ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: July 23, 2024

ClinicalTrials.gov ID: NCT05442775

Study Identification

Unique Protocol ID:	CY 5032
Brief Title:	A Phase 3, Open-Label Extension of COURAGE-ALS (CY 5031)
Official Title:	A Phase 3, Open-Label Extension of COURAGE-ALS (CY 5031)
Secondary IDs:	2021-004727-33 [EudraCT Number]

Study Status

Record Verification:	July 2024
Overall Status:	Terminated [The DMC recommended the trial be discontinued due to futility following a planned second interim analysis of the parent trial (CY 5031).]
Study Start:	August 4, 2022 [Actual]
Primary Completion:	June 7, 2023 [Actual]
Study Completion:	June 7, 2023 [Actual]

Sponsor/Collaborators

Sponsor:	Cytokinetics
Responsible Party:	Sponsor
Collaborators:	

Oversight

U.S. FDA-regulated Drug:	Yes
U.S. FDA-regulated Device:	No

U.S. FDA IND/IDE:	Yes
IND/IDE Information:	FDA Center: CDER IND/IDE Number: 134567 Serial Number: 0077 Has Expanded Access: No
Human Subjects Review:	Board Status: Approved Approval Number: 38820 Board Name: Horizon Health Network Research Ethics Board Board Affiliation: Phone: 506-648-6094 Email: ResearchEthics@Horizonnb.ca Address: Saint John Regional Hospital, 2nd Floor 400 University Ave. Saint John, New Brunswick, Canada E2L 4L2
Data Monitoring:	No
FDA Regulated Intervention:	Yes
Section 801 Clinical Trial:	Yes

Study Description

Brief Summary:	The purpose of this study is to assess the long-term safety and tolerability of reldesemtiv in patients with ALS who have successfully completed dosing in the Phase 3 clinical trial, CY 5031 (also known as COURAGE-ALS)
Detailed Description:	CY 5032 is an open-label extension (OLE) study of the selective fast skeletal muscle troponin activator, reldesemtiv, in patients with ALS who finished dosing (through Week 48) in CY 5031 (COURAGE-ALS). Approximately 400 patients from the sites that participated in CY 5031 are expected to be enrolled in the open-label extension, CY 5032. Following enrollment, patients will continue dosing with reldesemtiv, 300 mg twice a day for a 600 mg total daily dose (TDD) for a period of 48 weeks. At the end of 48 weeks, patients may transition to a reldesemtiv Managed Access Program (MAP) if the treating physician agrees to participate in the program.

Conditions

Conditions:	Amyotrophic Lateral Sclerosis
Keywords:	Amyotrophic Lateral Sclerosis ALS CK-2127107

Reldesemtiv

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 3
Interventional Study Model:	Single Group Assignment
Number of Arms:	1
Masking:	None (Open Label)
Allocation:	N/A
Enrollment:	71 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Reldesemtiv 300 mg twice daily Patients in this arm take 1 reldesemtiv 300 mg oral tablet twice a day for a 600 mg total daily dose (TDD). Participants who had been down titrated during the parent trail take 150 mg by mouth twice a day.	Drug: Reldesemtiv Oral tablet

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age:	18 Years
Maximum Age:	
Sex:	All
Gender Based:	No
Accepts Healthy Volunteers:	No
Criteria:	Inclusion Criteria:

- Able to comprehend and willing to sign an ICF and willing to comply with all study procedures and restrictions for the duration specified in the Schedule of Activities. If non-written consent is given, a Legal Designee of the patient must sign the ICF form.
- Completed dosing in CY 5031

Exclusion Criteria:

- Has taken investigational study drug (other than reldesemtiv) prior to dosing, within 30 days or five half-lives of the prior agent, whichever is greater
- Presence on Day 1 of any medically significant cardiac, pulmonary, gastrointestinal, musculoskeletal, or psychiatric illness that might interfere with the patient's ability to comply with study procedures or that might confound the interpretation of clinical safety or efficacy data.
- Use of a strong cytochrome P450 (CYP) 3A4 inhibitor within 7 days prior to first dose of reldesemtiv in CY 5032 or a strong CYP3A4 inducer within 14 days prior to first dose of reldesemtiv in CY 5032
- Use of a medication that is an OCT1/OCT2 substrate within 7 days prior to first dose of reldesemtiv in CY 5032
- Currently participating in another trial, managed access program, open label extension, early access program, or through the right to try act is receiving an investigational drug or received an investigational drug or device within 30 days (or 5 half-lives for drugs, whichever is longer) prior to Day 1. Patients also cannot be taking outside of a clinical trial certain investigational drugs (which includes drugs, supplements, and nutraceuticals) that are currently being studied or have been studied for the treatment of ALS.

Contacts/Locations

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IPDSharing

Plan to Share IPD:

References

Citations:

Links:

Available IPD/Information:

Documents

Study Protocol
Document Date: December 16, 2022
Uploaded: 06/07/2024 15:54

Statistical Analysis Plan
Document Date: June 16, 2023
Uploaded: 06/07/2024 15:54

Study Results

Participant Flow

Recruitment Details	Participants were enrolled from 41 trial centers in North America, Europe, and Australia. The first participant was enrolled on 04 Aug 2022 and the last participant completed on 07 Jun 2023.
Pre-assignment Details	A total of 71 participants who were previously enrolled in the double-blind placebo-controlled CY 5031 parent trial were enrolled in this trial and received at least one dose of reldesemtiv.

Reporting Groups

	Description
Reldesemtiv	Participants in this arm take 1 reldesemtiv 300 mg oral tablet twice a day for a 600 mg total daily dose (TDD) Reldesemtiv: Oral tablet

Overall Study

	Reldesemtiv
Started	71
Completed	0 [1]
Not Completed	71
Trial terminated	61
Lack of Efficacy	4
Withdrawal by Subject	4
Death	1
Participant removed at Sponsor request	1

[1] Trial was prematurely terminated by the Sponsor.

Baseline Characteristics

Baseline Analysis Population Description
Full Analysis Set

Reporting Groups

	Description
Reldesemtiv	Participants in this arm take 1 reldesemtiv 300 mg oral tablet twice a day for a 600 mg total daily dose (TDD) Reldesemtiv: Oral tablet

Baseline Measures

		Reldesemtiv
Overall Number of Participants		71
Age, Continuous Mean (Standard Deviation) Unit of measure: years	Number Analyzed	71 participants
		61.7 (11.62)
Sex: Female, Male Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	71 participants
	Female	31 43.66%
	Male	40 56.34%
Ethnicity (NIH/ OMB) Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	71 participants
	Hispanic or Latino	2 2.82%
	Not Hispanic or Latino	69 97.18%
	Unknown or Not Reported	0 0%
Race/Ethnicity, Customized Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	71 participants
White		65 91.55%
Other		3 4.23%
Asian		2 2.82%
Black or African American		1 1.41%

		Reldesemtiv
Region of Enrollment Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	71 participants
North America		53 74.65%
Europe		10 14.08%
Australia		8 11.27%
Time Since ALS Diagnosis at Screening in CY 5031 Mean (Standard Deviation) Unit of measure: months	Number Analyzed	71 participants
		17.9 (4.69)
Percent Predicted Forced Vital Capacity Mean (Standard Deviation) Unit of measure: percent predicted	Number Analyzed	71 participants
		70.6 (22.76)
ALSFRS-R Total Score [1] Mean (Standard Deviation) Unit of measure: scores on a scale	Number Analyzed	71 participants
		29.8 (8.47)
		[1] Measure Description: ALSFRS-R = Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised. ALSFRS-R total score range is from 0 to 48. A score of 48 reflects normal function.

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Long-term Safety and Tolerability
Measure Description	Incidence of treatment-emergent adverse events
Time Frame	Baseline to Week 34 (time the study was terminated prematurely)

Analysis Population Description
Safety Analysis Set

Reporting Groups

	Description
Reldesemtiv	Participants in this arm take 1 reldesemtiv 300 mg oral tablet twice a day for a 600 mg total daily dose (TDD) Reldesemtiv: Oral tablet

Measured Values

	Reldesemtiv
Overall Number of Participants Analyzed	71
Long-term Safety and Tolerability Measure Type: Count of Participants Unit of measure: participants	39 54.93%

2. Secondary Outcome Measure:

Measure Title	Long-term Effect of Reldesemtiv on ALSFRS-R Functional Outcomes
Measure Description	Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised (ALSFRS-R) total scores. ALSFRS-R total score range is from 0 to 48. A score of 48 reflects normal function.
Time Frame	Baseline to Week 32 (last timepoint before study was terminated prematurely)

Analysis Population Description
Full Analysis Set

Reporting Groups

	Description
Reldesemtiv	Participants in this arm take 1 reldesemtiv 300 mg oral tablet twice a day for a 600 mg total daily dose (TDD) Reldesemtiv: Oral tablet

Measured Values

		Reldesemtiv
Overall Number of Participants Analyzed		71
Long-term Effect of Reldesemtiv on ALSFRS-R Functional Outcomes Mean (Standard Deviation) Unit of measure: score on a scale	[Not specified]	
Week 12	Number Analyzed	47 participants
		29.5 (9.04)
Week 24	Number Analyzed	20 participants
		27.4 (11.86)
Week 32	Number Analyzed	9 participants
		26.6 (13.96)

Reported Adverse Events

Time Frame	up to 34 weeks (time the study was terminated prematurely)
Adverse Event Reporting Description	[Not specified]

Reporting Groups

	Description
Reldesemtiv	Participants in this arm take 1 reldesemtiv 300 mg oral tablet twice a day for a 600 mg total daily dose (TDD) Reldesemtiv: Oral tablet

All-Cause Mortality

	Reldesemtiv	
	Affected/At Risk (%)	# Events
Total All-Cause Mortality	5/71 (7.04%)	

Serious Adverse Events

	Reldesemtiv	
	Affected/At Risk (%)	# Events
Total	11/71 (15.49%)	
Cardiac disorders		
Stress cardiomyopathy [A] †	1/71 (1.41%)	1
Gastrointestinal disorders		
Abdominal pain [A] †	1/71 (1.41%)	1
Gastric ulcer haemorrhage [A] †	1/71 (1.41%)	1
Lower gastrointestinal haemorrhage [A] †	1/71 (1.41%)	1
Pneumoperitoneum [A] †	1/71 (1.41%)	1
Infections and infestations		
Klebsiella urinary tract infection [A] †	1/71 (1.41%)	1
Metapneumovirus infection [A] †	1/71 (1.41%)	1
Pneumonia aspiration [A] †	1/71 (1.41%)	1
Septic shock [A] †	1/71 (1.41%)	1
Urinary tract infection [A] †	1/71 (1.41%)	1
Injury, poisoning and procedural complications		
Tibia fracture [A] †	1/71 (1.41%)	1
Psychiatric disorders		
Assisted suicide [A] †	2/71 (2.82%)	2
Respiratory, thoracic and mediastinal disorders		

	Reldesemtiv	
	Affected/At Risk (%)	# Events
Respiratory failure [A] †	3/71 (4.23%)	3

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 26.0

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Reldesemtiv	
	Affected/At Risk (%)	# Events
Total	27/71 (38.03%)	
Gastrointestinal disorders		
Constipation [A] †	6/71 (8.45%)	6
Diarrhoea [A] †	7/71 (9.86%)	7
Nausea [A] †	4/71 (5.63%)	4
Infections and infestations		
Urinary tract infection [A] †	5/71 (7.04%)	5
Injury, poisoning and procedural complications		
Fall [A] †	5/71 (7.04%)	5

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 26.0

Limitations and Caveats

Based on interim analysis results of the Phase 3 parent trial CY 5031 which met the criteria for futility in participants with ALS, CY 5032 was prematurely terminated on 31 March 2023.

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There is NOT an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

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