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): June 27, 2023

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.)

275 Shoreline Drive, Suite 500, 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 June 27, 2023, Rezolute, Inc. (the "Company") issued a press release announcing an update to the Company's clinical programs. A copy of the press release is attached as Exhibit 99.1 to this Current Report on Form 8-K and is hereby incorporated by reference.

The information in Item 7.01 of this Current Report on Form 8-K, including the attached Exhibit 99.1 is being furnished pursuant to Item 7.01 and shall not be deemed to be "filed" for any purpose of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of such Section, and shall not be deemed to be incorporated by reference into any of the Company's filings under the Securities Act of 1933, as amended, or the Exchange Act, whether made before or after the date hereof and regardless of any general incorporation language in such filings, except to the extent expressly set forth by specific reference in such a filing.

Item 8.01. Other Events.

As set forth in Item 7.01 of this Current Report on Form 8-K, the Company is providing an update on its clinical program for congenital hyperinsulinism ("congenital HI").

Summary

In the fourth quarter of 2023, the Company plans to initiate a pivotal Phase 3 clinical study of RZ358 for the treatment of hypoglycemia in participants with congenital HI ("sunRIZE"). The sunRIZE study is a randomized, double-blind, placebo-controlled, parallel arm evaluation of RZ358 in participants with congenital HI who are not adequately responding to standard of care medical therapies. Topline results from the study are anticipated to be available in the first half of 2025. As of March 31, 2023, the Company had $129M in cash and cash equivalents with sufficient capital to sustain operations through the third quarter of 2025. The Phase 3 study follows the Company's multinational Phase 2b study ("RIZE") conducted in participants 2 years of age and older who were failing medical therapies. The RIZE study demonstrated that RZ358 was generally safe and well-

tolerated, as well as highly effective in improving hypoglycemia.

The Company has concluded its pre-Phase 3 regulatory and scientific advice meetings with health authorities outside of the US and has reached agreement on the design of the Phase 3 study that will include participants 3 months of age and older. In the US, the Company has had similar interactions with the US Food and Drug Administration ("FDA") culminating in a meeting held with the agency on May 24, 2023(as confirmed by meeting minutes received by the Company from FDA on June 22, 2023),and FDA has maintained an existing age restriction of 12 years of age and older on RZ358 clinical studies, and imposed dose level restrictions based on historical rat toxicology findings. The Company believes that the FDA restrictions make it infeasible to include the US in the Phase 3 study at this time, particularly given that the pediatric population with congenital HI has the greatest therapeutic need. The Company is evaluating potential nonclinical studies to address FDA's concerns in parallel with the initiation and advancement of the Phase 3 study outside of the US.

Regulatory Status

Toxicology studies in rats and monkeys were conducted as part of the early RZ358 development program and in these studies, rats demonstrated a microvascular liver injury at potentially clinically relevant doses and exposures ("rat findings"). However, there were no adverse liver findings in monkeys at dose levels that were more than 10 times higher than doses that were toxic in rats, and more than 4 times higher than human doses evaluated in clinical studies. Based on the absence of liver toxicity in monkeys and the lack of adverse liver findings in closely monitored human trials, the Company believes that the toxicity is unique to rats and unlikely relevant to humans.

As is customary in pediatric drug development, there is a progression of the inclusion of younger participants as a program advances through different stages and continues to demonstrate a good safety profile and a prospect of benefit for children based on previous stages. After the completion of Phase 1 adult healthy volunteer studies for RZ358, Phase 2a single-dose proof of concept studies ("Phase 2a") were conducted in participants with congenital HI who were 12 years of age and older in countries governed by regulatory authorities in the European Union and elsewhere in Europe (collectively, "European Authorities"). In the US, FDA restricted enrollment in Phase 2a to participants 18 years of age and older and, based on the rat findings, imposed a human drug exposure limit equating to repeat doses of approximately 3 mg/kg per week ("exposure cap").

Subsequently, in the RIZE study European Authorities and other regulatory bodies continued the expected downward age progression, lowering the age for study participants down from 12 years of age to 2 years of age and older. At the start of the RIZE study the clinical program in the US remained under the 18 years of age and older restriction as well as the exposure cap. However, in the first half of 2020, while the RIZE study was underway, the Company reached agreement with FDA to proceed with the RIZE study in the US at all dose levels (no exposure cap) and in younger participants (ages 12 and older). Following these developments, the study protocol was harmonized globally, other than a regional difference in the minimum permitted age (12 years and older in the US versus 2 years and older in all other geographies).

After the completion of the RIZE study, in the second half of 2022 and the first half of 2023, the Company conducted scientific advice meetings with European Authorities which resulted in alignment with the Company's proposed Phase 3 program including overall study design, dosing regimen, endpoints, sample size and patient population. Notably, with all available nonclinical (including the rat findings) and clinical information under review, European Authorities aligned with a further downward age progression whereby participants 3 months of age and older will be permitted to be enrolled in the Phase 3 study.

Prior to engaging FDA on Phase 3 planning in the US, the Company began interacting with the agency in the second half of 2022 to further liberalize the age restriction to achieve alignment with the parameters established by the European Authorities in the RIZE study. Over the course of these post-RIZE regulatory interactions with FDA, the agency revisited prior concerns regarding the rat findings and, despite the absence of new clinical or nonclinical data (other than the RIZE data), the agency decided to maintain the age restriction of 12 years and above and re-imposed the previous exposure cap which had been removed during the RIZE study (collectively, "New Restrictions"). In the second half of 2022 and the first half of 2023, the Company interacted with FDA to resolve the New Restrictions, particularly in the context of the advancement of the clinical program in the rest of the world. Nonetheless, FDA affirmed the New Restrictions at a meeting held with the Company on May 24, 2023.

The Company and FDA have discussed potential solutions that could enable removal of the New Restrictions and as a result, the Company is evaluating nonclinical studies to address FDA's concerns in parallel with the initiation and advancement of the sunRIZE study outside of the US. Assuming that the Company can conduct the appropriate nonclinical studies and that the results adequately address FDA's concerns, the Company believes that the New Restrictions could be removed. If the Company is unable to satisfy FDA's nonclinical concerns, the Company's development plans for congenital HI in the US could be negatively impacted.

Phase 3: "sunRIZE" study

The sunRIZE study will evaluate the safety and efficacy of RZ358 in participants with congenital HI who are unable to achieve control of low blood sugars (<70 mg/dL) with available medical therapies ("hypoglycemia"). The study will determine the ability of RZ358 to correct hypoglycemia as assessed by (i) hypoglycemia events using self-monitored blood glucose ("SMBG") and (ii) time in hypoglycemia using continuous glucose monitoring ("CGM") over 24 weeks of treatment. The study will also measure the levels of RZ358 and its effects on other important blood and clinical markers of hypoglycemia, as well as quality of life measures. The primary and key secondary efficacy endpoints are the following:

Primary efficacy endpoint:

- Change in average weekly occurrence of hypoglycemia events as measured by SMBG after 24 weeks

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Key secondary efficacy endpoint:

- Change in average daily percent time in hypoglycemia as measured by CGM after 24 weeks

The study will enroll approximately 56 participants between 3 months and 45 years of age. Participants between 1 and 45 years of age (approximately 48 participants) will be enrolled in a randomized, double-blind, placebo-controlled fashion to receive RZ358 or placebo at dose levels of 5 or 10 mg/kg while on standard of care. Infant participants between 3 months and 1 year of age (approximately 8 participants) will be enrolled in open label fashion to receive RZ358 at a starting dose level of 5 mg/kg, which may be increased to 10 mg/kg at the discretion of the investigator. Participants will receive RZ358 as an intravenous infusion every 2 weeks over an initial 4-week loading period (3 doses), followed by monthly doses over an additional 16-week maintenance period (4 doses), for a total of 7 doses over the total 24-week treatment period. Following the study period, participants may proceed into an open-label extension program where investigators shall be permitted to: (i) adjust the dose between 5 and 10 mg/kg; (ii) adjust the dosing frequency between 2 and 4 weeks; and (iii) wean or stop other background hypoglycemia therapies.

In summary, the study will be comprised of the following treatment groups:

- Participants ≥1 year old: 5 mg/kg (n = 16)

- Participants ≥1 year old: 10 mg/kg (n = 16)
- Participants ≥1 year old: placebo (n = 16)
- Infant Participants: starting at 5 mg/kg (n = 8)

Update on the Commercial Opportunity for Congenital HI

As the Company initiates the sunRIZE study in the fourth quarter of 2023, it recognizes the importance of advancing commercial readiness. Congenital HI, like many ultra-rare conditions, lacks robust epidemiology studies that accurately characterize the disease. Following RIZE, Rezolute has made a significant investment to understand the patient journey from diagnosis to treatment and to characterize the impact of current standard of care practices on patient outcomes. The Company has conducted primary research by engaging with patients, key opinion leaders, payers, and others to understand the significant unmet need and economic burden to patients, their families, and the healthcare system. The Company has also engaged specialized third parties to conduct claims-based market assessments to better characterize and quantify the number of individuals who live with congenital HI in primary markets. This body of work has been further validated by third party epidemiological analysis as well as the Company's engagement with centers of excellence and international advocacy organizations. Collectively, the output from this research provides increased certainty regarding certain fundamental characteristics of the disease:

- The estimated worldwide incidence of congenital HI is 1 in every 28,000 live births.[1]
- The average duration of therapy for an individual diagnosed with congenital HI is 25 years, particularly for those that are non-responsive to diazoxide.[2]
- Based on the live birth incidence and the average duration of therapy, the Company believes that the prevalence of congenital HI exceeds 10,000 individuals in primary markets, including approximately 3,500 individuals in each of the US and Western Europe. Importantly, the Company believes that more than half of these individuals lack adequate treatment options to control their hypoglycemia.

(1) Congenital Hyperinsulinism International (https://congenitalhi.org/congenital-hyperinsulinism/#overview)

(2) Clearview Healthcare Partners 2023 Commercial Assessment

Item 9.01 Financial Statements and Exhibits

(d) Exhibits.

Exhibit	Description
99.1	Press Release announcing an update to the Company's clinical programs dated June 27, 2023
104	Cover Page Interactive Data File (formatted as inline XBRL)

Cautionary Note Regarding *Forward-Looking Statements*

Certain statements made herein that are not historical facts are *forward-looking statements* for purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995. *Forward looking statements* generally are accompanied by words such as "believe," "may," "will," "estimate," "continue," "anticipate," "intend," "expect," "should," "would," "plan," "predict," "potential," "seem," "seek," "future," "outlook" and similar expressions that predict or indicate future events or trends or that are not statements of historical matters. These *forward-looking statements* include, but are not limited to, statements regarding future events and results, clinical trial plans and the locations and timing of such clinical trials, our ability to address FDA's exposure cap and other concerns through additional non clinical studies, our ability to conduct the sunRIZE study in Europe and elsewhere in the world, the design of the sunRize study, the timing of patient enrollment in the sunRize study, any potential outcomes of the sunRize study, our ability to attract patients to enroll into the sunRize study, potential dosing levels in the sunRize study, and the scope of the potential commercial opportunity for congenital HI and our ability to commercialize our therapies.

These statements are based on the current expectations of the Company and are not predictions of actual performance, and are not intended to serve as, and must not be relied on, by any investor as a guarantee, prediction, definitive statement, or an assurance, of fact or probability. These statements are only current predictions or expectations, and are subject to known and unknown risks, uncertainties and other factors which may be beyond our control. Actual events and circumstances are difficult or impossible to predict, and these risks and uncertainties may cause our or our industry's results, performance, or achievements to be materially different from those anticipated by these *forward-looking statements*. A further description of risks and uncertainties can be found in the sections captioned "Risk Factors" in our most recent annual report on Form 10-K, subsequent quarterly reports on Form 10-Q, and other filings with or submissions to, the U.S. Securities and Exchange Commission, which are available at https://www.sec.gov/. Except as otherwise required by law, the Company disclaims any intention or obligation to update or revise any *forward-looking statements*, which speak only as of the date they were made, whether as a result of new information, future events, or circumstances or otherwise.

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: June 27, 2023

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

Exhibit 99.1

Rezolute to Initiate a Pivotal Phase 3 Study of RZ358 in Participants 3 Months of Age and Older with Congenital Hyperinsulinism

Study to be initiated in Europe and other ex-US geographies in Q4 2023, with topline results expected 1H 2025

Conference call scheduled today at 4:30 p.m. ET

REDWOOD CITY, Calif., June 27, 2023 (GLOBE NEWSWIRE) -- Rezolute, Inc. (Nasdaq: RZLT), a clinical-stage biopharmaceutical company dedicated to developing transformative therapies with the potential to disrupt current treatment paradigms for devastating metabolic diseases, today provided an update on its clinical development plans for RZ358, the Company's product candidate for congenital hyperinsulinism (congenital HI). Rezolute plans to initiate sunRIZE, a pivotal Phase 3 clinical study of RZ358 in Europe and other geographies outside the US in Q4 2023, with topline results anticipated in the first half of 2025. The sunRIZE study is a randomized, double-blind, placebo-controlled, parallel arm evaluation of RZ358 in participants with congenital HI who are not adequately responding to standard of care medical therapies. The Phase 3 study follows the Company's successful Phase 2b RIZE study which demonstrated that RZ358 was generally safe and well-tolerated, as well as highly effective in improving hypoglycemia in participants who were failing available medical therapies.

The Company has concluded its pre-Phase 3 regulatory and scientific advice meetings with European health authorities and has reached agreement on the sunRIZE study design, that will include participants 3 months of age and older. In the US, the Company has had similar interactions with the US Food and Drug Administration (FDA), culminating in a meeting held with the agency on May 24, 2023, and FDA has maintained an existing age restriction of 12 years and older on RZ358 clinical studies and implemented dose level restrictions for RZ358 based on historical rat toxicology findings. The FDA restrictions make it infeasible to include the US in the sunRIZE study at this time, particularly given that the pediatric population with congenital HI has the greatest therapeutic need. The Company is evaluating potential nonclinical studies to address FDA's concerns in parallel with the initiation and advancement of sunRIZE outside of the US.

Nevan Charles Elam, Rezolute's Founder and Chief Executive Officer, stated, "We believe that RZ358 has tremendous potential to fulfill a significant unmet need for patients and families living with congenital HI around the world and we are delighted to have alignment for sunRIZE with regulators outside of the US. We believe that there may be a path forward to address FDA's nonclinical concerns and ensure that patients in the US have access to RZ358 should the therapy continue to demonstrate good safety and efficacy and be eligible for regulatory approval."

More information on sunRIZE and related regulatory interactions can be found in a filing made today on Form 8-K filed with the US Securities and Exchange Commission.

Conference Call Information

Rezolute will host a conference call today, June 27, 2023, at 4:30 p.m. EDT. To access the conference call, dial 1-877-270-2148 from the U.S. and Canada or 1-412-902-6510 internationally and ask to be joined into the Rezolute call. The live audio webcast of the call will be available under " Events" in the Investor section of the Company's website at https://ir.rezolutebio.com/news-events/ir-calendar.

About Congenital Hyperinsulinism (HI)

Congenital HI is the most common cause of recurrent and persistent hypoglycemia in children. Patients with congenital HI typically present with with signs or symptoms of hypoglycemia within the first month of life. These episodes can result in significant brain injury and death if not recognized and managed appropriately. Additionally, recurrent, or cumulative, hypoglycemia can lead to progressive and irreversible damage over time, including serious and devastating brain injury, seizures, neuro-developmental problems, feeding difficulties, and significant impact on patient and family quality of life. The two most-commonly used long-term medications, diazoxide and somatostatin analogs, are not Food and Drug Administration (FDA) approved for all forms of this condition and often are ineffective or have intolerable side effects. In cases of congenital HI that are unresponsive to medical management, surgical removal of the pancreas may be required. In those with diffuse congenital HI where the whole pancreas is affected, a near-total pancreatectomy can be undertaken, although about half of these children will continue to have hypoglycemia and require medical treatment for congenital HI.

About RZ358

RZ358 is a human monoclonal antibody that binds to a unique allosteric site on insulin receptors in the liver, fat, and muscle. The antibody counteracts the effects of elevated insulin in the body by modifying insulin's binding, signaling, and activity to maintain glucose levels in a normal range. Rezolute believes that RZ358 is ideally suited as a potential therapy for congenital hyperinsulinism (HI) and other conditions characterized by excessive insulin levels. As RZ358 acts downstream from the beta cells, it has the potential to be universally effective at treating congenital HI, regardless of the causative genetic defect.

RZ358 received Orphan Drug Designation in the United States and European Union as well as Pediatric Rare Disease Designation in the US.

About Rezolute, Inc.

Rezolute strives to disrupt current treatment paradigms by developing transformative therapies for devastating rare and chronic metabolic diseases. Its novel therapies hold the potential to both significantly improve outcomes and reduce the treatment burden for patients, the treating physician, and the healthcare system. Patient, clinician, and advocate voices are integrated in the Company's drug development process, enabling Rezolute to boldly address a range of severe conditions. Rezolute is steadfast in its mission to create profound, positive, and lasting impact on patients' lives. The Company's lead clinical asset, RZ358, is in late-stage development for the treatment of congenital hyperinsulinism, a rare pediatric endocrine disorder. Rezolute 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 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 future events and results, clinical trial plans and the locations of such clinical trials, the timing of the release of Phase 3 clinical trial results, our ability to address FDA's concerns through additional nonclinical studies, our ability to conduct the Phase 3 study in Europe and throughout the world, the effectiveness or future effectiveness of RZ358. 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 Rezolute's 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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