# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION
**WASHINGTON, DC 20549**

# FORM 8-K

**CURRENT REPORT**
**Pursuant to Section 13 or 15(d) of the**
**Securities Exchange Act of 1934**

**Date of report (Date of earliest event reported): February 22, 2022**

## REZOLUTE, INC.
**(Exact Name of Registrant as Specified in Charter)**

| Nevada | 001-39683 | 27-3440894 |
|---|---|---|
| (State or Other Jurisdiction of Incorporation) | (Commission File Number) | (I.R.S. Employer Identification No.) |

**201 Redwood Shores Pkwy, Suite 315, Redwood City, CA 94065**
**(Address of Principal Executive Offices, and Zip Code)**

**650-206-4507**
**Registrant's Telephone Number, Including Area Code**

**Not Applicable**
**(Former Name or Former Address, if Changed Since Last Report)**

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (*see* General Instruction A.2. below):

☐ Written communication pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communication pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communication pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

| Title of each class | Trading Symbol(s) | Name of each exchange on which registered |
|---|---|---|
| **Common Stock, par value $0.001 per share** | **RZLT** | **Nasdaq Capital Market** |

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (17 CFR §230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (17 CFR §240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

**Item 7.01. Regulation FD Disclosure.**

On February 22, 2022, Rezolute, Inc. issued a press release announcing positive topline results from its Phase 1b clinical study of RZ402. A copy of this press release is attached hereto as Exhibit 99.1.

**Item 9.01 Financial Statements and Exhibits.**

(d) *Exhibits*.

| Exhibit No. | Description |
|---|---|
| 99.1 | Press Release, dated February 22, 2022 |
| 104 | Cover Page Interactive Data File (embedded as Inline XBRL document) |

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

**REZOLUTE, INC.**

DATE: February 22, 2022

By: */s/ Nevan Elam*
Nevan Elam
Chief Executive Officer

**EXHIBIT INDEX**

| Exhibit No. | Description |
|---|---|
| 99.1 | Press Release, dated February 22, 2022 |
| 104 | Cover Page Interactive Data File (embedded as Inline XBRL document) |

**Exhibit 99.1**

**Rezolute Announces Positive Study Results for RZ402, an oral PKI being developed for DME**

Phase 2 proof-of-concept study anticipated in 2H 2022

**REDWOOD CITY, Calif., Feb. 22, 2022 (GLOBE NEWSWIRE)** -- Rezolute, Inc. (Nasdaq: RZLT), a clinical-stage biopharmaceutical company developing transformative therapies for metabolic diseases associated with chronic glucose imbalance, today announced topline data from its Phase 1b multiple-ascending dose (MAD) study of RZ402, a plasma kallikrein inhibitor (PKI) being developed as an oral therapy for the treatment of diabetic macular edema (DME). Results of the MAD study further validate and support the potential for once daily oral dosing and enable the company to initiate a Phase 2 proof-of-concept study later this year.

The recently completed MAD study showed dose-dependent increases in systemic exposures, with repeat-dosing to steady-state resulting in the highest concentrations of RZ402 explored to date, exceeding 200 ng/mL and 50 ng/mL at peak and 24-hour trough, respectively. Following the precedent established in systemic deliveries of PKIs in vascular diseases such as hereditary angioedema, steady-state plasma kallikrein activity in human plasma was measured on Day 14 as a biomarker of RZ402 target engagement. Daily dosing with RZ402 inhibited plasma kallikrein in a dose and concentration-dependent manner ($r=0.74$; $p < 0.001$). Given that the in-vivo $EC_{90}$ for RZ402 in animal models of DME is ~6 ng/mL, the results at both peak and 24-hour trough substantially exceeded target concentrations based on a combination of in-vitro and in-vivo profiling.

“As an oral therapy, RZ402 has the potential to substantially alter the treatment paradigm by providing an alternative that is less invasive for the patient and may lead to better clinical outcomes by getting patients on therapy sooner. By doing so, RZ402 may be able to prevent disease progression and treat vision loss for those suffering with DME,” said, Raj Agrawal, MD, Vice President at Rezolute. Dr. Agrawal continued, “There is a serious unmet need to treat DME patients, as anti-VEGF intraocular injections are a burdensome route of administration and ineffective in approximately half of all DME patients.”

The MAD study results showed that RZ402 was generally safe and well-tolerated, including at higher doses than previously tested in the SAD study. There were no serious adverse events, adverse drug reactions or identified risks.

“We are pleased to see that RZ402 benchmarks well in the human plasma kallikrein activity assay used routinely as an activity marker in hereditary angioedema,” said Brian Roberts, MD, Senior Vice President and Head of Clinical Development at Rezolute. Dr. Roberts continued, “We have consistently observed that RZ402 is even more potent at inhibiting kallikrein and bradykinin in vivo, which has translated to substantial reductions in vascular leakage in animal models of DME at low RZ402 concentrations, and suggests the possibility of unique compound properties that enhance compound activity at the vascular site of action. By safely exceeding these target concentrations by up to 30-fold in this study, we are encouraged and excited by the possibility of better efficacy in treating diseases associated with excessive kallikrein-kinin activity, including DME.”

Rezolute plans to present full study results at a medical conference this year.

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**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 RZ402-102**

RZ402-102 was a Phase 1, single-center, randomized, double-blind, placebo-controlled, multiple ascending dose study in healthy adult volunteers. The objectives of the study were to characterize the repeat-dose safety profile (including maximum tolerated dose) and pharmacokinetics of RZ402 administered as daily oral doses for 2 weeks. The study was conducted in a minimum of 40 subjects in four planned sequential ascending dose-level cohorts comprising ten subjects per cohort. Within each dose cohort, subjects were randomized in an 8:2 ratio to receive either RZ402 oral solution or matched placebo. Participants remained in-clinic throughout the 2-week dosing period for serial pharmacokinetic and safety assessments, before completing an outpatient follow-up visit at study day 28. Blood biomarkers of target engagement (kallikrein activity) were explored as a systemic surrogate for DME, using a precedent from studies of kallikrein inhibitors in a systemic vascular leakage syndrome (hereditary angioedema). The study concluded in the first quarter of 2022.

**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.

In 2021, Rezolute reported topline results from the first-in-human Phase 1a single-ascending dose study, demonstrating that RZ402 was generally safe and well-tolerated at all doses tested, without dose-limiting toxicities. In animal studies, RZ402 was shown to suppress vascular leakage (up to 90%) and retinal leukostasis (by > 90%).

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**About Rezolute, Inc.**

Rezolute is developing transformative therapies for metabolic diseases related to 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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