



## Clinical trial results:

### A randomised, placebo-controlled, multicentre phase IIb study evaluating the efficacy of pirenepamat on falls frequency in patients with Parkinson's disease

#### Summary

EudraCT number	2019-002627-16
Trial protocol	DE PL FR ES NL
Global end of trial date	09 January 2025

#### Results information

Result version number	v1 (current)
This version publication date	11 June 2026
First version publication date	11 June 2026
Summary attachment (see zip file)	Study report synopsis (IRL752C003_CSR synopsis_v1.0_10-Oct-2025_Bortredigerad.pdf) IRL752C003_Poster ADPD2026_REACT-PD results (eClinical_poster_IRL752_ADPD2026.pdf)

#### Trial information

##### Trial identification

Sponsor protocol code	IRL752C003
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05258071
WHO universal trial number (UTN)	-

Notes:

##### Sponsors

Sponsor organisation name	Integrative Research Laboratories Sweden AB (IRLAB)
Sponsor organisation address	Arvid Wallgrens Backe 20, Gothenburg, Sweden,
Public contact	Clinical Trial Information Desk, Integrative Research Laboratories Sweden AB (IRLAB), +46 31 757 38 00, info@irlab.se
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Notes:

##### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	19 March 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 December 2024
Global end of trial reached?	Yes
Global end of trial date	09 January 2025
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the effects of pirepemat on fall frequency as compared to placebo.

Protection of trial subjects:

To monitor safety of the trial subjects, measurements of vital signs, physical examinations, clinical laboratory safety tests and ECGs were performed regularly. Discontinuation protocol was in place if any of the protocol stopping criteria was met.

Background therapy:

All participants are receiving their standard Parkinson's treatment. Parkinson's treatment must be stable for at least 30 days prior to the start of IMP (Investigational Medicinal Product).

Evidence for comparator: -

Actual start date of recruitment	10 May 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Poland: 56
Country: Number of subjects enrolled	Spain: 14
Country: Number of subjects enrolled	Sweden: 5
Country: Number of subjects enrolled	France: 14
Country: Number of subjects enrolled	Germany: 14
Worldwide total number of subjects	104
EEA total number of subjects	104

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0

Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	19
From 65 to 84 years	85
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Recruitment was open from Jun-2022 to Sep-2024 at 38 trial centers across France, Germany, Poland, Spain, Sweden and the Netherlands.

### Pre-assignment

Screening details:

Screening period was between 4 and 6 weeks from the date of signature of the ICF by the subject. Participants were screened for eligibility according to study-specific inclusion/exclusion criteria. Key inclusion criteria: Parkinson's disease diagnostic with stable treatment, MoCA score between 10 and 26, 2 falls during the 4 weeks before baseline

### Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Pirepemat 300 mg

Arm description:

Pirepemat tablets, dose 50 mg, 2 tablets t.i.d. for 84 days

Arm type	Experimental
Investigational medicinal product name	IRL757
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

IRL757, 50 mg tablet, 2 tablets t.i.d.

<b>Arm title</b>	Pirepemat 600 mg
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Arm description:

Pirepemat tablets, dose 100 mg, 2 tablets t.i.d. for 84 days

Arm type	Experimental
Investigational medicinal product name	IRL757
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

IRL757, 100 mg tablet, 2 tablets t.i.d.

<b>Arm title</b>	Placebo
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Arm description:

Placebo tablets, 2 tablets t.i.d. for 84 days

Arm type	Placebo
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Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo, 2 tablets t.i.d.

<b>Number of subjects in period 1</b>	Pirepemat 300 mg	Pirepemat 600 mg	Placebo
Started	35	35	34
Completed	32	28	30
Not completed	3	7	4
Adverse event, serious fatal	-	-	1
Consent withdrawn by subject	1	4	2
Adverse event, non-fatal	1	1	1
Elevation of Liver Enzymes	1	2	-

## Baseline characteristics

### Reporting groups

Reporting group title	Overall trial
Reporting group description: -	

Reporting group values	Overall trial	Total	
Number of subjects	104	104	
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
geometric mean	71.6		
standard deviation	± 7.10	-	
Gender categorical			
Units: Subjects			
Female	41	41	
Male	63	63	

### Subject analysis sets

Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

The Full Analysis Set includes all patients who are randomized and treated, who receive at least 1 dose of IMP and who provide at least 1 post baseline efficacy assessment on primary or secondary endpoints.

Reporting group values	Full Analysis Set		
Number of subjects	101		
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
geometric mean	71.6		
standard deviation	± 7.10		
Gender categorical			
Units: Subjects			
Female	41		
Male	60		

## End points

### End points reporting groups

Reporting group title	Pirepemat 300 mg
Reporting group description: Pirepemat tablets, dose 50 mg, 2 tablets t.i.d. for 84 days	
Reporting group title	Pirepemat 600 mg
Reporting group description: Pirepemat tablets, dose 100 mg, 2 tablets t.i.d. for 84 days	
Reporting group title	Placebo
Reporting group description: Placebo tablets, 2 tablets t.i.d. for 84 days	
Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis
Subject analysis set description: The Full Analysis Set includes all patients who are randomized and treated, who receive at least 1 dose of IMP and who provide at least 1 post baseline efficacy assessment on primary or secondary endpoints.	

### Primary: Change in fall frequency as assessed with fall diary from baseline period to the end of treatment.

End point title	Change in fall frequency as assessed with fall diary from baseline period to the end of treatment.
End point description: The number of falls is being recorded using a paper fall diary (Patient Reported Outcome, PRO). Change in falls is reported as a relative fall rate (fall rate at evaluation period / fall rate at baseline period).	
End point type	Primary
End point timeframe: For the Baseline period, all collected data before first IMP administration are considered for baseline fall rate (min 28 days). For the fall rate at Evaluation period, the data collected during the last 28 days with full IMP dose are considered.	

End point values	Pirepemat 300 mg	Pirepemat 600 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	28	31	
Units: % of baseline fall rate	77	64	69	

### Statistical analyses

Statistical analysis title	Analysis 1 - MMRM with ranked relative fall rate
Statistical analysis description: Comparing high dose group vs placebo, using Mixed Model Repeated Measurements with ranked relative fall rate as dependent variable, with treatment group and acetylcholinesterase as covariates.	
Comparison groups	Placebo v Pirepemat 600 mg

Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority <sup>[1]</sup>
P-value	= 0.5753
Method	Ranked Relative Fall Rate MMRM
Parameter estimate	Median ratio
Point estimate	0.973
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.706
upper limit	1.274

Notes:

[1] - Estimate and confidence interval for primary analysis for Median Relative Fall Rate Ratio ((median relative fall rate of Pirepemat Group) / (median relative fall rate of placebo group)), is computed through bootstrap procedure (10000 estimates) described in the SAP. Confidence intervals are the 2.5 and 97.5% percentile values.

<b>Statistical analysis title</b>	Analysis 2 - Negative binomial regression
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Statistical analysis description:

Comparing high dose group vs placebo by means of negative binomial regression.

Comparison groups	Pirepemat 600 mg v Placebo
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority <sup>[2]</sup>
P-value	= 0.5156
Method	Negative binomial regression
Parameter estimate	Relative Fall Rate treatment/placebo
Point estimate	0.854
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	1.376

Notes:

[2] - Fall rate frequency and confidence intervals are calculated from a negative binomial regression in SAS Proc Genmod, with baseline days, log(fall rate at baseline) and strata for cholinesterase inhibitor use as covariates, treatment group as a factor

### **Secondary: Change in the total score of MDS-UPDRS part 2 (M-EDL) from baseline to end of full dose treatment (with pirepemat compared to placebo)**

End point title	Change in the total score of MDS-UPDRS part 2 (M-EDL) from baseline to end of full dose treatment (with pirepemat compared to placebo)
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End point description:

The total scoring range is 0-52, where a higher score indicates more severe impact on Motor Aspects of Experiences of Daily Living (M-EDL).  
The endpoint measure is the difference between the score measured at the last full dose visit and the score measured at baseline visit.

End point type	Secondary
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End point timeframe:

Baseline to end of full dose treatment (week 11)

<b>End point values</b>	Pirepemat 300 mg	Pirepemat 600 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	32	28	29	
Units: point	0	1	2	

## Statistical analyses

<b>Statistical analysis title</b>	Analysis MDS-UPDRS
Comparison groups	Pirepemat 600 mg v Placebo
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	superiority
P-value	$\leq 0.05$
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.04
upper limit	3.65

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from signature of ICF to completion of trial (20-22 weeks). The AE presented here in the results are only treatment-emergent AEs (meaning AE occurring once the study treatment was started).

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	27.1

### Reporting groups

Reporting group title	Pirepemat 300 mg
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Reporting group description:

Pirepemat tablets, dose 50 mg, 2 tablets t.i.d. for 84 days

Reporting group title	Pirepemat 600 mg
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Reporting group description: -

Reporting group title	Placebo
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Reporting group description: -

Serious adverse events	Pirepemat 300 mg	Pirepemat 600 mg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 35 (11.43%)	4 / 35 (11.43%)	3 / 34 (8.82%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	1
Investigations			
Cystatin C increased			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glomerular filtration rate decreased			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Papillary thyroid cancer			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Bradykinesia			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neurodegenerative disorder			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Gastrointestinal disorders			
Duodenal ulcer			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatitis cholestatic			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis toxic			

subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Delusion			
subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

<b>Non-serious adverse events</b>	Pirepemat 300 mg	Pirepemat 600 mg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 35 (74.29%)	27 / 35 (77.14%)	18 / 34 (52.94%)
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	7 / 35 (20.00%)	4 / 35 (11.43%)	0 / 34 (0.00%)
occurrences (all)	7	4	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 35 (0.00%)	2 / 35 (5.71%)	0 / 34 (0.00%)
occurrences (all)	0	2	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 35 (5.71%)	0 / 35 (0.00%)	3 / 34 (8.82%)
occurrences (all)	2	0	3
Head injury			
subjects affected / exposed	4 / 35 (11.43%)	1 / 35 (2.86%)	0 / 34 (0.00%)
occurrences (all)	4	1	0
Joint injury			

subjects affected / exposed occurrences (all)	1 / 35 (2.86%) 1	1 / 35 (2.86%) 1	2 / 34 (5.88%) 2
Fall subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0	2 / 35 (5.71%) 2	1 / 34 (2.94%) 1
Skin abrasion subjects affected / exposed occurrences (all)	2 / 35 (5.71%) 2	1 / 35 (2.86%) 1	0 / 34 (0.00%) 0
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	2 / 35 (5.71%) 2	0 / 35 (0.00%) 0	1 / 34 (2.94%) 1
Surgical and medical procedures Dental implantation subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0	0 / 35 (0.00%) 0	2 / 34 (5.88%) 2
Nervous system disorders Headache subjects affected / exposed occurrences (all)	3 / 35 (8.57%) 3	1 / 35 (2.86%) 1	1 / 34 (2.94%) 1
Dizziness subjects affected / exposed occurrences (all)	1 / 35 (2.86%) 1	3 / 35 (8.57%) 3	0 / 34 (0.00%) 0
Freezing phenomenon subjects affected / exposed occurrences (all)	2 / 35 (5.71%) 2	1 / 35 (2.86%) 1	0 / 34 (0.00%) 0
Somnolence subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0	2 / 35 (5.71%) 2	1 / 34 (2.94%) 1
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all)	1 / 35 (2.86%) 1	2 / 35 (5.71%) 2	0 / 34 (0.00%) 0
Fatigue subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0	2 / 35 (5.71%) 2	0 / 34 (0.00%) 0

Gastrointestinal disorders			
	Diarrhoea		
	subjects affected / exposed	4 / 35 (11.43%)	3 / 35 (8.57%)
	occurrences (all)	4	3
	Nausea		
	subjects affected / exposed	1 / 35 (2.86%)	3 / 35 (8.57%)
	occurrences (all)	1	3
Endocrine disorders			
	Hypothyroidism		
	subjects affected / exposed	2 / 35 (5.71%)	0 / 35 (0.00%)
	occurrences (all)	2	0
Musculoskeletal and connective tissue disorders			
	Arthralgia		
	subjects affected / exposed	2 / 35 (5.71%)	3 / 35 (8.57%)
	occurrences (all)	2	3
	Pain in extremity		
	subjects affected / exposed	3 / 35 (8.57%)	1 / 35 (2.86%)
	occurrences (all)	3	1
	Musculoskeletal chest pain		
	subjects affected / exposed	2 / 35 (5.71%)	1 / 35 (2.86%)
Infections and infestations			
	Urinary tract infection		
	subjects affected / exposed	1 / 35 (2.86%)	3 / 35 (8.57%)
	occurrences (all)	1	3
	COVID-19		
	subjects affected / exposed	0 / 35 (0.00%)	2 / 35 (5.71%)
	occurrences (all)	0	2
	Nasopharyngitis		
	subjects affected / exposed	1 / 35 (2.86%)	2 / 35 (5.71%)
	occurrences (all)	1	2

**More information**

**Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 September 2023	Correction of discrepancies and clarifications and update following implementation of urgent safety measure (adding a visit for safety laboratory assessments at week 3). Removal of two safety follow-up visits.
23 January 2024	Re-estimation of the sample size. Revision of analysis model for the primary endpoint. Clarification of the primary outcome measure and revision of secondary, tertiary objectives classification. Correction of discrepancies.

Notes:

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**Interruptions (globally)**

Were there any global interruptions to the trial? No

**Limitations and caveats**

None reported