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HCU Network America announces the recipient of its sixth research grant, awarding Syntis Bio, to develop new treatments for classical homocystinuria. The research led by Dr. Vasa Sethuraman aims to optimize oral dosing for a novel GI-stable Methionine-Gamma-Lyase (MGL) enzyme to treat HCU. Dr. Sethuraman is the Head of Research and Development at Syntis Bio.

Classical Homocystinuria (HCU) is a rare genetic disorder that follows an autosomal recessive inheritance pattern. The disorder is caused by a faulty Cysteine-Beta-Synthase (CBS) enzyme, leading to high levels of homocysteine and methionine. The severity of Classical HCU varies and depends on whether the faulty CBS enzyme is completely inactive or can still metabolize some homocysteine. Left untreated, HCU can lead to a range of health problems over time, affecting the eyes, skeleton, brain, and blood vessels. Common consequences experienced by untreated or uncontrolled individuals include lens dislocation, blood clots and strokes, and varying degrees of cognitive impairment

There are two forms of HCU: a 'milder' form that responds to vitamin B6 (pyridoxine)and a more 'severe' pyridoxine non-responsive form. About 40% of individuals with CBS-deficient homocystinuria are pyridoxine responsive. People who do not respond adequately to pyridoxine need to be on a special diet that is low in protein and consequently low in methionine, as well as administration of a medication called betaine to help metabolize homocysteine. Medical formula is also given to provide non-methionine amino acids for those on a low protein diet. While effective, adherence to a low-protein diet and the medical formula is extremely difficult and is very often poor, especially in late-diagnosed patients. If a safe and effective new treatment could result from this strategy, it could reduce the need for a low-protein diet and formula.

While the exact incidence is unknown and varies globally, it is estimated that CBS-deficient homocystinuria impacts at least 1 in 200,000 people worldwide. The U.S. Office of Rare Diseases Research has classified it as a rare disease, and it is included as part of the newborn screening panel in many countries.

According to the principal investigator, Dr. Vasa Sethuraman, "the project aims to determine the most effective site for gut-restricted enzyme activity to maximize disease impact and uncover new insights into managing synthetic methionine and total homocysteine levels in HCU patients."

"We are honored to receive this award from HCU Network America," said Rahul Dhanda, Co-founder and CEO of Syntis Bio. "We are grateful to be a part of their mission to improve lives in the HCU community, and this grant will help us advance a breakthrough therapy to do exactly that."

Syntis Bio is a clinical-stage biopharmaceutical company developing oral therapies that harness the small intestine's unique biology to provide more accessible, effective, and sustainable solutions across the healthcare spectrum, from rare genetic disorders to the world's most prevalent conditions. The company's lead program, SYNT-101, is a once-daily oral pill for the treatment of obesity that mimics the

effects of gastric bypass surgery. The company is also developing a portfolio of enzyme replacement therapies to treat orphan metabolic diseases and broad digestive disorders. For more information, please visit www.syntis.bio and follow on LinkedIn.

HCU Network America Board President Margie McGlynn said: "This project has the potential to advance the development of an orally active enzyme that could be administered to HCU patients with food, to break down methionine from that food in the gut and prevent its absorption and conversion to homocysteine, which would be expected to have a very beneficial effect on their clinical status and quality of life."

The founders of Syntis Bio, from left to right: Giovanni Traverso, Rahul Dhanda, and Bob Langer.

HCU Network America thanks the community of supporters whose contributions made this grant possible.

The Hummel Family

Margie McGlynn
via the
Hempling Foundation
for HCU Research

In memory of her
sisters Judy and Susie

Team Dayton

Ellie's Entourage

About HCU Network America:
HCU Network America is a 501c (3) non-profit organization founded in 2016 dedicated to helping patients and their families affected by Homocystinuria (HCU) and related disorders. The organization's mission is to inform and provide resources for patients and families, create connections, influence state and federal policy, and support the advancement of diagnosis and treatment for HCU and related disorders.