September 2, 2025

Rezolute Announces Alignment with FDA on Streamlined Design for Ongoing Phase 3 Trial of Ersodetug in Tumor Hyperinsulinism

Open-label study in as few as 16 tumor hyperinsulinism (HI) patients

Study initiated and enrolling patients in the U.S. and Europe

Topline data expected in the second half of 2026

REDWOOD CITY, Calif., Sept. 02, 2025 (GLOBE NEWSWIRE) -- Rezolute, Inc. (Nasdaq: RZLT) ("Rezolute" or the "Company"), a late-stage rare disease company focused on treating hypoglycemia caused by hyperinsulinism, today announced that the Company has gained alignment with FDA on a significantly streamlined clinical development path for its ongoing Phase 3 study (upLIFT) of ersodetug for the treatment of hypoglycemia caused by tumor HI.

At a meeting held with FDA on August 19, 2025, the agency agreed to modifications to the design of the study including removing the need to conduct a double-blind randomized placebo-controlled trial. The truncated study will include as few as 16 participants and will be limited to the single-arm open-label portion of the upLIFT study, which has been the focus of the Company's patient recruitment efforts. FDA also confirmed that Rezolute's pivotal sunRIZE trial in congenital HI, which is on track to report topline results in December 2025, would serve as confirmatory clinical evidence, and is demonstrative of FDA's recognition of the broad applicability of ersodetug in multiple forms of HI.

"We are absolutely delighted with this regulatory outcome," said Nevan Charles Elam, Chief Executive Officer and Founder of Rezolute. "The FDA's staff and leadership have been very vocal about the desire to responsibly simplify clinical development for rare diseases, particularly when there is real-world evidence of benefit combined with mechanistic plausibility. We believe that the alignment we have achieved with the agency exemplifies this innovative approach and is substantially based upon the favorable outcomes that we have observed over the last two years treating more than 10 patients with tumor HI under our Expanded Access Program."

Brian Roberts, M.D., Chief Medical Officer at Rezolute went on to say, "This revised and simplified plan for the upLIFT study and approval pathway marks an important development for us as well as the community of healthcare providers, patients, and families living with serious hypoglycemia caused by tumor HI. By focusing on an open-label study in upLIFT, while building upon the robust clinical foundation established in the congenital HI indication, we are expediting development with the goal of making this therapy available as efficiently

as possible.”

About upLIFT

The Phase 3 registrational study is a single-arm, open-label, pivotal trial in approximately 16 participants with insulinoma or non-islet cell tumors who have uncontrolled hypoglycemia caused by tumor hyperinsulinism (HI). Eligible participants requiring continuous intravenous (IV) glucose will receive ersodetug 9 mg/kg per week for 8 weeks, as an add-on to standard of care. Following this 8-week pivotal treatment period, all participants may receive ersodetug in long-term extension. The primary endpoint is the number of participants achieving at least a 50 percent reduction from baseline in IV glucose requirements (glucose infusion rate; GIR). Additional endpoints include the number of participants and time to discontinuation of GIR, time to discharge from the hospital, extent of hypoglycemia events and hypoglycemia time in the outpatient setting by self-monitored blood glucose and continuous glucose monitor, respectively, and patient reported quality of life.

About Tumor Hyperinsulinism

Tumor hyperinsulinism (HI) is a rare disease that may be caused by two distinct types of tumors: islet cell tumors (ICTs) and non-islet cell tumors (NICTs), both of which lead to hypoglycemia as a result of over-activation of the insulin receptor. Insulinomas are the most common type of ICT and cause hypoglycemia by stimulating the over production of insulin. A variety of different NICTs, particularly hepatocellular carcinoma, can cause hypoglycemia by producing and secreting insulin-like paraneoplastic substances such as IGF-2 that bind to and activate the insulin receptor. With high morbidity and mortality rates within tumor HI, there remains a significant unmet need for new therapies directed at hypoglycemia treatment. Ersodetug has shown real-world benefit in patients with insulinoma and NICTs.

About Ersodetug

Ersodetug is a fully human monoclonal antibody that binds allosterically to the insulin receptor to decrease receptor over-activation by insulin and related substances (such as IGF-2) in the setting of hyperinsulinism (HI), thereby improving hypoglycemia. Because ersodetug acts downstream from the pancreas, it has the potential to be universally effective at treating hypoglycemia due to any congenital or acquired form of HI.

About Rezolute, Inc.

Rezolute is a late-stage rare disease company focused on treating hypoglycemia caused by hyperinsulinism (HI). The Company’s antibody therapy, ersodetug, is designed to treat all forms of HI and has shown meaningful benefit in clinical trials and real-world use for the treatment of both congenital and tumor HI. For more information, visit www.rezolutebio.com.

Forward-Looking Statements

This release, like many written and oral communications presented by Rezolute and our authorized officers, may contain certain forward-looking statements regarding our prospective performance and strategies within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act of 1934, as amended. We intend such forward-looking statements to be covered by the safe harbor provisions for forward-looking

statements contained in the Private Securities Litigation Reform Act of 1995 and are including this statement for purposes of said safe harbor provisions. Forward-looking statements, which are based on certain assumptions and describe future plans, strategies, and expectations of Rezolute, are generally identified by use of words such as "anticipate," "believe," "estimate," "expect," "intend," "plan," "project," "seek," "strive," "try," or future or conditional verbs such as "could," "may," "should," "will," "would," or similar expressions. These forward-looking statements include, but are not limited to, statements regarding the potential efficacy of ersodetug in the congenital HI and tumor HI patient populations, the timeline for achieving results in the upLIFT studies and the potential approval and commercialization of ersodetug. Our ability to predict results or the actual effects of our plans or strategies is inherently uncertain. Accordingly, actual results may differ materially from anticipated results. Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this release. Except as required by applicable law or regulation, Rezolute undertakes no obligation to update these forward-looking statements to reflect events or circumstances that occur after the date on which such statements were made. Important factors that may cause such a difference include any other factors discussed in our filings with the SEC, including the Risk Factors contained in the Rezolute's Annual Report on Form 10-K and Quarterly Reports on Form 10-Q, which are available at the SEC's website at www.sec.gov. You are urged to consider these factors carefully in evaluating the forward-looking statements in this release and are cautioned not to place undue reliance on such forward-looking statements, which are qualified in their entirety by this cautionary statement.

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