Amicus Therapeutics Presents Positive Preclinical Fabry Disease Gene Therapy Data at the 17th Annual WORLDSymposium™ 2021

February 8, 2021

Amicus Optimized Transgene Show Greater Substrate Reduction than Wild Type Construct Across All Tissues and Doses

Further Validates Combining Amicus-Engineered Transgenes with Penn's AAV Gene Therapy Technologies to Develop Next Generation Gene Therapies

PHILADELPHIA, Feb. 08, 2021 (GLOBE NEWSWIRE) -- Amicus Therapeutics (Nasdaq: FOLD) today announced initial preclinical data from its investigational adeno-associated viral (AAV) gene therapy program for Fabry disease in mice. The results are featured in a virtual poster presentation at the 17th Annual WORLD*Symposium* ™ 2021, being held February 8-12, 2021. The poster is also available in the Events and Presentations section of the Amicus Therapeutics corporate website.

Fabry disease is an inherited lysosomal disorder caused by deficiency of the enzyme alpha-galactosidase A (GLA). Reduced or absent levels of GLA lead to accumulation of disease substrate leading to cellular disfunction and organ damage, which results in the clinical manifestations of Fabry disease. Amicus, in collaboration with the Gene Therapy Program of the Perelman School of Medicine at the University of Pennsylvania (Penn), is developing a novel gene therapy for Fabry disease that combines the Amicus protein-engineering expertise and deep knowledge and experience in Fabry disease with Penn's adeno associated virus (AAV) gene transfer technologies.

This initial preclinical study assessed a range of single doses of AAV in *Gla* knockout (KO) mice with either natural unmodified hGLA ("wildtype hGLA") or Amicus/Penn engineered hGLA transgenes ("engineered hGLA"). The Amicus/Penn engineered hGLAs are designed for improved stability which is believed to provide a larger window for the enzyme to stay active while in circulation prior to being taken up into the target tissues and for additional stabilization after cell uptake. The lead Amicus/Penn engineered hGLA declared as an IND candidate is designated as AT-GTX-701.

Preclinical Poster Highlights for Amicus/Penn AAV Gene Therapy for Fabry Disease:

- **Improved for stability:** In vitro characterization of two stabilized alpha-Gal A constructs with engineered disulfide bonds demonstrated stable homodimer formation, enhanced temperature, plasma, and neutral pH stability compared to wildtype.
- **Dose dependent response**: The lowest tested dose of AT-GTX-701 in *Gla* KO mice showed partial substrate reduction, while highest tested dose resulted in near complete substrate reduction.
- **Significantly greater substrate reduction vs. wildtype transgene**: AT-GTX-701 demonstrated significantly greater lyso-Gb3/GL-3 substrate reduction across all Fabry disease relevant tissues including the dorsal root ganglia (DRG), kidney, and heart, with reductions at low dose being equal to or greater than the reductions observed at higher doses with wildtype transgene.
- **First evidence of dorsal route ganglia storage reduction**: DRG are affected in Fabry disease and associated with neuropathic pain. AT-GTX-701's stabilized transgene provided the first evidence for DRG storage reduction in a Fabry mouse model treated with an AAV gene therapy.
- **Amicus/Penn Gene Therapy Platform:** Further validates the potential of this platform to design constructs that enhance proteins across multiple lysosomal disorders.
- Additional preclinical studies, IND enabling studies, and GMP manufacturing process development are underway.

Hung Do, Ph.D., Chief Science Officer of Amicus Therapeutics, stated, "These very important preclinical results validate our capabilities to develop engineered proteins via a gene therapy that can result in superior substrate reduction compared with a wildtype transgene. This is the second program in our collaboration with Penn that has demonstrated the potential advantages of optimizing the target protein in these disorders, and may be applicable to other lysosomal disorders as we continue to combine our understanding of the molecular basis of these diseases and expertise in protein engineering, together with Penn's vector engineering expertise, to develop novel gene therapies."

Amicus is currently developing AAV gene therapies in collaboration with Penn for Pompe disease, Fabry disease, CDD, CLN1, MPS IIIB, a next generation program in MPS IIIA, as well as Angelman Syndrome. The agreement between Amicus and Penn is a Research, Collaboration and License Agreement, providing funding to Penn to advance the preclinical research programs in the Wilson Lab and to license certain technologies invented under the funded Research Collaboration.

About Fabry Disease

Fabry disease is an inherited lysosomal disorder caused by deficiency of an enzyme called alpha-galactosidase A (alpha-Gal A), which is the result of mutations in the GLA gene. The primary biological function of alpha-Gal A is to degrade specific lipids in lysosomes, including globotriaosylceramide (referred to here as GL-3 and also known as Gb3). Lipids that can be degraded by the action of alpha-Gal A are called "substrates" of the enzyme. Reduced or absent levels of alpha-Gal A activity lead to the accumulation of GL-3 in the affected tissues, including the central nervous system, heart, kidneys, and skin. Progressive accumulation of GL-3 is believed to lead to the morbidity and mortality of Fabry disease, including pain, kidney failure, heart disease, and stroke. The symptoms can be severe, differ from patient to patient, and begin at an early age. All Fabry disease is progressive and may lead to irreversible organ damage regardless of the time of symptom onset.

About Amicus Therapeutics

Amicus Therapeutics (Nasdaq: FOLD) is a global, patient-dedicated biotechnology company focused on discovering, developing and delivering novel high-quality medicines for people living with rare metabolic diseases. With extraordinary patient focus, Amicus Therapeutics is committed to advancing and expanding a robust pipeline of cutting-edge, first- or best-in-class medicines for rare metabolic diseases. For more information please visit the company's website at www.amicusrx.com, and follow us on Twitter and LinkedIn.

Forward-Looking Statements

This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, including statements relating to initial preclinical data from its investigational adeno-associated viral (AAV) gene therapy program for Fabry disease in mice and the potential implications of these data for the future advancement and development of a gene therapy for Fabry disease and other lysosomal disorders and development of potential platform technologies. Words such as, but not limited to, "look forward to," "believe," "expect," "anticipate," "estimate," "intend," "confidence," "encouraged," "potential," "plan," "targets," "likely," "may," "will," "would," "should" and "could," and similar expressions or words identify forward-looking statements. The forward looking statements included in this press release are based on management's current expectations and belief's which are subject to a number of risks, uncertainties and factors, including that the preliminary data reported before completion of the study will not be predictive of future results, that results of additional preliminary data or data from the completed study or any future study will not yield results that are consistent with the preliminary data presented, that later study results will not support further development, or even if such later results are favorable, that the Company will not be able to successfully complete the development of, obtain regulatory approval for, or successfully commercialize. In addition, all forward looking statements are subject to the other risks and uncertainties detailed in our Annual Report on Form 10-K for the year ended December 31, 2019 and the Quarterly Report filed on Form 10-Q for the quarter ended September 30, 2020. As a consequence, actual results may differ materially from those set forth in this press release. You are cautioned not to place undue reliance on these forward looking statements, which speak only of the date hereof. All forward looking statements are qualified in their entirety by this cautionary statement and we undertake no obligation to revise this press release to reflect events or circumstances after the date hereof.

CONTACTS:

Investors:
Andrew Faughnan
Sr. Director, Investor Relations
afaughnan@amicusrx.com
(609) 662-3809

Media:
Diana Moore
Head of Global Corporate Communications
dmoore@amicusrx.com
(609) 662-5079

FOLD–G