M6P Therapeutics Presents Promising Preclinical Data in Lysosomal Storage Disorders at the 17th Annual WORLD*Symposium*™ 2021

- Study Results Highlight Potential Utility of Targeting Mannose 6-Phosphate Pathway to Treat Gaucher Disease and Mucolipidosis II -

ST. LOUIS, Mo., – Feb. 11, 2021 – M6P Therapeutics, a privately held life sciences company developing next-generation recombinant enzyme and gene therapies for lysosomal storage disorders (LSDs), announced today the presentation of promising preclinical data at the 17th Annual WORLD*Symposium*™, a research conference dedicated to lysosomal diseases being held virtually Feb. 8-12, 2021. In two separate poster presentations, M6P Therapeutics' researchers report preclinical efficacy and safety results for Gaucher disease and mucolipidosis II (MLII) respectively.

M6P Therapeutics developed its novel bicistronic-S1S3 technology platform to maximize the natural mechanism for trafficking enzymes to lysosomes by enhancing phosphorylation of lysosomal enzymes for both recombinant enzyme and gene therapies. By increasing levels of mannose 6-phosphate, a specialized carbohydrate structure found on the surfaces of lysosomal enzymes, therapies created through the Company's proprietary platform are designed to improve biodistribution and cellular uptake of therapeutic enzymes to target tissues and to enable efficient cross-correction for gene therapies.

"Targeting the mannose 6-phosphate pathway for recombinant enzymes and gene therapies shows tremendous promise because it may lead to better tissue distribution, enhanced cellular uptake, and greater efficacy, compared to current therapeutic approaches for lysosomal storage disorders," commented Lin Liu, Ph.D., Director of R&D at M6P Therapeutics. "The preclinical data we are presenting at the WORLD*Symposium* suggest that increasing the mannose 6-phosphate content on lysosomal enzymes may enable targeting of more cells within the body, possibly easing the disease burden for patients living with these devastating disorders."

M6P Therapeutics will present the following posters at the WORLD*Symposium*:

Poster LB-30: M011 for the Potential Treatment of Patients with Gaucher Disease

Details:

> **Title:** *Phosphorylated acid β-glucosidase (M011, GCase^{M6P}) enzyme replacement therapy leads to better tissue distribution, cellular uptake, and efficacy in the Gaucher D409A mouse model compared to conventional α-mannosyl terminated β-glucosidase.*
> **Date and Time:** Friday, Feb. 12, 2021, between 2:30 – 3:30 PM
> **Session:** Translational Research Abstracts
> **Presenter:** Lin Liu, Ph.D.

Gaucher disease is a rare, inherited metabolic disorder in which deficiency of the enzyme β-glucosidase results in harmful accumulation of glycolipids, specifically glucocerebroside, within the bone marrow, spleen, and liver.

M011, a highly phosphorylated recombinant β-glucosidase (GCase) enzyme with a high affinity for the cation independent mannose 6-phosphate receptor (CI-MPR), demonstrated superiority to imiglucerase, the enzyme currently used for enzyme replacement therapy (ERT) in Gaucher disease, in terms of binding to the CI-MPR and uptake by Gaucher patient fibroblasts.

In multiple *in vivo* experiments in a Gaucher mouse model, M011 was more efficacious than imiglucerase in several key parameters, including broader tissue and cell distribution, reduction of macrophage infiltration into liver and lung tissue, and reduction in the number and size of Gaucher storage cells.

"The main therapeutic advantage of M011 lies in its targeting of the ubiquitous CI-MPR pathway and its ability to achieve superior biodistribution across multiple tissues, overcoming limits associated with current enzyme replacement therapies used to treat Gaucher disease," said Dr. Liu. "We hope to validate these preclinical results through further studies of this promising recombinant enzyme in patients with Gaucher disease."

Poster LB-18: M002 for the Potential Treatment of Mucolipidosis II

Details:

> **Title:** *Mucolipidosis type II AAV9 gene therapy pilot study (M002): In vivo safety of over-expressing modified GlcNAc-1-phosphotransferase (S1S3) in wild-type mice.*
> **Date and Time:** Friday, Feb. 12, 2021, between 2:30 – 3:30 PM
> **Session:** Translational Research Abstracts
> **Presenter:** Russell Gotschall, M.S.

M002 is a gene therapy approach utilizing S1S3, a modified GlcNAc-1-phosphotransferase (S1S3 PTase) that M6P Therapeutics is evaluating as a potential transgene for adeno-associated virus-9 (AAV9)-delivered gene therapy for MLII, one of the most severe LSDs for which there are no approved therapies.

MLII is caused by a deficiency of GlcNAc-1 PTase, a key enzyme responsible for forming M6P on lysosomal hydrolases, which is required for targeting proteins to the lysosome via the CI-MPR. Mutations in the gene that codes for this enzyme can lead to a loss of GlcNAc-1 PTase activity, resulting in inefficient targeting of lysosomal proteins. Consequently, children with MLII typically have significant developmental delays and multiple bone abnormalities, many of which are present at birth. Most affected individuals do not survive past early childhood.

M6P Therapeutics conducted a long-term study to establish the safety of M002 in wild-type mice, with evaluations at two, four, and six months to demonstrate that the constant expression of S1S3 would not lead to unexpected pathology. The investigators reported that expression of M002 did not affect animal wellbeing, weight gain or blood chemistry, and there was sustained expression of the modified, membrane-bound enzyme. Three doses were studied, and 22 tissues were evaluated. There were no macroscopic findings, and the only microscopic

pathological finding was minimal to mild fibrosis of the myocardium of animals who received the highest dose.

"These data appear to justify the continued development of M002 as a potential gene therapy for the treatment of patients with MLII," noted Russell Gotschall, M.S., Vice President of R&D at M6P Therapeutics. "We plan to complete efficacy evaluation of M002 in the MLII mouse model, as well as initiate safety studies in non-human primates."

Both poster presentations will be available in the Publications section on the Company's website at the time of the poster session.

About the Annual WORLDSymposium™
The WORLDSymposium™ is designed for basic, translational and clinical researchers, patient advocacy groups, clinicians, and all others who are interested in learning more about the latest discoveries related to lysosomal diseases and the clinical investigation of these advances. For additional information on the 17th Annual WORLD Symposium™, please visit https://worldsymposia.org/.

About M6P Therapeutics
M6P Therapeutics is a privately held, venture-backed biotechnology company developing the next-generation targeted recombinant enzyme and gene therapies for lysosomal storage disorders (LSDs). M6P Therapeutics' proprietary bicistronic-S1S3 platform has the unique ability to enhance phosphorylation of lysosomal enzymes for both recombinant enzyme and gene therapies, leading to improved biodistribution and cellular uptake of recombinant proteins and efficient cross-correction of gene therapy product. This can potentially lead to more efficacious treatments with lower therapy burden, as well as new therapies for currently untreated diseases. M6P Therapeutics' team, proven in rare diseases drug development and commercialization, is dedicated to fulfilling the promise of recombinant enzyme and gene therapies by harnessing the power of protein phosphorylation using its bicistronic-S1S3 platform. M6P Therapeutics' mission is to translate advanced science into best-in-class therapies that address unmet needs within the LSD community. For more information, please visit: www.m6ptherapeutics.com.

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