

Fast-track approval for gene silencing therapies for Huntington's disease will expand treatment options for terminal patients

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Globally, there are currently 24 products in clinical development for the treatment of Huntington's disease, which is a rare, inheritable neurodegenerative condition. Symptoms are typically noticed between the ages of 30 and 50 and include memory loss, anxiety, depression, and compulsive behaviours.

Research strategies to develop efficacious therapeutics to treat Huntington's disease include efforts to improve cell survival by optimizing synaptic communication and employing neuroprotective agents to reduce damage to nerve cells. Also being explored in clinical trials is the possibility of using antisense therapy to inactivate mutated huntingtin (htt), which is the gene that causes Huntington's disease.

Spread across various stages of development, 13 (54%) products are in Phase I, 10 (42%) products are in Phase II, and one drug candidate is at Phase III. Although small molecules make up the majority (70%) of products with a disclosed molecule type, biologics make up half of all products granted fast track designation by the FDA.

A monoclonal antibody drug candidate, pepinemab, is being developed by US biotech company Vaccinex. Although the product is primarily an anti-neoplastic agent and inhibits angiogenesis, pepinemab also enhances the differentiation of oligodendroglia, which is expected to improve the cognitive and psychomotor symptoms of Huntington's disease. Another product with fast track designation is drug candidate AMT-130 being developed by UniQure, a biopharmaceutical company headquartered in the Netherlands. AMT-130 is a product that employs RNA interference (RNAi) technology to suppress the expression of mutated huntingtin and prevent its aggregation within cells of the nervous system.

Both products involving RNAi-based mechanisms of action are in Phase II trials and are expected to enter the market for Huntington's disease from 2021.

Other drug candidates in development for the treatment of Huntington disease include RG-6042 and WVE-120102, being developed by Roche and WAVE Life Sciences, respectively. Both of these products utilize antisense technology, inhibit the production of mutant huntingtin, and have shown efficacy in clinical trials. Mutant huntingtin protein was seen to be reduced by between 40–60% in the cerebrospinal fluid (CSF) of patients treated with RG-6042 in a Phase I/II clinical trial. Concerns about RG-6042 mainly revolve around the fact that the drug candidate can potentially reduce the production of non-mutant huntingtin protein.

Despite this, RG-6042 was awarded PRIME designation by the European Medicines Agency for Huntington disease for its potential to address the unmet need of developing efficacious treatments for the condition, which currently has no cure.

In addition, opportunities for strategic partnerships between key players in the field of gene therapy will continue to bolster efforts to produce refined drug candidates that specifically and effectively target genes causing diseases such as Huntington's. An example of this would be the partnership deal between Roche and Ionis Pharmaceuticals formed to develop drugs that employ antisense technology to treat genetic diseases.

With promising results in preclinical studies and in animal models, it is not unexpected that gene suppression including RNAi and antisense therapies are on course to outperform current treatment options in the foreseeable future and the years beyond.