REZOLUTE

Corporate Presentation

A Metabolic and Orphan Disease Company

NASDAQ: RZLT

Forward Looking Statements

The information provided herein contain "forward-looking statements" within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. Forward-looking statements can be identified by words such as "anticipate," "intend," "plan," "goal," "seek," "believe," "project," "estimate," "expect," "strategy," "future," "likely," "may," "should," "will" and similar references to future periods. These Forward-Looking statements include, but are not limited to, statements regarding the sunRIZE clinical study, the DME RZ402 study, the RIZE study, the ability of RZ358 and RZ402 to become effective treatments, the effectiveness or future effectiveness of RZ358 and RZ402 as treatments, and statements regarding clinical trial timelines for either treatment. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based only on Rezolute's current beliefs, expectations and assumptions regarding the future of its businesses, results of and timing of clinical trials, financial condition and results of operations, future plans and strategies, projections, anticipated events and trends, the economy and other future conditions. Because forward-looking statements relate to the future, they are subject to inherent uncertainties, risks and changes in circumstances that are difficult to predict and many of which are outside of Rezolute's control. Rezolute's actual results including the timing and results of clinical trials may differ materially from those indicated in the forward-looking statements. Therefore, you should not place undue reliance on any of these forward-looking statements. Important factors that could cause Rezolute's actual results including the timing and results of clinical trials to differ materially from those indicated in the forward-looking statements are discussed or identified in Rezolute's filings made with the U.S. Securities and Exchange Commission. Any forward-looking statements made by Rezolute in this information are based only on information currently available to Rezolute and speak only as of the date on which the statement is made. Rezolute undertakes no obligation to update any forward-looking statement, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise except as required by applicable law.

Creating Long-term Value By Advancing Transformative Therapies

RZ358: Monoclonal antibody addressing all forms of hyperinsulinism (HI)

- Congenital HI: Global Phase 3 trial (sunRIZE); **topline results expected mid-2025**
- Tumor HI: **success in multiple cases under our Expanded Access Program (EAP)**

RZ402: Once daily oral therapy in Phase 2 for diabetic macular edema (DME)

- Potential to change treatment paradigm dominated by eye injections
- **Topline results expected Q2 2024**

Seasoned management team

- Demonstrated success from early development through commercialization

Cash runway through Q3 2025

- Past topline results for both programs

Strong investor base focused on long-term value

Each program has potential >$1B+ market opportunity

- Potential upside with expanded indications

EAP: expanded access program.

Pipeline

Program	Target	Status	Preclinical	Phase 1	Phase 2	Phase 3
RZ358	**Congenital Hyperinsulinism (HI)** ***rare*** *pediatric disease*	Currently enrolling				**Mid-2025**
	Tumor Hyperinsulinism (HI) ***rare*** *disease*	EAP Enabled Emergency Use Authorization			**Alignment with FDA for potential late-stage clinical study**	
RZ402	**Oral PKI for Diabetic Macular Edema** *(DME)*	Fully enrolled				**2Q 2024**

EAP: expanded access program

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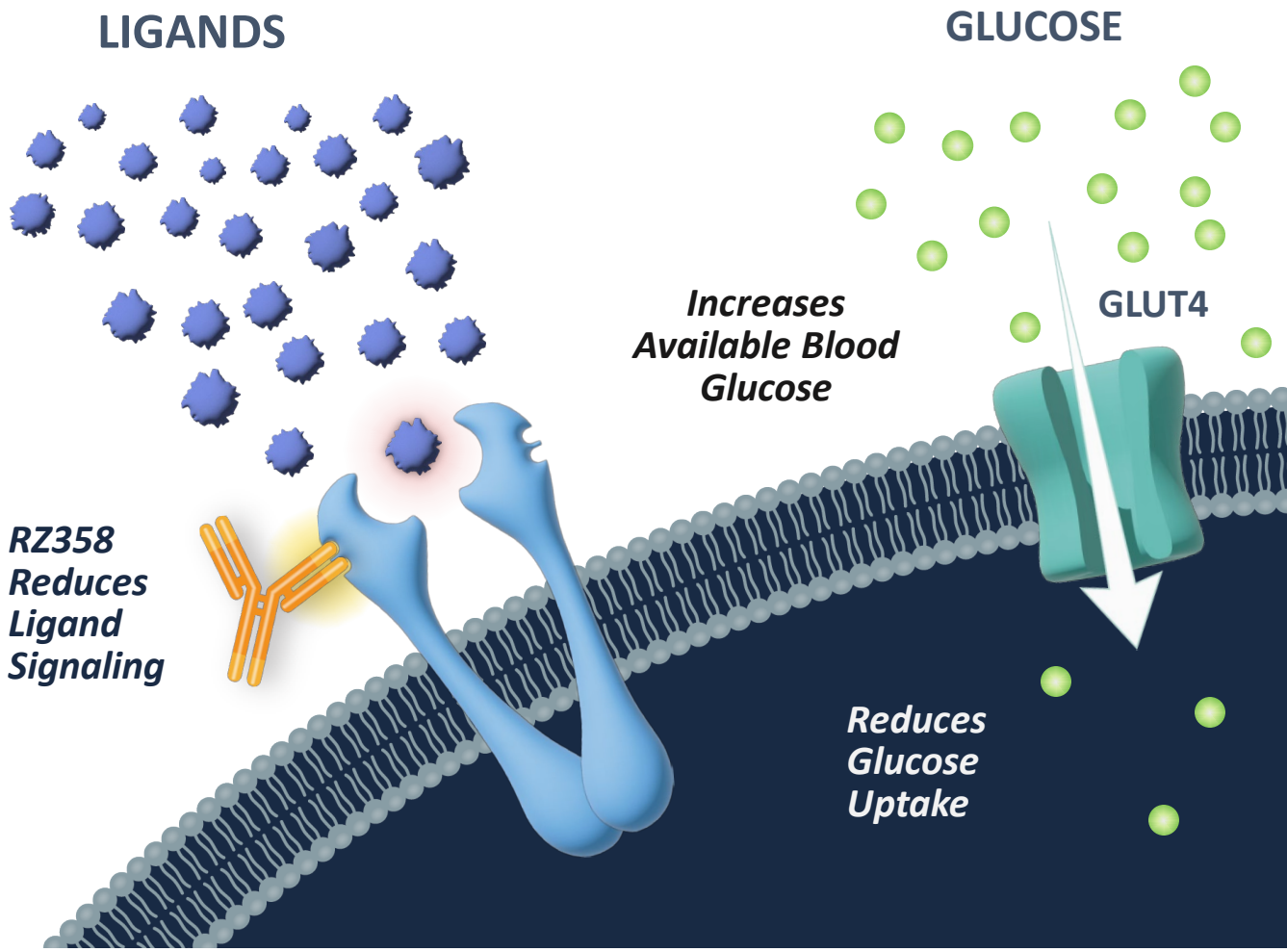
RZ358

Antibody for Hyperinsulinism (HI)

An Antibody Created to Address all Forms of HI

- **RZ358 allosterically binds to the insulin receptor** to modulate the **signaling effect of ligands such as insulin and other substances** to maintain glucose values in a healthy range
- Novel mechanism of action by **operating downstream from pancreatic insulin over-secretion (usual SOC target)**
- **Administered by IV infusion** every 2 to 4 weeks



HI: hyperinsulinism. SOC: standard of care. GLUT4: glucose transporter type 4.

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Congenital HI

Pediatric rare genetic disease characterized by dysregulated and excessive insulin production

Congenital HI Disease Background

- **1 in 28,000 live births in the US**
  - 25 years of treatment required on average
  - ~3500 cases in the US
  - Often presents within first month of life
- **Most common cause of persistent hypoglycemia in infants and children**
- **Symptoms often not recognized until life-threatening**
- **Risk of coma, death, and other serious complications**
- **50% of children have neurological deficiencies**
- **No therapy has been developed and approved for this indication**

Psychosocial and Financial Burden

"Everything I see just drives home the fact we will never lead a normal life. So many of my hopes and dreams for our family and for our little one are shattered."[1]

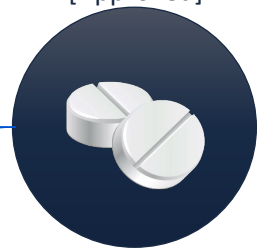
Carbohydrate Supplementation

Dependence on nutritional support limits the ability to have normal lives, especially in social situations[1]

HI: hyperinsulinism. SOC: standard of care. **1.** Banerjee I, et al. *Orphanet J Rare Dis.* 2022;17(1):61.

Available Treatment Options are Suboptimal

Diazoxide
[Approved]

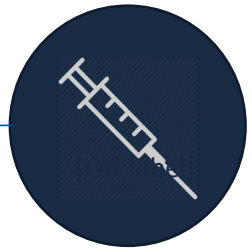


- Ineffective in 50% of patients (with K_{ATP} mutations)
- FDA black box for pulmonary hypertension
- Fluid retention affecting heart/lungs
- Facial changes and excessive hair growth

Carbohydrate Supplementation

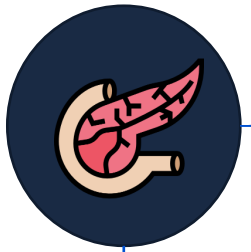
- Frequent, glucose-enriched oral feeds or continuous enteral feeds via NG/GT
- Multifactorial feeding aversions affect a large proportion of children with cHI
- Negative impact on normal daily activities and social interactions

Glucagon



- Current formulations short-acting
- Temporary measure for emergent glucose correction
- Repeated use may deplete liver glucose stores
- Long-term efficacy is modest

Pancreatectomy



Resection for diffuse disease

- Invasive procedure, not done globally
- Hypoglycemia may persist for years in up to half of patients
- Eventually insulin therapy required
- Requires adjuvant medical management, and/or repeat surgery

Resection for focal disease

- Limited number of overall cases
- Only done at specialized centers
- Can be curative for patients

Somatostatin Analogues
[Off label]

- Marginal efficacy, effects wane with repeat dosing
- Gastrointestinal side effects
- Risk of NEC, particularly in newborns
- Potential interaction with pituitary hormones (growth and thyroid)

Congenital HI Treatment Landscape

Diagnosis and Treatment Pathway

~3,500 congenital HI patients in the US

Diazoxide Trial Period
(up to 15 mg/kg/day)

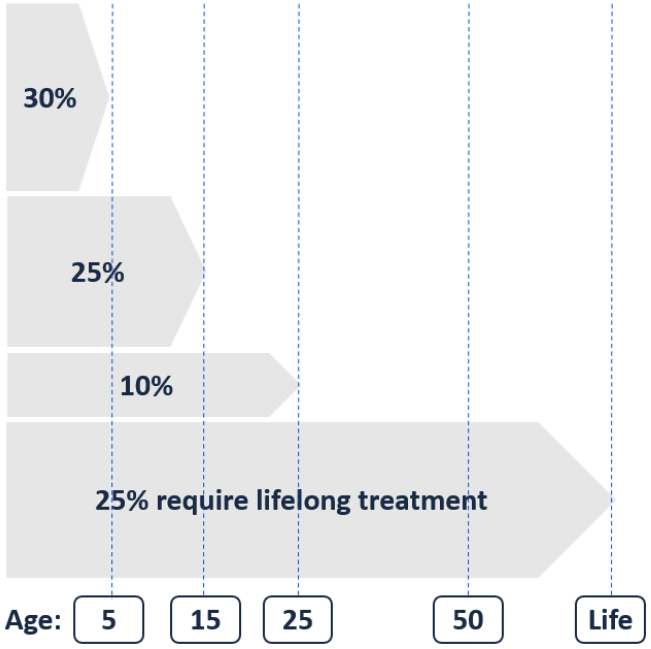
After 5-Day Treatment:

- **Responsive to DZ** — 40%
  - **Tolerated** — ~70%
  - **Unacceptable Side Effects** — ~30% or 420 pts
- **Unresponsive to DZ** — 60%
  - **Diffuse** — ~60% or 2100 pts
  - **Focal** — ~40%

RZ358 Addressable Patient Population ~2,500

Surgical Candidates

Duration of Treatment
(Age when Patient No Longer Needs Therapy)



HI: hyperinsulinism. DZ: diazoxide.

Phase 2b RIZE Study Results

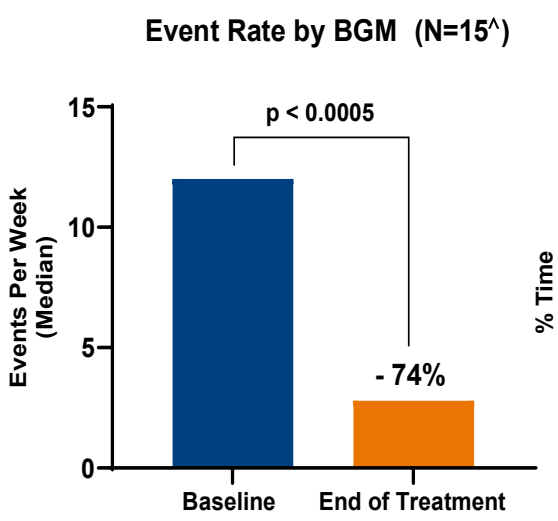
- **23 participants enrolled**
  - Average age ~6.5 (16 participants were between 2-6 years of age)
  - Diverse group across gender and genetics
- **~20% average daily time in hypoglycemia and 13 hypoglycemia events per week at baseline**
  - Participants were on SOC
- **Generally safe and well-tolerated**
  - No adverse drug reactions
  - No study terminations
  - No clinically-significant hyperglycemia or hyperglycemia AEs
- **Study exceeded expectations for glucose correction:**
  - Average improvement in hypoglycemia of up to ~90%
  - Nearly universal response rate at the top dose
- **Predictable and dose-dependent pharmacokinetics**

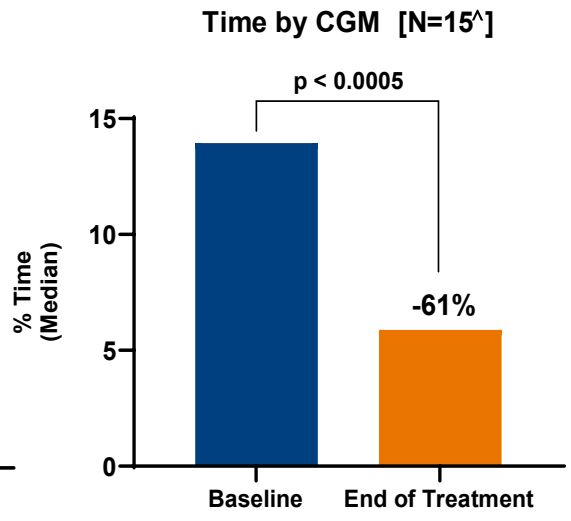
SOC: standard of care. AEs: adverse events.

Substantial Improvement in All Hypoglycemia Metrics

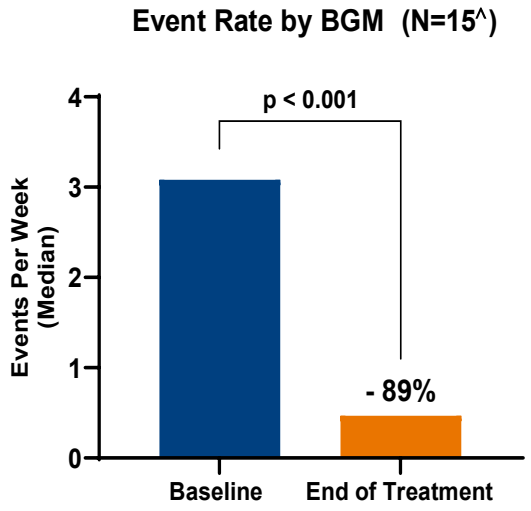
Clinically-Relevant Threshold of ≥ 25% Hypoglycemia Correction
(Time and Events) Was Met and Exceeded

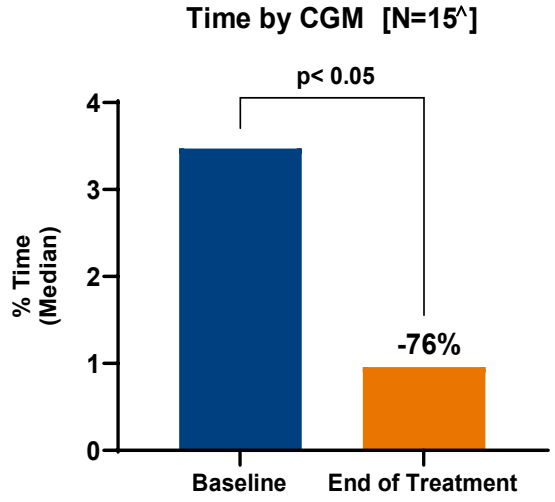
Hypoglycemia (<70 mg/dL)





Severe Hypoglycemia (<50 mg/dL)



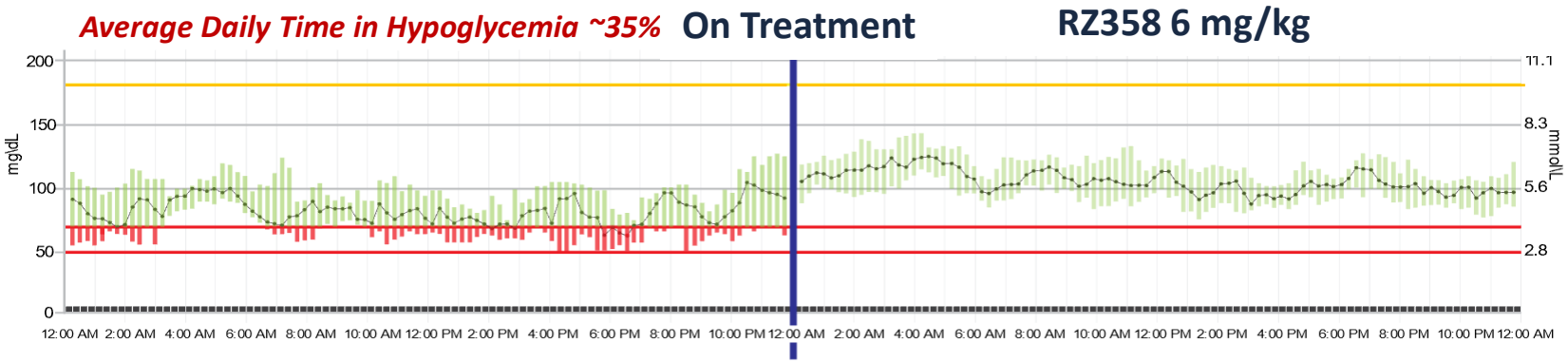


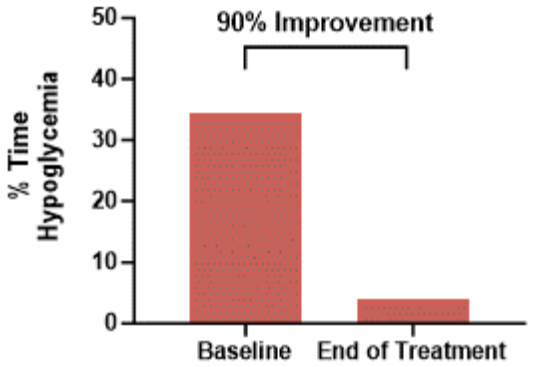
Pooled 6 and 9 mg/kg dose levels representative of Phase 3 dosing and group sizes

BGM: blood glucose monitoring. CGM: continuous glucose monitoring. One 9 mg/kg participant excluded from analyses for stopping background therapy while on study; two others wore CGM incorrectly which impacted efficacy by CGM but were included in analyses.

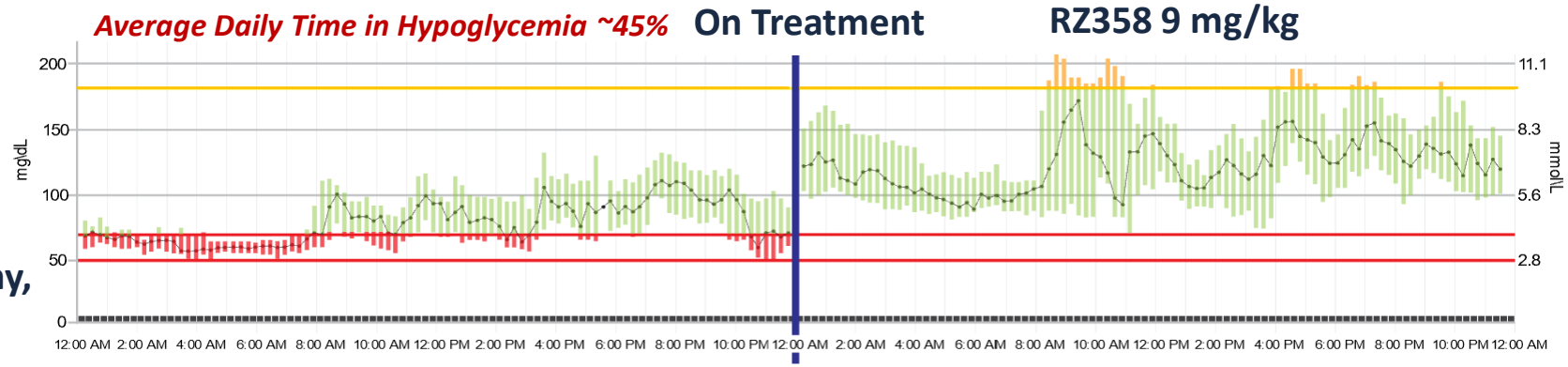
Exemplary Hypoglycemia Improvement

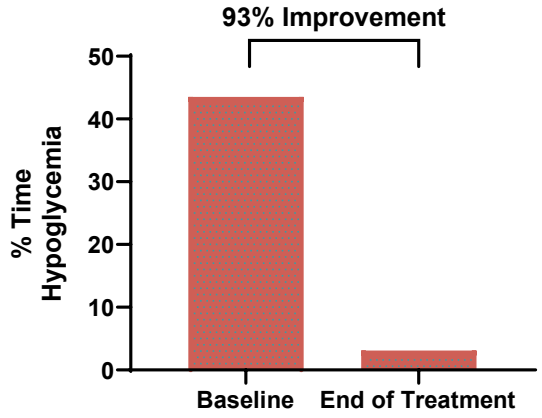
2-Year-Old Patient on Somatostatin Analog





6-Year-Old; Failed Other Therapies 65% pancreatectomy, No meds





Baseline CGM period (≥10 days) **Treatment Evaluable CGM (2-weeks)**

CGM: continuous glucose monitoring.

Phase 3: The sunRIZE Study

sunRIZE RZ358-301

- **Multi-center safety and efficacy registrational study**
- **56 participants**
  - Ages 3 months and above who have not achieved adequate glycemic control with standard of care medical management
- **Primary endpoint: change in average hypoglycemia events per week**
  - Secondary endpoints include change in average daily percent time in hypoglycemia, change in severe hypoglycemia events and time, time in a target glucose range, and symptomatic hypoglycemia events
- **Pivotal treatment arms**
  - ~48 participants ages 1 year and above randomized in double blind, placebo-controlled fashion
  - Three bi-weekly loading doses, then 4 monthly doses over a total 6-month treatment period
    - 5 mg/kg (+ SOC) (n = 16)
    - 10 mg/kg (+ SOC) (n = 16)
    - Placebo (SOC only) (n = 16)
  - Open label treatment arm: ~8 participants ages 3 months to 1 year
  - Eligible participants may continue in a long-term extension study following pivotal treatment
- **Topline results expected mid-2025**

Congenital HI Addressable Market

- **~10K individuals in primary markets**
  - 1 in 28,000 live births and up to 1 in 2,500 live births in certain populations due to consanguinity
  - In RZ358 addressable patient population, disease persists for more than 25 years on average
- **At Launch >50% of the market is addressable**
  - <50% of patients are adequately managed by standard of care
  - Growing percentage of patients on standard of care experience unacceptable side effects
- **Rapid patient identification and concentrated prescriber base enables accelerated adoption**
  - 60% of patients are diagnosed within 1 month of presentation
  - 80% of patients are managed at centers of excellence that are participating the Phase 3 clinical trial
- **Regulatory Designations: Orphan, Pediatric Rare Disease (FDA), PRIME (EMA), ILAP (UK)**
- **Potential for expanded indications such as tumor HI**

$1B+ market opportunity with analogous rare pediatric disease drug pricing

HI: hyperinsulinism.

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Tumor Hyperinsulinism

Hypoglycemia resulting from excessive activation of the insulin receptor caused by tumors

Tumor HI Background

Severe hypoglycemia resulting from excessive activation of the insulin receptor, caused by two distinct tumor types

- **Islet cell tumors (ICTs)**
  - Characterized by the excessive secretion of insulin, insulinomas are the most common type of ICTs
  - ~1,500 individuals in US have malignant/unresectable ICTs with severe and uncontrolled hypoglycemia
  - Under our EAP four individuals with ICT hypoglycemia (ICTH) have been successfully treated with RZ358
- **Non-islet cell tumors (NICTs)**
  - Produce and secrete insulin-like substances such as IGF-2 that bind to the insulin receptor
  - Hypoglycemia may occur in more than 15 different tumor types, 60% of which are malignant
  - ~3,000 individuals in the US have NICT hypoglycemia (NICTH)
  - In an insulin receptor cell model, RZ358 was proven to similarly blunt both IGF-2 and insulin-mediated insulin-receptor signaling, at levels that are disease-relevant in humans
- **Combined RZ358 tumor HI addressable market is 4,500 patients in the US**
  - Normalization of glucose levels is crucial to enable patients to receive cancer therapies and to reduce mortality
  - Significant unmet need for treatment options with improved efficacy and tolerability

Alignment with FDA to pursue late-stage clinical trial of RZ358 in tumor HI

HI: hyperinsulinism. EAP: expanded access program. IGF-2: insulin-like growth factor 2

Tumor HI Hypoglycemia Correction Under our EAP

- **Four hospitalized patients have successfully received RZ358**
  - Refractory to usual SOC therapies for chronic management of hypoglycemia
  - Required continuous high volume/concentration intravenous dextrose or nutritional infusion
  - Hospitalized and in life-threatening or hospice-bound condition because of uncontrollable hypoglycemia
  - Further treatment with tumor-directed therapies (e.g., embolization, radiotherapy, chemotherapy) deferred because of debilitating hypoglycemia
  - RZ358 resulted in substantial hypoglycemia improvement, discontinuation of intravenous dextrose, and hospital discharge

Stanford MEDICINE

Joslin Diabetes Center | HARVARD MEDICAL SCHOOL AFFILIATE

OHSU

EAP: expanded access program. SOC: standard of care. 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

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RZ402

An Oral Once Daily Plasma Kallikrein Inhibitor (PKI) for Diabetic Macular Edema (DME)

The Diabetes Epidemic Drives the DME Market

537M people worldwide have diabetes [2]

- **22M** affected by DME [4]
- **>1M** DME patients - US

>$1.5B

Commercial Market Opportunity

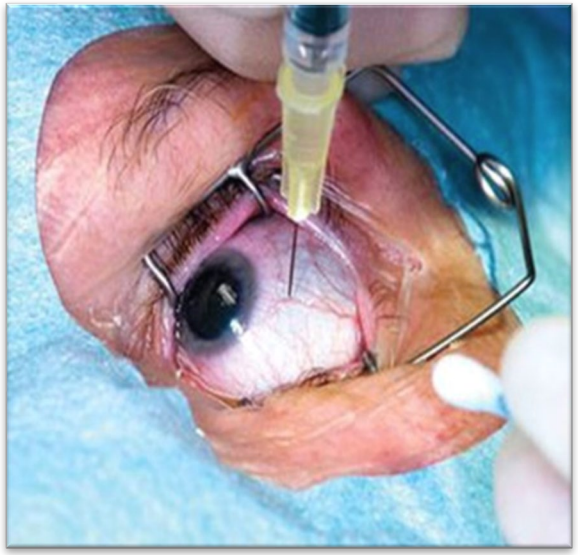
- DME is the leading cause of blindness in adults worldwide
- Only 50% of DME patients respond to anti-VEGF treatments [1]
- Invasive injections and time-consuming office visits lead to poor compliance causing treatment gaps between injections [3]
- No approved therapy provides adequate and sustained systemic plasma kallikrein inhibition to the site of action at the retinal vasculature
- Real world evidence demonstrated frequent intravitreal injections were not sustainable, compromising the ability to maintain visual gains [5]

DME: diabetic macular edema. **Sources: 1.** https://www.idf.org/our-activities/care-prevention/eye-health.html **2.** Lee R et al. Epidemiology of diabetic retinopathy, diabetic macular edema and related vision loss. Eye Vis (Lond). 2015; 2-17 **3.** Kita et al, Diabetes. 2015 Oct; 64 (10): 3588-3599 **4.** Yau JW et al.; Meta-Analysis for Eye Disease (META-EYE) Study Group. Global prevalence and major risk factors of diabetic retinopathy. Diabetes Care 2012;35:556–564 **5.** SIERRA-AMD, Khanani A, et al. Ophthal. Retina 2020 Feb; 4(2):122-123

The Limitations of Standard of Care

Anti-VEGF injectable therapies

- 40-50% of patients treated with anti-VEGF therapies are unresponsive to the therapy[1]
- Furthermore, invasive administration leads to delayed treatment, poor patient compliance and suboptimal real-world outcomes[2]
- Requires two separate injections if both eyes are affected
- Anti-VEGF injections are resource intensive (patient turn-around time, billing, processing pre-authorizations) limiting patient access to retinal specialists



An effective oral therapy may enable earlier treatment and better outcomes

Sources: 1.Kita et al, Diabetes. 2015 Oct; 64 (10): 3588-3599 **2.** Holz FG et al. Br J Ophthalmol 2015; 99 (2): 220-226

Inhibiting Plasma Kallikrein: An Alternative Approach for DME

KKS: an Alternative Pathway to Target DME

- KKS is part of the first line of defense against vascular injury
- KKS over activation leads to edema in the macula
- Vitreous KKS levels are universally elevated in DME
  - Only ~50% of patients have elevated VEGF

RZ402: An Oral Once Daily PKI for DME

- Possible treatment alternative for patients with suboptimal response to anti-VEGF therapies
- Intended as monotherapy or combination with anti-VEGF injections
- Oral dosing and systemic levels enables sustained drug exposures for kallikrein inhibition at retinal blood vessel site of action
- Added advantage of treating both eyes

Potential systemic treatment and opportunity for early intervention to support prevention or treatment of DME

KKS: kallikrein-kinin system. PKI: plasma kallikrein inhibitor.

Phase 2 Study Fully Enrolled

- **Multi-Center, Randomized, Double-Masked, Placebo-Controlled Parallel-Arm Study**
- **94 participants enrolled in the US**
  - Newly diagnosed treatment naïve DME patients
  - CST of ≥320 µm
  - BCVA of ≤78 ETDRS letters (≤20/25 on Snellen chart)
- **Dosing regimen**
  - Once daily oral administration for 3 months
  - Three active arms (50mg, 200mg, 400mg) compared to placebo
- **Study endpoints**
  - Primary endpoints: safety; change in CST
  - Secondary endpoints
    - Change in BCVA; change in DRSS; changes in non-study eye
    - Repeat dose pharmacokinetics
- **Study goals**
  - Improvement vs placebo in CST, BCVA
  - Dose-response
  - Binocular (2-eye) composite responses
- **Topline data expected Q2 2024**

DME: diabetic macular edema.

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