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): May 2, 2022 (May 1, 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 May 1, 2022, Rezolute, Inc. (the "Company") issued a press release announcing the pricing of an underwritten registered direct offering of an aggregate of 18,026,315 shares of its common stock at a public offering price of $3.80 per share and, to certain investors, pre-funded warrants to purchase up to 12,921,055 shares of its common stock at a public offering price of $3.799 per pre-funded warrant, which represents the per share public offering price for the common stock less the $0.001 per share exercise price for each pre-funded warrant, and a concurrent private placement offering of pre-funded warrants to purchase up to 3,263,157 shares of the Company's common stock at the same price as the public offering price of the pre-funded warrants in the underwritten registered direct offering. Gross proceeds from the underwritten registered direct offering and the concurrent private placement offering before deducting underwriting discounts and commissions, placement agent commissions and other offering expenses are expected to be approximately $130 million. The text of the press release is included as Exhibit 99.1 to this Form 8-K and is incorporated herein by reference.

In addition, on May 1, 2022, the Company issued a press release announcing positive data from its Phase 2b (RIZE) study of RZ358 in patients with congenital hyperinsulinism. The text of the press release is included as Exhibit 99.2 to this Form 8-K and is incorporated herein by reference.

Item 8.01. Other Events.

On May 1, 2022, the Company made available an updated Corporate Presentation on the Investor Relations page of its website, which will be used at investor and other

meetings. A copy of the Corporate Presentation is attached hereto as Exhibit 99.3 to this Current Report on Form 8-K and is incorporated herein by reference. The Company does not undertake to update this presentation.

Item 9.01 Financial Statements and Exhibits.

(d) *Exhibits*.

Exhibit No.	Description
99.1	Rezolute, Inc. Press Release announcing pricing of the offerings, dated May 1, 2022
99.2	Rezolute, Inc. Press Release for study results, dated May 1, 2022
99.3	Rezolute, Inc. Corporate Presentation, May 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: May 2, 2022

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

Rezolute, Inc. Announces Aggregate $130 Million Registered Direct Offering and Concurrent Private Placement Priced At-the-Market

REDWOOD CITY, Calif., May 1, 2022 (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 announced the pricing of an underwritten registered direct offering of an aggregate of 18,026,315 shares of its common stock at an offering price of $3.80 per share, and, to certain investors in lieu of common stock, pre-funded warrants to purchase up to 12,921,055 shares of common stock at an offering price of $3.799 per pre-funded warrant, which represents the per share offering price for the common stock less the $0.001 per share exercise price for each pre-funded warrant. Certain of the pre-funded warrants offered to investors are only exercisable upon receipt of stockholder approval of an increase in the authorized shares of Rezolute's common stock which Rezolute will first seek to obtain at an annual meeting of stockholders to be held by June 30, 2022, and the shares of common stock underlying such pre-funded warrants are not being registered under the Securities Act of 1933, as amended (the "Securities Act"). Concurrent with the underwritten registered direct offering, certain existing investors agreed to purchase pre-funded warrants to purchase up to 3,263,157 shares of common stock in a private placement at the same offering price as the offering price of the pre-funded warrants offered in the underwritten registered direct offering. Gross proceeds from the underwritten registered direct offering and the concurrent private placement before deducting underwriting discounts and commissions, placement agent fees and other offering expenses are expected to be approximately $130 million. The pre-funded warrants issued in the private placement and the shares of our common stock issuable upon exercise of such pre-funded warrants are not being registered under the Securities Act, but are being offered pursuant to the exemption provided in Section 4(a)(2) under the Securities Act and Rule 506(b) promulgated thereunder.

All of the shares of common stock and pre-funded warrants sold in the underwritten registered direct offering and the concurrent private placement were sold by Rezolute. The closing of the offerings is expected to occur on or about May 4, 2022, subject to the satisfaction of customary closing conditions. The closing of the underwritten registered direct offering and the closing of the concurrent private placement are not contingent upon each other.

Rezolute intends to use the net proceeds from these offeringsto fund the continued activities for development of RZ358 for Congenital Hyperinsulinism and RZ402 for Diabetic Macular Edema and other pipeline development, working capital, and general corporate purposes.

Jefferies is acting as the lead book-running manager, Cantor is acting as passive bookrunner, Canaccord Genuity and JMP Securities, A Citizens Company, are acting as co-lead managers and H.C. Wainwright & Co. is acting as co-manager for the underwritten registered direct offering. Jefferies is acting as lead placement agent, Cantor is acting as placement agent, and Canaccord Genuity, JMP Securities, A Citizens Company, and H.C. Wainwright & Co. are acting as co-placement agents for the concurrent private placement.

The underwritten registered direct offering of shares of common stock and pre-funded warrants (but not the pre-funded warrants to be issued in the concurrent private placement and the shares of common stock issuable thereunder) is being made pursuant to an effective shelf registration statement on Form S-3 (File No. 333-251498) previously filed with the U.S. Securities and Exchange Commission (the "SEC") and declared effective by the SEC on June 23, 2021. Such securities are being offered only by means of a prospectus. A final prospectus supplement and the accompanying prospectus relating to and describing the terms of the underwritten registered direct offering will be filed with the SEC, and will be available on the SEC's website at http://www.sec.gov; by contacting Jefferies LLC, Attention: Equity Syndicate Prospectus Department, 520 Madison Avenue, New York, NY 10022, by telephone at (877) 821-7388, or by email at prospectus_department@jefferies.com.

This press release shall not constitute an offer to sell or the solicitation of an offer to buy any of the securities described herein, nor shall there be any sale of these securities in any state or jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state or jurisdiction.

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 statements include, but are not limited to, the offerings. 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, but are not limited to, market risks and uncertainties, the satisfaction of customary closing conditions for an offering of securities, and 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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Exhibit 99.2

Rezolute Announces Positive Data from its Phase 2b (RIZE) Study of RZ358 in Patients with Congenital Hyperinsulinism

Results Presented Today at the Pediatric Endocrine Society's 2022 Annual Meeting

- *Highly significant ~75% reduction in hypoglycemia events at anticipated therapeutic doses*
- *≥50% improvement in hypoglycemia in 100% of patients in high-dose cohort, with no adverse drug reactions or clinically significant hyperglycemia*
- *Study exceeded expectations for correction of hypoglycemia across multiple metrics, including hypoglycemia events and time in hypoglycemia*
- *Predictable and dose-dependent exposures with a clear dose-response*
- *Good safety and tolerability across all doses with no study discontinuations or adverse drug reactions*
- *Results are Phase-3 enabling and demonstrate the potential for RZ358 to be used as a monotherapy as well as a potential universal therapy for all forms of hyperinsulinism*
- *Company hosting Analyst and Investor Conference Call, Sunday, May 1 at 2:30 p.m. ET*

REDWOOD CITY, Calif., May 1, 2022 (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 announced positive results from its Phase 2b RIZE study of RZ358 in patients with congenital hyperinsulinism (HI), which were unveiled today in a late-breaking oral presentation at the Pediatric Endocrine Society 2022 Annual Meeting. The study exceeded expectations for correction of hypoglycemia, including a highly significant reduction of ~75% in hypoglycemia events by blood glucometer (BGM) as well as time in hypoglycemia by continuous glucose monitoring (CGM).

"Patients with congenital hyperinsulinism often have continued hypoglycemia in spite of available therapies, as has been clearly demonstrated in the RIZE study," said Dr. Paul Thornton, a Pediatric Endocrinologist at Cook Children's Hospital. Dr. Thornton continued, "The magnitude of improvement in hypoglycemia in this study demonstrates the potential for RZ358 to become a much-needed therapy for treating congenital hyperinsulinism."

The RIZE study enrolled a diverse group of congenital HI patients with an average age of 6.5 years, including 16 patients between the ages of 2 and 6 years old, and with substantial continued hypoglycemia despite being on currently available therapies. During a robust screening and baseline run-in period on stable standard of care, the average RIZE study patient was hypoglycemic for 23% of their overall monitored time on a CGM, corroborated by having an average of 16 hypoglycemia events per week by point-of-care blood glucometer. There was also a significant amount of severe hypoglycemia at baseline (defined by glucose values below 50 mg/dL). RZ358 was administered via a thirty-minute intravenous infusion every other week for an 8-week treatment period in four sequential cohorts ranging from 3 to 9 mg/kg.

RZ358 led to a better than 50% reduction from baseline in overall (<70 mg/dL) and severe (<50 mg/dL) hypoglycemia events (by BGM) and time in hypoglycemia (by CGM) in the pooled group of patients across all doses (see Table 1). A larger magnitude of improvement of ~75% was seen at the anticipated therapeutic doses of 6 mg/kg and 9 mg/kg.

The blood concentrations of RZ358 were highly predictable and dose-proportional, with no apparent impact from factors relevant to this patient population, such as age distribution, food aversions, or gastrointestinal absorption and tolerability. A clear dose and exposure response was observed with RZ358.

A safety review committee comprised of three expert investigators in congenital HI met over the course of the study to review and confirm safety prior to dose escalation. RZ358 was generally safe and well-tolerated across the studied dose and age range. There were no adverse drug reactions, study discontinuations, or occurrences of clinically significant hyperglycemia. The observed blood levels of RZ358 were well below levels that were safely tested in long term toxicology studies in non-human primates.

Table 1: Mean Hypoglycemia Time (by CGM) and Events (by BGM)

Mean (Range)	RZ358 3 mg/kg (n=4) #	RZ358 6 mg/kg (n=8)	RZ358 9 mg/kg (n=7)^	RZ358 Titrate (3-9 mg/kg) (n=3)	RZ358 Total Pooled (n=22)
Time in Hypoglycemia (<70 mg/dL) by CGM (%)					
Baseline	16.1	22.2	26.5	29.1	23.3 (6-86)
End of Treatment	10.5	9.2	9.4	15.8	10.4 (0.3-33)
% Change from BL (p-value)	***-35% (p=0.05)***	***-59% (p<0.01)***	***-65% (p=0.07) ^***	***-46% (p=0.10)***	***-56% (p=0.0002)***
Time in Severe Hypoglycemia (<50 mg/dL) by CGM (%)					
Baseline	1.8	5.1	4.3	3.3	3.9 (0-21)
End of Treatment	1.3	1.4	1.7	1.6	1.5 (0-5)
% Change from BL (p-value)	***-25% (NS)***	***-73% (p<0.05)***	***-61% (NS)^***	***-52% (NS)***	***-63% (p=0.01)***
Hypoglycemia Events (<70 mg/dL) by BGM (events/week)					
Baseline	10.1	19.2	16.7	8.0	15.5 (4.5-77.8)
End of Treatment	7.8	9.9	5.3	5.3	7.5 (0-30.3)
% Change from BL (p-value)	***-22% (NS)***	***-48% (p=0.1)***	***- 68% (p<0.01)***	***-34% (p<0.05)***	***-52% (p=0.002)***
Severe Hypoglycemia Events (<50 mg/dL) by BGM (events/week)					
Baseline	1.6	5.5	4.2	0.5	3.8 (0.5-23.8)
End of Treatment	1.5	1.2	1.1	0.4	1.1 (0-5.5)
% Change from BL (p-value)	***-8% (NS)***	***-77% (p=0.1)***	***-74% (p<0.05)***	***-20% (NS)***	***-71% (p=0.01)***

One patient at 3 mg/kg was excluded from the per protocol BGM analyses for failing to meet pre-specified minimum glucometer testing

^ One patient at 9 mg/kg was excluded from the per protocol CGM and BGM analyses for stopping background therapy while on study;
Two 2-year-old patients in 9 mg/kg group wore CGM on the arm which may have impacted their results, but were included in analysis

There was a high patient response rate to RZ358, as shown by the percentage of patients who achieved improvements in hypoglycemia across different clinically relevant thresholds (see Table 2). Notably, at the top dose, all patients achieved at least a 50% improvement, and all but one patient achieved at least a 75% improvement, indicating that the substantial reductions in hypoglycemia observed on average were nearly universally experienced by the wide variety of congenital HI patients across the study.

Table 2: Patient Response Rates to RZ358

Responders N (%)	RZ358 3 mg/kg (n=4)#	RZ358 6 mg/kg (n=8)	RZ358 9 mg/kg (n=7)^	RZ358 Titrate 3-9 mg/kg (n=3)	RZ358 Total (n=22)
≥25% Correction of Hypoglycemia					
Severe (<50 mg/dL)	3 (75%)	7 (88%)	7 (100%)	2 (67%)	19 (86%)
Overall (<70 mg/dL)	3 (75%)	7 (88%)	7 (100%)	3 (100%)	20 (91%)
≥50% Correction of Hypoglycemia					
Severe (<50 mg/dL)	3 (75%)	6 (75%)	7 (100%)	2 (67%)	18 (82%)
Overall (<70 mg/dL)	1 (2%)	7 (88%)	7 (100%)	1 (33%)	16 (73%)
≥75% Correction of Hypoglycemia					
Severe (<50 mg/dL)	1 (25%)	5 (63%)	6 (86%)	2 (67%)	14 (64%)
Overall (<70 mg/dL)	1 (25%)	3 (38%)	5 (71%)	1 (33%)	10 (45%)

“These data show a very pronounced effect of RZ358 in improving hypoglycemia, across a broad range of patient characteristics, thereby demonstrating the potential for RZ358 to be a safe and effective therapy for all forms of congenital HI,” said Dr. Brian Roberts, an Endocrinologist and Senior Vice President of Clinical Development for Rezolute. Dr. Roberts continued, “We are extremely pleased by the results, which we believe enable the continued advancement of RZ358 into a Phase 3 registrational program. We’re also extremely thankful for the contributions of the RIZE Investigators and their study staff, patient advocacy organizations, and particularly the participating patients and families, and we are looking forward to further advancing our combined efforts to find better therapies for congenital hyperinsulinism.”

Julie Raskin, Founding Member and Executive Director of Congenital Hyperinsulinism International, added, “I am happy to learn of the encouraging topline data from the RZ358 Phase 2b study. The current treatment options for many children and adults with congenital HI are very limited and suboptimal, and many with the condition don’t have any treatment option approved for their condition. Babies born with HI typically face long hospital stays and once home, their parents face a dauntingly complicated care regime. The constant activities of feeding and monitoring blood sugar crowd out the typical experiences babies and their families should have, and this pattern can go on for years. The threat of hypoglycemia and the ensuing damage that can occur from it often rules the lives of families who have a child with HI. Novel treatments that keep hypoglycemia at bay are urgently needed. RZ358 gives the HI community hope for a better future.”

Conference Call & Webcast Information

Rezolute management will host a conference call at 2:30 p.m. ET on Sunday, May 1, 2022. Analysts and investors are invited to participate in the conference call by dialing (855) 645-1306 from the U.S. and Canada or (442) 268-1087 internationally and using the conference ID 6063004. The live webcast can be accessed on the investor page of Rezolute’s website at ir.rezolutebio.com. A replay of the webcast will be available on Rezolute’s website approximately two hours after the completion of the event and will be archived for up to 30 days.

About the RIZE Study

RIZE is a Phase 2b, multicenter, open label, repeat-dose study, designed to assess the safety and tolerability, pharmacokinetics, and glycemic efficacy of RZ358 administered bi-monthly for 8 weeks in patients with congenital hyperinsulinism whose hypoglycemia was not adequately controlled on standard of care therapies. A total of 23 patients participated in the study in four sequential dosing cohorts ranging from 3 mg/kg to 9 mg/kg. The effects of RZ358 on hypoglycemia were assessed by continuous glucose monitor (hypoglycemia time) and glucometer self-monitored blood glucose (hypoglycemia events).

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 Congenital Hyperinsulinism (HI)

Congenital HI is the most common cause of recurrent and persistent hypoglycemia in children. It typically presents early in life, with about 60% of infants with congenital HI experiencing 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 mostcommonly 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 Rezolute, Inc.

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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, 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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Forward Looking Statements

Statements in this presentation that are not descriptions of historical facts are forward-looking statements relating to future events, and as such all forward-looking statements are made pursuant to the Securities Litigation Reform Act of 1995. Statements may contain certain forward-looking statements pertaining to future anticipated or projected plans, performance and developments, as well as other statements relating to future operations and results. Any statements in this presentation that are not statements of historical fact may be considered to be forward-looking statements. Words such as "may," "will," "expect," "believe," "anticipate," "estimate," "intends," "goal," "objective," "seek," "attempt," or variations of these or similar words, identify forward-looking statements.

These forward-looking statements by their nature are estimates of future results only and involve substantial risks and uncertainties, including but not limited to risks associated with the uncertainty of clinical trial results, future financial results, additional financing requirements, development of new products, the impact of competitive products or pricing, technological changes, the effect of economic conditions and other uncertainties detailed from time to time in our reports filed with the Securities and Exchange Commission.

Our actual results may differ materially from expectations based on the above factors and other factors more fully described in our public filings with the U.S. Securities and Exchange Commission, which can be reviewed at www.sec.gov.

Targeting Diseases Associated With Chronic Glucose Imbalance

RZ358 for Congenital Hyperinsulinism (HI)

- Congenital HI is over-production of insulin resulting in life-threatening hypoglycemia and neurologic damage
- RZ358 is a fully humanized monoclonal antibody, works downstream from the pancreas, binds to the insulin receptor at a non-competitive site (not an antagonist) and agnostic to genetic causes
- Open-label Phase 2b study results demonstrated up to ~75% improvement in hypoglycemia at the 6 mg/kg and 9 mg/kg cohorts (the expected therapeutic doses)
- Interactions with Health Authorities planned for in 2H 2022, Phase 3 start anticipated in 1H 2023
- Orphan designation in US and EU, Pediatric Rare Disease designation
- Potential for expanded indications: post bariatric surgery hypoglycemia, insulinoma

RZ402 for Diabetic Macular Edema (DME)

- Microvascular complication of diabetes results in breakdown of the blood-retinal barrier and eventual blindness
- Potent, selective small molecule kallikrein inhibitor
- Oral therapy offering the potential to treat DME earlier and to address the disease at the vascular source
- Phase 1 program complete and demonstrated good bioavailability, with drug levels that safely exceeded target efficacious concentrations, supporting potential for once daily dosing
- Planning for initiating a Phase 2 proof-of-concept study 4Q 2022
- Potential for expanded indications: diabetic retinopathy, hereditary angioedema, systemic inflammatory syndromes and others

Two clinical stage programs with transformative therapies targeting diseases of dysglycemia

Leadership with deep expertise in metabolic drug development

Nevan Charles Elam, JD
Founder & CEO

- SAVARA
- Aerogen
- NEKTAR
- HARVARD UNIVERSITY

Brian Roberts, MD
Head of Clinical Development

- FibroGen
- CYMABAY
- STANFORD UNIVERSITY
- GEORGETOWN UNIVERSITY

Michael Covarrubias
Head of CMC

- Seagen
- AMGEN
- Genentech, A member of the Roche Group
- INDIANA UNIVERSITY

Erin O'Boyle
Head of Clinical Operations

- FibroGen
- HERON THERAPEUTICS
- STONEHILL COLLEGE

Michael Deperro
Head of Operations

- Patheon
- MERCK
- Alkermes
- UNIVERSITY OF NOTRE DAME

Davelyn Eaves Hood, MD
Scientific & Patient Affairs

- CHI Congenital Hyperinsulinism International
- HI GLOBAL REGISTRY
- aetna
- UTHealth The University of Texas Health Science Center at Houston

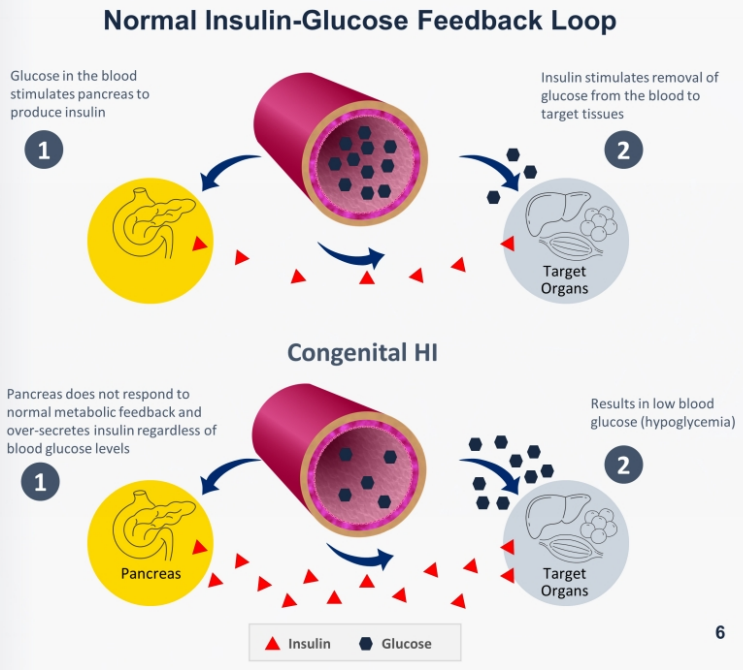
RZ358

A MONOCLONAL ANTIBODY IN PHASE 2B CLINICAL DEVELOPMENT FOR CONGENITAL HYPERINSULINISM

REZOLUTE

Congenital HI Disease State

- Ultra-rare disease
- 1 in 25,000 to 1 in 50,000 live births
  - Less than 10,000 in US and EU each
- Excessive insulin secretion from pancreatic beta cells regardless of blood sugar levels
- Most common cause of persistent hypoglycemia in infants and children
  - Brain (highly dependent on glucose as its main fuel source) is starved of energy
  - Symptoms often not recognized until life-threatening
  - Risk of neurological complications, coma, and death



Congenital HI Standard of Care is Deficient

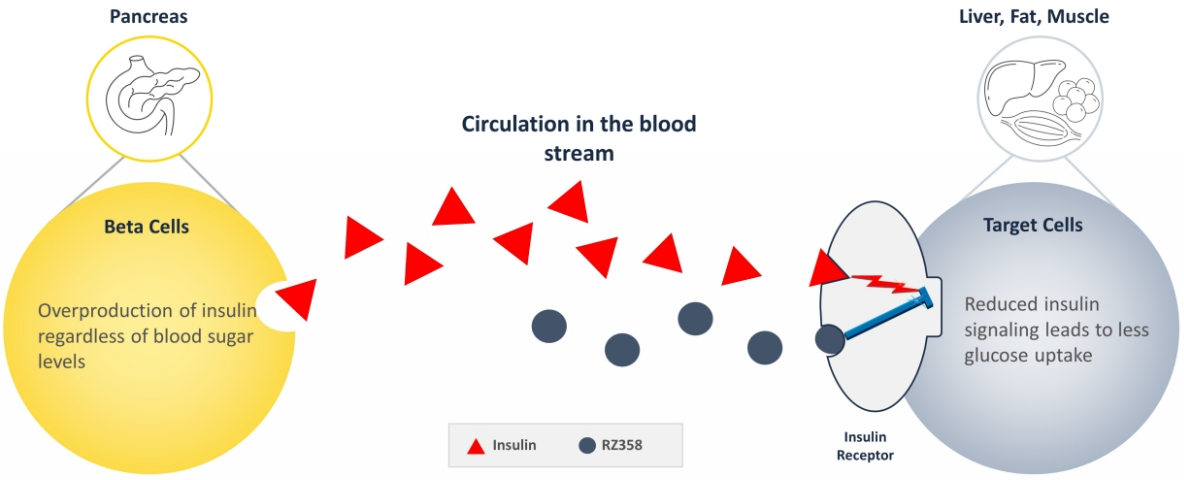
- No FDA-approved therapy for Congenital HI
- Existing treatments used by physicians are suboptimal:

Glucagon	Diazoxide	Somatostatin Analogues	Pancreatectomy
Opposes insulin's actions	***K_{ATP} channel agonist***	***Octreotide/Lanreotide***	***Resection for diffuse disease***
− Current formulations short-acting	− Ineffective in 50% of patients (with K_{ATP} mutations)	− Effects wane with repeat doses	− Invasive procedure, not done globally
− Temporary measure for emergent glucose correction	− FDA black box for pulmonary hypertension	− Marginal efficacy	− Hypoglycemia may persist for years in up to half of patients
− Repeated use may deplete liver glucose stores	− Fluid retention affecting heart/lungs	− Gastrointestinal side effects	− Requires adjuvant medical management, and/or repeat surgery
− Long-term efficacy is modest	− Facial changes and excessive hair growth	− Risk of necrotizing enterocolitis particularly in newborns	− Eventually insulin therapy required
		− Potential interaction with pituitary hormones (growth and thyroid)	***Resection for focal disease***
			− Limited number of overall cases
			− Only done at specialized centers
			+ Can be curative for patients

RZ358: Monoclonal Antibody Developed for Congenital HI

- Fully humanized monoclonal antibody, works downstream from the pancreas and agnostic to genetic causes
- Mechanism of Action (MOA) is uniquely suited for Congenital HI: antibody developed specifically for the disease
  - Binds to the insulin receptor at a non-competitive site (not an antagonist), normalizing insulin activity to prevent hypoglycemia
  - Normalized insulin activity protects against hyperglycemia
  - Highly selective to the insulin receptor (does not bind to the IGF-1 receptor)
  - Dose dependent pharmacokinetics with a half life greater than 2 weeks

RZ358's Unique MOA Normalizes Glucose Levels



RZ358 Unique MOA: Potential for Universal Treatment for all Forms of Congenital HI

	Current Standard of Care	RZ358
Targeting	− Beta cells only	+ Insulin receptor/signal on insulin-dependent target organs
Development	− Not developed for Congenital HI	+ Tailored for Congenital HI
Impact	− Marginally effective, invasive, and/or significant AEs	+ Normalizes insulin activity for optimal glucose range
Relevancy	− Genetics-dependent narrow targeting	+ Potentially universal treatment

Completed Clinical Studies Demonstrate Proof-of-Concept

- **PHASE 1:**
  - Insulin administration (ITT) in a subset of 29 healthy volunteers (to mimic Congenital HI) conducted before and after single-dose administration of RZ358
    - Prevented insulin-induced hypoglycemia

- **PHASE 2a:**
  - RZ358 administered to Congenital HI patients with a range of glucose values between normal and severely hypoglycemic
    - Subjects with hypoglycemia restored to normal range
    - Subjects with normal blood glucose levels remained the same
      - No evidence of hyperglycemia
    - Effect persisted for 4 weeks, consistent with PK/PD observed in Phase 1
    - Safe and well-tolerated
    - Established proof of concept
    - Informed Phase 2b entry criteria and endpoints

Phase 2a: RZ358 Brings Congenital HI Patients into Glucose Target Range

Design

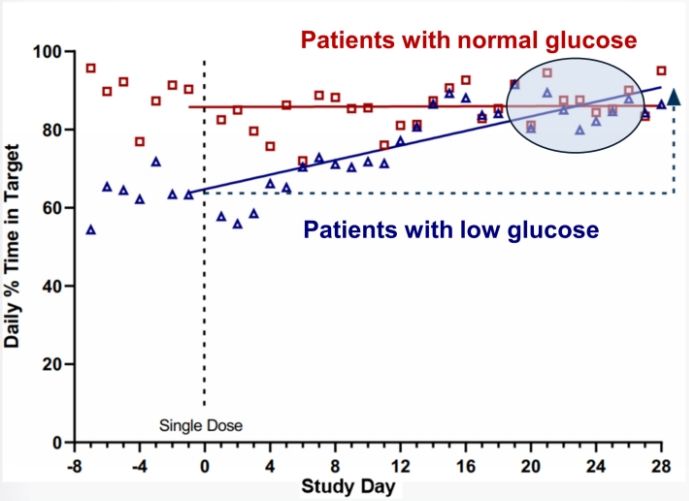
- Single IV doses of 1 to 9 mg/kg in patients with congenital hyperinsulinism
- 14 patients; ages ≥ 12 in Europe and ≥ 18 in the US
- Congenital hyperinsulinism patients by subgroup:
  - hypoglycemic at baseline (n=9)
  - normal baseline glucose (n=5)

Results

After a single dose of RZ358:

- Group with baseline hypoglycemia (n=9) achieved glucose normalization by 2 weeks
  - Equating to a 50% improvement from study baseline
- No hyperglycemia in patients with normal baseline glucose (n=5)
  - Confirmation of mechanism of action
- Effect persisted for 4 weeks, consistent with Phase 1 PK/PD
- Safe and well-tolerated
- Establishes proof of concept
- Informed Phase 2b entry criteria and endpoints

Time in Glucose Target Range (70-180 mg/dL) by CGM*



Glucose normalization achieved after two weeks with single dose of RZ358 in Congenital HI patients

**Phase 2b (RIZE) study primary endpoint*

Phase 2b Study (RIZE) Overview

Design	Population	Duration	Assessments/ Endpoints	Topline Results
Open-label, repeat-dose study in 4 sequential ascending dosing cohorts (up to 8 patients per cohort)	Congenital HI ≥ 2 years old with continued hypoglycemia on SOC, by specified continuous glucose monitoring (CGM) and self-monitored BG (SMBG) thresholds	~26 weeks • Screening – up to 5 weeks • Treatment – 8 weeks • Follow Up – 13 weeks	Primary: Time within range (70-180 mg/dL) by CGM Secondary: duration/incidence of hypoglycemia by CGM/SMBG/fasting	Enable registrational Phase 3 planning and preparation for regulatory interactions

Dosing Cohort	Dose Levels and Bi-Weekly Dosing Regimen (mg/kg)			
	Week 1	Week 3	Week 5	Week 7
1	3	3	3	3
2	6	6	6	6
3	9	9	9	9
4	3	6	9	9

Topline results presented in 2Q 2022

Study Objectives and Endpoints

- Repeat-dose safety and pharmacokinetics (PK) in children
- Open-label, dose-ranging (3-9 mg/kg) to inform Phase 3
  - Dose or exposure-response relationship to validate the treatment effect
  - Fixed dose level(s) and dose regimen that optimize treatment and benefit across all patients
- Assessed glycemic efficacy across a range of CGM and BGM-based principle glycemic endpoints to inform Phase 3, including:
  - Time in Range (70-180mg/dL) [TIR] measured by continuous glucose monitoring (CGM)
  - Time in hypoglycemia measured by CGM
  - Hypoglycemia events measured by blood glucose monitoring (BGM)

RIZE Study Expectations: Glycemic Efficacy

- Any reduction in the number of events and duration of hypoglycemia is significant
- 25% improvement from the patient's baseline is very clinically-meaningful
  - Expect reduced monitoring and rescue interventions, as well as liberalization of common activities such as exercise, school and third-party caregiver interactions
  - Expect reduced emergent or severe hypoglycemia events (such as seizures, coma, or hospitalizations), and improved neurodevelopmental outcomes
- RIZE study is expected to demonstrate:
  - At least a 25% improvement in hypoglycemia for the primary endpoint (time in target range) and key secondary endpoints (hypoglycemia events and duration of hypoglycemia)
  - A dose or exposure response relationship, yielding credibility to a treatment-effect
  - Fixed dose level(s) and regimen that optimizes benefit across all Congenital HI patients

Phase 2b RIZE Study Results

REZOLUTE

RIZE Study Summary

- Study was conducted primarily in a young pediatric population: average ~6.5 years of age
  - Diverse group of patients in the study across gender and genetics
  - Whether on SOC therapies, patients had to have substantial hypoglycemia to be enrolled
    - Patients enrolled had an average of 25% time in a hypoglycemic range at baseline
- RZ358 demonstrated:
  - ~50% improvement in hypoglycemia across all doses and cohorts
  - ~75% improvement in hypoglycemia at the 6 mg/kg and 9 mg/kg cohorts
    - These are the likely two dosing levels to be studied in Phase 3
- RZ358 was generally safe and well-tolerated
- Expected RZ358 concentrations achieved
- Dose and exposure-dependent responses were observed
  - 100% patient response rate with > 50% Hypoglycemia correction at the top dose

Patient Disposition and Study Status

Enrollment	N
Sites (Countries) that Enrolled	12 (10)
Screened	34
Screen Failed	11
Enrolled	23
Completed Treatment and Efficacy Evaluable Period	23
Completed Study (through 3-month follow-up)	13
Early Terminated	0

Patient Demographics and Baseline Characteristics

Parameter	Cohort 1: 3 mg/kg (N=4)	Cohort 2: 6 mg/kg (N=8)	Cohort 3: 9 mg/kg (N=8)	Cohort 4: 3-9 mg/kg (N=3)	RZ358 Total (N=23)
Age (Mean, Range)	5.8 (2-12)	9.3 (2-22)	5.8 (2-17)	4.0 (2-6)	6.7 (2-22); N=16 ages 2-6
Gender (n, M / F)	4 / 0	5 / 3	3 / 5	1 / 2	13 / 10
Genetics (n, kATP / Other / Unknown)	1 / 0 / 3	5 / 1 / 2	4 / 1 / 3	1 / 1 / 1	11 / 3 / 9
CHI Rx (n, %)	4	7	6	3	20 (87%)
Diazoxide	2	3	1	2	8 (35%)
SSA (Long-acting/Short-Acting)	2 / 0	1 / 2	3 / 4	1 / 0	7 / 6 (56%)
Other (inc 2+ meds, pancreatectomy, enteral feeding)	0	2	6	1	9 (39%)
% Time Hypoglycemia (<70 mg/dL) by CGM (Mean, Range, PP Population)	16 (12-20; n=4)	22 (12-34; n=8)	26 (6-86; n=7)	29 (10-43)	23 (6-86; n=22)
Hypoglycemia Events / Wk by BGM (Mean, Range, PP Population)	10 (6-14; n=3)	19 (5-78; n=8)	17 (8-28; n=7)	8 (5-11; n=3)	16 (5-78; n=21)

- Patients enrolled on stable background therapies had:
  - Clinically-significant, and in many cases, substantial residual hypoglycemia indicating an unmet treatment need
  - Some hyperglycemia (>180 mg/dL) at baseline

RZ358 Was Generally Safe and Well Tolerated Across Doses

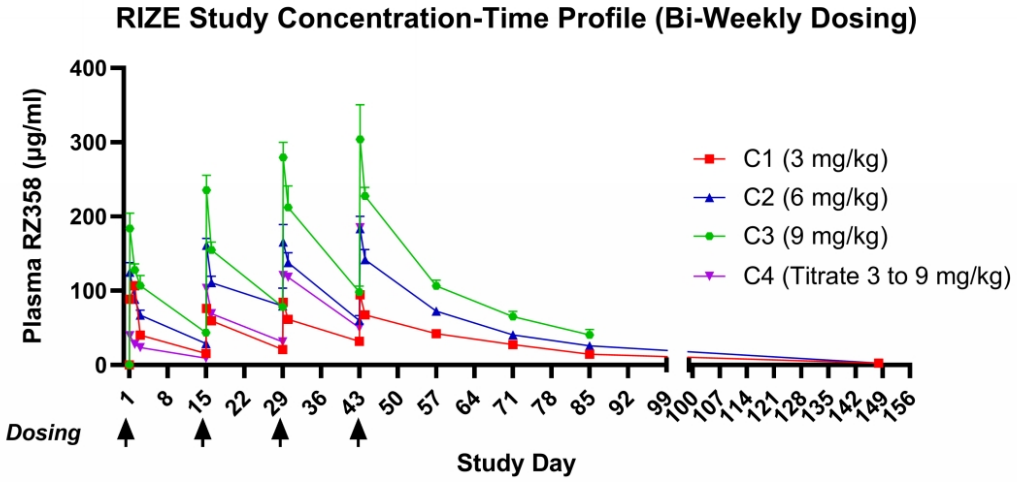
- No adverse drug reactions, AEs leading to study discontinuation, or dose-limiting toxicities
- In RZ358 treated subjects overall, 15 subjects (65%) experienced a total of 43 treatment-emergent AEs, compared to 10 subjects (43%) who experienced a total of 13 AEs outside of the defined treatment-emergent period (pre-treatment or >+42 days post-treatment)
  - No difference in time (or exposure)-adjusted AE rates
  - No dose-response
  - Generally mild and unrelated to study drug
  - No issues with GI tolerability
- Three patients experienced mild adverse events that were judged by Investigator(s) as related to study drug (hyperactivity, mild/transient infusion site rash, dizziness)
- Three patients experienced three unrelated SAEs (hospitalization), all deemed related to background conditions
- Mild hyperglycemia (>180 mg/dL) worsened from baseline in this patient group on SOC with some baseline hyperglycemia
- No increase from baseline in clinically relevant hyperglycemia (≥ 250 mg/dL) and no hyperglycemia AEs or adverse metabolic changes

Treatment Emergent Adverse Event Overview

	Non-TEAE (Pre/42d Post-Rx) (n=23)	RZ358 3 mg/kg (n=4)	RZ358 6 mg/kg (n=8)	RZ358 9 mg/kg (n=8)	RZ358 Titrate (n=3)	RZ358 Total TEAE (n=23)
Subjects with Adverse Events (AEs), n (%)	10 (43%)	2 (50%)	7 (87%)	4 (50%)	2 (50%)	15 (65%)
Total AEs	13	2	30#	7	4	43
Subjects with Serious AEs (SAEs), n (%)	0 (0%)	0 (0%)	2 (25%)	1 (13%)	0 (0%)	3 (13%)
Total SAEs	0	0	2	1	0	3
Subjects with PI-Judged Related AEs, n (%)	n/a	0 (0%)	2 (25%)	1 (13%)	0 (0%)	3 (13%)
Total Related AEs	n/a	0	3	1	0	4
Subjects with AEs by Severity, n (%)						
Grade 1	8 (35%)	2 (50%)	7 (87%)	2 (25%)	2 (50%)	13 (57%)
Grade 2	2 (9%)	0 (0%)	3 (38%)	1 (13%)	0 (0%)	4 (17%)
≥ Grade 3	1 (4%)	0 (0%)	2 (25%)	1 (13%)	0 (0%)	3 (13%)
Subjects Discontinued due to AEs, n (%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

 # Majority of AEs in Cohort 2 were mild, judged unrelated to study drug, and experienced by 2 patients.

Dose-Dependent and Predictable Drug Concentrations

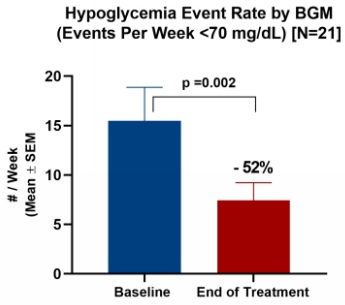


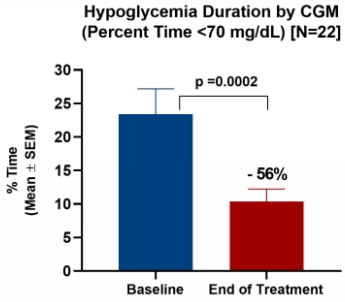
- Dependable concentrations independent of congenital HI patient factors (absorption, PO aversion, GI tolerability, etc)
- Half-Life > 2 weeks
- No apparent age dependencies
- Well below exposures in monkey toxicology studies (≥ 4-fold margin at highest dose)

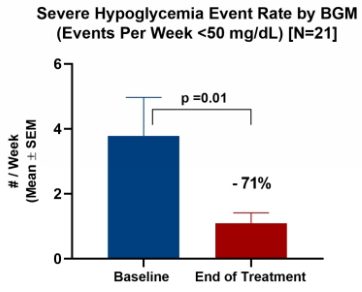
Topline Glycemic Results: Far Exceeded Expectations

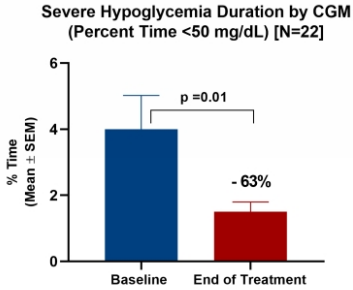
- Low starting dose (3 mg/kg) was selected for safety with minimal expectations for efficacy
  - Notably, an improvement in hypoglycemia of ~25% was achieved
- Improvements in hypoglycemia of ~75% at the mid (6 mg/kg) and top doses (9 mg/kg) and a high patient response rate
  - Improvements were comparable between both BGM (hypoglycemia events) and CGM (hypoglycemia time)
- Better than expected hypoglycemia correction resulted in an increase from baseline in mild, self-limiting, non-clinically meaningful hyperglycemia in patients taking background therapies
  - TIR (70-180 mg/dL) by CGM improved 8% across all doses, 16% at the top dose, and more significantly (>25%) in patients without baseline hyperglycemia on SOC
- Clear dose-response observed
- Results demonstrate that RZ358 can be administered at fixed dose levels with the potential to be an effective combination or monotherapy in all patients with congenital and syndromic HI

Expectations of ≥ 25% Hypoglycemia Correction (Time and Events) Were Met and Exceeded Across Multiple Metrics









Highly Significant Dose-Dependent Improvements in Hypoglycemia Events (BGM) and Time (CGM) Exceeded Study Expectations

Mean (Range)	RZ358 3 mg/kg (n=4) #	RZ358 6 mg/kg (n=8)	RZ358 9 mg/kg (n=7) ^	RZ358 Titrate (3-9 mg/kg) (n=3)	RZ358 Total Pooled (n=22)
Time in Hypoglycemia (<70 mg/dL) by CGM (%)					
Baseline	16.1	22.2	26.5	29.1	23.3 (6-86)
End of Treatment	10.5	9.2	9.4	15.8	10.4 (0.3-33)
% Change from BL (p-value)	***-35% (p=0.05)***	***-59% (p<0.01)***	***-65% (p=0.07)*** ^	***-46% (p=0.10)***	**-56% (p=0.0002)**
Time in Severe Hypoglycemia (<50 mg/dL) by CGM (%)					
Baseline	1.8	5.1	4.3	3.3	3.9 (0-21)
End of Treatment	1.3	1.4	1.7	1.6	1.5 (0-5)
% Change from BL (p-value)	***-25% (NS)***	***-73% (p<0.05)***	***-61% (NS)*** ^	***-52% (NS)***	**-63% (p=0.01)**
Hypoglycemia Events (<70 mg/dL) by BGM (events/week)					
Baseline	10.1	19.2	16.7	8.0	15.5 (4.5-77.8)
End of Treatment	7.8	9.9	5.3	5.3	7.5 (0-30.3)
% Change from BL (p-value)	***-22% (NS)***	***-48% (p=0.1)***	***- 68% (p<0.01)***	***-34% (p<0.05)***	***-52% (p=0.002)***
Severe Hypoglycemia Events (<50 mg/dL) by BGM (events/week)					
Baseline	1.6	5.5	4.2	0.5	3.8 (0.5-23.8)
End of Treatment	1.5	1.2	1.1	0.4	1.1 (0-5.5)
% Change from BL (p-value)	***-8% (NS)***	***-77% (p=0.1)***	***- 74% (p<0.05)***	***-20% (NS)***	***-71% (p=0.01)***

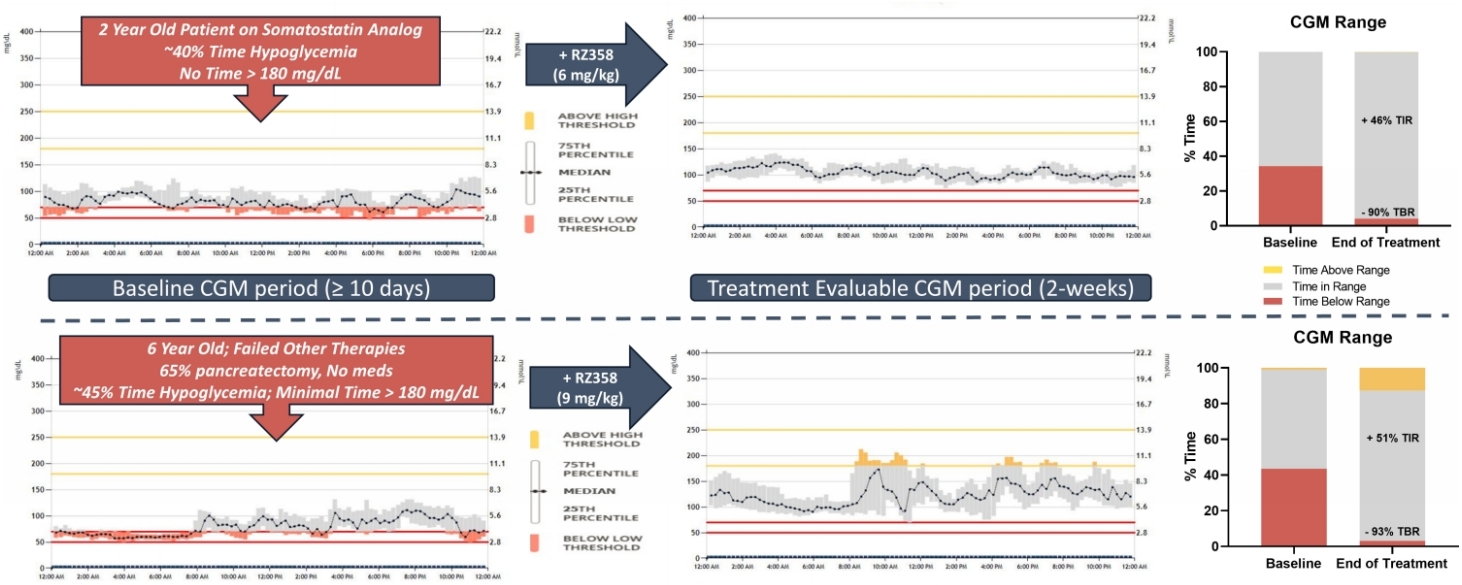
One patient at 3 mg/kg was excluded from the per protocol BGM analyses for failing to meet pre-specified minimum glucometer testing

^ One patient at 9 mg/kg was excluded from the per protocol CGM and BGM analyses for stopping background therapy while on study; Two 2 year-old patients in 9 mg/kg group wore CGM on the arm which may have impacted their results, but were included in analysis

High Patient Response Rate at Clinically-Relevant Correction Thresholds

Responders N (%)	RZ358 3 mg/kg (n=4)	RZ358 6 mg/kg (n=8)	RZ358 9 mg/kg (n=7)	RZ358 Titrate 3-9 mg/kg (n=3)	RZ358 Total (n=22)
≥25% Correction of Hypoglycemia					
Severe (<50 mg/dL)	3 (75%)	7 (88%)	7 (100%)	2 (67%)	19 (86%)
Overall (<70 mg/dL)	3 (75%)	7 (88%)	7 (100%)	3 (100%)	20 (91%)
≥50% Correction of Hypoglycemia					
Severe (<50 mg/dL)	3 (75%)	6 (75%)	7 (100%)	2 (67%)	18 (82%)
Overall (<70 mg/dL)	1 (25%)	7 (88%)	7 (100%)	1 (33%)	16 (73%)
≥75% Correction of Hypoglycemia					
Severe (<50 mg/dL)	1 (25%)	5 (63%)	6 (86%)	2 (67%)	14 (64%)
Overall (<70 mg/dL)	1 (25%)	3 (38%)	5 (71%)	1 (33%)	10 (45%)

Potential for RZ358 to be an Effective Monotherapy Treatment



Summary of Results

- RZ358 was safe and effective in a diverse group of congenital HI patients (across age, gender, and genetics) who had continued hypoglycemia and some hyperglycemia on background SOC
- Improvements in hypoglycemia of ~75% at the mid (6 mg/kg) and top doses (9 mg/kg) and a high patient response rate
  - Improvements were comparable by both BGM (hypoglycemia events) and CGM (hypoglycemia time)
- Better than expected hypoglycemia correction resulted in mild, self-limiting, non-clinically meaningful hyperglycemia in patients taking background therapies
  - TIR (70-180 mg/dL) by CGM improved 8% across all doses, 16% at the top dose, and more significantly (>25%) in patients without baseline hyperglycemia on SOC
- Clear dose-response observed
- Results demonstrate the potential for RZ358 to be an effective combination or monotherapy for patients with congenital and syndromic HI

RZ402

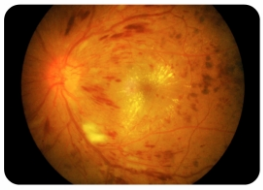
A SELECTIVE AND POTENT PLASMA KALLIKREIN INHIBITOR (PKI) – IN DEVELOPMENT AS A POTENTIAL ORAL THERAPY FOR DIABETIC MACULAR EDEMA (DME)

REZOLUTE

Diabetic Macular Edema (DME)

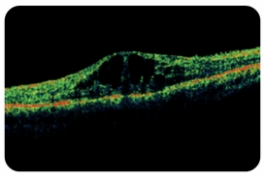
- DME is a microvascular complication of diabetes affecting the retinal blood vessels and a primary cause of blindness in the US
  - Chronic exposure to high blood sugar levels leads to loss of the blood-retinal-barrier resulting in leakage and fluid infiltration into the retina
  - Manifests as blind spots, floaters, blurry vision, and ultimately blindness

Increased Retinal Vascular Permeability



Leakage of fluid from vascular compartment into the retina

Macular Edema



Swelling of the central macula

Progressive Vision Loss and Blindness

10M have diabetic retinopathy[2] in US and 1-2M have DME[3,4]

REZOLUTE

1. CDC National Diabetes Statistics Report, 2020. 2. JAMA. 2010, 304(6):649-656. 3. JAMA Ophthalmology. 2014, 132(11):1334-1340. 4. Diabetes Care. 2012, 35(3):556-564.

Current SOC: Anti-VEGF Therapies Are Inadequate

- Anti-VEGF injections into the eye are the current standard of care (e.g., Lucentis and Eylea)
- Problematic route of administration
    - Initiation of therapy is delayed as disease progresses
    - Poor compliance with monthly injection regimen
    - Must be administered in clinical setting
    - Invasive injection and sub-optimal compliance limits potential market size
- Not effective in many patients as VEGF may not be implicated in all DME patients

1. Diabetes 2015, 64(10): 3588-3599 2. Ther Adv Endocrinol Metab. 2013, 4(6): 151–169

RZ402: Oral Therapeutic Alternative for DME

- Targets a different pathway, the Kallikrein–Kinin System (KKS), to address inflammation and vascular leakage
    - RZ402 potently inhibits kallikrein activation in human plasma
    - In dose dependent fashion, RZ402 potently suppresses vascular leakage (up to 80%) in relevant animal models
    - Possible treatment alternative for patients with a suboptimal response to anti-VEGF therapies
- Oral delivery provides for patient-controlled regimen and systemic exposure
    - Advantages in comfort and convenience – anticipated once daily capsule or tablet
    - Intended as monotherapy or combination with anti-VEGF injections
    - For prevention or treatment of DME
    - Continuous drug levels, targeting the vasculature, not the eye

Oral route of delivery may lead to earlier intervention, reach more patients and lead to better overall clinical outcomes

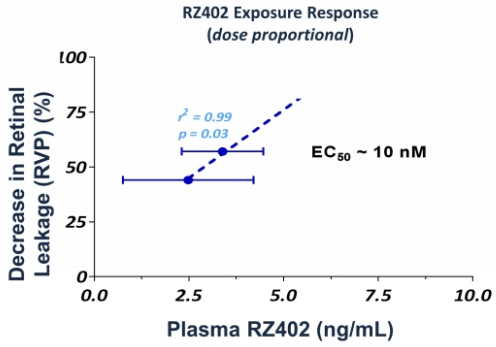
Disease Models Highlight RZ402 Efficacy

- Retinal vascular permeability (indicative of macular edema) was inhibited by RZ402 in rodent models of DME
- Low nanomolar potency was exhibited in rodent DME models

RZ402 Inhibits Retinal Vascular Permeability in Diabetic and Hypertensive Rodent Models

Animal Model	End Point	RZ402 Dose*	Inhibition
Diabetes	RVP	0.25 – 0.6 mg/kg/day	43-83%
Hypertension	RVP	0.2 – 0.4 mg/kg/day	60-92%
Diabetes	***Hematoma Expansion***	*0.4 mg/kg/day*	***85%***
Retinal Hemorrhage	***Retinal Leukostasis***	*1 mg/kg/day*	***>90%***

RZ402 is Highly Potent and Dose Proportional in Treating Vascular Permeability

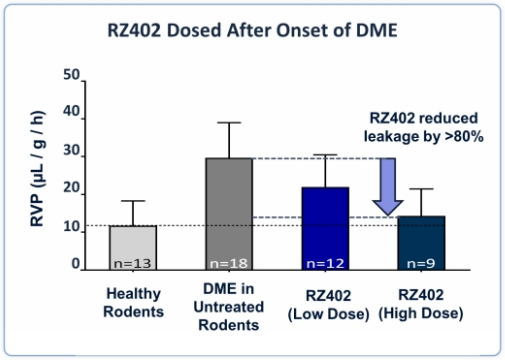


*Subcutaneous administration

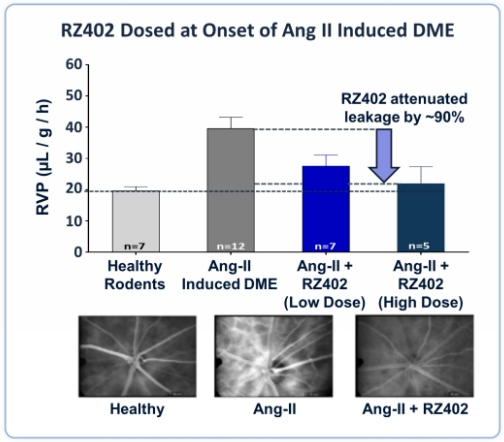
Systemic Delivery *Reversed* & *Prevented* Retinal Vascular Leakage

- Reversal of retinal vascular permeability (RVP) was seen when RZ402 was dosed in rodent DME models
- Angiography studies in a rodent DME model highlighted that RZ402 may prevent Angiotensin II induced RVP

RZ402 reversed vascular leakage by >80%



RZ402 prevented vascular leakage by ~90%



Hypertension 2009, 53:175-181; Diabetes. 2011 May; 60(5): 1590–1598

RZ402: Phase 1 (SAD and MAD) Study Results Support Once Daily Oral Dosing

Design/Dosing	Population	Primary Objectives	Exploratory Objectives	Timeline
Single center, randomized, double-blind, placebo-controlled study in 3 sequential dosing cohorts in the SAD study (25, 100, 250 mg) and an additional 4th cohort (500 mg) in the MAD study administered once-daily	Each cohort comprised of 10 healthy volunteers randomized 8:2 active vs placebo, for a total of 30 participants in the SAD study and 40 participants in the MAD study	Assess the safety and tolerability of once-daily oral administration of RZ402 and determine the PK profile; achieve steady-state target concentrations	Investigate effects of repeat doses of RZ402 on biomarkers of target engagement (plasma kallikrein inhibition) and related PD effects	SAD study concluded in 2Q 2021 MAD study concluded in 1Q 2022 Phase 2 proof-of-concept study planned for 4Q 2022

- The Phase 1 program met its primary safety and pharmacokinetic endpoints and enables a Phase 2 proof-of-concept study:
  - RZ402 was safe and well tolerated across all doses, without dose-limiting toxicities
  - RZ402 was adequately bioavailable with dose-dependent increases in systemic exposures
  - Repeat-dosing to steady-state resulted in the highest concentrations of RZ402 explored to date
  - Results at both peak and 24-hour trough substantially exceeded target concentrations based on a combination of in-vitro and in-vivo profiling

MAD Study Results: Safety

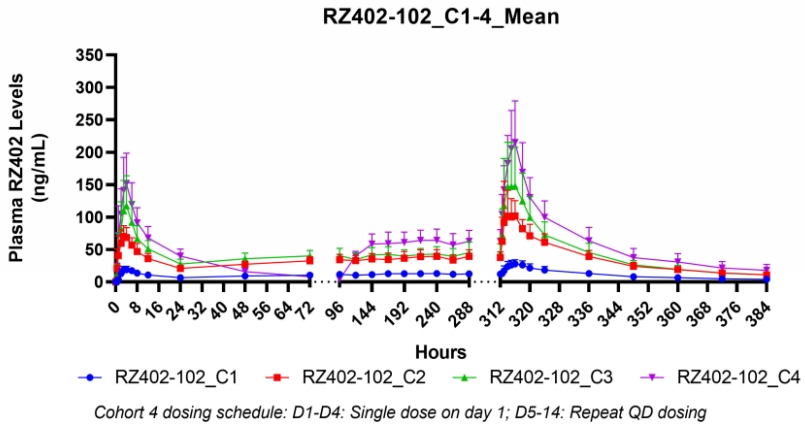
- No adverse drug reactions, serious adverse events, or study discontinuations
- 19 subjects (59%) in treatment group had a total of 48 AEs compared to 5 subjects (63%; 15 AEs) in placebo group
- Some GI events were reported but they were mild and not dose-dependent, so relationship to study drug is unclear
- No effect on blood pressure or heart rate
- Comprehensive safety eye exams were unremarkable
- Laboratory evaluations unremarkable (including coagulation studies)

	RZ402 25-mg (N = 8)	RZ402 100-mg (N = 8)	RZ402 250-mg (N = 8)	RZ402 500-mg (N = 8)	Placebo (N = 8)	Combined RZ402 (N = 32)	Overall (N = 40)
Subjects with at least 1 TEAE, n (%)	6 (75.0)	5 (62.5)	3 (37.5)	5 (62.5)	5 (62.5)	19 (59.4)	24 (60.0)
Subjects with a related TEAE, n (%)	4 (50.0)	2 (25.0)	1 (12.5)	4 (50.0)	2 (25.0)	11 (34.4)	13 (32.5)
Subjects with a grade 3 or greater TEAE, n (%)	0	0	0	0	0	0	0
Subjects with a serious TEAE, n (%)	0	0	0	0	0	0	0
Subjects with a related serious TEAE, n (%)	0	0	0	0	0	0	0
Subjects with a TEAE leading to study discontinuation, n (%)	0	0	0	0	0	0	0
Subjects with a related TEAE leading to study discontinuation, n (%)	0	0	0	0	0	0	0
Number of TEAEs	24	8	6	10	15	48	63
Number of related TEAEs	10	2	3	6	5	21	26
Number of grade 3 or greater TEAEs	0	0	0	0	0	0	0
Number of serious TEAEs	0	0	0	0	0	0	0
Number of related serious TEAEs	0	0	0	0	0	0	0
Number of TEAEs leading to study discontinuation	0	0	0	0	0	0	0
Number of related TEAEs leading to study discontinuation	0	0	0	0	0	0	0

RZ402 was generally safe and well-tolerated

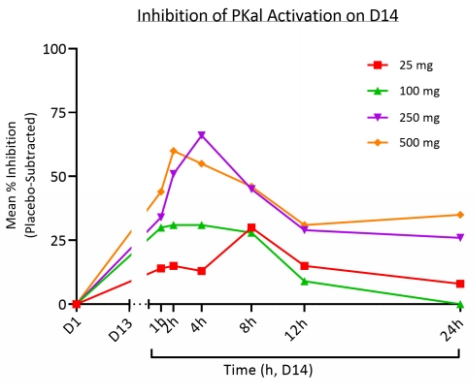
MAD Study Results: Single and Repeat Dose Pharmacokinetics

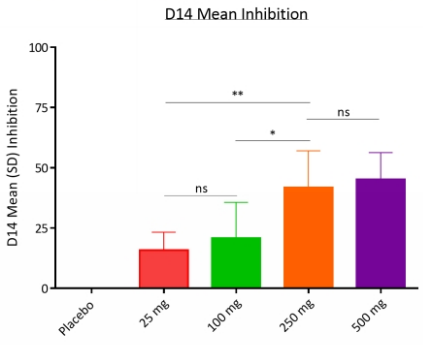
- Dose-dependent increase in systemic exposures
- Highest concentrations explored to date
- Drug accumulation following repeat dosing ≤ 2-fold
- 24-hour levels and half-life of ~20h support potential for once daily oral dosing
- Good safety profile observed in the clinic, and large safety margins to animal toxicology doses and exposures

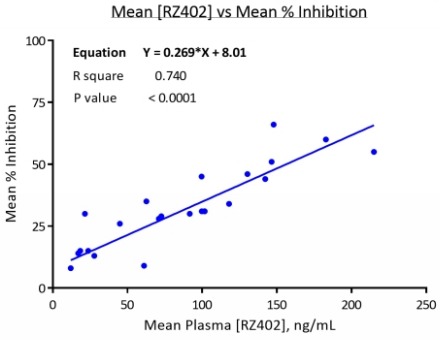


Cohort 4 dosing schedule: D1-D4: Single dose on day 1; D5-14: Repeat QD dosing

MAD Study Results: Steady-State Pharmacodynamics / Target Inhibition



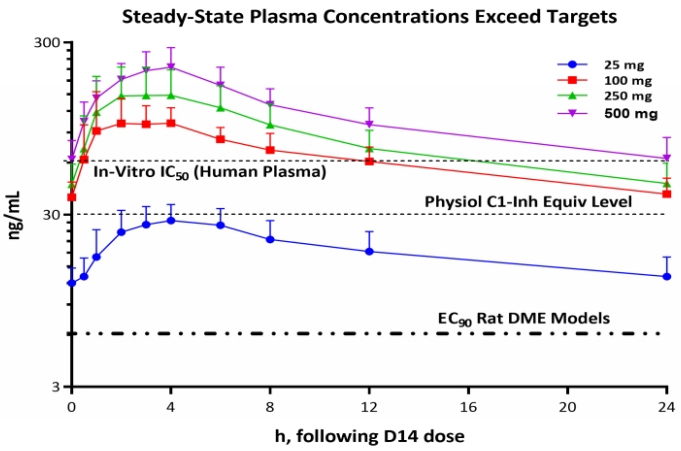




- Patient plasma samples from D14 were activated using an ellagic acid-based commercial aPTT reagent, and PKal activity determined using a PKal-specific chromogenic peptide substrate
- Percent inhibition of PKal activation at each D14 timepoint was determined by comparison to same patient pre-dose plasma samples (D1)
- Mean percent inhibition for timepoints in each cohort were corrected for placebo changes
- Mean inhibition over the 24h period on D14 was calculated by averaging percent inhibitions for each time point

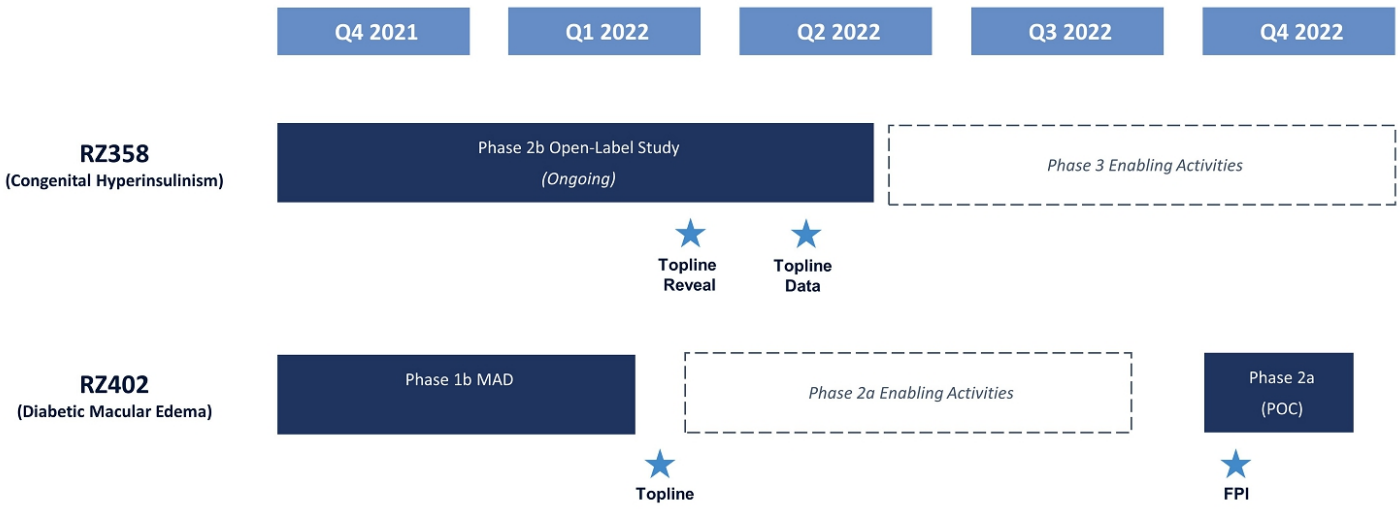
MAD Study Results: Pharmacologic Target Concentrations Achieved with Once Daily Oral Dosing

- Target concentrations achieved at the lowest dose administered and between daily doses (trough levels)
  - Daily dosing with RZ402 inhibited plasma kallikrein in a dose and concentration-dependent manner throughout the 24-hour dosing interval
- Potent *in-vivo* efficacy has been established with RZ402 in several animal models
  - ***In-vivo*** EC_{50-90}: 3-7 ng/mL (C_{ss})
  - RZ402 may localize at the blood vessel site of action to exert greater pharmacologic effects
  - Highly potent in-vivo effects may predict higher translatability into the clinic, with better efficacy than current oral therapies



Milestones

Near-term Catalysts



REZOLUTE