May 1, 2022

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 01, 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 (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%)

“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 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 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, 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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