REZOLUTE

A Late-stage Rare Disease Company Treating Hyperinsulinism

Corporate Presentation

NASDAQ: RZLT

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 complete removal of the partial clinical holds on RZ358 for the treatment of hypoglycemia, the Investigational New Drug (IND) application for RZ358 (ersodetug), the ability of RZ358 to become an effective treatment, the effectiveness or future effectiveness of RZ358 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.

A Rare Disease Company Treating Hyperinsulinism

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

Two rare disease Phase 3 programs evaluating ersodetug to treat hypoglycemia in congenital HI and tumor HI

Compelling real-world evidence of patient benefit under the Company's Expanded Access Program

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

Seasoned management team with demonstrated success from early development through commercialization

$105 million in cash with runway into Q2 2026

Management Team

Nevan Charles Elam
Founder & Chief Executive Officer

Brian Roberts
Chief Medical Officer

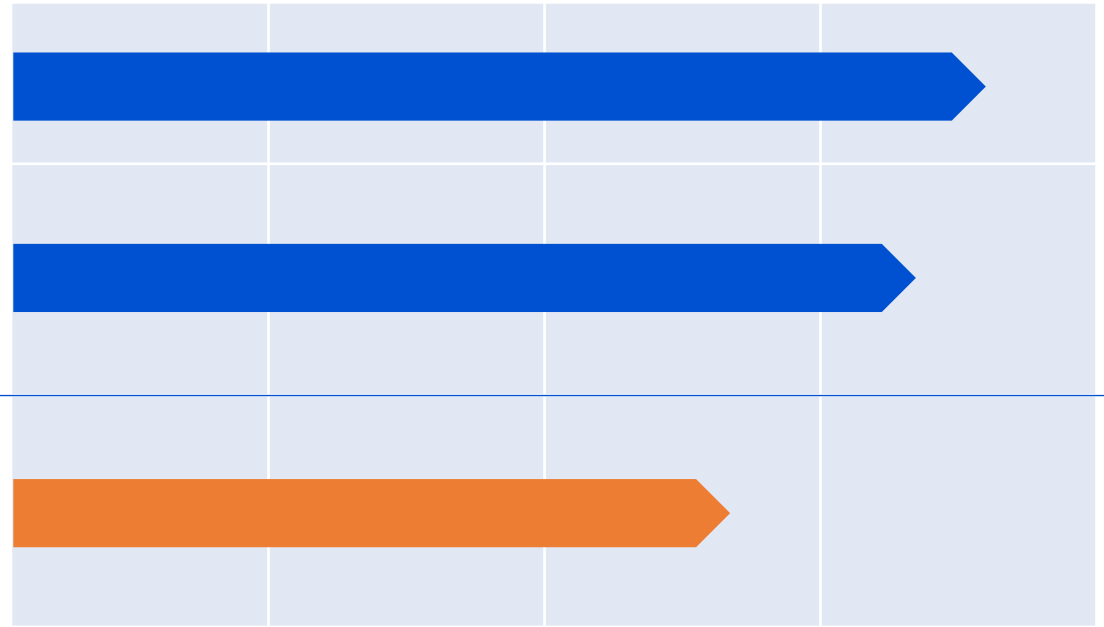
Daron Evans
Chief Financial Officer

Susan Stewart
Chief Regulatory Officer

Michael Deperro
SVP, Corporate Development

Two Phase 3 Indications Targeting Hyperinsulinism

Program	Target	IND-Enabling	Phase 1	Phase 2	Phase 3	Next Milestone	Milestone Expected
RZ358 (ersodetug)	Congenital Hyperinsulinism					Topline data	2H 2025
RZ358 (ersodetug)	Tumor Hyperinsulinism					Patient enrollment in Phase 3 study	1H 2025
RZ402	Diabetic Macular Edema					POC complete; Available for partnering	N/A



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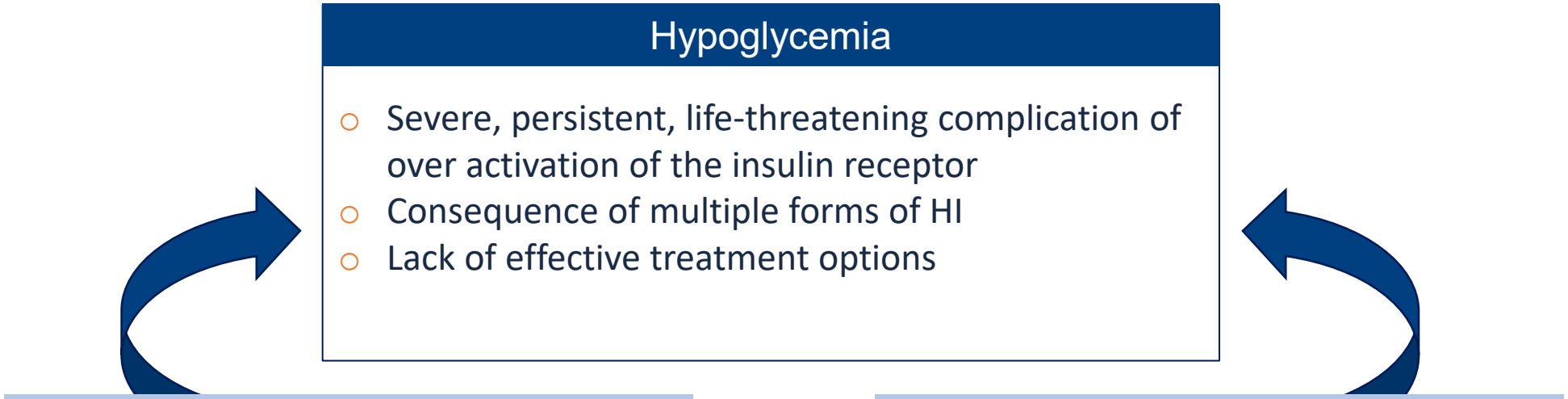
Ersodetug

Treatment for Hyperinsulinism (HI)

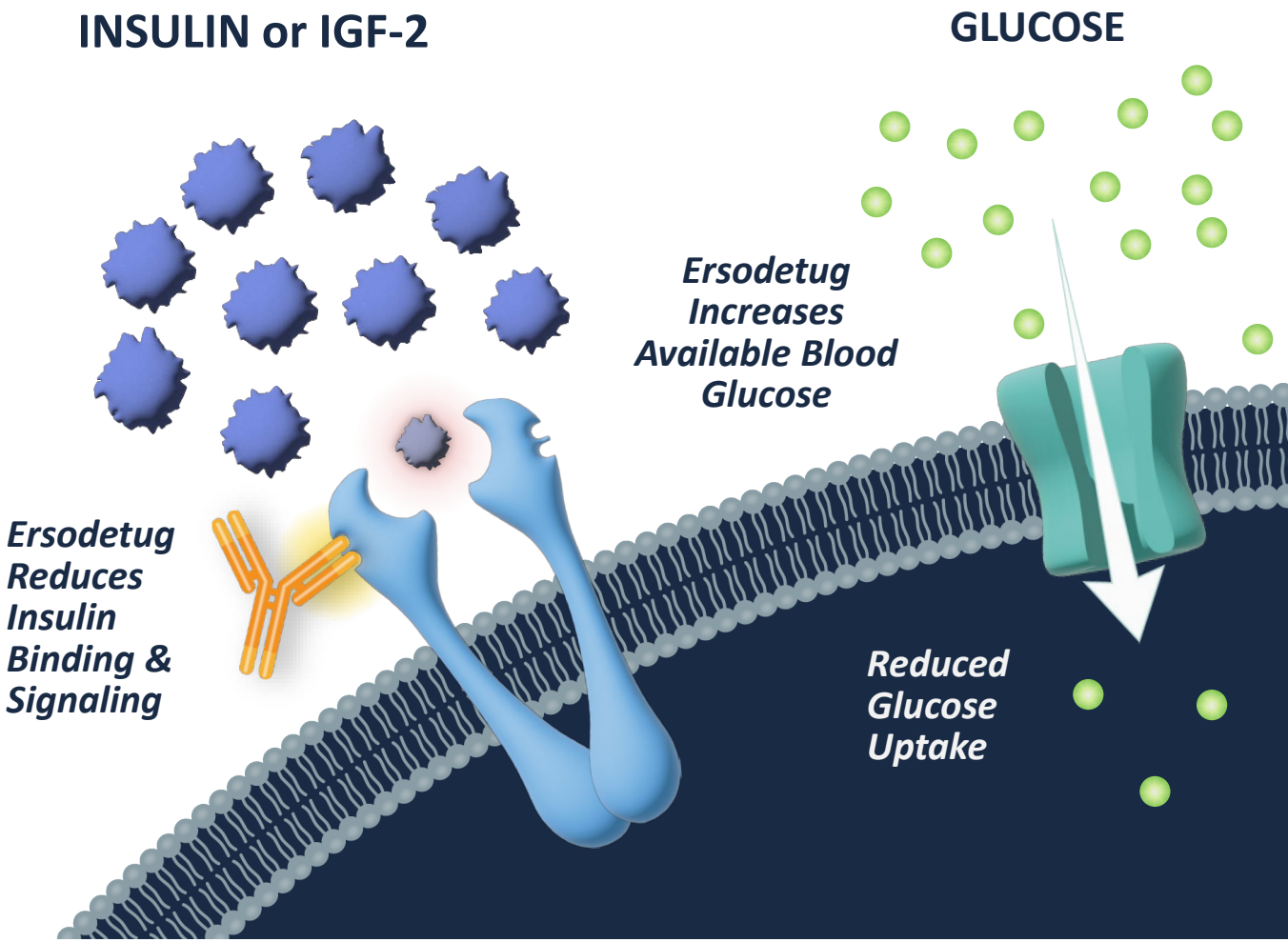
Hypoglycemia as a Result of HI



Ersodetug has shown substantial benefit in studies and real-world use for treatment of HI

Antibody Designed to Treat All Forms 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 related hormones (e.g. IGF)
- Modulating effect helps maintain glucose values in a healthy range
- Administered by IV infusion every 2 to 4 weeks



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Congenital HI

Disease Background

- 1 in 28,000 live births in the US[1], translating to approximately 130 new patients per year
- Often presents within first month of life
- Most common cause of persistent hypoglycemia in infants and children
- Requires constant monitoring as serious hypoglycemic lows are often missed
- Risk of coma, death, and other serious complications
- 50% of children have neurological deficiencies caused by hypoglycemic lows
- No therapy has been developed and approved for chronic treatment[2]

Source: 1) The birth prevalence of congenital hyperinsulinism: a narrative review of the epidemiology of a rare disease: https://www.rezolutebio.com/wp-content/uploads/2024/06/The-birth-prevalence-of-congenital-hyperinsulinism_a-narrative-review-of-the-epidemiology-of-a-rare-disease.pdf. 2) 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.

Inadequate 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
  - May experience frequent and serious adverse reactions including volume overload, heart failure, and pulmonary hypertension
  - Patients report[1] intolerable side effects including increased body hair (92%), loss of appetite (43%), swelling (27%), facial changes (27%), 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
  - Pancreatectomy is an invasive option in DZ non-responsive patients, but frequently requires adjuvant medications until insulin-dependent diabetes eventually ensues
  - Intensive feeding regimens (e.g. tube feeding) often underlie all of these approaches
  - Each of these therapies can contribute to a cycle of poor appetite and feeding aversions

Source: 1) HI Global Registry 2024 Annual Report: 223patients surveyed, 183 have taken DZ.

Therapies in Development

Ersodetug is a fully human monoclonal antibody designed to treat all forms of HI and has shown substantial benefit in clinical trials and real-world use

Asset	Mechanism	Stage	Dosing	HI Indication	Clinical Barriers
Ersodetug	**Insulin receptor allosteric modulator**	**Phase 3**	**IV[1], once monthly**	**Congenital, Tumor, PBH[2]**	**N/A**
Dasiglucagon (Zealand)	Glucagon analogue	Phase 3	Continuous Infusion Pump	Congenital	• Utility in chronic use unproven; likely need to combine with other therapies
Avexitide (Amylyx)	GLP-1 receptor antagonist	Phase 3	IV, 1-2 times daily	PBH	• No plans to pursue cHI • MOA suited to PBH
HM-15136 (Hanmi)	Glucagon analogue	Phase 2	SC injection, once weekly	Congenital	• Earlier in development • Similar drawbacks as dasiglucagon
CRN-04777 (Crinetics)	SST5 agonist	IND-enabling	Oral, once daily	Congenital	• Early stage after failed program • No clear development plans at this time

Source: 1) formulation allows for subcutaneous dosing. 2) Phase 2 data supports potential use. SC: subcutaneous. SOC: standard of care. PBH: post-bariatric hypoglycemia. MOA: mechanism of action.

Phase 2b RIZE Study Results

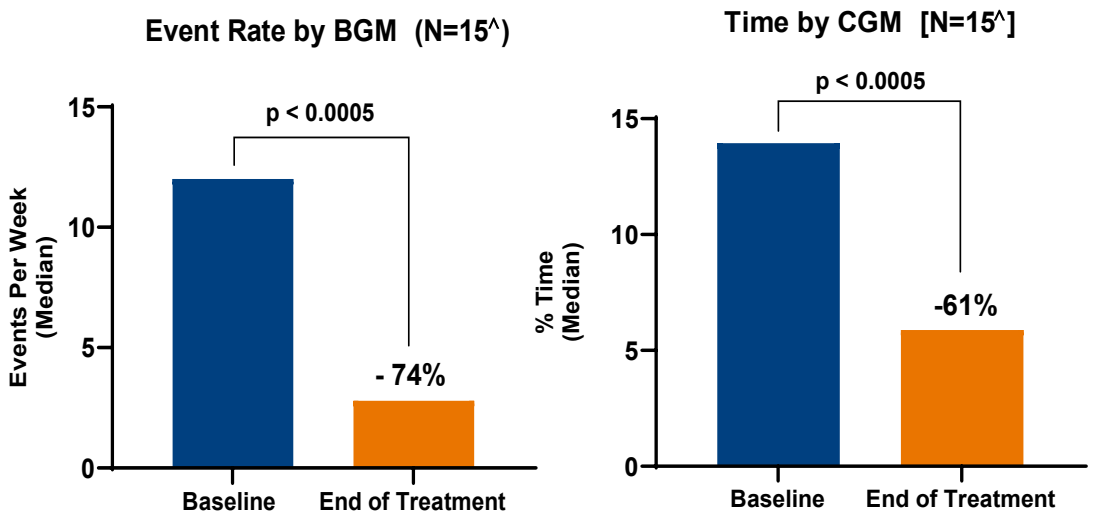
- **23 participants**
  - Average age ~6.5 (16 participants were between 2-6 years of age)
  - Diverse group across gender and genetics
- **~20% average daily time in hypoglycemia and 13 hypoglycemia events per week at baseline**
  - Participants were on standard of care
- **Predictable and dose-dependent pharmacokinetics**
- **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:**
  - Improvement in hypoglycemia time and events of up to ~90% at top doses
  - Nearly universal response rate at the top dose

SOC: standard of care. AEs: adverse events.

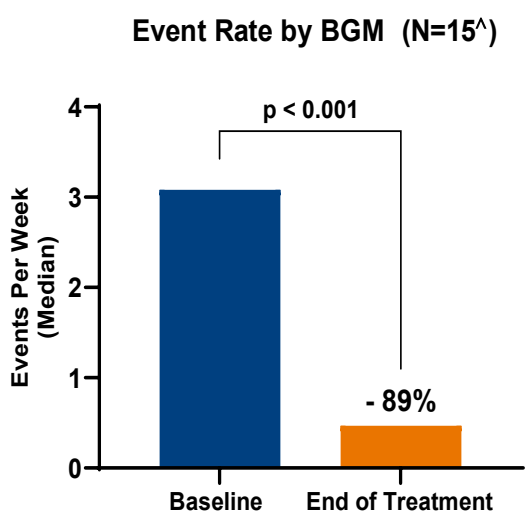
Substantial Improvement in All Hypoglycemia Metrics

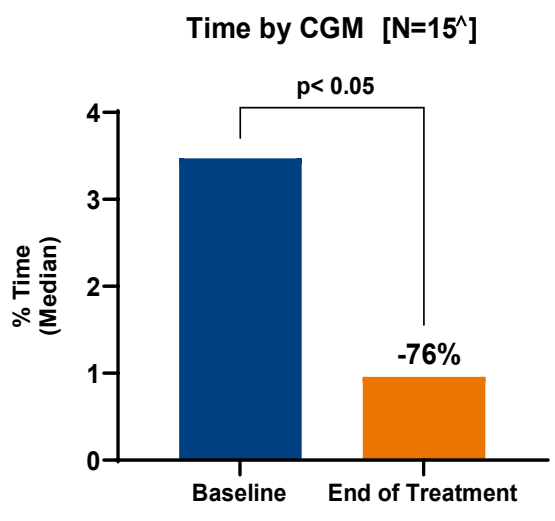
Pooled 6 and 9 mg/kg dose levels representative of Phase 3 population and dosing

Hypoglycemia (<70 mg/dL)



Severe Hypoglycemia (<50 mg/dL)



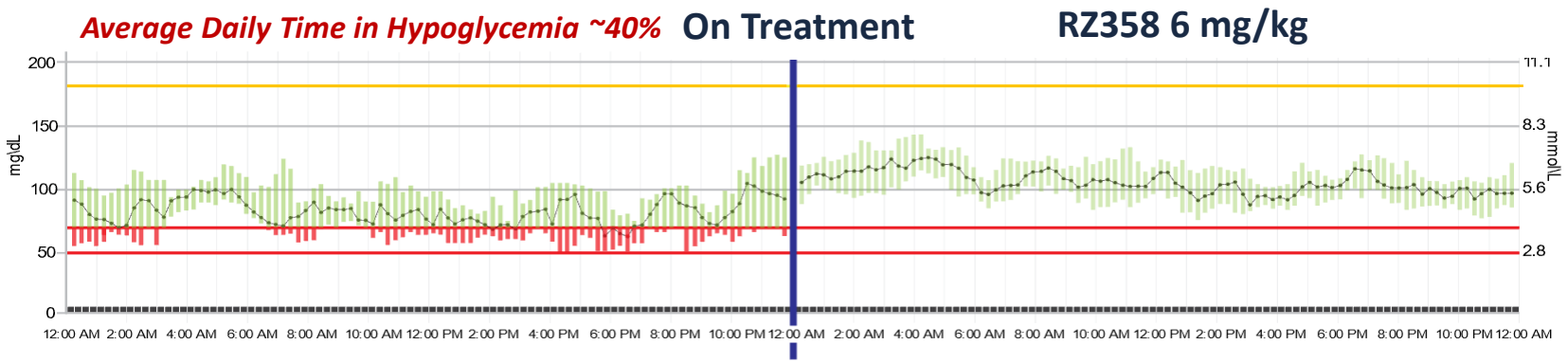


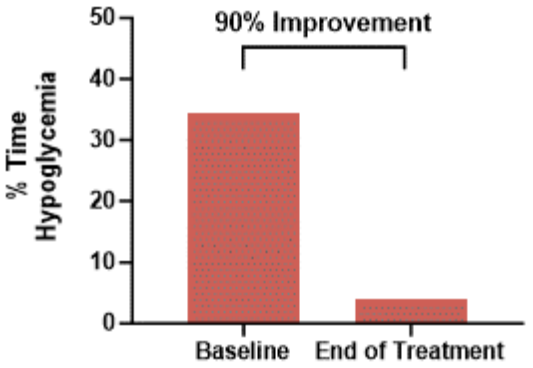
Improvement in time in hypoglycemia and overall events of ~75% and up to ~90% at top doses

BGM: blood glucose monitoring. CGM: continuous glucose monitoring. Median data presented. 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.

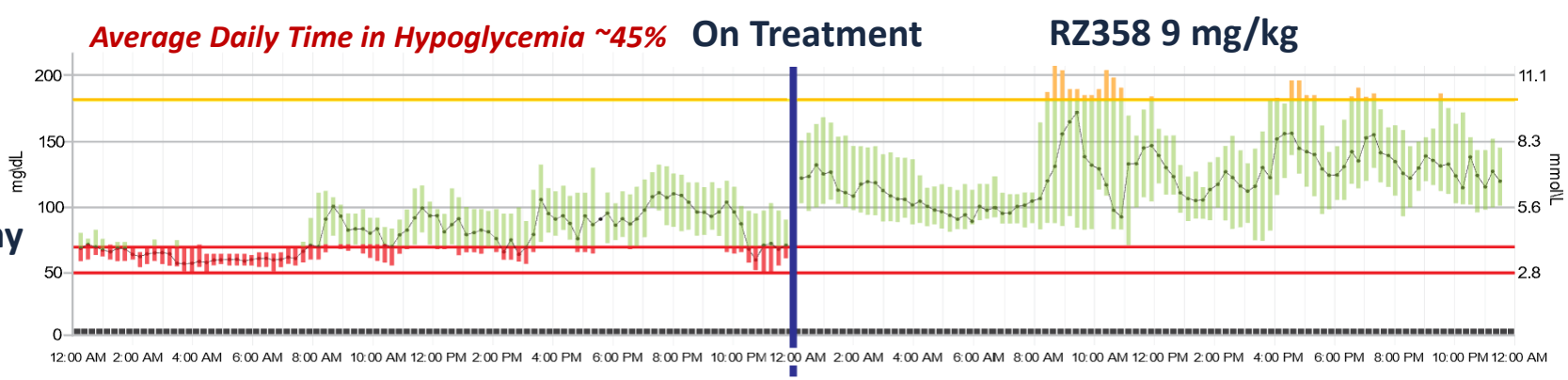
Compelling Patient Responses

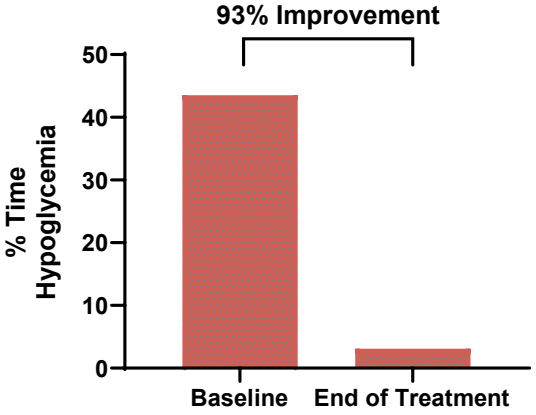
2-Year-Old on SSA





6-Year-Old; Failed meds, pancreatectomy





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

Nearly universal patient response rate (>50% hypoglycemia correction) observed at mid and top doses

SSA: Somatostatin Analog. CGM: continuous glucose monitoring.

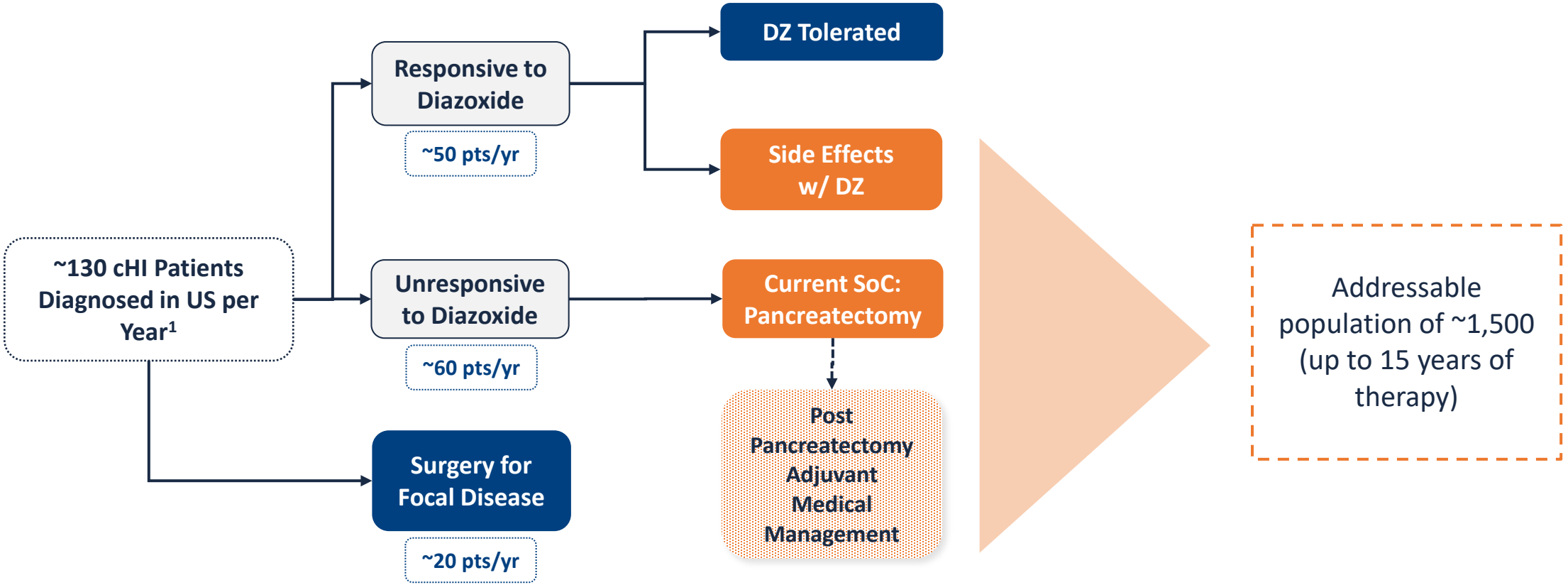
Phase 3: The sunRIZE Study

sunRIZE RZ358-301

- **Global, multi-center, double-blind, randomized, controlled, safety and efficacy registrational study**
- **Patient population (n=56)**
  - Ages 3 months + who do not have 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 second half 2025**

SOC: standard of care.

Addressable U.S. Market Driven by Both Diazoxide-Responsive and Diazoxide-Unresponsive Patients



Source: 1) The birth prevalence of congenital hyperinsulinism: a narrative review of the epidemiology of a rare disease: https://www.rezolutebio.com/wp-content/uploads/2024/06/The-birth-prevalence-of-congenital-hyperinsulinism_a-narrative-review-of-the-epidemiology-of-a-rare-disease.pdf. HI: hyperinsulinism. DZ: Diazoxide. DZR: Diazoxide Responsive. DZNR: Diazoxide Non-Responsive (kATP channel defect).

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Tumor HI

Disease Background

- **Hypoglycemia caused by two distinct tumor types:**
  - 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 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
  - Can require hospitalization (often prolonged and in ICU) and interferes with patient quality of life
  - May prevent adjuvant tumor treatment

Treatment Options and Unmet Need

- **Tumor-directed therapies do not directly treat hypoglycemia**
  - Adequate hypoglycemia management is required prior to initiation of tumor-targeted therapies
- **Therapies to treat malignant insulinoma are often ineffective or poorly tolerated**
  - Diazoxide (DZ) is the only approved treatment
    - Suboptimal response rates and serious side effects
  - Somatostatin analogs (SSAs)
    - Used off-label with limited success
    - May worsen hypoglycemia in tumor HI setting
  - mTOR-inhibitors
    - Used off-label and have potentially severe side effects
- **Limited and often ineffective treatment options for hepatocellular carcinoma (HCC)**
  - Medical therapies directed at suppressing insulin secretion such as DZ and SSAs do not work in non-islet cell tumors (NICTs) where HI is caused by non-insulin substances such as IGF-2

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

Real-world Patient Benefit in Expanded Access Program of Ersodetug

- **Multiple ICT patients with severe refractory hypoglycemia**
  - Hospitalized and in life-threatening or hospice-bound condition
  - Required continuous high volume/concentration intravenous dextrose or nutritional infusion
  - Tumor-directed therapies (e.g., embolization, radiotherapy, chemotherapy) deferred because of hypoglycemia
  - Physician-requested use of ersodetug
- **Administration of ersodetug resulted in:**
  - Substantial hypoglycemia improvement with no significant side effects[1]
  - Discontinuation of intravenous dextrose
  - Discharge from in-patient to out-patient care
  - Resumption of tumor-directed therapies

Joslin Diabetes Center | HARVARD MEDICAL SCHOOL AFFILIATE

BRIGHAM HEALTH
BWH BRIGHAM AND WOMEN'S HOSPITAL

Stanford MEDICINE

MOFFITT CANCER CENTER

Hôpital Cochin Port-Royal AP-HP

OHSU

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

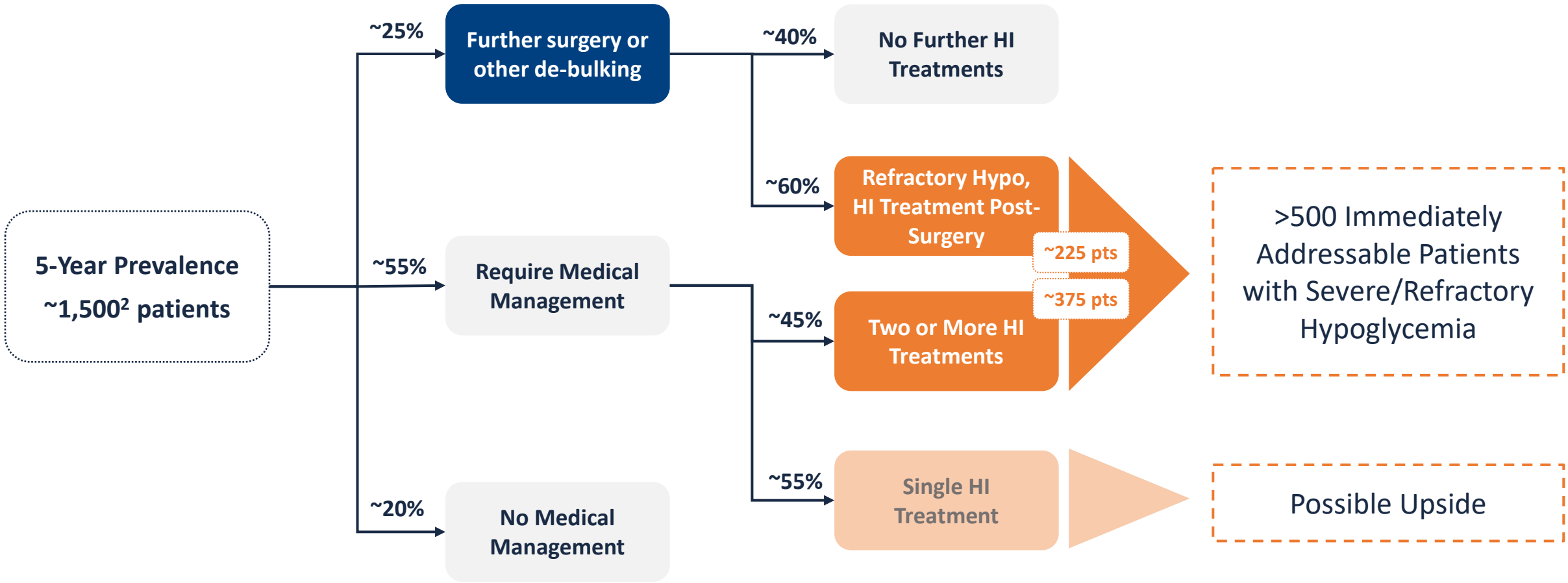
Phase 3 Study Overview

- **Multi-center, double-blind, randomized, controlled, safety and efficacy registrational study**
- **Patient population (n= up to 48)**
  - Adult ICT and NICT patients with HI who have not achieved adequate hypoglycemia control with SOC therapies
  - 24 participants in double-blind, placebo-controlled arm (to evaluate primary endpoint/hypoglycemia events)
  - Up to 24 participants in open label arm: initial 6 NICT patients and any hospitalized participants on IV glucose
- **Primary endpoint: change in average hypoglycemia events per week by self-monitored blood glucose**
  - Secondary/additional endpoints: change in average daily percent time in hypoglycemia, change in Level 1 hypoglycemia events and time, hospitalization, patient reported quality of life
  - Open-label arm to evaluate change in IV glucose requirements in hospitalized participants
- **Treatment arms and dosing regimen**
  - Once weekly administration over 8-week pivotal treatment period
    - 9 mg/kg RZ358 (+ SOC) (n = 12)
    - Matched placebo (SOC only) (n = 12)
    - 9 mg/kg RZ358 Open Label Arm (n ≤ 24)
  - Eligible participants may continue in a long-term extension study following pivotal treatment
- **IND filed and cleared: start-up activities in progress to enable patient enrollment in 1H 2025**

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

Immediately Addressable U.S. ICT Market

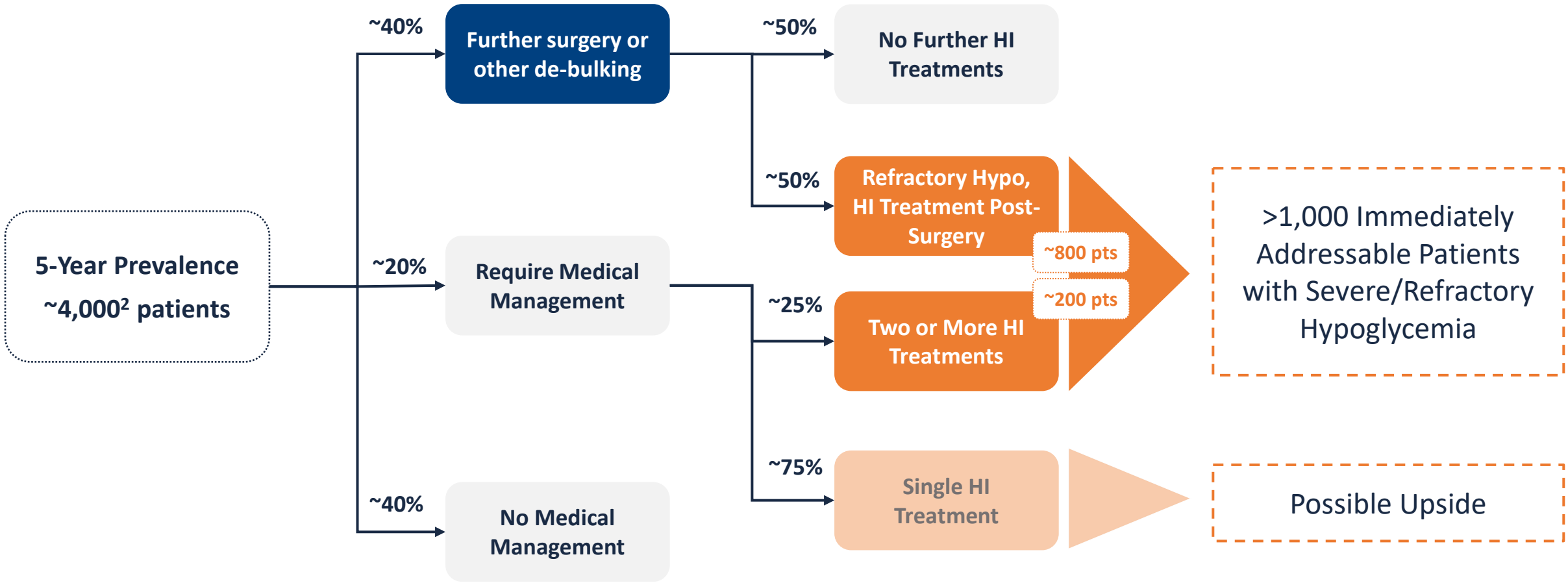
Malignant Insulinoma Hypoglycemia (Hypo) Diagnosis and Treatment Pathway[1]



ICT: islet cell tumor. Source: 1) Based on analysis of seven years of data from the Komodo Claims Assessment;
2) Approximate, average 5-year prevalence of patients with malignant insulinoma or other malignant pancreatic cancer w/ diagnosed hypoglycemia, who may or may not have already had de-bulking surgery.

Immediately Addressable U.S. NICT Market

Hepatocellular Carcinoma + Hypoglycemia (Hypo) Diagnosis and Treatment Pathway[1]



NICT: non-islet cell tumor. Source: 1) Based on analysis of five years of data from the Komodo Claims Assessment.
2) Komodo incidence applied to to SEER: The Surveillance, Epidemiology, and End Results database. Does not include multiple other cancer types with known NICT etiology.

Commercial Opportunity

- **Potential to Address Two Rare Disease Markets**
  - ~1,500 addressable cHI patients in US; equivalent patient population in Europe
  - >500 islet cell tumor patients and >1,000 non-islet cell tumor patients addressable in the US
- **Highly Concentrated Physician Base for cHI**
  - 60% of patients are diagnosed within 1 month of presentation
  - 80% of addressable patients are seen by centers of excellence (many participating in sunRIZE study)
- **Tumor HI Patients Identified and treated by both Endocrinologists and Oncologists**
- **Regulatory Designations: Breakthrough Therapy (FDA), Orphan, Pediatric Rare Disease (FDA), PRIME (EMA), ILAP (UK)**

$1B+ global market opportunity across two indications with rare disease drug pricing

HI: hyperinsulinism.

A Rare Disease Company Treating Hyperinsulinism

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

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

Compelling real-world evidence of patient benefit under the Company's Expanded Access Program

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

$105 million in cash with runway into Q2 2026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