REZOLUTE

A Late-stage Ultra-rare Disease Company Treating Refractory Hypoglycemia

Corporate Presentation

Forward Looking Statements

This presentation, 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," "prove," "potential," "seek," "strive," "try," or future or conditional verbs such as "predict," "could," "may," "likely," "should," "will," "would," or similar expressions. These Forward-Looking statements include, but are not limited to, statements regarding the sunRIZE clinical study, the RIZE study, the upLIFT study, the potential efficacy of RZ358 (ersodetug) in treating hypoglycemia, the Investigational New Drug (IND) application for ersodetug, the ability of ersodetug to become an effective treatment, the effectiveness or future effectiveness of ersodetug as a treatment, statements regarding clinical trial timelines for the treatment. 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 our 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. This presentation shall not constitute an offer to sell or the solicitation of an offer to buy, nor shall there be any sale of these securities in any state or other 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 other jurisdiction.

@2026 Rezolute, Inc. All Rights Reserved.

An Ultra-rare Disease Company Treating Refractory Hypoglycemia

RZ358 (ersodetug) is an antibody designed to treat refractory hypoglycemia caused by all forms of hyperinsulinism (HI)

Two late-stage programs evaluating ersodetug to treat refractory hypoglycemia in congenital HI and tumor HI

Compelling evidence that ersodetug is active against hypoglycemia in patients under the Company's Expanded Access Program

Total $1B+ global market opportunity with additional upside through expansion

Seasoned management team with demonstrated success from early development through commercialization

Well-capitalized for execution – $120 million in cash with runway to mid-2028

@2026 Rezolute, Inc. All Rights Reserved.

Late-Stage Clinical Programs Targeting Hyperinsulinism

Program	Target	IND-Enabling	Phase 1	Phase 2	Phase 3	Next Milestone	Milestone Expected
Ersodetug	Congenital Hyperinsulinism					Pending FDA discussions	2H 2026
Ersodetug	Tumor Hyperinsulinism					Topline data	2H 2026
Ersodetug	GI-Surgery Hypoglycemia (including PBH)					Regulatory Discussions	Q1 2027

Pipeline expansion opportunities to treat additional causes of hyperinsulinism

@2026 Rezolute, Inc. All Rights Reserved.

Ersodetug

Treatment for Hyperinsulinism (HI)

Refractory Hypoglycemia as a Result of HI

Hypoglycemia

- Severe, persistent, life-threatening complication of over activation of the insulin receptor
- Lack of effective treatment options

Congenital HI

Ultra-rare pediatric genetic disease characterized by excessive insulin production

Tumor HI

Ultra-rare disease caused by tumors that produce insulin or insulin-like substances such as IGF-2

GI-Surgery

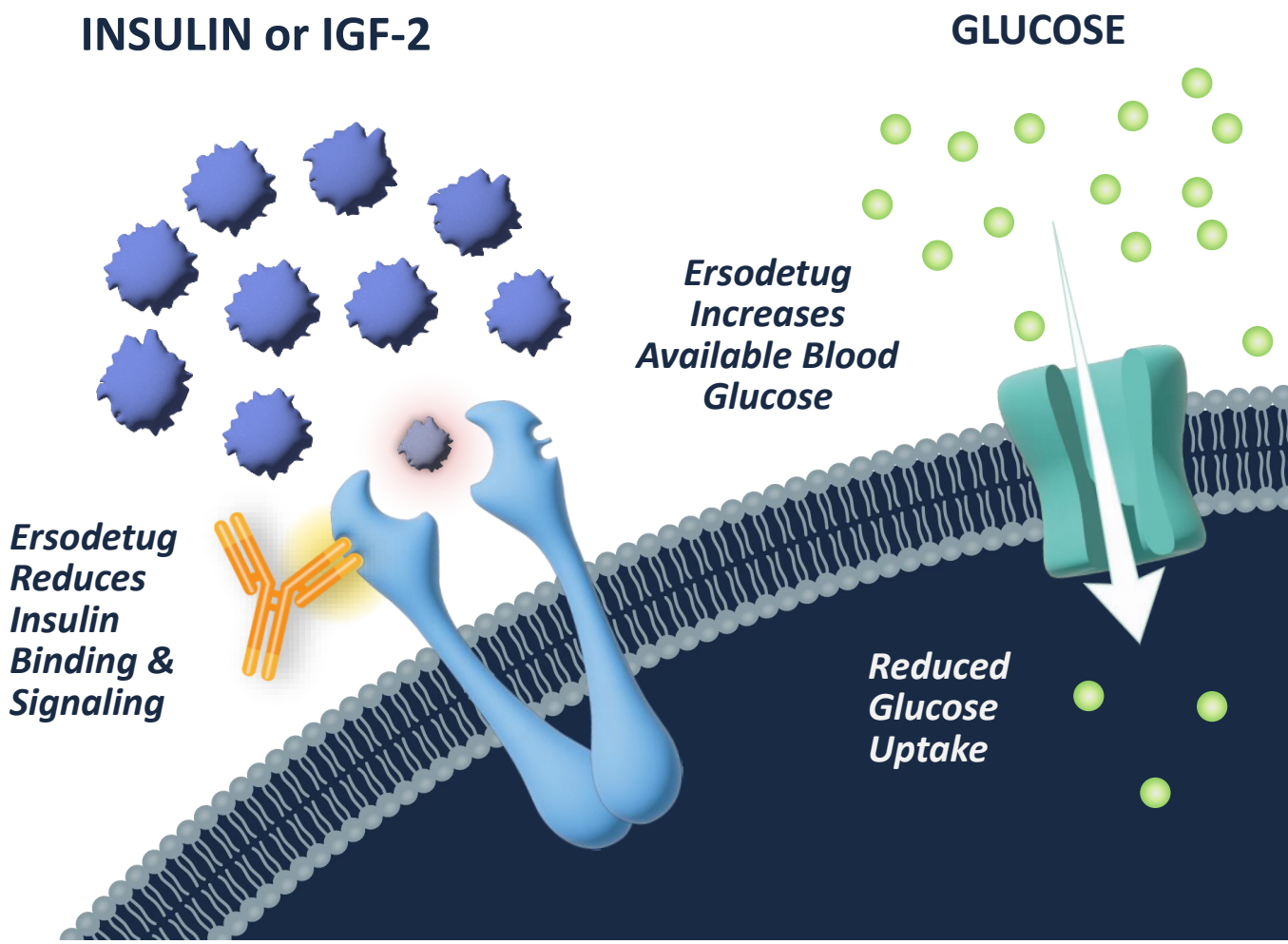
Hyperinsulinism mediated by dysregulated GLP-1 and resulting insulin production following bariatric and non-bariatric surgery

Ersodetug has been studied in clinical trials and a real-world expanded access program (EAP)

@2026 Rezolute, Inc. All Rights Reserved.

Downstream MOA at Insulin Receptor Addresses any Form of HI

- Fully human monoclonal antibody with a novel mechanism acting downstream from production source (e.g., pancreas)
- Allosterically binds to the insulin receptor to counteract excess signaling by insulin or paraneoplastic insulin-like substances (e.g., IGF-2 variants)
- Modulating effect helps maintain glucose values in a healthy range
- Administered by IV infusion



@2026 Rezolute, Inc. All Rights Reserved.

Congenital HI

Disease Pathophysiology, Incidence, and Clinical Features

- Multiple gene causes of dysregulated insulin production and signaling
- 1 in 22,000 live births in the US[1], translating to approximately 165 new patients per year
- Most common cause of persistent hypoglycemia in infants and children
- Often presents within first month of life
  - 70% of cases present with seizure[2]
- Risk of coma, death, and other serious complications if undiagnosed or undertreated
- Requires constant monitoring as serious hypoglycemic lows are often missed
- 50% of children with congenital HI have neurological deficiencies caused by hypoglycemic lows
- No therapy has been developed and approved for chronic treatment of all genetic forms[3]

[1] Based on the Forian and Compass claims data. [2] Meissner T, et al. *EUR J Endocrinol*. 2003;149(1):43-51. [3] Based on the RIZE clinical trial outcomes and the evidence of benefit in this serious condition with substantial unmet medical need, ersodetug was granted Breakthrough Therapy Designation by the US Food and Drug Administration (FDA), a priority medicines (PRIME) designation by the European Medicines Agency (EMA), an Innovation Passport designation by the U.K. Innovative Licensing and Access Pathway (ILAP) Steering Group, and Orphan Drug Designation in the US and EU for the treatment of hypoglycemia due to congenital HI.

@2026 Rezolute, Inc. All Rights Reserved.

High Unmet Medical Need with Current Standard of Care

- Diazoxide (DZ) is first line treatment and the only approved medication for hypoglycemia caused by HI
  - ~60% of patients do not respond to DZ
  - Can cause frequent and serious adverse reactions including volume overload, heart failure, and pulmonary hypertension
  - Patients report[1] intolerable side effects including increased body hair (91%), loss of appetite (45%), swelling (27%), facial changes (28%), and gastrointestinal upset (26%)
- Other available treatment options are suboptimal
  - Glucagon tends to be temporizing and short-term
  - Somatostatin analogs have marginal efficacy and potentially serious pediatric side effects
  - Intensive feeding regimens (e.g., tube feeding) often underlie all of these approaches
  - May contribute to a cycle of poor appetite and feeding aversions
  - Pancreatectomy is an invasive option in DZ non-responsive patients, but frequently requires adjuvant medications until insulin-dependent diabetes eventually ensues

[1] HI Global Registry 2025 Annual Report: 360 patients surveyed, 259 have taken DZ.

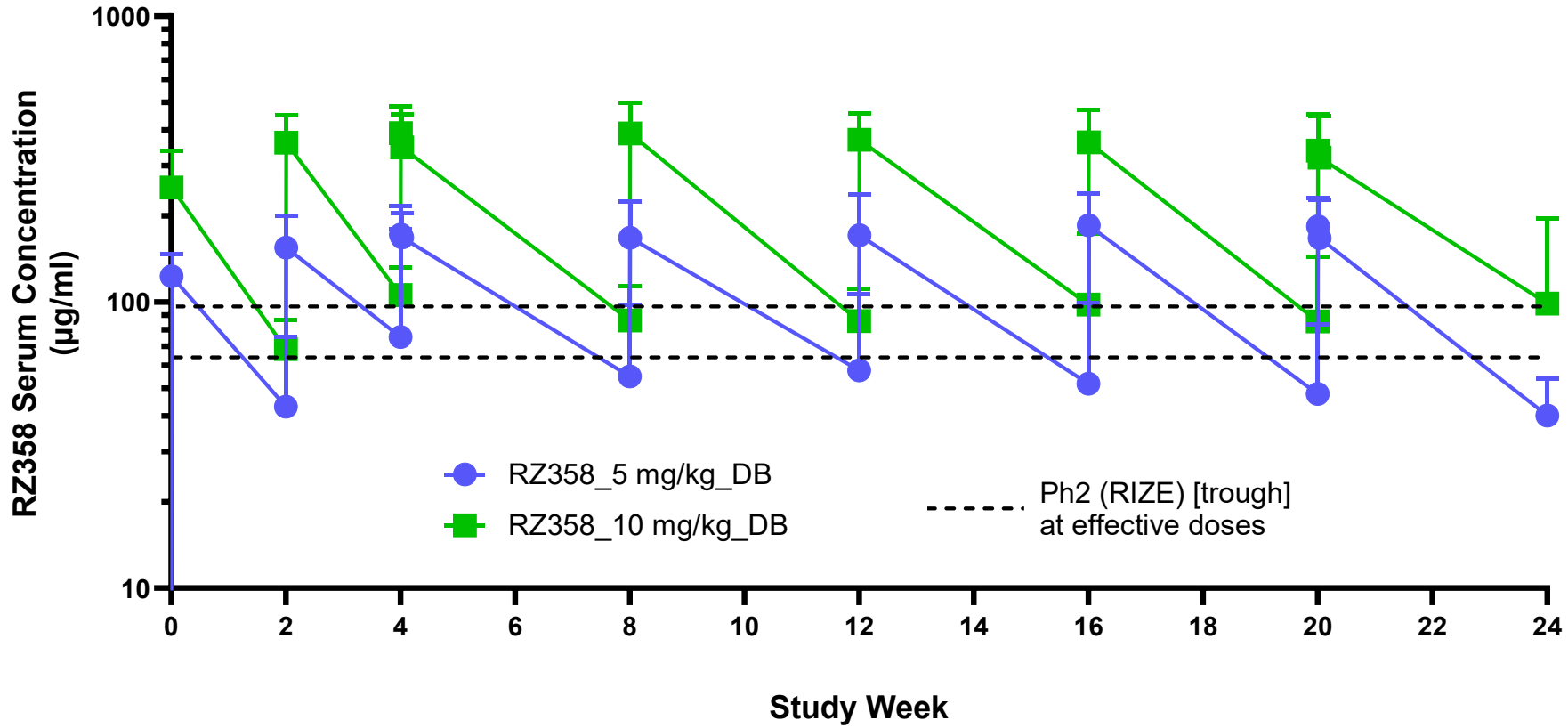
@2026 Rezolute, Inc. All Rights Reserved.

Phase 3 sunRIZE Study Highlights

- Study status
  - Phase 3 pivotal study completed; open-label extension (OLE) ongoing
  - 100% roll-over to OLE and very high retention rate
  - Significant number of patients have stopped other therapies and remain on ersodetug as monotherapy
- Efficacy (Pivotal, RCT period)
  - Primary endpoint (SMBG weekly hypoglycemia events) not met due to confounding placebo/study effect caused by functional unblinding of the endpoint
  - Several CGM outcomes showed consistent and clinically meaningful reductions in hypoglycemia
- Safety
  - Reassuring safety profile
  - 2% systemic hypersensitivity reactions; mild hypertrichosis observed
- Long-term experience
  - Significant exposure experience with continued glycemic benefit
  - ~48 months of exposure in Expanded Access Program (EAP)
- FDA currently reviewing analysis datasets and summary tables and will provide guidance on path forward
  - Program update expected in 2H26

@2026 Rezolute, Inc. All Rights Reserved.

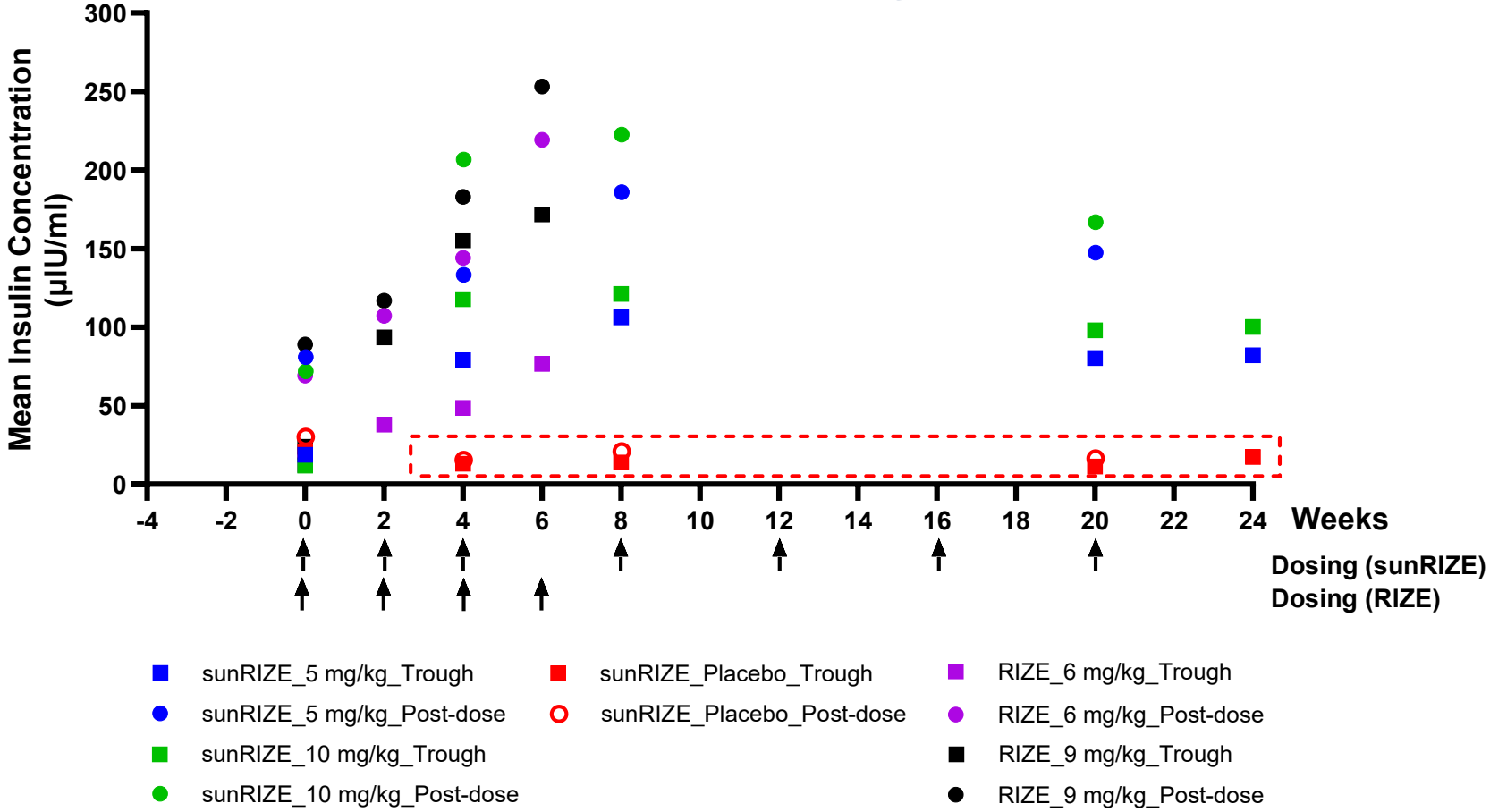
Preliminary PK: Therapeutic and Age-Comparable Concentrations



@2026 Rezolute, Inc. All Rights Reserved.

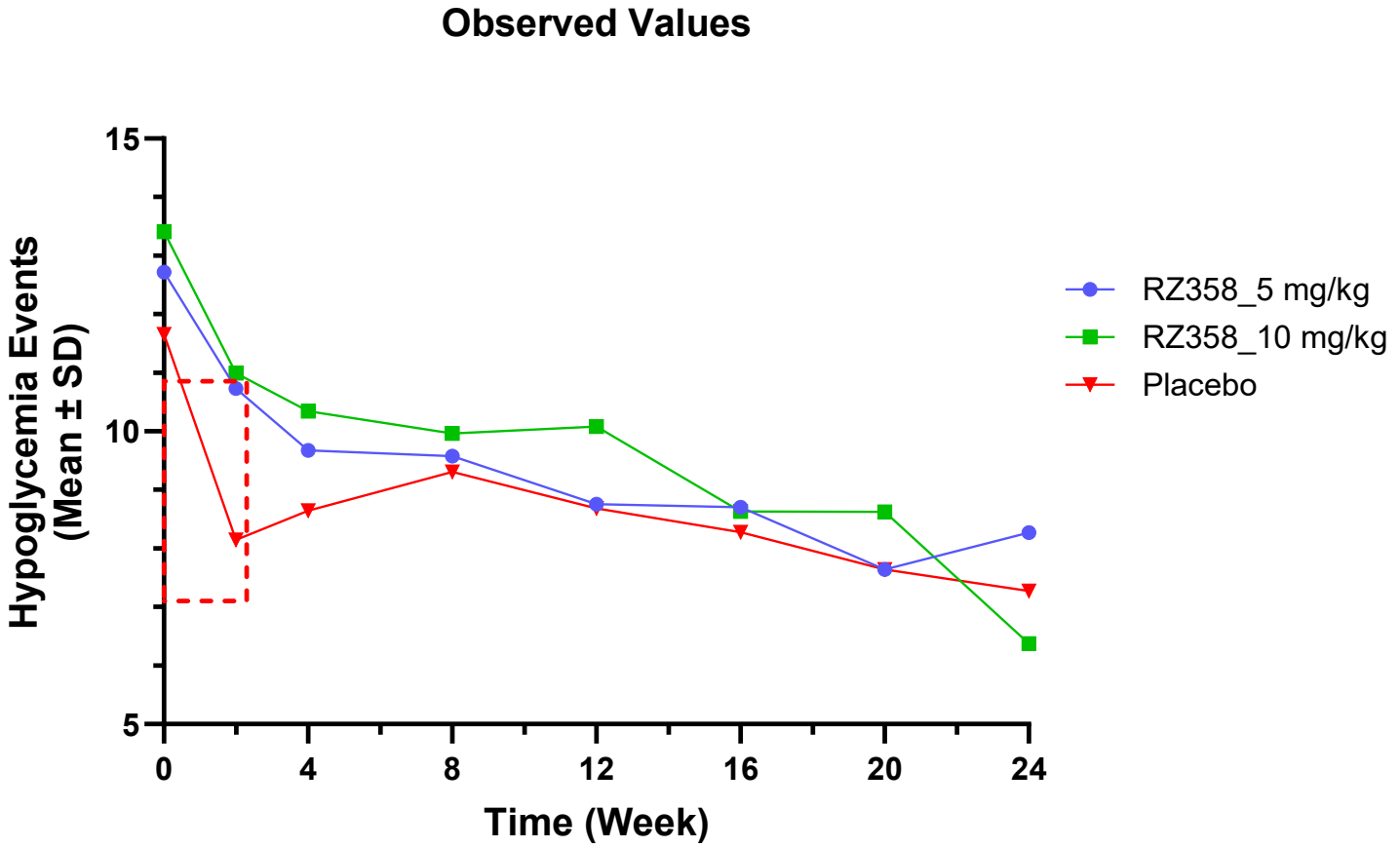
Decrease in Cleared Insulin Indicates Drug Activity at Insulin Receptor Target, and is Comparable to Ph2 RIZE Study

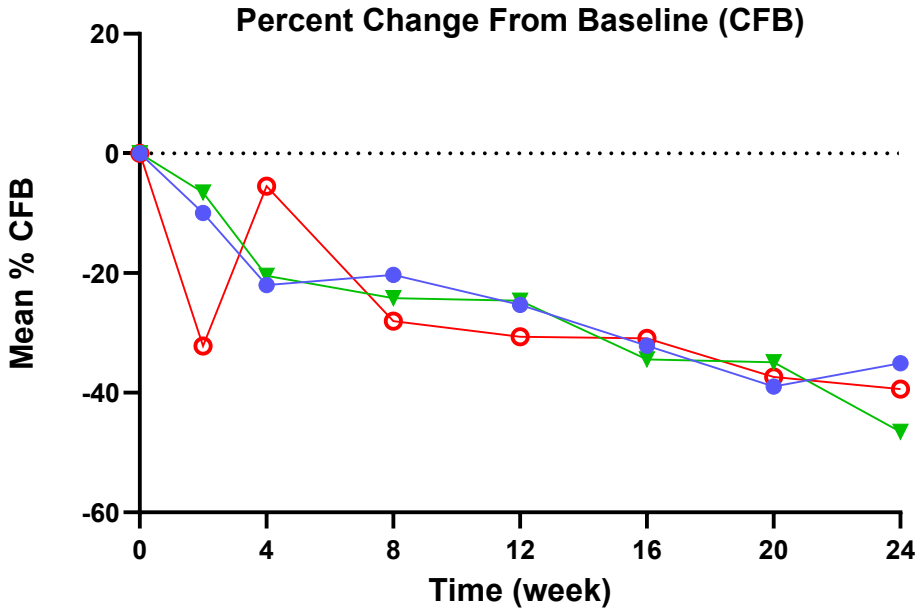
Circulating Insulin:
Sensitive Biomarker of Drug Activity

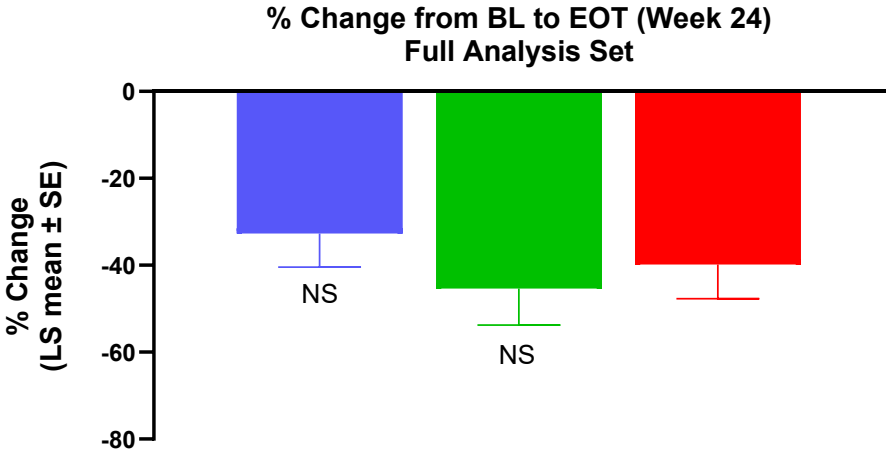


@2026 Rezolute, Inc. All Rights Reserved.

Study Effect on Unblinded SMBG Occurred Early in Dosing: Primary Endpoint Not Met (Change in Avg Weekly Hypo Events by SMBG)





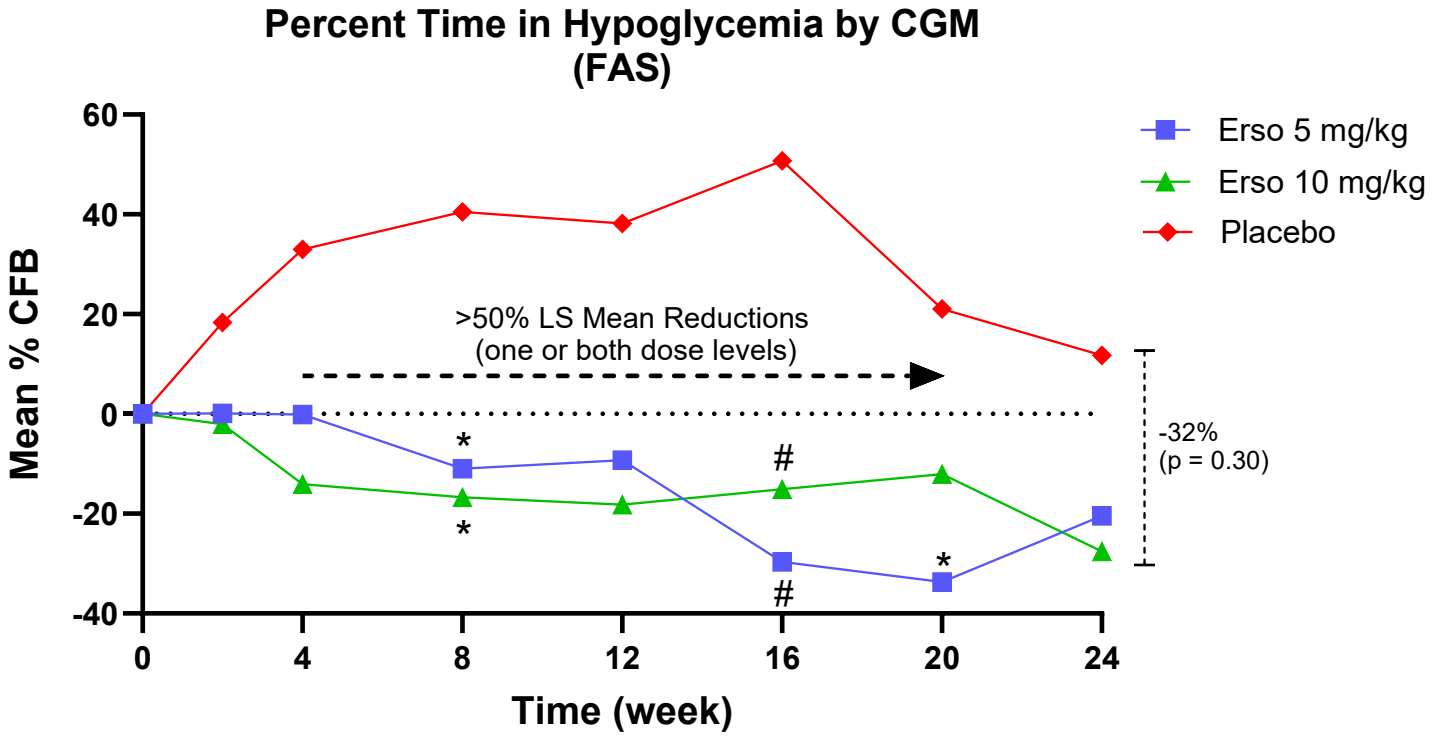


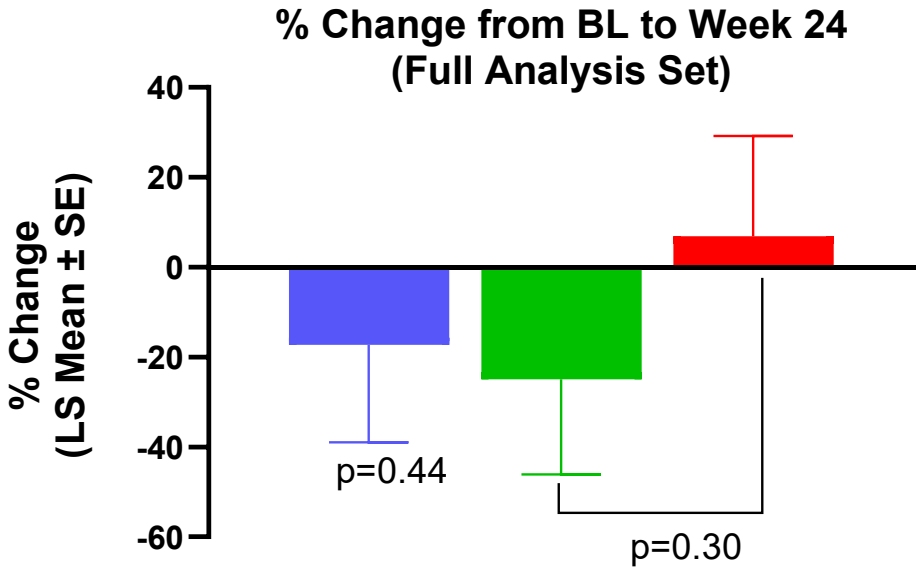
SMBG = self-monitored blood glucose, BL = baseline, EoT = end of treatment

@2026 Rezolute, Inc. All Rights Reserved.

Secondary Endpoint: Clinically Significant Reductions in Time in Hypoglycemia (CGM) not Stat. Sig. at Wk24/EOT

- Reductions of >50% compared to placebo with nominal statistical significance at the noted timepoints
- Not statistically significant at SAP-specified Week 24/EOT analysis window (-32%; p=0.30 at 10 mg/kg)





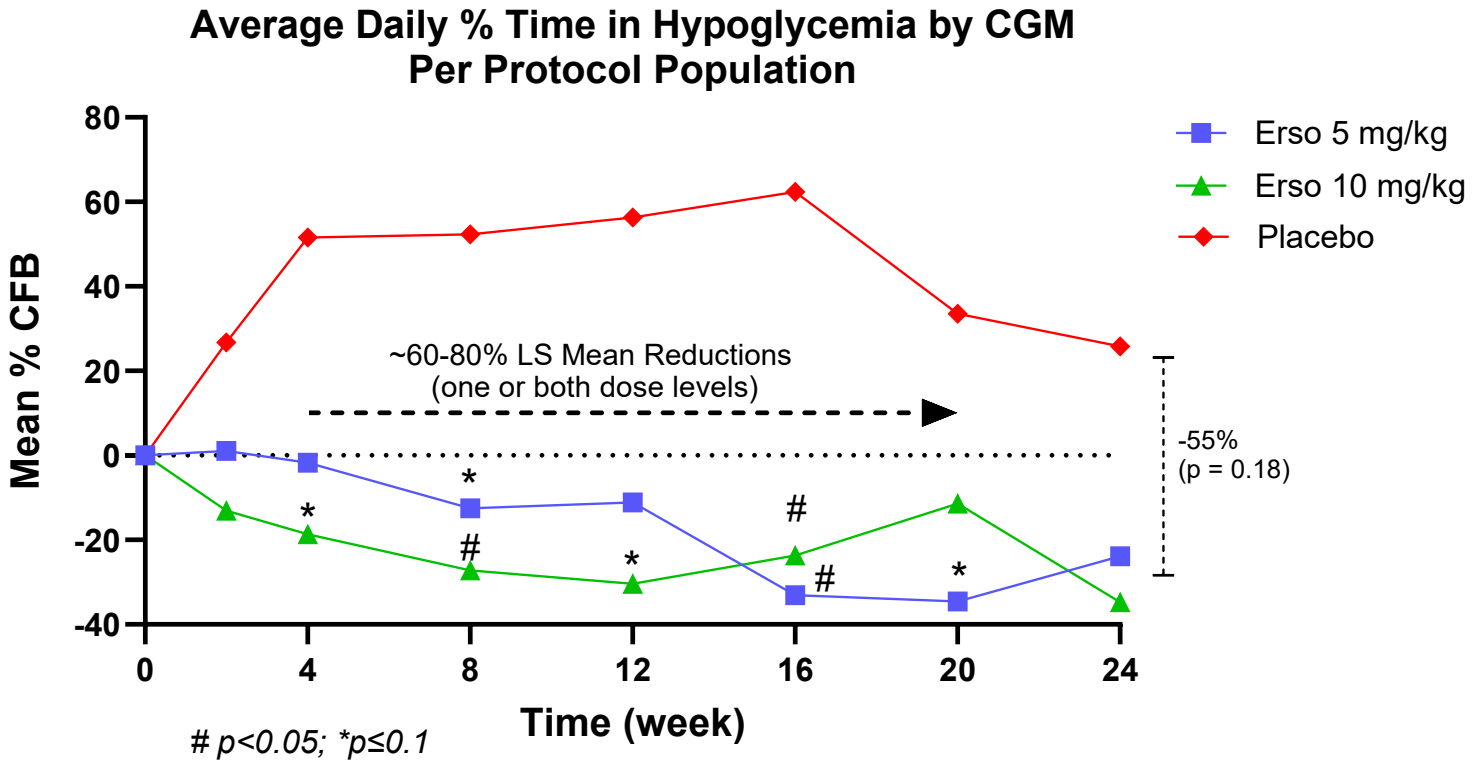
 # Significant reduction vs PBO (p<0.05; both doses) at Week 16;
**p≤0.1 at Weeks 8 (both doses) and 20 (5 mg/kg)*

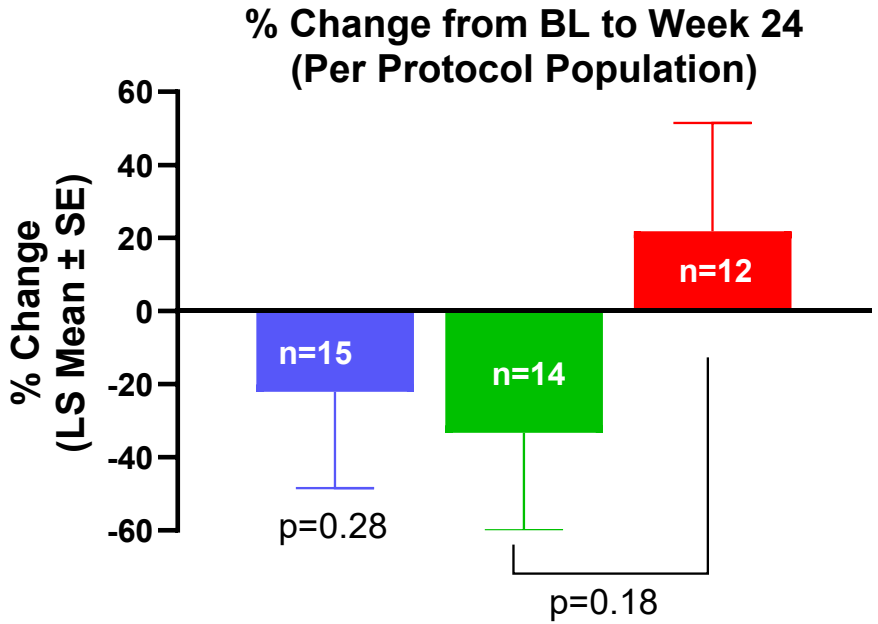
CGM = continuous glucose monitor, SAP = statistical analysis plan, FAS = full analysis set; CFB = change from baseline, PBO = placebo, BL = baseline

@2026 Rezolute, Inc. All Rights Reserved.

Time in Hypoglycemia Reductions (CGM) More Significant in the Per Protocol Set (PPS)* (n=41)

- Reductions of ~60-80% compared to placebo with nominal statistical significance at the noted timepoints
- Not statistically significant at SAP-specified Week 24/EOT analysis window (-55%; p=0.18 at 10 mg/kg)

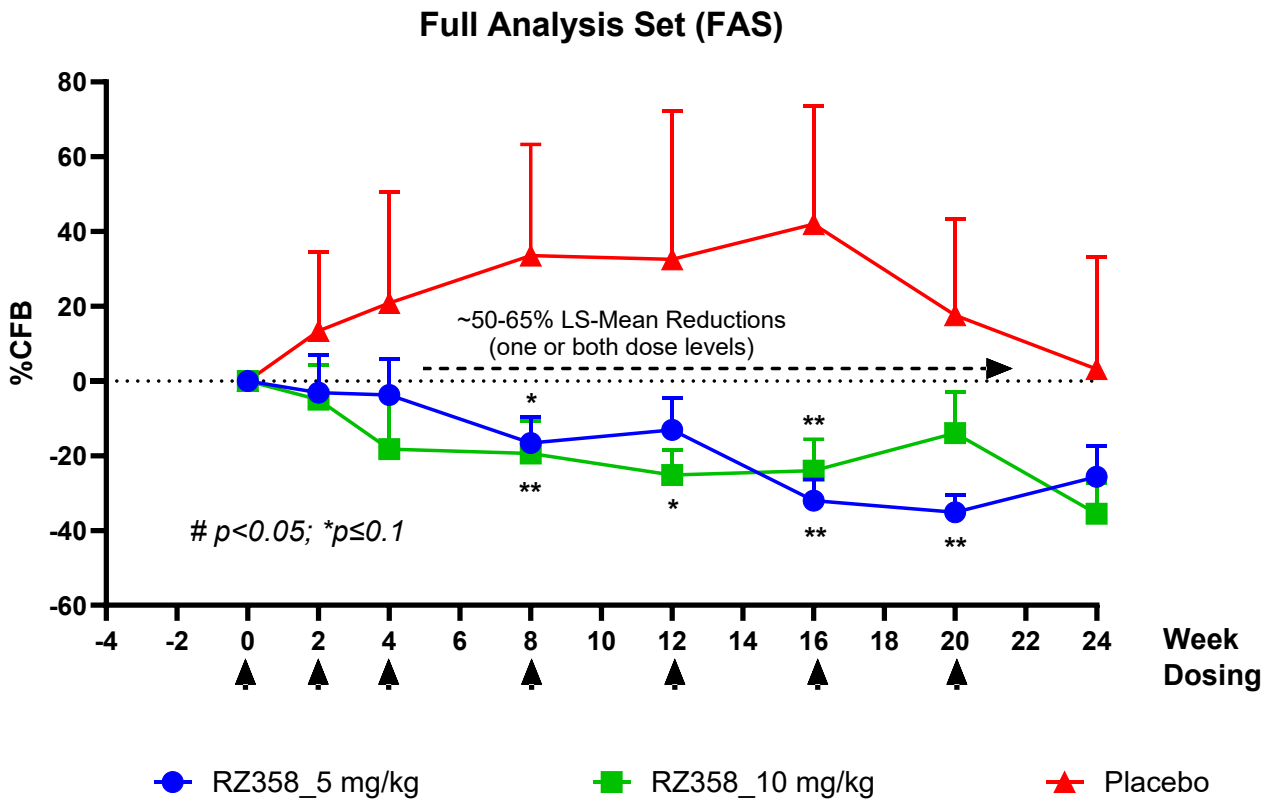


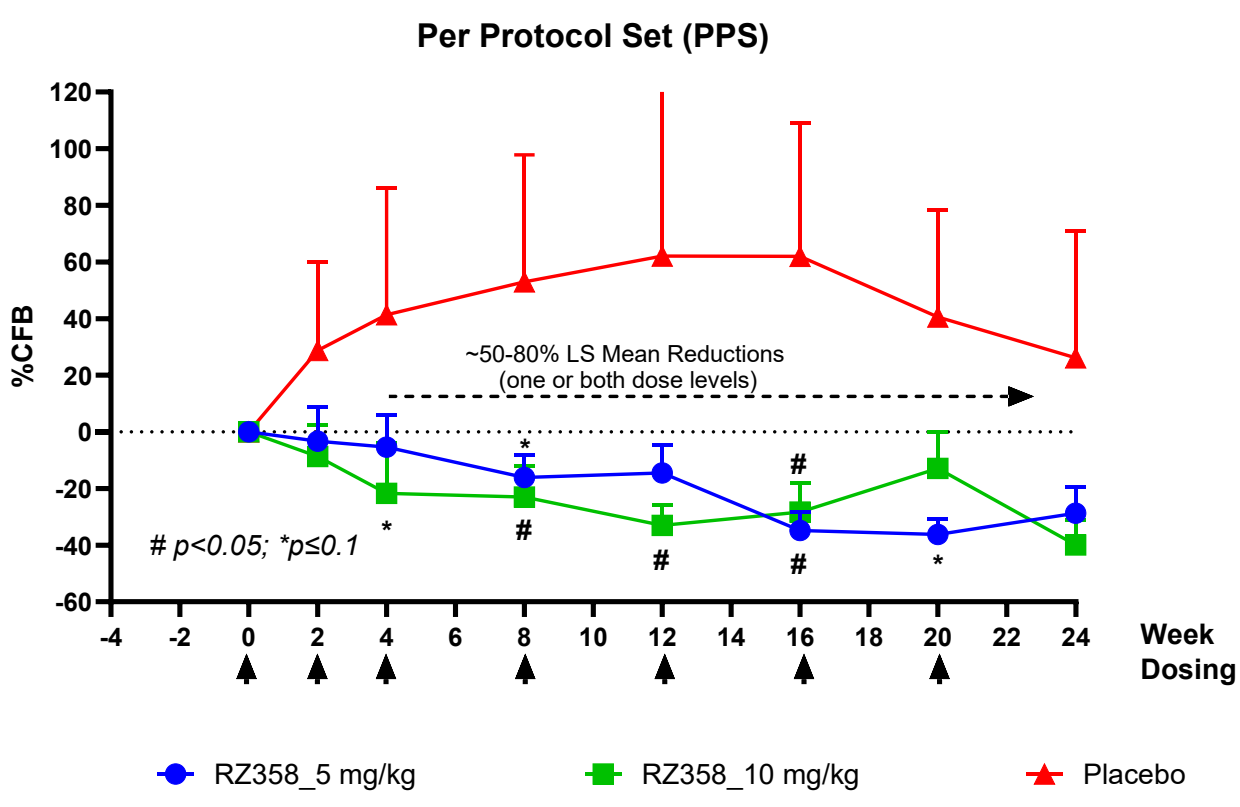


*Per-Protocol Set (PPS): Defined in blinded fashion prior to database lock and excludes participants with below threshold SMBG/CGM data collection, significant escalation in background SOC, and early discontinuations.
CGM = continuous glucose monitor, SAP = statistical analysis plan, EOT = end of treatment, CFB = change from baseline, BL = baseline, SMBG = self-monitored blood glucose, SOC = standard of care

@2026 Rezolute, Inc. All Rights Reserved.

Significant Reductions in Average Weekly Hypoglycemia Events by CGM in FAS and PPS Populations (Pre-Specified Endpoint)



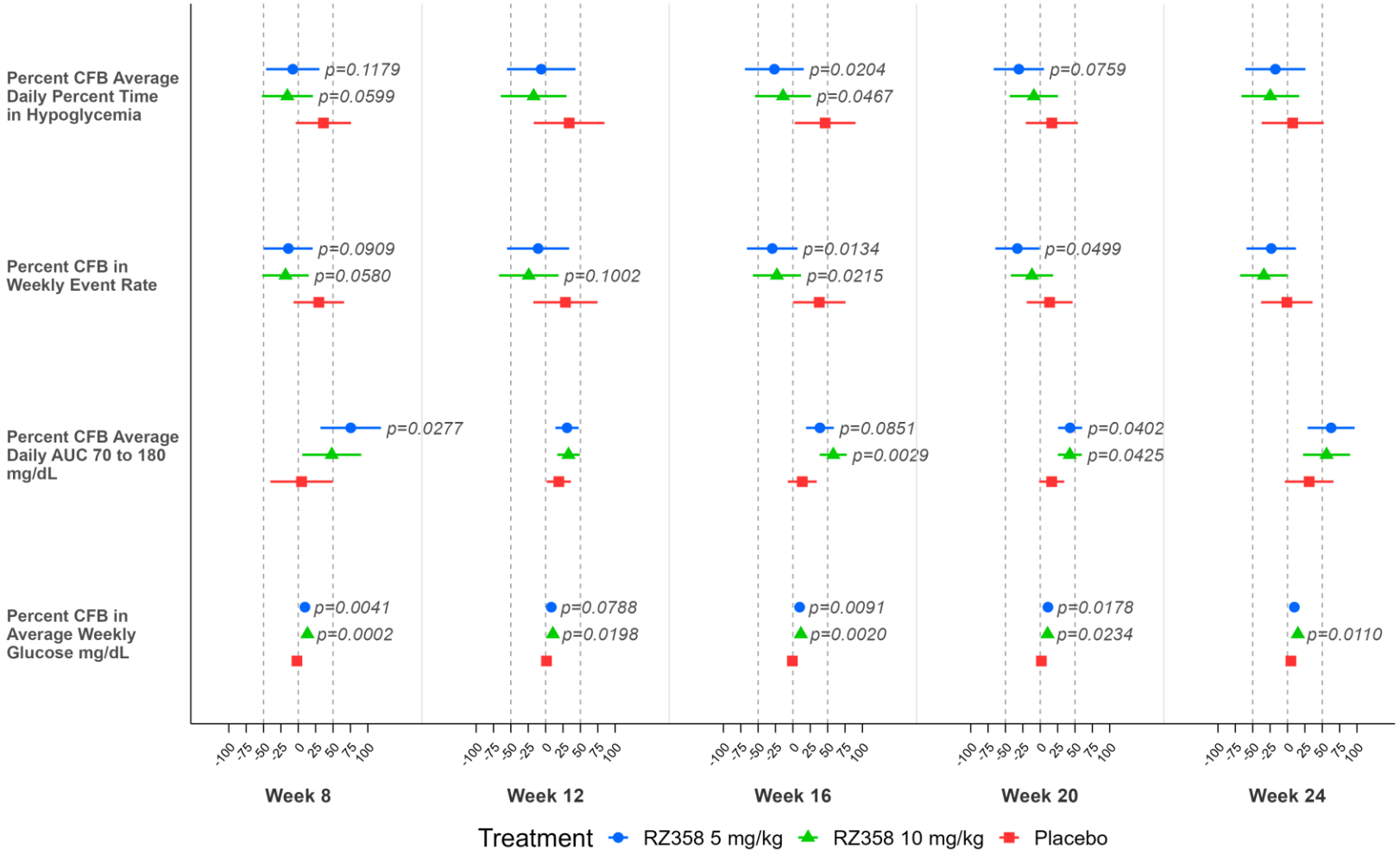


CGM = continuous glucose monitor, FAS = full analysis set, PPS = per protocol set,
CFB = change from baseline

@2026 Rezolute, Inc. All Rights Reserved.

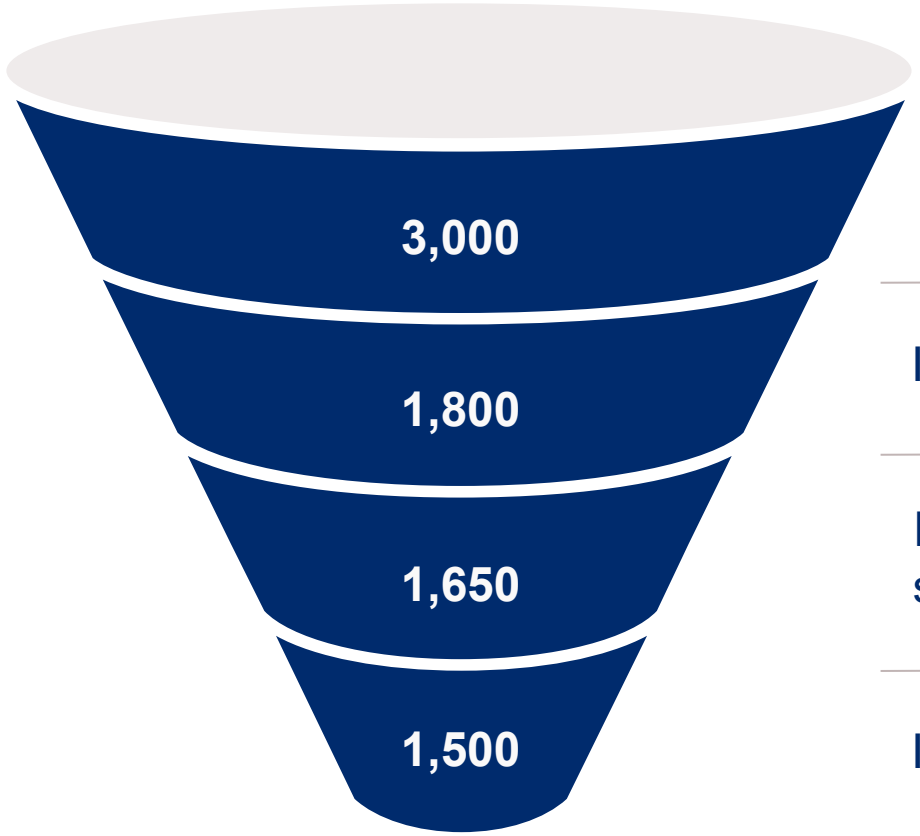
Consistent and Significant Glycemic Improvements Across Multiple CGM Outcomes in the Maintenance Phase of Dosing (every 4 weeks)

LS-Mean (95% CI) Percent Change from Baseline; FAS Population



@2026 Rezolute, Inc. All Rights Reserved.

~1,500 Initially Addressable Pediatric Patients in U.S.



Verified in the claims database[1]
- *Hypoglycemia + SOC congenital HI medical therapies**

Initial market after removing ~40% DZ responsive patients

Initial market after removing ~5% patients with a surgically curable focal lesion

Initially addressable pediatric patients at launch

Addressable market may grow with use in DZ responsive patients with significant side effects

[1] Claims database: Forian and Veeva Compass. *SOC = Standard of Care which includes Diazoxide (DZ), Somatostatin Analogs (SSAs), and NTP. There is no specific ICD-10 code for congenital HI.

@2026 Rezolute, Inc. All Rights Reserved.

Tumor HI

Pathophysiology and Clinical Presentation

- Hypoglycemia caused by two distinct tumor categories:
  - Islet Cell Tumors (ICT)
    - Excessive secretion of insulin
    - Malignant insulinomas are the most common ICTs that cause hypoglycemia
  - Non-Islet Cell Tumors (NICT)
    - Produce and secrete insulin-like paraneoplastic substances such as IGF-2 that over activate the insulin receptor
    - Hepatocellular carcinomas (HCC) are the most common NICTs that cause hypoglycemia in addition to several other tumor types including fibrosarcomas and mesotheliomas
- Significant unmet need across both tumor types
  - Resulting hypoglycemia is often severe and may have serious adverse outcomes
  - Limited treatment options with poor efficacy and safety profiles
  - High morbidity and mortality rates
  - Frequent prolonged hospitalization
  - Leads to frequent deferral of tumor treatment
  - Significant adverse impact on patient quality of life

@2026 Rezolute, Inc. All Rights Reserved.

High Unmet Medical Need with Current Standard of Care

- Unmet need for medical therapies to directly treat hypoglycemia over the entire course of the patient cancer journey
- Therapies to treat hypoglycemia caused by malignant insulinoma are often ineffective or poorly tolerated
  - Diazoxide (DZ) is the only approved treatment but has suboptimal response rates and serious side effects
  - Somatostatin analogs (SSAs) are used off-label with limited success, and may cause paradoxical worsening of hypoglycemia
  - mTOR-inhibitors are used off-label and have potentially serious side effects
- Limited and often ineffective treatment options for NICTH
  - DZ and SSAs do not work in NICTs because HI is not mediated by insulin

ICT: islet-cell tumor. NICT: non-islet cell tumor. SOC: standard of care.

@2026 Rezolute, Inc. All Rights Reserved.

Real-world Patient Benefit in Expanded Access Program of Ersodetug

- Multiple tumor HI patients with severe refractory hypoglycemia
  - Hospitalized and in life-threatening or hospice-bound condition
  - Required continuous high volume/concentration parenteral glucose
  - Tumor-directed therapies (e.g., embolization, radio therapy, chemotherapy) deferred because of hypoglycemia
  - Physician-requested use of ersodetug
- Administration of ersodetug through EAP has resulted in:
  - Substantial hypoglycemia improvement with no significant side effects[1]
  - Complete discontinuation of IV dextrose/total parenteral nutrition (TPN) in 75% of patients[2]
  - Discharge from inpatient to outpatient care
  - Ability to resume regular activities (e.g., driving, walking dog)
  - Resumption of tumor-directed therapies

Joslin Diabetes Center | HARVARD MEDICAL SCHOOL AFFILIATE

Stanford MEDICINE

BRIGHAM HEALTH
BWH BRIGHAM AND WOMEN'S HOSPITAL

OHSU

Hôpital Cochin Port-Royal AP-HP

MOFFITT CANCER CENTER

[1] Based on real-world patient benefit demonstrated in Expanded Access Program the US Food and Drug Administration (FDA) granted Orphan Drug Designation to ersodetug for the treatment of hypoglycemia due to tumor HI. Sources: n engl j med 389;8 Aug24,2023 - https://www.nejm.org/doi/full/10.1056/NEJMc2307576?query=TOC&cid=NEJM+eToc%2C+August+24%2C+2023+DM2279684_NEJM_Non_Subscriber&bid=1754093795

[2]Mary Elizabeth Patti, MD et al. A Case Series on the Compassionate Use of Ersodetug, an Insulin Receptor Modulating Antibody, in Patients with Refractory Hypoglycemia Due to Malignant Insulin-Secreting Tumors. Poster #087. ENDO 2026, Chicago

@2026 Rezolute, Inc. All Rights Reserved.

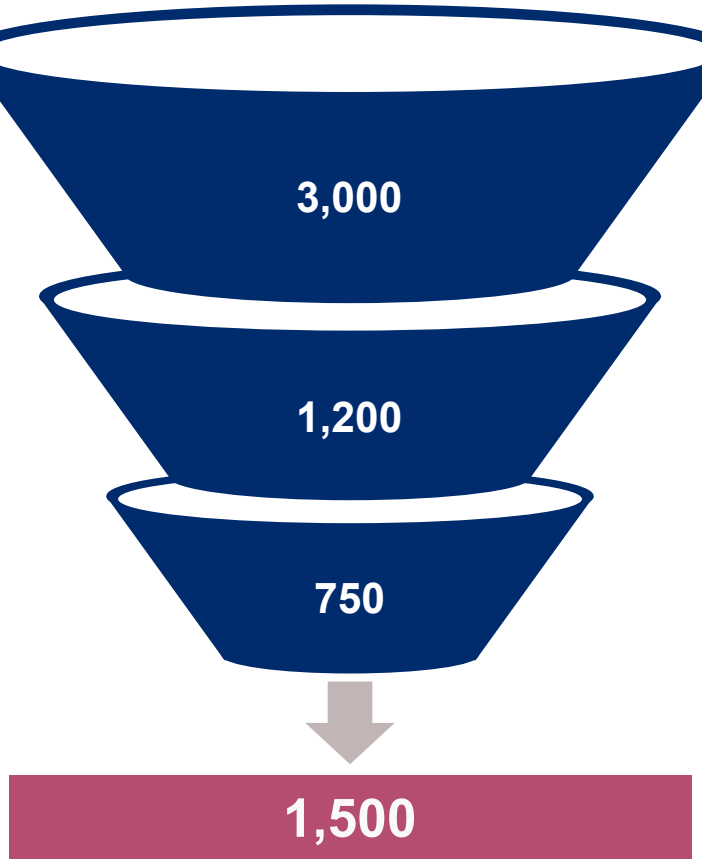
Ongoing Phase 3 (upLIFT) Study

- Global, multi-center, single-arm, open-label registrational study
- Patient population (n=~16)
  - Adult ICT and NICT patients with HI who have not achieved adequate hypoglycemia control with SOC therapies
- Primary endpoint: number of participants achieving ≥50% reduction from baseline IV glucose requirements (glucose infusion rate; GIR)
  - Additional endpoints for GIR, time to discharge from the hospital, and extent of hypoglycemia in the outpatient setting, ECOG status, and patient reported quality of life
- Treatment arms and dosing regimen
  - Once weekly administration of 9 mg/kg per week as add on to SOC over 8-week pivotal treatment period
  - All participants may receive ersodetug in long-term extension
- Topline results expected second half of 2026
  - Interim open-label outcomes are favorable

ICT: islet-cell tumor. NICT: non-islet cell tumor. SOC: standard of care.

@2026 Rezolute, Inc. All Rights Reserved.

~1500 Initially Addressable Malignant Insulinoma Patients in the U.S.



Malignant insulinoma patients identified in claims (includes two or more C25.4 or E31.21+)

~40% patients refractory to surgery and medical management including DZ

Initial commercial effort: refractory patient population at nationally recognized cancer institutes or academic centers

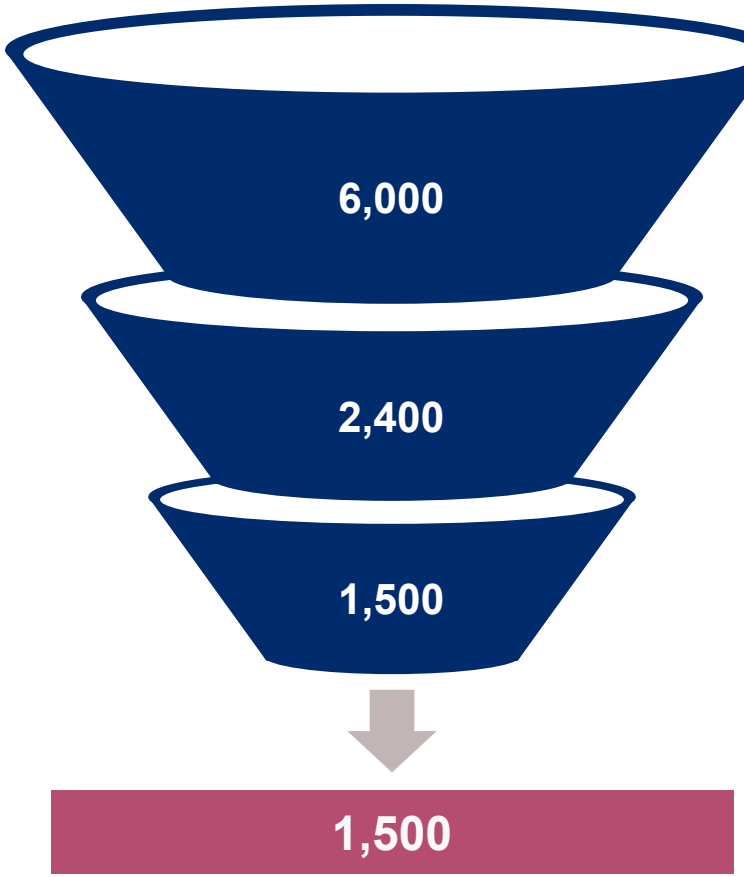
Estimated treatment duration for ~750 patients is 2 years

- 5-year survival rate in this population is between ~24% to 67%
- *Entire refractory population = significant market expansion opportunity*

The ICD-10 code C25.4 is for malignant neoplasm of the endocrine pancreas, which refers to cancer of the endocrine pancreas. The above analysis shows the unique patient count based on claims data from Forian and Veeva Compass; +The ICD-10 code E31.21 is for multiple endocrine neoplasia [MEN] type I, also known as Wermer's syndrome. Included in the above analysis are MEN1 patients with hypoglycemia and treated for hypoglycemia; DZ = Diazoxide; * 60% of these patients respond to DZ (https://www.ncbi.nlm.nih.gov/books/NBK544299/).

@2026 Rezolute, Inc. All Rights Reserved.

~1,500 Initially Addressable NICTH Patients in the U.S.



Severe NICTH patients identified in claims*
(Tumor Diagnosis + Hypoglycemia + Steroids + Hospitalization)

~40% patients refractory to SOC (tumor-directed and/or steroids) and requiring hospital stays + IV glucose*

Initial commercial effort: refractory patient population at nationally recognized cancer institutes or academic centers

Estimated treatment duration of 1 year

- 5-year survival rates from 8% to 39%+
- *Entire refractory population = significant market expansion opportunity*

* Analysis identified patients in the Forian and Veeva Compass claims database that matched phase 3 tumor HI clinical inclusion/exclusion criteria.

@2026 Rezolute, Inc. All Rights Reserved.

Combined Commercial Opportunity in Congenital and Tumor HI Indications

Weight-based Dosing Applies to Both Indications

Tumor HI patients require ~3X more vials compared to congenital HI patients

- Each vial is 80 mg/mL
- Congenital HI maintenance dose: 10 mg/kg
  - Pediatric patient average weight: ~24 kg
  - Patients will use 3 vials per infusion
  - 39 vials per year per patient assuming infusion every four weeks
- Tumor HI maintenance dose: 9 mg/kg
  - Adult patient average weight: ~80 kg
  - Patients will use 9 vials per infusion
  - 117 vials per year per patient assuming infusion every four weeks

@2026 Rezolute, Inc. All Rights Reserved.

Initial Combined U.S. Market Opportunity: 4,500 Patients

- Congenital HI Market
  - Pediatric ultra-rare disease pricing
  - Lead indication establishes clinical effectiveness and payer access pathway for ersodetug in HI
  - Addressable market of ~1,500 pediatric patients
- Tumor HI Market
  - Malignant Insulinoma
    - Immediate opportunity with high awareness and concentration of patients among national cancer institutes
    - Addressable market of ~1,500 patients
  - NICTH
    - Nascent market with low disease awareness and underdiagnosis
    - Addressable market of ~1,500 patients
  - High prescriber overlap between the two indications among adult endocrinologists

Tumor HI weight-based pricing at ~3X congenital HI represents significant revenue opportunity

@2026 Rezolute, Inc. All Rights Reserved.

An Ultra-rare Disease Company Treating Refractory Hypoglycemia

Mission-driven to improve outcomes for individuals with refractory hypoglycemia caused by hyperinsulinism (HI)

RZ358 (ersodetug) is an antibody designed to treat refractory hypoglycemia caused by all forms of (HI)

Ersodetug has been studied in clinical trials and used in real-world cases for the treatment of HI

Total $1B+ global market opportunity with additional upside through expansion

Well-capitalized for execution – $120 million in cash with runway to mid-2028

@2026 Rezolute, Inc. All Rights Reserved.

Rezolutebio.com