RZ358

CHI: Program Updates
22 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

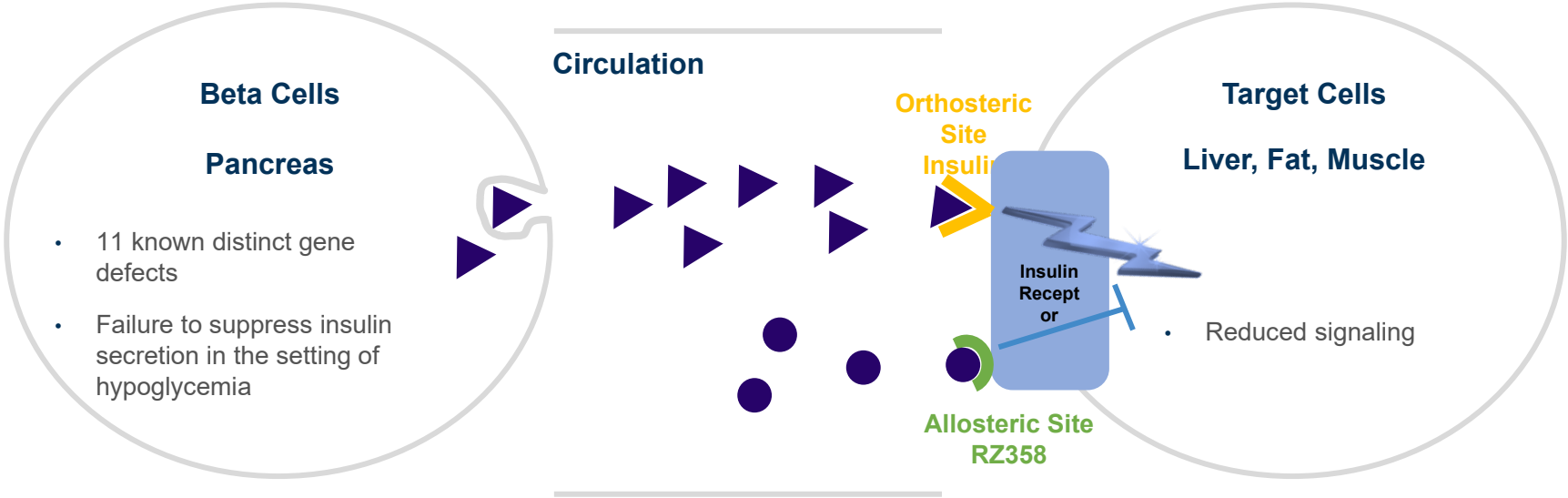
Continuous Glucose Monitoring (CGM) for Two Weeks: Summary of Results

- 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

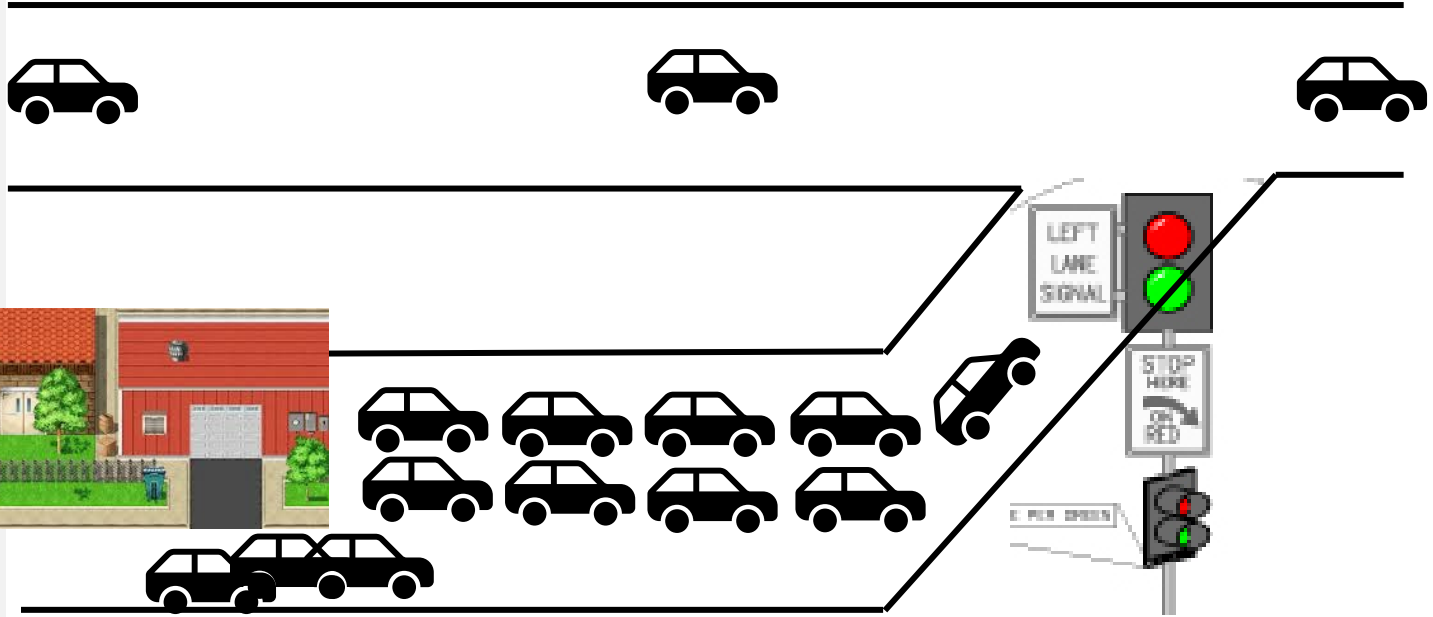


- High affinity binding to the insulin receptor at the allosteric site
- High selectivity to the insulin receptor (no IGF-1 interaction)
- Insulin still binds and signals
- Dims the insulin signal when insulin is elevated

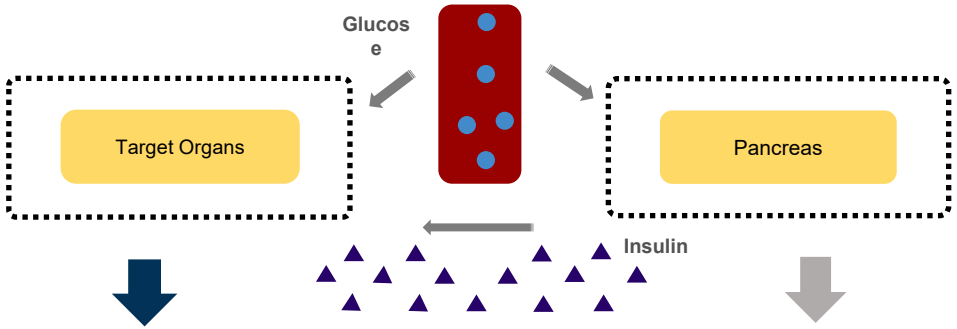
Insulin

RZ358

RZ358 Works Like a Freeway Metering Light



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
Relevancy	▲ Potentially universal treatment	▼ Genetics-dependent narrow targeting
Impact	▲ Reversibly counteracts insulin only when insulin is elevated	▼ Marginally effective, invasive, and/or significant side effects

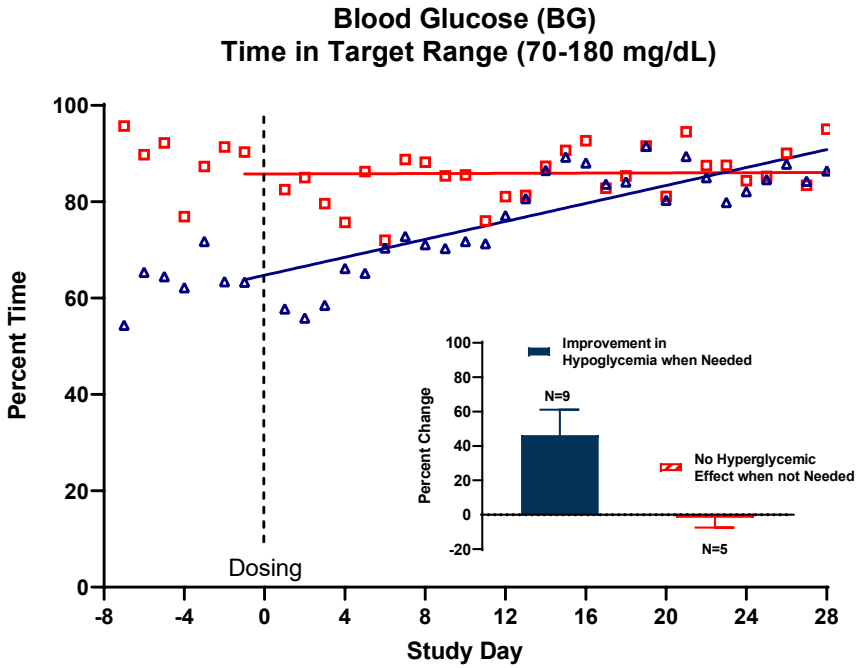
Phase 2a – Completed Proof of Concept

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 ≥ 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

GET THE STUDY'S INSIDE SCOOP!

RIZE

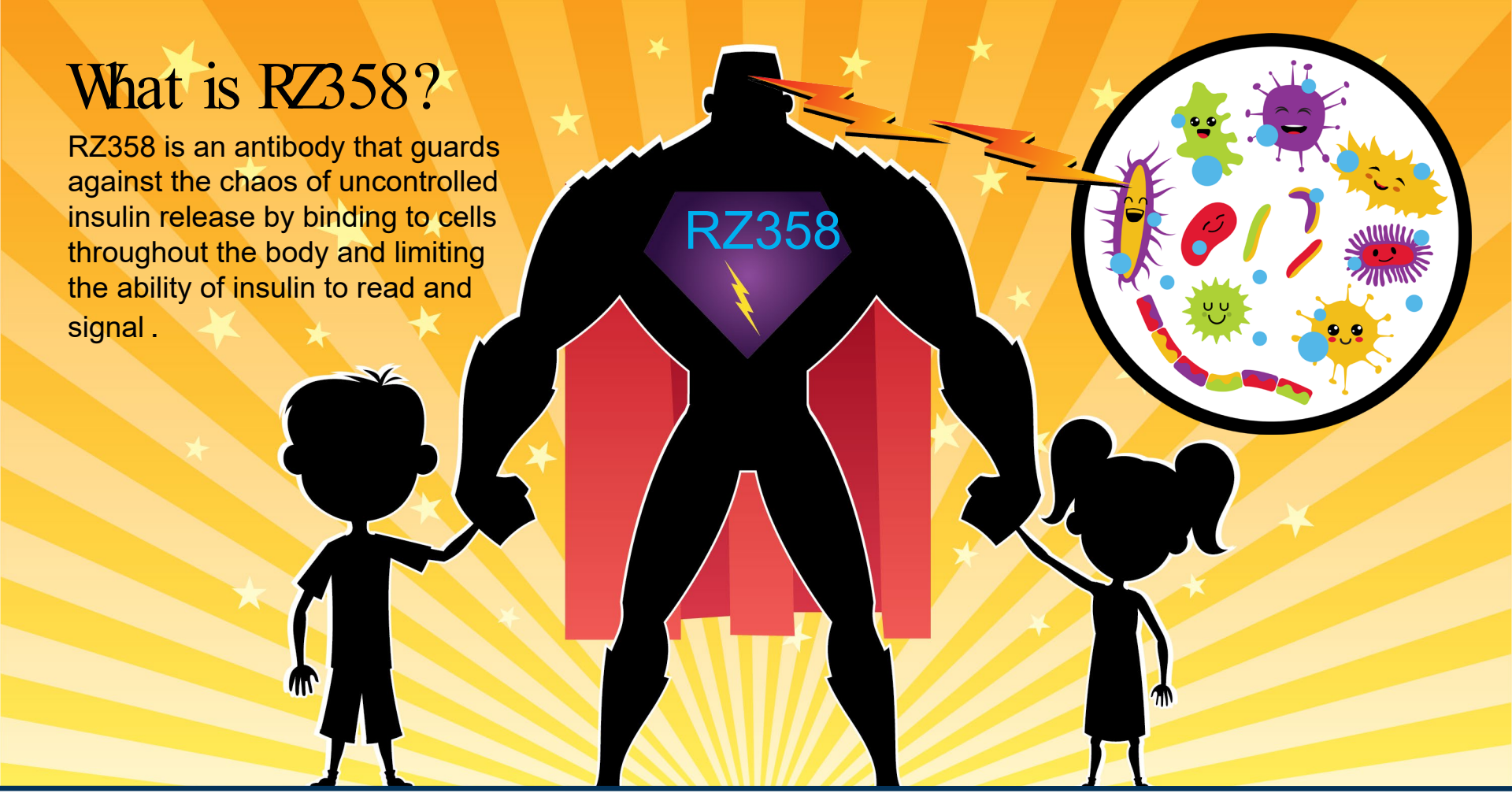
RZ358-606

What CHI does to the body…

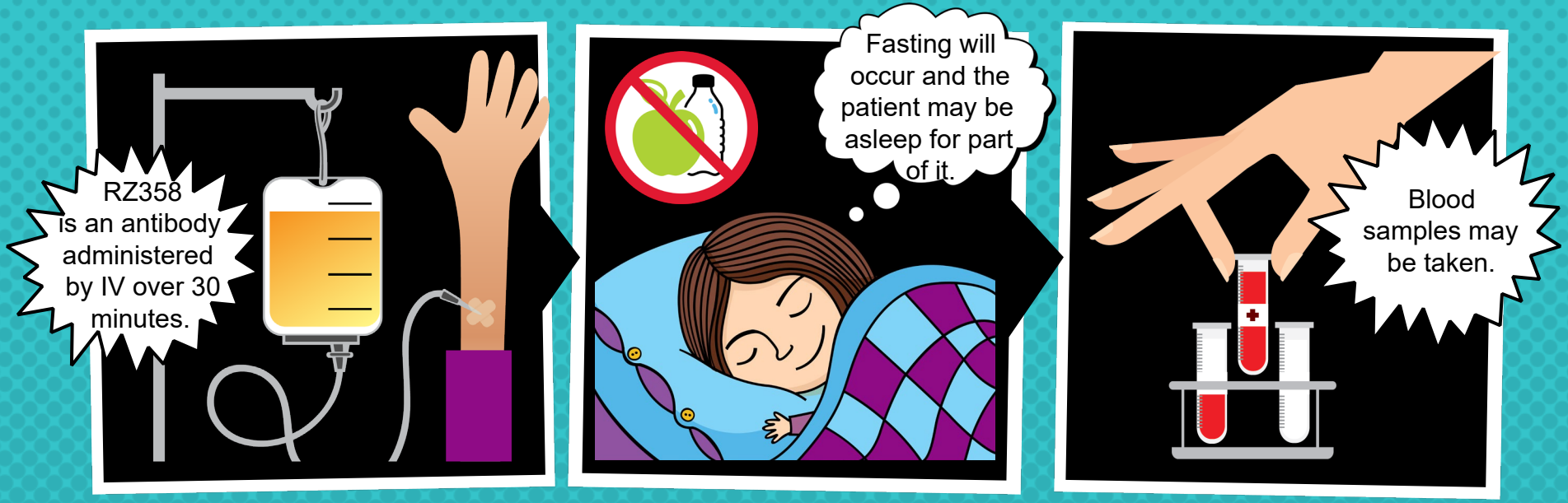
If you live with CHI, you live with the uncontrolled release of insulin from the pancreas which floods your body, leaving you with dangerously low blood sugar levels.

What is RZ358?

RZ358 is an antibody that guards against the chaos of uncontrolled insulin release by binding to cells throughout the body and limiting the ability of insulin to read and signal .



What are some things that will be done during the study?

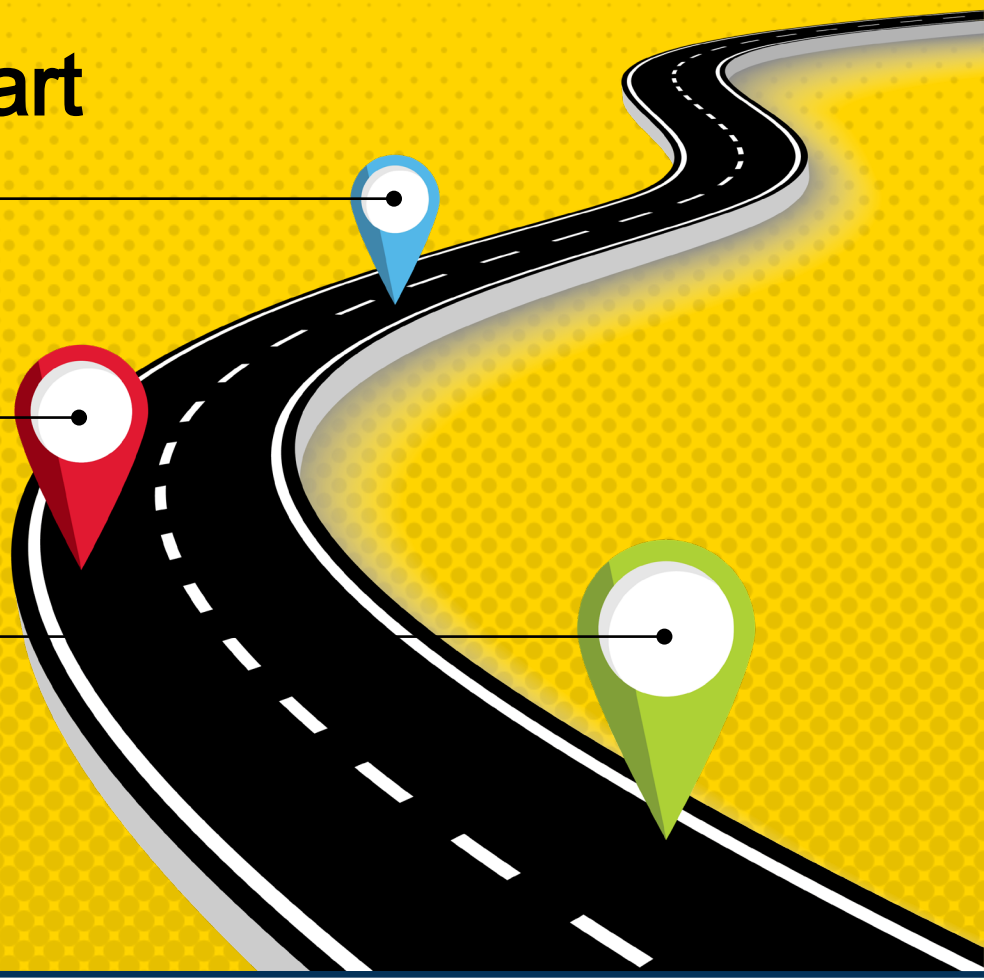


What are some things the doctor will ask during study?

RZ358 has been tested in previous studies in patients with chi and healthy volunteers.

Road Map to Study Start

1. **Health Authority Submissions**
   - Country Level
   - Local Level
2. **Site Identification and Start-up Activities**
   - Site Needs
   - Patient/Caregiver Needs
   - Training
3. **Site Activations in Q4 2019**
   - Screening
   - Enrollment



Clinical Trial Participation – Your rights!

- To receive adequate information (written and verbal) about:
  - Aim of the study
  - What will happen during the study and what is expected of you: procedures, medications, diaries, etc.
  - Which possible benefits AND possible risks or side effects you can expect
  - Which alternative treatments are available
- To be allowed sufficient time to ask questions and to make an informed decision
- To refuse to participate or to change your mind at any time
  - This will NOT influence your further care
- Your privacy will be protected in accordance with national/regional legislation (GDPR)
  - Only anonymized data will be collected during the study
- A special insurance is in place, which covers any potential damage resulting from participation in the study

Clinical Trial Participation – Your responsibilities

- To follow instructions with regard to:
  - Study drug intake
  - Visit schedule
  - Maintaining diary
  - Other study procedures (in this case: CGM-device)

- Report to the site's study team:
  - Any observation/untoward event (possible side effect)
  - Any changes in medications
  - Any significant changes in behavior, food intake, etc.

- Maintain own health and avoid unnecessary risks

Questions?