment in the study long-term follow-up phase.

"*These initial results underline the full potential of this new dopamine-based device-assisted therapy (DAT), which promises to be the best representative of the DAT class in the long term, offering an alternative not only to patients who have failed current therapies, but also to those who are not considering treatment with available DATs. In addition to demonstrating the benefits for Parkinson's disease, this work also validates the concept of cerebral infusion as a personalized treatment for other neurological pathologies*," state **Professors Devos and Moreau, neurologists at Lille University Hospital, University of Lille and INSERM, and co-founders and scientific advisors of InBrain Pharma.**

"*Given the major therapeutic progress and public health impact to expect from this dopamine-based DAT showing a fully different activity profile from that of L-dopa-or related drug based DATs, we are doing our utmost to confirm these results as quickly as possible on a larger scale, with a Phase III program that will guarantee the fastest possible market access by the end of this decade under early accesses, and by the very beginning of the next decade for a full access*", concludes **Dr Véronique Foutel, CEO of InBrain Pharma.**

A major medical breakthrough to enhance patient quality of life

In the 21st century, medical priorities have evolved due to the decline in mortality and the increase in life expectancy, leading to greater focus on morbidity and quality of life. The goal is no longer merely to extend life but to improve patients' physical condition and autonomy, especially in the context of disabling chronic diseases.

Dopamine supplementation in the treatment of Parkinson's disease aligns with this approach of reducing the burden and consequences of a highly disabling illness and should remain an essential therapeutic strategy regardless of future innovations in the field. Following the era of hormonal supplementation aimed at correcting symptoms caused by endocrine secretion deficits, a new era of personalized central supplementation with deficient neurotransmitters is emerging to address medical disorders.

About InBrain Pharma
InBrain Pharma, a biopharmaceutical company, created in 2018, exploits through a worldwide exclusive patent license signed with SATT Nord, a novel therapeutic approach to Parkinson's disease based on the research work of Prof. David DEVOS and Prof. Caroline MOREAU in their academic research team at the University of Lille, Lille Neuroscience & cognition UMR-S 1172 INSERM and Lille University Hospital. In July 2024, Professors Devos and Moreau were finalists in the Research category of the European Inventor Award 2024 organized by the European Patent Office. InBrain Pharma was also a winner of the University of Lille Foundation Prize, the i-Lab competition, and received Deeptech support.

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