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Rezolute Announces Positive RZ402 Study Results Demonstrating Potential for Once Daily Dosing of an Oral Plasma Kallikrein Inhibitor for Diabetic Macular Edema

Results allow the Company to advance development, including planning for its multiple-ascending dose clinical study

REDWOOD CITY, Calif., May 04, 2021 (GLOBE NEWSWIRE) -- **Rezolute, Inc.** (Nasdaq: RZLT), a clinical-stage biopharmaceutical company developing novel therapies for diseases caused by chronic glucose imbalance, today announced positive topline results from its first-in-human Phase 1a clinical study of RZ402, the Company's investigational oral plasma kallikrein inhibitor (PKI), for the treatment of diabetic macular edema (DME). Single dose oral administration of RZ402 resulted in plasma concentrations that substantially exceeded target pharmacologically active drug levels, demonstrating the potential for once daily dosing, and supporting the advancement of developmental activities toward Phase 2, including a Phase 1b multiple-ascending dose study. RZ402 was generally safe and well-tolerated at all doses tested, without dose-limiting toxicities.

"We're in need of new treatments in the clinical care of patients with diabetic eye diseases," said Robert B. Bhisitkul, M.D., Ph.D., Professor of Ophthalmology and Retinal Specialist at the University of California San Francisco School of Medicine's Department of Ophthalmology, and member of Rezolute's Scientific Advisory Board. "Pioneering research has strongly implicated the kallikrein-kinin system in the development of diabetic retinopathy and macular edema. A novel plasma kallikrein inhibitor has potential to give patients with diabetic macular edema an alternative therapeutic option. Oral delivery would provide the possibility of earlier treatment intervention and enable a patient-controlled regimen with advantages in comfort, convenience, and continuous drug levels in the retinal microvasculature. I look forward to the continued development of RZ402 for patients at risk of losing their sight from DME."

RZ402-101 is a first-in-human Phase 1a, single-center, randomized, double-blind, placebo-controlled, single ascending dose (SAD) study in healthy adult volunteers. The study objectives were to characterize the safety profile and pharmacokinetics of RZ402 administered as single oral doses. The study enrolled 30 subjects in three planned sequential dose-level cohorts of 25 mg, 100 mg, and 250 mg. Within each ten-subject dose cohort, subjects were randomized 8:2 to receive either RZ402 oral solution or matched placebo. After receiving single doses, participants remained in the clinic for seven days for serial pharmacokinetic and safety assessments, before completing two outpatient follow-up visits at study days 14 and 30. Dose advancement proceeded following blinded reviews of safety and pharmacokinetic data from the preceding cohort(s).

Single doses of RZ402 resulted in dose-dependent increases in systemic exposure. Plasma concentrations of RZ402 exceeded the 3.5 ng/mL target concentration that was pharmacologically active in animal models of DME for a 24-hour period after receipt of the 25 mg starting dose, and by > 20 and > 5-fold at maximum concentration and 24 hours after dosing, respectively, at the highest dose tested. Across this dose and exposure range, there were no serious adverse events, adverse drug reactions, or discontinuations due to adverse events, and no imbalance of adverse events between the treatment and placebo control groups. Similarly, regular laboratory, hemodynamic, cardiac, and ophthalmologic safety examinations were unremarkable.

“We are excited to share these encouraging results from the first clinical trial of the systemic delivery of an oral plasma kallikrein inhibitor for the treatment of DME. Given that DME is a consequence of diseased microvascular at the back of the eye, we believe that systemic exposure may be crucial in treating the disease,” said Brian Roberts, M.D., Rezolute’s Senior Vice President and Head of Clinical Development. “It is noteworthy that a single oral dose of RZ402 safely, durably, and substantially exceeded target blood concentrations that have been shown in animal models of DME to reduce retinal inflammation and fluid leakage, the physiological hallmarks of this microvascular disease. These results support the advancement of RZ402 into a Phase 1b multiple ascending dose study, which we expect to initiate in the third quarter of this year.”

About RZ402 and the contact activation kallikrein-kinin system

The contact-activation kallikrein-kinin system promotes increased vascular permeability and inflammation via key downstream mediators, including bradykinin, and activation of the intrinsic pathway of coagulation. Pathophysiologic upregulation of this system has been linked to a variety of diseases which are characterized by vascular dysfunction, including diabetic macular edema.

RZ402 is a selective and potent plasma kallikrein inhibitor (PKI) being developed as a potential oral therapy for the chronic treatment of diabetic macular edema (DME). By inhibiting the formation of kallikrein, RZ402 is designed to block downstream bradykinin production and the pro-inflammatory, pro-coagulant, and fluid-leakage contact-activation cascade.

About Diabetic Macular Edema (DME)

Diabetic retinopathy (DR) affects approximately one third of adults with diabetes and is the leading cause of vision loss in the working age population. DME is a severe vision-threatening complication of DR characterized by swelling of the retina and thickening of the macula, the part of the eye that is responsible for high-resolution vision. Anti-vascular growth factor (anti-VEGF) injections into the eye are the current standard of care for DME, requiring continued administration over long periods of time to preserve vision. Due to their invasive route of administration and occasional serious side effects, there is a tendency to delay treatment until later in the disease course, and long-term compliance with eye injection regimens can be difficult for patients. Coupled with inadequate responsiveness in some patients, this leads to overall undertreatment and suboptimal vision outcomes in DME patients.

About Rezolute, Inc.

Rezolute is advancing novel therapies for diseases caused by chronic glucose imbalance. The Company's lead clinical asset, RZ358, is in Phase 2b development for treatment of congenital hyperinsulinism (CHI), a rare pediatric endocrine disorder. The Company is also developing RZ402, an orally available plasma kallikrein inhibitor, for the treatment of diabetic macular edema. For more information, visit www.rezolutebio.com or follow us on Twitter.

Forward-Looking Statements

This release, like many written and oral communications presented by Rezolute, Inc. 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 the Company, 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. 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.

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