M6P Therapeutics Presents Promising Preclinical Data in Lysosomal Storage Disorders at the 18th Annual WORLD*Symposium*™ 2022

- Study Results Highlight Potential Utility of Targeting Mannose 6-Phosphate Pathway to Treat Multiple Lysosomal Storage Disorders -

ST. LOUIS, Mo., – February 11, 2022 – M6P Therapeutics ("M6PT" or "the Company"), a privately held life sciences company developing next-generation enzyme replacement and gene therapies for lysosomal storage disorders (LSDs), today announced the presentation of promising preclinical data at the 18th Annual WORLD*Symposium*™, a research conference dedicated to lysosomal diseases. In four poster presentations, including two Contemporary Forum presentations, M6P Therapeutics' researchers reported preclinical efficacy results for LSDs, including Sanfilippo B syndrome, Gaucher disease, and Pompe disease.

"We are thrilled to showcase our S1S3 co-expression platform technology at the WORLD*Symposium*," said Pawel Krysiak, President and CEO at M6PT. "The preclinical data we presented demonstrate the tremendous promise of targeting the mannose 6-phosphate pathway to enable enhanced biodistribution and tissue uptake across both enzyme replacement and gene therapy modalities and may represent next-generation treatments for LSDs."

The following posters were presented at the WORLD*Symposium*™:

Poster #70: NAGLU-M6P for the Potential Treatment of Sanfilippo B Syndrome

Title: *Co-expression of S1S3 phosphotransferase in production cell line improves mannose 6-phosphorylation and cellular uptake of alpha-N-acetylglucosaminidase (Sanfilippo syndrome type B)*

Date and Time: Monday, Feb. 7, 2022, from 3:00 – 5:00 PM PT (6:00 – 8:00 PM ET)

Session: Basic Science Abstracts
Presenter (In-person): Steven Le from Dr. Patricia Dickson's lab, Division of Genetics and Genomic Medicine, Washington University of St. Louis

Sanfilippo B syndrome is characterized by a defect in the gene providing instructions for producing the enzyme alpha-N-acetylglucosaminidase (NAGLU), located in lysosomes, resulting in accumulation of glucosaminoglycans (GAGs).

NAGLU-M6P is an enzyme replacement therapy approach utilizing co-expression of recombinant human NAGLU and S1S3, a modified GlcNAc-1-phosphotransferase, designed to increase M6P content and enhance subsequent cellular uptake of the enzyme. Binding experiments demonstrated superior binding up to 40% of NAGLU-M6P to the cation independent mannose 6-phosphate receptor (CI-MPR) compared to NAGLU produced without S1S3.

In Sanfilippo B patient fibroblasts, NAGLU-M6P exhibited robust M6P-dependent uptake into cells and reduction of intracellular heparan sulfate. *In vivo* experiments in a Sanfilippo B mouse model showed broader distribution of NAGLU enzyme activity in mice that received NAGLU-M6P versus NAGLU.

"These data show the potential utility of recombinant NAGLU and S1S3 co-expression as an effective enzyme replacement therapy in Sanfilippo B syndrome," said Dr. Lin Liu, Vice President, Research &

Development at M6PT. “We look forward to continued development of this promising therapeutic approach and hope to validate these preclinical results in patients with Sanfilippo B syndrome.”

Poster #120: S1S3 Gene Therapy for the Potential Treatment of Lysosomal Disorders

Title: *A novel S1S3 phosphotransferase co-expression gene therapy platform for lysosomal disorders*

Date and Time:
Contemporary Forum Talk (including live moderated Q&A): Thursday, Feb. 10, 2022, from 10:30 – 11:30 AM PT (1:30 – 2:30 PM ET) followed by:

Poster Session: Thursday, Feb. 10, 2022, from 3:00 – 5:00 PM PT (6:00 – 8:00 PM ET)
Session: Contemporary Forum Poster Presentations
Presenter (In-person): Dr. Andrew Hedman, M6PT Scientist

LSDs are rare, genetic, life-threatening diseases marked by defects in specific lysosomal enzymes.

M6PT has developed a gene therapy platform utilizing adeno-associated virus-9 (AAV9) vector to deliver S1S3 phosphotransferase (PTase) and recombinant lysosomal enzymes in LSDs. This co-expression gene therapy is designed to enhance M6P content on the enzyme, allowing for correct targeting to the lysosome.

Investigators reported the potential utility of this gene therapy platform using various LSD models. In a mouse model of Mucolipidosis type II, an LSD with GlcNAc-1-phosphotransferase deficiency, AAV9 expression of S1S3 PTase restored phosphorylation of lysosomal enzymes. In addition, M6P content was increased in mouse tissues treated with AAV9 vectors co-expressing S1S3 PTase and α-Gal A, an enzyme involved in Fabry disease, as compared to treatment with an AAV9 vector expressing α-Gal A alone.

“We are encouraged by the positive preclinical results from our gene therapy co-expression studies,” said Dr. Hedman. “We believe that an S1S3-based gene therapy platform can improve lysosomal enzyme cross-correction in a variety of LSDs and represents a potential advancement in the treatment of these disorders.”

Poster #105: M011 for the Potential Treatment of Gaucher Disease

Title: *M011: A novel highly phosphorylated β-glucocerebrosidase enzyme with broader tissue biodistribution for the treatment of Gaucher disease*

Date and Time:
Contemporary Forum Talk: Thursday, Feb. 10, 2022, from 1:00 – 2:00 PM PT (4:00 – 5:00 PM ET) followed by:

Poster Session: Thursday, Feb. 10, 2022, from 3:00 – 5:00 PM PT (6:00 – 8:00 PM ET)
Session: Contemporary Forum Poster Presentations
Presenter (Virtual): Russell Gotschall, Vice President, Research & Development, M6PT

Gaucher disease is a rare, autosomal recessive metabolic disorder in which deficiency of the enzyme β-glucosidase results in harmful accumulation of glucosylceramide in tissue macrophages and other cells.

M011 is a novel recombinant human β-glucosidase (rhGCase) enzyme co-expressed with S1S3 PTase that produces rhGCase with a high M6P levels, resulting in high levels of bis-phosphorylated glycans and high binding affinity for the CI-MPR.

In vivo experiments in a Gaucher mouse model showed that M011 reduced glucosylshpingosine from the liver and spleen and cleared bone and skeletal muscle substrate more effectively than imiglucerase, the enzyme currently used for enzyme replacement therapy in Gaucher disease. In addition, M011 showed more efficient cellular uptake and broad distribution in tissues.

“The superior efficacy and broad distribution of M011 demonstrate its potential as a viable treatment approach for Gaucher disease, including in types affecting the central nervous system,” said Mr. Gotschall. “We are encouraged by these highly promising results and look forward to continued development of M011.”

Poster #106: M021 for the Potential Treatment of Pompe Disease

Title: *M021: A uniquely glycosylated, highly phosphorylated acid-alpha glucosidase enzyme replacement therapy for the treatment of Pompe disease*

Date and Time: Thursday, Feb. 10, 2022, from 3:00 – 5:00 PM PT (6:00 – 8:00 PM ET)
Session: Contemporary Forum Poster Presentations
Presenter (Virtual): Russell Gotschall, Vice President, Research & Development, M6PT

Pompe disease is a rare, inherited metabolic disorder in which deficiency of the enzyme α-glucosidase (GAA) results in defective lysosomal glycogen catabolism.

M021 is a novel recombinant human GAA (rhGAA) enzyme co-expressed with S1S3 PTase that enhances M6P levels, resulting in high levels of bis-phosphorylated glycans, high affinity for the CI-MPR, and low levels of neutral oligosaccharides.

In vivo experiments in GAA deficient mice showed that M021 significantly reduced glycogen accumulated in muscles compared to alglucosidase alfa, the current enzyme replacement therapy for Pompe disease.

“These data demonstrate the continued development potential of M021 as a next-generation treatment for Pompe disease,” said Mr. Gotschall. “We plan to complete efficacy evaluations of M021 in mice and hope to advance this potential therapeutic approach to future clinical studies.”

For more information, registration details and to access the live streamed events, presentations, and Q&A sessions, please go to WORLD*Symposium*™. The abstracts will also be made available on the Publications section of M6PT’s corporate website following the presentations.

About the Annual WORLD*Symposium*™
The WORLD*Symposium*™ 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 18th 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 of targeted enzyme replacement and gene therapies for lysosomal storage disorders (LSDs). M6P Therapeutics’ proprietary S1S3 co-expression platform has the unique ability to enhance phosphorylation of lysosomal enzymes for both enzyme replacement 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 enzyme replacement

and gene therapies by harnessing the power of protein phosphorylation using its S1S3 co-expression 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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