

The ReInspire Study

Initial Data from Adults and Adolescents 12 and up
with *PIK3CA*-Driven Vascular Malformations Treated
with the Investigational Drug Zovegalisib (RLY-2608)

ReInspire Study: A Clinical Trial Evaluating the Investigational Drug Zovegalisib (RLY-2608) for the Treatment of Adults and Children with *PIK3CA*-driven Vascular Malformations

What is the ReInspire Study?

The ReInspire study is a clinical trial evaluating the safety and effectiveness of the investigational drug, zovegalisib (RLY-2608), for the treatment of individuals with *PIK3CA*-driven vascular malformations. *PIK3CA*-driven vascular malformations include lymphatic malformations, venous malformations, and *PIK3CA*-related overgrowth spectrum (PROS) conditions such as K-T syndrome, CLOVES, FAVA, M-CM/MCAP, and more.

These conditions are caused by mutations or changes in the *PIK3CA* gene, which creates a malfunctioning form of the protein PI3Kα. When mutated, PI3Kα can cause vascular malformations and/or overgrowths throughout the body, along with other symptoms.

What is Zovegalisib (RLY-2608)?

Zovegalisib (RLY-2608) is an investigational drug designed to selectively target the PI3Kα protein causing the disease. This means zovegalisib has not yet been approved by the US Food and Drug Administration (FDA) or any other regulatory agency and is not available outside of a clinical research study. The safety and efficacy of zovegalisib have not been established.

Individuals with *PIK3CA*-driven vascular malformations have both normal and mutated PI3Kα proteins in their body. Zovegalisib (RLY-2608) is a mutant-selective drug. This means it is designed to specifically hinder the mutated PI3Kα protein that can cause *PIK3CA*-driven vascular malformations and limit impact on the normal protein that everyone needs for regular body functions which may have lesser side effects. Zovegalisib (RLY-2608) is the only known mutant-selective drug in clinical trials for individuals with vascular malformations. It is taken orally.

What is the design of the ReInspire Study?

There are three age groups and three parts to the ReInspire Study.

AGE GROUPS:

Group 1 adults and adolescents 12 years or older

Group 2 children 6-11 years old

Group 3 children 2-5 years old

PARTS:

Part 1 is intended to determine the dose(s) of zovegalisib (RLY-2608) that provide the most benefit with the least side effects

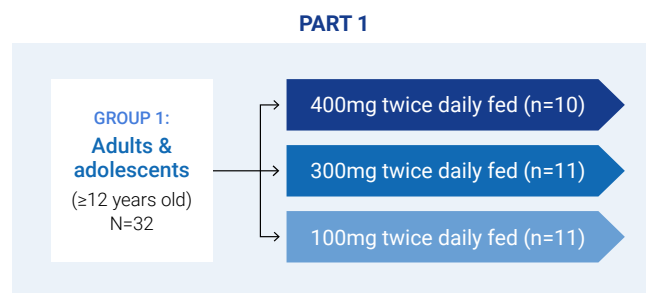
Part 2 will continue to collect data on the safety and effectiveness of the recommended dose(s) based on data collected in Part 1

Part 3 will open after Parts 1 and 2 and is intended to further confirm the treatment effect of the drug

The initial data in this document were reported on May 19, 2026, and are from Group 1 participants (adults and adolescents 12 and up) who enrolled in Part 1 and were randomly assigned to one of three doses. All initial data included in this document are as of April 15, 2026.

What is the background of the participants represented in this initial data?

- 32 participants with *PIK3CA*-driven vascular malformation
 - 69% with a PROS-specific diagnosis
 - 25% with a lymphatic malformation diagnosis
 - 6% with a venous malformation diagnosis
- 19% of participants did not have a documented mutation
- The median age was about 25 years old, with approximately 2/3 of patients aged 18 or older and 1/3 of patients aged 12-17
- 72% had previously been treated with sirolimus and/or alpelisib
- 59% had prior disease-related surgery



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What was the initial safety data from Part 1 of the ReInspire Study?

Side effects in clinical trials are graded by severity with Grade 1 being mild, Grade 2 being moderate and Grade 3 being severe but not life-threatening. In Part 1 of the ReInspire Study side effects were generally low-grade, manageable, and reversible in the participants treated at the lower dose levels of 100mg and 300mg twice daily, which is the dose range prioritized for further development in the next part (Part 2) of the ReInspire Study.

AT 100MG AND 300MG TWICE DAILY:

- The most common treatment-related side effect was headache, and it was generally mild (Grade 1)
- Other common side effects were fatigue, nausea, diarrhea and decreased appetite, all low grade (Grade 1-2)
- Low grade (Grade 1-2) hyperglycemia (increased blood sugar) was observed at 300mg twice daily; it was not observed at 100mg twice daily
- No treatment-related severe, life-threatening side effects were observed

Zovegalisib – Treatment-Related Adverse Events ≥15% of Participants

	100mg Twice Daily				300mg Twice Daily				400mg Twice Daily			
	All Gr	Gr 1	Gr 2	Gr 3+	All Gr	Gr 1	Gr 2	Gr 3+	All Gr	Gr 1	Gr 2	Gr 3+
Headache	18%	18%	-	-	73%	73%	-	-	50%	30%	20%	-
Fatigue	18%	9%	9%	-	55%	36%	18%	-	20%	10%	10%	-
Nausea	27%	18%	9%	-	45%	36%	9%	-	70%	40%	30%	-
Diarrhea	27%	27%	-	-	18%	18%	-	-	10%	-	10%	-
Hyperglycemia (increased blood sugar)	-	-	-	-	45%	18%	27%	-	40%	20%	10%	10%
Decreased appetite	18%	9%	9%	-	18%	9%	9%	-	20%	10%	10%	-

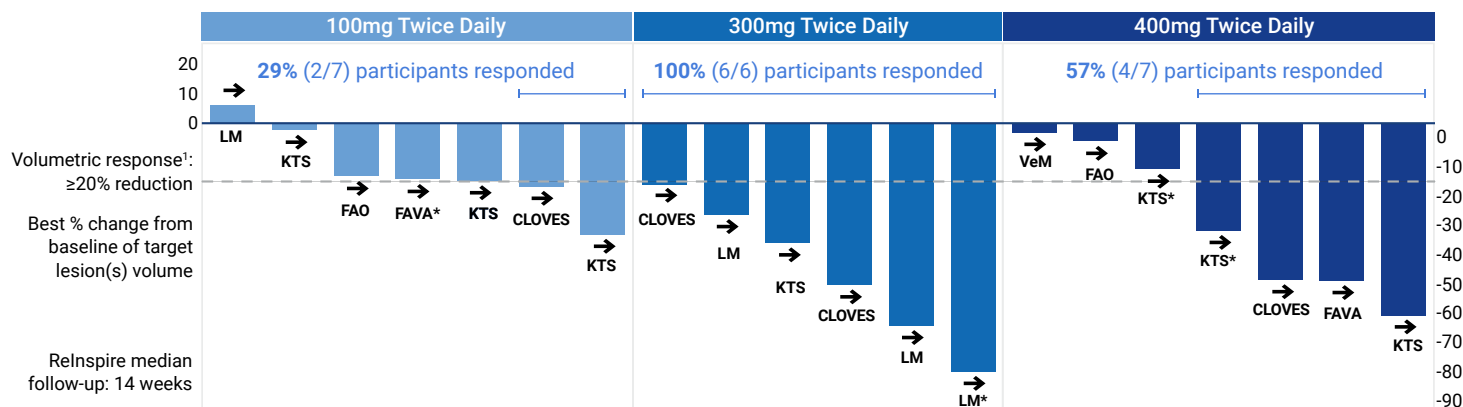
Gr = grade.

What was the initial volumetric response rate and clinical outcome assessment data from Part 1 of the ReInspire Study?

Additional data from Part 1 of the ReInspire Study measured Volumetric Response and Clinical Outcome Assessments (COAs).

VOLUMETRIC RESPONSE

The volumetric response rate looks at the volumetric reduction or change in size of an identified vascular malformation and/or overgrowth (called target lesions). A response is a ≥20% reduction of a target lesion(s) which is measured by MRIs. At the time of the data cut 20 of the 32 participants had at least one MRI scan, so the volumetric response rates reported below are based off of these 20 participants.



¹Includes both confirmed and unconfirmed responses *unknown mutation; LM= lymphatic malformation, FAVA= Fibroadipose vascular anomaly, KTS= Klippel-Trenaunay syndrome, FAO= Fibro Adipose hyperplasia or Overgrowth, VeM = venous malformation.

CLINICAL OUTCOME ASSESSMENTS (COAs)

COAs are questionnaires answered by physicians and patients that measure how a participant is feeling and functioning.

89% 

(17/19) of **physician assessments*** reported improved symptoms at Week 12 across doses

79% 

(11/14) of **patient assessments†** reported improved symptoms at Week 12 across doses

71% 

(11/14) of **pain symptoms‡** at week 12 were reported as improved by physicians across doses

*Investigator Global Impression of Change (IGIC): Assesses overall change of symptoms since baseline as reported by physicians. †Patient Global Impression of Change (PGIC): Assesses overall change of symptoms since baseline as reported by patients. ‡Investigator Assessment of Disease-Related Signs and Symptoms Assesses (IADRSS): Assesses change of 1-3 participant-specific symptoms collaboratively selected by investigator & patient.

What are the next steps of the ReInspire Study?

For adults and adolescents 12 and up, doses between 100mg twice daily and 300mg twice daily have been chosen to study in the next part of the trial (Part 2) to further define a dose(s) with the most benefit and least side effects.

The ReInspire Study continues to enroll eligible participants in the different parts and age groups.

Where can I learn more about the ReInspire Study?

To learn more about the ReInspire Study, visit: ReInspireStudy.com or reach out to clinicaltrials@relaytx.com



Relay would like to thank the participants and their families whose commitment and participation makes the ReInspire Study possible.

- The initial data from the ReInspire Phase 2 Study included in this document are based on a preliminary data cut from an ongoing clinical trial and reflect results from a limited number of participants. These data are early in nature and should be interpreted with caution.
- The study remains open to enrollment, and additional participants, longer follow up, and ongoing analyses may materially affect the results and conclusions as the trial progresses. As such, the initial results presented here may not be predictive of future outcomes.
- Zovegalisib (RLY-2608) has not been approved for any use, and the safety and efficacy of zovegalisib (RLY-2608) have not been established.