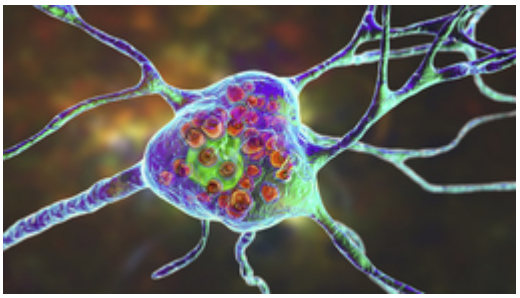
INNOVATION PARTNERSHIPS
UNIVERSITY OF MICHIGAN

Pyridine Inhibitors of Glucosylceramide Synthase

TECHNOLOGY NUMBER: 2019-268



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Category
Therapeutics and Vaccines
Life Sciences

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OVERVIEW

Novel class of glucosylceramide synthase inhibitors

- Best in class efficacy in treating lipid storage diseases
- Replacement for more invasive therapeutic options

BACKGROUND

Lipids are important parts of the membranes found within and between each cell as well as in the myelin sheath that coats and protects nerves. Lipid storage diseases are rare metabolic disorders that cause a dangerous build-up of lipids within cells and tissues throughout the body. This lipid build up can cause permanent cellular damage, particularly in the nervous system, liver, spleen, and bone marrow. Several diagnoses fall into the category of lipid storage diseases, including Gaucher, Fabry, Sandhoff, and Tay-Sachs diseases.

These disorders have historically been treated with enzyme replacement therapies (ERTs). ERTs are administered by delivering recombinant proteins (glucocerebrosidase) through intravenous injections to aid in the breakdown of lipids. Even given their successes, ERTs are not suitable for all patients, and their beneficial effects can vary between affected organs and can also be difficult to assess in any given patient. Furthermore, this class of medicines is not free of side effect risks and requires lifelong intravenous administrations that can be expensive. Therefore, a need exists for new options to treat illnesses which make up this disease class.

INNOVATION

Researchers have discovered novel pyrimidine-based inhibitors of glucosylceramide synthase that can be used to treat both neuronopathic and peripheral lipid storage diseases, including

Gaucher, Sandhoff, Tay-Sachs and Fabry. This substrate reduction therapy (SRT) represents a new class of glucosylceramide synthetase inhibitors that provide chemically distinct and diverse scaffolds that are capable of treating these lipid storage diseases. SRTs are orally administered and therefore do not require the inconvenience or risks associated with intravenous administration. The inhibition of glucosylceramide synthetase permits a broad range of potentially therapeutic effects, including decreases in glucosylceramide in Gaucher as well as overproduction of glycosphingolipids in Tay-Sachs, Sandhoff, and Fabry.