NEWS RELEASE

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Lille, September 11th, 2024– InBrain Pharma, a biopharmaceutical company specialized in neurodegenerative disease management, announces the publication of an article entitled “Effectiveness of Continuous Dopaminergic Therapies in Parkinson's Disease: A Review of L-DOPA Pharmacokinetics/Pharmacodynamics” on the pharmacokinetic and pharmacodynamic limitations of L-DOPA in Parkinson's patients published in July 2024 in the Journal of Parkinson's Disease.

The article consists of a review of the existing literature on the limitations of L-DOPA, a mainstay in the treatment of Parkinson's disease, especially when used in the context of continuous dopaminergic stimulation, highlighting the need for new therapeutic avenues.

Parkinson's disease is characterized by striatal dopamine deficiency. Since dopamine cannot cross the digestive and blood-brain barriers, its precursor, levodopa (L-DOPA), remains the mainstay of treatment. However, the significant

pharmacokinetic and pharmacodynamic limitations of L-DOPA, combined with the progression and severity of Parkinson's disease, trigger motor and non-motor complications after a few years, having led to the development of therapies providing continuous dopaminergic stimulation, but remaining largely inadequate.

After selecting the 10 most relevant articles in the literature, it is shown that pharmacokinetic and pharmacodynamic problems include: restricted digestive and cerebral passage, unnecessary peripheral distribution, short half-life, age- and Parkinson's disease-induced decline in central aromatic L-amino acid decarboxylase, poor distribution in many cells and pulsatile stimulation of dopaminergic receptors. Current L-DOPA based treatments beyond oral do not provide a satisfactory response to these limitations.

“These new data help to highlight that many of L-DOPA's pharmacokinetic and pharmacodynamic constraints are not resolved by existing subcutaneous or enteral continuous dopaminergic stimulation therapies. This highlights the significant gap between these treatments and the ideal of continuous dopaminergic stimulation. Medical needs in the management of Parkinson's disease remain very great. It is against this backdrop that we have developed pharmacological neuromodulation by continuous personalized delivery of the deficient neurotransmitter - dopamine - administered via the intracerebroventricular (i.c.v.) route to treat people with advanced Parkinson's disease with severe late complications refractory to L-Dopa treatment”, explains Professor Caroline Moreau, neurologist at Lille University Hospital and co-founder of InBrain Pharma.

“A-dopamine treatment considerably reduced the periods during which patients suffered from dopamine-dependent tremors, slowness, pain and difficulty walking and communicating, as well as L-dopa-induced abnormal symptoms (involuntary movements, agitation) limiting their autonomy and quality of life,” comments Professor David Devos, neurologist and pharmacologist at Lille University Hospital and co-founder of InBrain Pharma.

A-dopamine, administered intracerebroventricularly, improves the autonomy of patients affected by Parkinson's disease by reducing both the symptoms associated with a lack of dopamine, such as tremors, slowness, stiffness, pain and difficulties in walking and communicating, and the abnormal symptoms induced by L-dopa-based treatment, characterized by involuntary movements and agitation, through the tapering down of the oral optimized background regimen.

Preliminary results from the DIVE-I phase I/II clinical trial, conducted in collaboration with Lille University Hospital and launched in September 2020, have confirmed the treatment's excellent ergonomics, high safety profile and remarkable clinical effect in controlling severe motor symptoms, enabling the dosage of underlying oral L-dopa-based treatments to be reduced.

The final results of the DIVE-I phase I/II clinical trial will be announced at the International Congress of Parkinson's Disease and Movement Disorders, to be held in Philadelphia at the end of September 2024.

In the near future, this new therapeutic modality will change the treatment paradigm for Parkinson's disease and other neurodegenerative diseases. It paves the way for precision medicine in neurology, bringing this discipline fully into the 21st century.

For more information on this article, please click on :
https://pubmed.ncbi.nlm.nih.gov/38848195/

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. The final results of its first phase I/IIb clinical trial, DIVE-I, will be announced shortly.

About Parkinson’s disease

Parkinson's disease is the world's fastest-growing neurological disorder, prevalence having doubled over the last 25 years. 2.6 million people1 are affected in the top 5 EU markets2, the United States and Japan, half of them being in advanced stage. The disease is caused by a progressive dopaminergic neuron loss, triggering a dopamine deficit, and leading to major painful motor disability, coupled to cognitive-behavioral and psychiatric disorders. Today therapeutic options in advanced stage rely on few device-aided therapies, useful for less than 50% of patients, given either their limited efficacy or their invasiveness or both. The brain infusion of dopamine is a disruptive treatment modality contributing to address this unmet need.

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1 GlobalData’s figures
2 France, Spain, United-Kingdom, Germany and Italy

Attachment

- **InBrainPharma_PR_Publication_Journal_of_Parkinson_Disease_VDEF**

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