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Rezolute Announces Initiation of Phase 1 Study of RZ402, an Oral Plasma Kallikrein Inhibitor for the Treatment of Diabetic Macular Edema

RZ402 is a plasma kallikrein inhibitor being investigated as a potential once-daily, oral therapy for DME

Trial initiation marks expansion of the Company's pipeline to a second clinical-stage program, reinforcing its commitment to advancing novel therapies for patients with serious unmet metabolic diseases

REDWOOD CITY, Calif., Jan. 12, 2021 (GLOBE NEWSWIRE) -- **Rezolute, Inc.** (Nasdaq: RZLT), today announced the initiation of dosing in a Phase 1 first-in-human clinical study of RZ402, an investigational oral plasma kallikrein inhibitor (PKI), for the treatment of diabetic macular edema (DME). The study (RZ402-101) is a single-center, randomized, double-blind, placebo-controlled, single ascending dose study to evaluate the safety, tolerability, and pharmacokinetics of RZ402 in healthy adult volunteers. The Company expects to complete the study in the first half of 2021.

"With the initiation of our clinical trial with RZ402 we now have a second program in clinical development, further highlighting our commitment to build a broad pipeline of novel and targeted therapies with the potential to change the lives of patients suffering from serious metabolic diseases," said Brian Roberts, M.D., senior vice president and head of clinical development at Rezolute.

Dr. Roberts continued, "Plasma kallikrein is a validated therapeutic target in hereditary angioedema, and we believe it has important potential therapeutic implications in other conditions characterized by vascular leakage, such as occurs at the retinal microvasculature in DME. Clinical trials investigating intravitreal injections of PKIs in DME have highlighted the potential of this therapeutic target, and we are uniquely positioned to favorably shift the clinical development and treatment paradigm in DME with RZ402's novel oral dosing. Oral-systemic administration of RZ402 may optimize kallikrein inhibitor levels at the retinal microvasculature, while providing patients with the comfort and convenience of a once-daily, oral treatment."

About Diabetic Macular Edema (DME)

Diabetic retinopathy (DR) affects approximately one third of adults with diabetes and can lead to loss of vision. 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 sharp, straight ahead vision. Anti-vascular growth factor (anti-VEGF) injections into the

eye are the current standard of care for DME, but require frequent treatment 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 a significant percentage of patients, this leads to overall undertreatment and suboptimal vision outcomes in DME patients.

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 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 RZ402-101

RZ402-101 is a first-in-human Phase 1, single-center, randomized, double-blind, placebo-controlled, single ascending dose study in healthy adult volunteers. The objectives of the study are to characterize the safety profile (including maximum tolerated dose) and pharmacokinetics of RZ402 administered as single oral doses in sequential ascending dose fashion. The study will be conducted in a minimum of 30 subjects in at least three planned sequential dose-level cohorts comprising ten subjects per cohort. Within each dose cohort, subjects will be randomized in an 8:2 ratio to receive either RZ402 oral solution or matched placebo. After receiving single blinded doses, participants will remain in-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 will proceed in staggered fashion every two weeks as appropriate, following blinded reviews of data from the preceding cohort(s). The study is expected to conclude in the first half of 2021.

About Rezolute, Inc.

Rezolute is advancing targeted therapies for rare, metabolic, and life-threatening diseases. Its lead clinical asset, RZ358, is in Phase 2b development as a potential treatment for congenital hyperinsulinism (HI), a rare pediatric endocrine disorder. Its pipeline also includes RZ402, an orally available plasma kallikrein inhibitor in Phase 1 development as a potential treatment for 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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