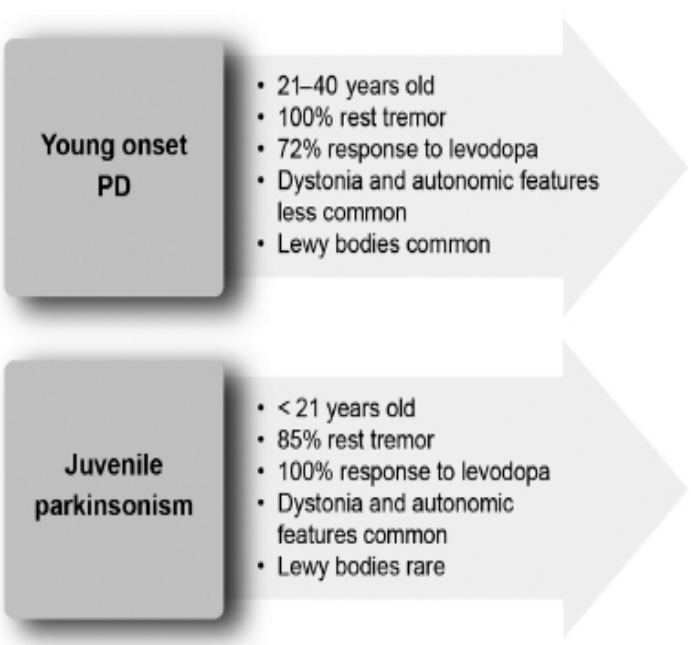
DRD1 AAV Gene Therapy: A Novel Therapeutic Approach to Treat Juvenile Parkinson's Disease

Background



Parkinson's disease (PD) is a neurodegenerative disease primarily of the central nervous systems, affecting both motor and non-motor systems. Symptoms typically develop gradually, with non-motor issues becoming more prevalent as the disease progresses. Young-onset Parkinson's disease (YOPD) is a rare subtype of PD, occurring between 3% and 6% of all PD cases[1], with specific symptoms, defined genetic correlations, and limited treatment options. YOPD is defined as the diagnosis of PD between the ages of 21 and 40; while a positive PD diagnosis under the age of 21 is referred to as "Juvenile Parkinson's" (JP)[2]. Although most clinical features of JP and YOPD are the same, increased occurrence of dystonia and PD are found in families of patients with JP[3]. The age of diagnosis matters for a variety of reasons, from probable causes of early cases to symptoms and treatment. Traditional treatments for Parkinson's disease, such as dopamine agonists and L-dopa, provide temporary symptom relief but are associated with severe side effects, particularly in JP. These therapies exacerbate disease burden and often lead to poor long-term outcomes due to:

- **Dyskinesia and Motor Fluctuations:** Uncontrolled, erratic movements are common with long-term use of agonists.
- **Neuropsychiatric Side Effects:** Including anxiety, depression, hallucinations, and impulse control disorders.
- **Short Duration of Action:** Daily dosing creates compliance challenges and fluctuating symptom control, especially in pediatric populations.

AAV Gene Therapy: DRD1 Receptor Upregulation

Pathways Neuro Pharma, Inc. (Pathways) innovative therapy focuses on upregulating the DRD1 dopamine receptor using a proprietary **AAV6.2 FF viral vector**, representing a safer, more effective, and transformative approach to treatment of JP. Our therapy directly addresses PD:

- **Non-Agonist Mechanism:** By upregulating the DRD1 dopamine receptor without using agonists, we avoid side effects like augmentation (worsening of restless leg syndrome (RLS) symptoms with long-term agonist use) and neuropsychiatric issues.

- **Sustained Symptom Relief:** With a single injection lasting up to 15 months, patients experience consistent improvement in symptoms, particularly during sleep.

- **Improved Quality of Life:** Addressing RLS alongside motor symptoms enables pediatric patients to maintain better sleep patterns, critical for their development and overall health.

Our Approach

By targeting both the motor and non-motor symptoms of Parkinson's disease, our therapy offers a comprehensive solution that sets it apart from traditional approaches. Our therapy avoids the use of agonists, focusing instead on upregulating the DRD1 dopamine receptor to restore natural dopaminergic function. By utilizing the **AAV6.2 FF viral vector**, our approach achieves:

- **Non-Agonist Mechanism:** Eliminating the side effects associated with overstimulation of dopaminergic pathways.

- **Fast Onset:** The AAV6.2 FF vector delivers rapid symptom relief, addressing a critical need for pediatric patients.

- **Sustained Efficacy:** A single injection provides therapeutic benefits for up to 15 months, dramatically reducing the treatment burden and improving compliance.

Advantages Over Traditional Therapies

- **Improved Safety Profile:** By avoiding dopamine agonists, we eliminate common side effects such as nausea, low blood pressure, dyskinesia, and neuropsychiatric complications. This is particularly critical for pediatric patients with developing brains.

- **Enhanced Quality of Life:** JP patients benefit from a single-dose therapy that maintains symptom control over 15 months, reducing the need for daily medications and frequent physician visits.

- **Addressing Compliance Challenges:** JP patients and their families often struggle with complex treatment regimens. Our one-time injection simplifies disease management.

Potential Impact

This therapy has the potential to redefine the treatment landscape for rare pediatric Parkinson's disease by:

- **Improving Long-Term Outcomes:** With a superior safety profile and sustained symptom control, patients can experience improved quality of life and reduced disease progression.

- **Revolutionizing Pediatric Care:** Our innovative approach addresses the unique challenges of treating pediatric patients, providing a long-term, non-invasive solution.

- **Comprehensive Symptom Management:** By addressing both motor and non-motor symptoms such as RLS, the therapy provides holistic relief for pediatric patients and their families.

- **Accelerating Approval Pathways:** The rare pediatric disease designation and associated voucher create a clear pathway to expedited regulatory approval and faster commercialization.

Product development

Our focus on DRD1 receptor upregulation via the AAV6.2 FF vector represents a transformative leap forward for JP disease treatment. By addressing both motor and non-motor symptoms such as RLS, we provide a safer, more effective alternative to traditional therapies. With its unmatched safety profile, prolonged efficacy, and strategic opportunities, this therapy is poised to deliver life-changing benefits to patients and their families while driving meaningful progress in clinical and commercial settings. Further research and clinical exploration are crucial to fully realizing the potential of these advancements in the biotechnological landscape.

About the team

Pathways Neuro Pharma, Inc. is developing the first pharmaceutical treatments that target the pathways in the brain that regulate and control the root causes of alcoholism, substance abuse, depression and associated neurological conditions. Pathways is led by Bradley Thompson, Chief Technology Officer (CTO), with over 39 years' experience in autoimmune disease, oncology, and infectious disease, and Anthony Mack, Chief Executive Officer (CEO), with 35-years' experience in the pharmaceutical and biotech industries as a C-level executive overseeing the successful development and licensure of several innovative drugs in pain and addiction.

Contact: Anthony Mack: Anthony.mack@pathwaysnp.com

References:

1. Young-Onset Parkinson's | Parkinson's Foundation
2. Klepac N, Habek M, Adamec I, Barusic AK, Bach I, Margetic E, Lusic I. An update on the management of young-onset Parkinson's disease. Degener Neurol Neuromuscul Dis. 2013 Oct 4;2:53-62. doi: 10.2147/DNND.S34251. PMID: 30890879; PMCID: PMC6065598.
3. Post B, van den Heuvel L, van Prooije T, van Ruissen X, van de Warrenburg B, Nonnekes J. Young Onset Parkinson's Disease: A Modern and Tailored Approach. J Parkinsons Dis. 2020;10(s1):S29-S36. doi: 10.3233/JPD-202135. PMID: 32651336; PMCID: PMC7592661.

Patents:

Neuroreceptor Compositions and Methods of Use, US Patent Number: 11760788