M6P Therapeutics Presents M002 Gene Therapy Preclinical Proof-of-Concept Data for the Treatment of Mucolipidosis Type II at the ASGCT 24th Annual Meeting

- Preclinical data provide proof of concept for M002 to restore cellular uptake and lysosomal delivery and attenuate phenotype in mouse models of mucolipidosis type II -

- M002 leverages the Company's proprietary S1S3 bicistronic platform technology in an AAV9 gene therapy to restore mannose 6-phosphate recognition marker on lysosomal enzymes -

ST. LOUIS, Mo., – May 11, 2021 – M6P Therapeutics ("the Company"), a privately held life sciences company developing next-generation recombinant enzyme and gene therapies for lysosomal storage disorders (LSDs), today announced the presentation of preclinical proof-of-concept data for M002, its gene therapy candidate for mucolipidosis type II (MLII), at the American Society of Gene & Cell Therapy (ASGCT) 24th Annual Meeting.

"These preclinical data mark an important milestone for M6P Therapeutics, providing proof of concept for our S1S3 bicistronic platform technology in one of our lead gene therapy programs," said Pawel Krysiak, president and chief executive officer of M6P Therapeutics. "This approach utilizing our proprietary S1S3 GlcNAc-1 PTase variant is the only technology capable of modulating N-glycan processing *in vivo* to add mannose 6-phosphate, or M6P, to lysosomal proteins, which is essential for improving their cellular uptake and lysosomal delivery in target tissues and what we believe is the key to providing transformative treatments for lysosomal storage disorders. MLII, caused by mutations in the GlcNAc-1 PTase gene itself, is an ideal indication to demonstrate that our S1S3 variant restores PTase activity *in vivo*, via its truncated form that facilitates expression and delivery via AAV9. Our results show that in mouse models of MLII, treatment with M002 results in S1S3 expression, which restores PTase enzymatic activity in target tissues, ultimately improving disease manifestations on a cellular and behavioral level.

Mr. Krysiak continued, "Together, these results provide a strong foundation for our broader gene therapy pipeline, which leverages our S1S3 bicistronic platform to enhance M6P content across lysosomal enzymes. We look forward to advancing our programs to the clinic, leveraging our platform to improve tissue distribution and cellular uptake, which we believe has the potential to translate to improved efficacy and safety across our gene and recombinant enzyme therapies to overcome the existing limitations in treating lysosomal storage disorders."

Presentation highlights from the poster titled, "*M002, a novel AAV9-mediated gene therapy in a mouse model of mucolipidosis type II*" include:

- In a mouse model of MLII, mice lacking the GNPTAB gene, which encodes the α/β subunits of GlcNAc-1 phosphotransferase (PTase), were treated with M002, an AAV-9-mediated gene therapy which delivers a truncated PTase (S1S3)
- Preliminary data from MLII mice treated with M002 showed:
    - Expressed S1S3 in a number of tissues including heart, liver, and salivary gland
    - Increased enzyme binding to the cation-independent mannose 6-phosphate receptor (CI-MPR)
    - Restored PTase activity with restored phosphorylation of a number of lysosomal enzymes
    - Partially decreased levels of lysosomal enzymes secreted in serum, with concurrent increased intracellular levels in tissues including liver, heart, brain, and salivary gland
    - Improved the phenotype of secretory lesions of exocrine glands, measured in the pancreas and salivary glands, which is associated with loss of PTase
    - Improved sensorimotor activity

The e-poster presentation will be available on ASGCT's website at the time of the poster session.

About Mucolipidosis II
Mucolipidosis II or MLII (also known as I-cell disease) is a progressively debilitating, ultra-rare autosomal recessive disorder caused by mutations in the GNPTAB gene. The mutation leads to GlcNAc-1-phosphotransferase deficiency and inability to phosphorylate (add mannose 6-phosphate, or M6P) lysosomal enzymes. As a result, lysosomal enzymes are not trafficked to lysosomes where they are needed to breakdown large molecules into smaller ones to be reused by the cell; consequently, the enzymes remain in cytoplasm or leak out to serum. Most affected individuals do not survive past early childhood. Although its exact prevalence is unknown, it is estimated to occur in about 1 in 100,000 to 400,000 individuals worldwide. MLII is apparent at birth, and slowly progressive until death in childhood. MLII is characterized by growth delays, skeletal abnormalities, facial dysmorphism, stiff skin, developmental delay, cardiomegaly, and respiratory insufficiency.

About M6P Therapeutics
M6P Therapeutics is a privately held, venture-backed biotechnology company developing the next-generation of targeted recombinant enzyme and gene therapies for lysosomal storage disorders (LSDs). M6P Therapeutics' proprietary S1S3 bicistronic 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 S1S3 bicistronic 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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