Galectin Therapeutics Reports the Positive Outcome of the Fifth Data and Safety Monitoring Board Meeting for NAVIGATE Phase 2b/3 Study of Belapectin in Patients with Cirrhotic Portal Hypertension Caused by Metabolic Dysfunction-Associated SteatoHepatitis

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- **Data and Safety Monitoring Board (DSMB) recommends the continuation, without modifications, of the adaptive Phase 2b/3 NAVIGATE study of belapectin in metabolic dysfunction-associated steatohepatitis (MASH) liver cirrhosis**
- **Fifth positive recommendation further supports favorable tolerability and safety profile of belapectin**
- **Interim Phase 2b efficacy readout anticipated in Q4 2024**

NORCROSS, Ga., April 09, 2024 (GLOBE NEWSWIRE) -- Galectin Therapeutics, Inc. (NASDAQ: GALT), the leading developer of therapeutics that target galectin-3, today reported the positive outcome of its fifth independent data and safety monitoring board (DSMB) meeting for NAVIGATE, its seamless, adaptive, Phase 2b/3 study of belapectin in patients with cirrhotic portal hypertension caused by Metabolic Dysfunction-Associated SteatoHepatitis (MASH).

The objective of this fifth DSMB meeting was to further review the emerging tolerance and safety profiles of belapectin. Based on its deliberation, which included an unblinded review of the data collected thus far, the DSMB concluded that NAVIGATE can continue as designed, without modifications.

The Phase 2b/3 NAVIGATE study is a global, seamless, adaptive, randomized, placebo-controlled, double-blind trial. This is the first study of its kind in cirrhotic patients with an innovative adaptive design and an innovative primary outcome of efficacy, the prevention of esophageal varices, a clinical marker of portal hypertension which is an essential mechanism underlying the relentless progression of the disease. The adaptive study includes two stages: The Phase 2b portion, or Stage 1, has been fully enrolled with 357 patients who have clinical signs of portal hypertension, no cirrhosis decompensations, and no esophageal varices. Portal hypertension is the consequence of the unrelenting inflammatory and fibrotic process occurring in the liver and dramatically increases the risk of developing esophageal varices, a potentially life-threatening complication of liver cirrhosis.

Enrolled patients have been randomized to receive every two weeks a blinded infusion of belapectin at 2 mg/kg/LBM or 4 mg/kg/LBM or placebo. An interim analysis of safety and efficacy will be conducted once the last patient randomized into Stage 1 has been followed up for 18 months, and has had a second esophago-gastric endoscopy to evaluate for the presence or absence of esophageal varices. The results of this stage 1 interim analysis will determine if the study progresses into the Phase 3 portion of the trial, or Stage 2 , and which of the pre-specified protocol adaptations are to be integrated into this second stage.

The Stage 1 interim analysis has three possible outcomes: stop NAVIGATE because of overwhelming efficacy or because of futility, or initiate NAVIGATE Stage 2 because there is a favorable conditional probability of success regarding the final analysis that will take place at the end of Stage 2 (Phase 3). In this third scenario, adaptations to be selected include the choice of the best dose of belapectin and the final number of new patients to be randomized for ensuring an adequate study power for the Final Analysis.

Dr. Pol Boudes, M.D., Chief Medical Officer of Galectin Therapeutics, said: “The fifth positive recommendation of the DSMB to continue the trial without any modification confirms that our NAVIGATE study remains on track for an interim readout by the end of the year. Moreover, the recommendation further strengthens our confidence that belapectin appears generally safe and well tolerated, which is of great importance given the patients in our trial suffer from several co-morbidities and are on multiple medications, which increases the overall risk of severe complications. This safety profile can tip the balance in favor of the drug’s risk-benefit ratio, an essential element to support any drug approval. The innovative design of the NAVIGATE trial is essential to bring new momentum to clinical development in cirrhosis, a field that has not seen enough medical breakthroughs over the past 50 years. I am convinced that we must change the way we do clinical research if we want to bring hope to our patients. Our adaptive design, as well as our clinical efficacy criteria, represent a new way to evaluate cirrhosis treatment and we hope, if we are successful, that this approach will be emulated. The next DSMB meeting, in addition to the evaluation of belapectin profile, will evaluate the results of the interim analysis and provides its recommendation to Galectin Therapeutics. We are excited to continue our journey to bring patients with liver cirrhosis a potentially efficacious and safe treatment.”

The topline results from the Interim analysis of the Phase 2b (Stage 1) portion of NAVIGATE is expected in the fourth quarter of 2024.

About Belapectin
Belapectin is a complex carbohydrate drug that targets galectin-3, a critical protein in the pathogenesis of NASH/MASH and fibrosis. Galectin-3 plays a major role in diseases that involve scarring of organs, including fibrotic disorders of the liver, lung, kidney, heart and vascular system. Belapectin binds to galectin-3 and disrupts its function. Preclinical data in animals have shown that belapectin has robust treatment effects in reversing liver fibrosis and cirrhosis. A Phase 2 study showed belapectin may prevent the development of esophageal varices in MASH cirrhosis, and these results provide the basis for the conduct of the NAVIGATE Phase 2b/3 trial (NCT04365868) to evaluate the efficacy and safety of belapectin for the prevention of esophageal varices in MASH cirrhosis. Galectin-3 has a significant role in cancer, and the Company has supported a Phase 1b study in combined immunotherapy of belapectin and KEYTRUDA in advanced melanoma and in head and neck cancer. This trial provided a strong rationale for moving forward into a Company-sponsored Phase 2 development program, which the company is exploring.

About liver cirrhosis due to MASH and portal hypertension
Metabolic Dysfunction-Associated Steatohepatitis, formerly known as nonalcoholic steatohepatitis or NASH, has become a common disease of the

liver with the rise in obesity and other metabolic diseases. MASH is estimated to affect up to 28 million people in the U.S. It is characterized by the presence of excess fat in the liver along with inflammation and hepatocyte damage (ballooning) in people who consume little or no alcohol. Over time, patients with NASH can develop excessive fibrosis, or scarring of the liver, and ultimately liver cirrhosis. Liver cirrhosis is further complicated by portal hypertension which is one of the main mechanisms leading to decompensated liver cirrhosis. It is estimated that as many as 1 to 2 million individuals in the U.S. will develop cirrhosis as a result of MASH, for which liver transplantation is the only curative treatment available. Approximately 9,000 liver transplants are performed annually in the U.S. There are no drug therapies approved for the treatment of liver cirrhosis.

About Galectin Therapeutics

Galectin Therapeutics is dedicated to developing novel therapies to improve the lives of patients with chronic liver disease and cancer. Galectin's lead drug belapectin is a carbohydrate-based drug that inhibits the galectin-3 protein, which is directly involved in multiple inflammatory, fibrotic, and malignant diseases, for which it has Fast Track designation by the U.S. Food and Drug Administration. The lead development program is in metabolic dysfunction-associated steatohepatitis (MASH, formerly known as nonalcoholic steatohepatitis, or NASH) with cirrhosis, the most advanced form of MASH-related fibrosis. Liver cirrhosis is one of the most pressing medical need and a significant drug development opportunity. Additional development programs are in treatment of combination immunotherapy for advanced head and neck cancers and other malignancies. Advancement of these additional clinical programs is largely dependent on finding a suitable partner. Galectin seeks to leverage extensive scientific and development expertise as well as established relationships with external sources to achieve cost-effective and efficient development. Additional information is available at **www.galectintherapeutics.com**.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These statements relate to future events or future financial performance, and use words such as "may," "estimate," "could," "expect", "look forward", "believe", "hope" and others. They are based on management's current expectations and are subject to factors and uncertainties that could cause actual results to differ materially from those described in the statements. These statements include those regarding the hope that Galectin's development program for belapectin will lead to the first therapy for the treatment of MASH, formerly known as NASH, with cirrhosis and those regarding the hope that our lead compounds will be successful in cancer immunotherapy and in other therapeutic indications. Factors that could cause actual performance to differ materially from those discussed in the forward-looking statements include, among others, that trial endpoints required by the FDA may not be achieved; Galectin may not be successful in developing effective treatments and/or obtaining the requisite approvals for the use of belapectin or any of its other drugs in development; the Company may not be successful in scaling up manufacturing and meeting requirements related to chemistry, manufacturing and control matters; the Company's current clinical trial and any future clinical studies may not produce positive results in a timely fashion, if at all, and could require larger and longer trials, which would be time consuming and costly; plans regarding development, approval and marketing of any of Galectin's drugs are subject to change at any time based on the changing needs of the Company as determined by management and regulatory agencies; regardless of the results of any of its development programs, Galectin may be unsuccessful in developing partnerships with other companies or raising additional capital that would allow it to further develop and/or fund any studies or trials. Galectin has incurred operating losses since inception, and its ability to successfully develop and market drugs may be impacted by its ability to manage costs and finance continuing operations. For a discussion of additional factors impacting Galectin's business, see the Company's Annual Report on Form 10-K for the year ended December 31, 2023, and subsequent filings with the SEC. You should not place undue reliance on forward-looking statements. Although subsequent events may cause its views to change, management disclaims any obligation to update forward-looking statements.

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