WVE-120102 is a new medication designed to treat Huntington's disease. It is developed by Wave Life Sciences and is being tested in clinical trials together with its companion compound, WVE-120101.

Both compounds belong to a new class of medication called antisense oligonucleotides (ASO). These are designed to target molecules called messenger RNAs (mRNA), or copies of a gene that will be read by the protein-making machinery of the cell. WVE-120102 is a stereopure nucleic acid therapeutic, meaning that similar, but distinct, forms of the ASO produced as byproducts in the manufacturing process are eliminated.

How WVE-120102 works

Huntington's disease is caused by a mutation or defect in the huntingtin (HTT) gene, which contains the instructions for cells to produce the Huntingtin protein. It is not yet known what this protein normally does in the body, but it is thought to play an important role in the proper function of nerve cells.

The mutation that is seen in Huntington's disease results in the production of a longer Huntingtin protein than what is normally produced. Parts of this longer protein may be cut into smaller pieces that accumulate and bind together inside nerve cells and are toxic. This disrupts the normal function of the nerve cells and eventually causes their death, leading to the symptoms of the disease.

WVE-120102 is designed to prevent the production of mutant Huntingtin protein by inhibiting its corresponding mRNA. It specifically targets the mRNA produced from the mutant HTT gene, but not the mRNA from the normal HTT gene.

Roughly two-thirds of people with Huntington's disease carry either one of two markers that identify the mutant HTT gene called a single nucleotide polymorphism (SNP). WVE-120101 is designed to treat people with SNP1 and WVE-120102 is designed to treat people with SNP2.

WVE-120102 in clinical trials

A Phase 1b/2a clinical trial (NCT03225846) called PRECISION-HD2 is testing the safety and tolerability of WVE-120102 in an estimated 48 patients with Huntington's disease, ages 25 to 65. The trial, which is still recruiting participants in Canada and Poland, will test four different doses of WVE-120102 against a placebo. The compound's pharmacokinetics (the study of the interactions of a medication and the body), and pharmacodynamics (the body's response to a medication) also will be assessed. Clinical improvement will be evaluated using the Unified Huntington's Disease Rating Scale (UHDRS). The clinical features and course of the disease will be assessed using the Short Problems Behavior Assessment (PBA-s) and a psychiatric assessment, as well as magnetic resonance imaging (MRI) of the brain.