Polaryx Therapeutics, Inc.
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Patient-friendly treatments for neuronal ceroid lipofuscinoses

Polaryx Therapeutics is working to bring patient-friendly treatments to people with ultra-rare genetic disorders known as neuronal ceroid lipofuscinoses (NCLs), the most common of which is Batten disease. The strategy is centered on the repurposing of oral small molecules to provide NCL patients with safe and effective treatment options as soon as possible.

NCL patients experience seizures, deterioration of mental and motor functions, and visual failures. There is no cure, and attempts to control symptoms can fall short. Drug developers have utilized highly experimental approaches, such as gene, stem cell, and enzyme-replacement therapies. However, faced with genetically complicated diseases, they have yet to find a safe and effective treatment.

Polaryx has taken a different approach. Using a drug-repurposing tactic in preclinical testing, Polaryx identified PLX-200, an approved oral small molecule potentially effective against CLN2 disease (Late infantile NCL), which is associated with deficiency or loss of function of tripeptidyl peptidase 1 (TPP1) caused by the *CLN2* gene mutation. PLX-200 upregulates *CLN2* mRNA expression when a residual copy of the *CLN2* gene is present. The drug also enhances lysosome biogenesis in animal models and patient-derived fibroblasts. In TPP1-deficient animals, PLX-200 is neuroprotective and prolongs lifespan.

PLX-200 was originally developed to lower cholesterol, but Polaryx has shown on the basis of its mechanism of action that it could also be used to treat CLN2 disease patients. Encouraged by preclinical data supporting the rationale for the use of PLX-200 in these patients, Polaryx is moving the drug toward clinical trials.

Polaryx is spending 2017 generating preclinical data on PLX-200 and talking to the US Food and Drug Administration (FDA) about the best path forward for this candidate. The goal is to submit an investigational new drug (IND) application to the FDA in the first quarter of 2018. If clinical development is successful, Polaryx will seek FDA approval under the 505(b)(2) pathway. Polaryx is also testing the drug in juvenile NCL animal models, thus positioning the company to increase the number of NCL patients it can help.

In parallel, Polaryx is working on PLX-100, a drug that combines PLX-200 with another approved, repurposed molecule, all-trans retinoic acid (ATRA). The addition of ATRA to PLX-200 is intended to provide a synergistic effect leading to the minimum effective dose. Preclinical tests so far have confirmed the effectiveness of this unique combination. This lower dose combination may be a safer treatment option for the younger pediatric NCL patients.

The focus on safe small molecules that have already been used is significant. Polaryx aims to rapidly develop safe and convenient drugs. The speed and existing safety repurposing data, as well as the convenience of oral small molecules, facilitate this goal.

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