Gyre Therapeutics Announces Publication in Journal of Gastroenterology and Hepatology

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SAN DIEGO, June 18, 2024 (GLOBE NEWSWIRE) -- Gyre Therapeutics ("Gyre") (Nasdaq: GYRE), a clinical-stage, self-sustainable biotechnology company developing anti-fibrotic therapeutics for a variety of chronic organ diseases, today announced the publication of the manuscript titled "Hydronidone induces apoptosis in activated hepatic stellate cells through endoplasmic reticulum stress-associated mitochondrial apoptotic pathway" in the *Journal of Gastroenterology and Hepatology.* This publication includes both *in vivo* and *in vitro* studies supporting the potential of hydronidone (F351), a novel derivate of pirfenidone, as a promising therapy for the treatment of liver fibrosis.

"Preclinical animal studies have shown that treatment with hydronidone attenuated liver fibrosis by inhibiting the activation of hepatic stellate cells (HSCs), although the underlying mechanisms of action are still not fully understood," said Han Ying, Ph.D., CEO of Gyre. "The findings of these *in vivo* and *in vitro* studies demonstrate that hydronidone induces apoptosis in activated HSCs (aHSCs) via the endoplasmic reticulum stress (ERS)-associated mitochondrial apoptotic pathway and suggest that hydronidone may contribute to the improvement of liver fibrosis. These findings further enhance our understanding of hydronidone and underscore its therapeutic potential in treating liver fibrosis."

Liver fibrosis is characterized by the progressive accumulation of extracellular matrix (ECM), which disrupts the normal liver architecture. Research has shown that quiescent HSCs undergo activation and transform into myofibroblast-like cells to produce ECM in chronic liver disease, and therefore that liver fibrosis can be reversed by eliminating aHSCs. This study found that treatment with hydronidone significantly promoted apoptosis in aHSCs in both the CCl_4- and DDC-induced liver fibrosis in mice and LX-2 cells. Mechanistic studies revealed that hydronidone triggered ERS and subsequently activated the IRE1α-ASK1-JNK pathway and subsequent dysfunction of the mitochondria, ultimately resulting in the apoptosis of aHSCs.

Gyre Pharmaceuticals, Gyre's majority indirectly owned subsidiary in the People's Republic of China (PRC), is currently evaluating hydronidone in a Phase 3 trial for the treatment of Chronic Hepatitis B (CHB)-associated liver fibrosis in the PRC with topline data anticipated by early 2025. The trial is evaluating 248 patients with a primary endpoint of the reduction of the liver fibrosis score (Ishak Scoring System) by at least one grade after taking hydronidone in combination with entecavir. Pending results from the Phase 3 trial, Gyre intends to initiate a Phase 2a proof-of-concept trial to evaluate hydronidone for the treatment of NASH-associated liver fibrosis in 2025.

About Gyre Therapeutics

Gyre Therapeutics is a biopharmaceutical company headquartered in San Diego, CA, with a primary focus on the development and commercialization of F351 (Hydronidone) for the treatment of NASH-associated fibrosis in the U.S. Gyre's development strategy for F351 in NASH is based on the company's experience in NASH rodent model mechanistic studies and CHB-induced liver fibrosis clinical studies. Gyre is also advancing a diverse pipeline in the PRC through its indirect controlling interest in Gyre Pharmaceuticals, including ETUARY therapeutic expansions, F573, F528, and F230.

Forward-Looking Statements

This press release contains "forward-looking statements" within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995, which statements are subject to substantial risks and uncertainties and are based on estimates and assumptions. All statements, other than statements of historical facts included in this press release, are forward-looking statements, including statements concerning: the expectations regarding Gyre's research and development efforts and timing of expected clinical readouts, including timing of topline data from Gyre Pharmaceuticals' Phase 3 clinical trial evaluating F351 for the treatment of CHB-associated liver fibrosis in the PRC and initiation of Gyre's Phase 2a trial in the U.S. for F351. In some cases, you can identify forward-looking statements by terms such as "may," "might," "will," "objective," "intend," "should," "could," "can," "would," "expect," "believe," "design," "estimate," "predict," "potential," "plan" or the negative of these terms, and similar expressions intended to identify forward-looking statements. These statements reflect our plans, estimates, and expectations, as of the date of this press release. These statements involve known and unknown risks, uncertainties and other factors that could cause our actual results to differ materially from the forward-looking statements expressed or implied in this press release. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation: Gyre's ability to execute on its clinical development strategies; positive results from a clinical trial may not necessarily be predictive of the results of future or ongoing clinical trials; the timing or likelihood of regulatory filings and approvals; competition from competing products; the impact of general economic, health, industrial or political conditions in the United States or internationally; the sufficiency of Gyre's capital resources and its ability to raise additional capital. Additional risks and factors are identified under "Risk Factors" in Gyre's Annual Report on Form 10-K for the year ended December 31, 2023 filed on March 27, 2024 and in other filings with the Securities and Exchange Commission.

Gyre expressly disclaims any obligation to update any forward-looking statements whether as a result of new information, future events or otherwise, except as required by law.

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