

RZ358




CHI: Program Updates 7-Sep 2019



Background



Rezolute:
A Metabolic and Orphan Disease Company With a Diversified Pipeline

| Program | Description | Preclinical  | Phase 1  | Phase 2  |
|--------------|------------------|--|---|---|
| RZ358 | Antibody for CHI | Phase 2b dosing anticipated 2H'19  | | |
| RZ402 | Oral PKI for DME | IND anticipated mid- year '20  | | |
| AB101 | Weekly insulin | Top-line results anticipated 2H'19  | | |

Observational Study Demonstrates Unmet Need



Conducted in partnership

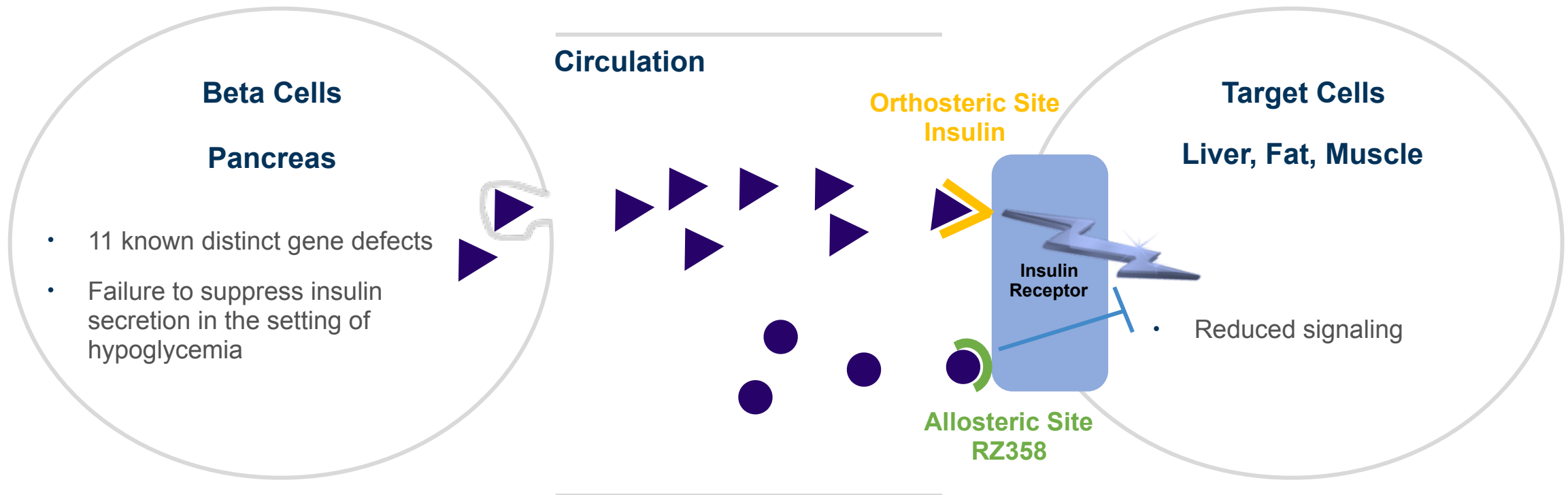
Continuous Glucose Monitoring (CGM) for Two Weeks: Summary of Results

- Blood glucose <70 mg/dL is hypoglycemia
- On average, patients had ~3 hours / day (~180 min) of hypoglycemia, even on standard of care (SOC) medications
- Younger ages are particularly vulnerable

| Glucose Threshold (mg/dL) | All Patients | | Patients on SOC Medication | |
|---------------------------|-------------------|------------------------|----------------------------|-----------------------|
| | All Ages (N = 22) | 2-6 Year Olds (N = 12) | All Ages (N = 15) | 2-6 Year Olds (N = 9) |
| <70 | 174 | 207 | 174 | 223 |
| <60 | 56 | 74 | 54 | 81 |
| <50 | 15 | 22 | 14 | 24 |

CGM reveals current therapies are ineffective at controlling hypoglycemia

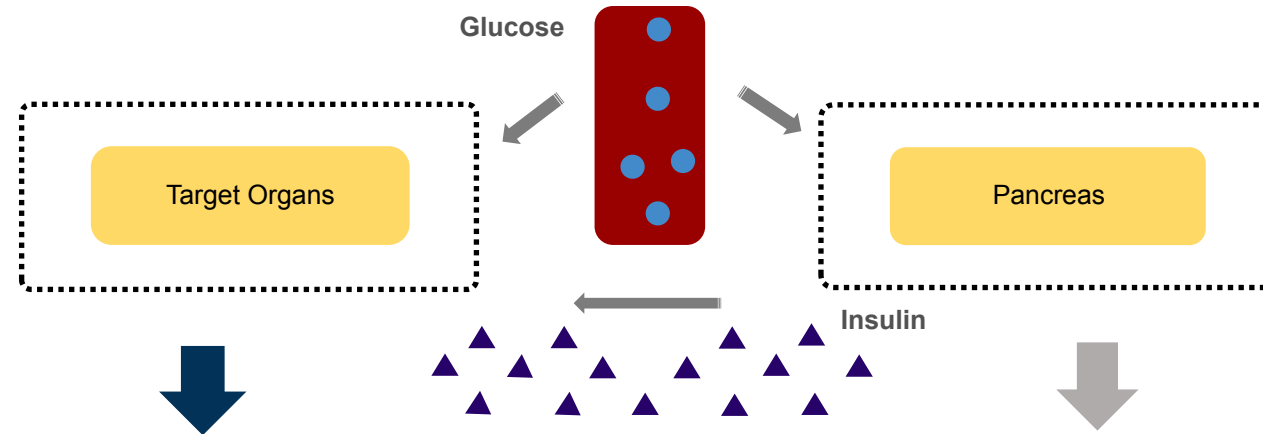
Unique Mechanism Attenuates Insulin Effects



- High affinity binding to the insulin receptor at the allosteric site
- High selectivity to the insulin receptor (no IGF-1 interaction)
- Insulin still binds and signals
- Dims the insulin signal when insulin is elevated



Potential to Address Limitations of Standard of Care



| | RZ358 (Broad Focus) | Standard of Care (Narrow Focus) |
|-------------|--|---|
| Development | ▲ Tailored for CHI | ▼ Not developed for CHI |
| Targeting | ▲ Insulin receptor/signal on insulin-dependent target tissues | ▼ Beta cell only |
| Reversancy | ▲ Potentially universal treatment | ▼ Genetics-dependent narrow targeting |
| Impact | ▲ Reversibly counteracts insulin only when insulin is elevated | ▼ Marginally effective, invasive, and/or significant side effects |

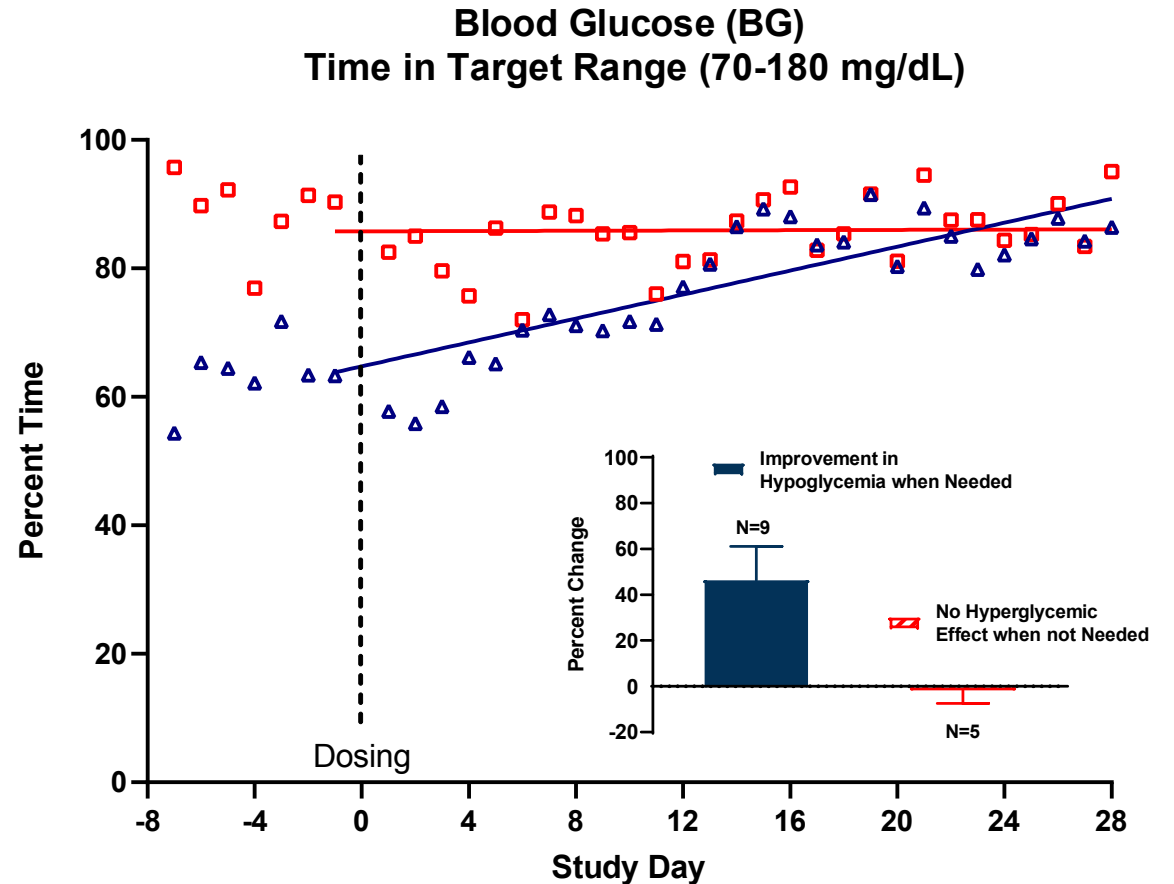
Phase 2a – Completed Proof of Concept

Design

- Single IV doses of 1 to 9 mg/kg in patients with CHI
- Ages ≥ 12 in Europe and ≥ 18 in the US

Results

- PK comparable with healthy volunteers
- Baseline and post-treatment CGM
 - **Near universal normalization of glucose across a variable group of patients**
 - **Approximately 50% improvement in patients with baseline hypoglycemia**
 - **No hyperglycemia in patients without a present need**
 - Effect persisted for several weeks, consistent with Ph1 PK/PD
 - Established proof-of-mechanism and efficacy in CHI patients
- Safe and well-tolerated



RZ358-606: Phase 2b Study Protocol



RZ358-606: Phase 2b Study Overview

- **Design:** Open-label, repeat-dose study in 4 sequential ascending dosing cohorts (6-8 patients per cohort)
- **Population:** CHI \geq 2 years old with baseline hypoglycemia by specified CGM thresholds
- **Duration of individual participation:** ~27 weeks
- **Principal assessments / endpoints:** CGM Glycemic Endpoints and Modified Overnight Fast
- **Interim Analysis:** Open label design provides opportunity for interim discussions with health authorities

| Dosing Cohort | Induction Dosing | | | | Maintenance Dosing | |
|---------------|----------------------------------|--------|--------|--------|--------------------|----------|
| | Weekly RZ358 for 4 weeks (mg/kg) | | | | RZ358 for 4 weeks | |
| | Week 1 | Week 2 | Week 3 | Week 4 | mg/kg | Interval |
| 1 | 3 | 3 | 3 | 3 | 3 | 14 Days |
| 2 | 6 | 6 | 6 | 6 | 6 | 14 Days |
| 3 | 9 | 9 | 9 | 9 | 9 | 14 Days |
| 4 | 3 | 6 | 9 | 12 | 9 | 14 Days |

Road Map to Study Start



Questions?

