EU Clinical Trials Register

Clinical trial results:
An adaptive seamless randomized, double-blind, placebo-controlled, dose ranging study to investigate the efficacy and safety of LNP023 in primary IgA nephropathy patients

EudraCT number	2017-000891-27
Trial protocol	GB SE FI DE BE NL DK CZ HU FR IT
Global end of trial date	22 June 2021

Result version number	v1 (current)
This version publication date	30 June 2022
First version publication date	30 June 2022

Sponsor protocol code	CLNP023X2203

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03373461
WHO universal trial number (UTN)	-

Notes:

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com
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Notes:

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:

Analysis stage	Final
Date of interim/final analysis	22 June 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 June 2021
Was the trial ended prematurely?	No

Notes:

Main objective of the trial:

To evaluate the dose response relationship of LNP023 on the reduction in proteinuria versus placebo after 90 days of treatment

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 February 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Country: Number of subjects enrolled	Argentina: 2
Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	Belgium: 14
Country: Number of subjects enrolled	Brazil: 4
Country: Number of subjects enrolled	China: 9
Country: Number of subjects enrolled	Colombia: 1
Country: Number of subjects enrolled	Czechia: 1
Country: Number of subjects enrolled	Denmark: 4
Country: Number of subjects enrolled	Finland: 1
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Germany: 5
Country: Number of subjects enrolled	Hong Kong: 2
Country: Number of subjects enrolled	India: 3
Country: Number of subjects enrolled	Israel: 4
Country: Number of subjects enrolled	Japan: 5
Country: Number of subjects enrolled	Korea, Republic of: 1
Country: Number of subjects enrolled	Malaysia: 1

Country: Number of subjects enrolled	Netherlands: 2
Country: Number of subjects enrolled	Norway: 5
Country: Number of subjects enrolled	Singapore: 2
Country: Number of subjects enrolled	Sweden: 3
Country: Number of subjects enrolled	Taiwan: 8
Country: Number of subjects enrolled	Thailand: 14
Country: Number of subjects enrolled	Turkey: 5
Country: Number of subjects enrolled	United Kingdom: 10
Worldwide total number of subjects	112
EEA total number of subjects	36

Notes:

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)	109
From 65 to 84 years	3
85 years and over	0

Recruitment details: -

Screening details:

There were 99 participants screened and 46 randomized participants completed in Part 1. There were 162 screened in Part 2 and 66 were randomized. All participants completed a run-in period of at least 30 days. Participants randomized to Part 1 could not participate in Part 2.

Period 1 title	Part 1 (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

Are arms mutually exclusive?	Yes
	LNP023 10 mg BID
Arm description: 10 mg taken twice a day	
Arm type	Experimental
Investigational medicinal product name	iptacopan
Investigational medicinal product code	LNP023
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: 10 mg taken twice a day	
	LNP023 50 mg BID
Arm description: 50 mg taken twice a day	
Arm type	Experimental
Investigational medicinal product name	iptacopan
Investigational medicinal product code	LNP023
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: 50 mg taken twice a day	
	LNP023 100 mg BID - Part 2
Arm description: 100 mg taken orally twice a day	
Arm type	Experimental
Investigational medicinal product name	iptacopan
Investigational medicinal product code	LNP023
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details: 100 mg taken twice a day

	LNP023 200 mg BID
Arm description: 200 mg taken twice a day	
Arm type	Experimental
Investigational medicinal product name	iptacopan
Investigational medicinal product code	LNP023
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: 200 mg taken twice a day	

	Placebo
Arm description: Placebo identical to LNP023 taken orally twice a day	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: Placebo identical to LNP023 taken twice a day	

	LNP023 10 mg BID	LNP023 50 mg BID	LNP023 100 mg BID - Part 2
Started	20	19	22
Started Part 1	9 [1]	8 [2]	15 [3]
Completed Part 1	9 [4]	8 [5]	15 [6]
Started Part 2	11 [7]	11 [8]	22
Completed Part 2	11 [9]	10 [10]	22
Completed	20	18	22
Not completed	0	1	0
Adverse event, non-fatal	-	1	-

	LNP023 200 mg BID	Placebo
Started	26	25
Started Part 1	14 [11]	14 [12]
Completed Part 1	14 [13]	14 [14]
Started Part 2	11 [15]	11 [16]

Completed Part 2	11 [17]	10 [18]
Completed	26	24
Not completed	0	1
Adverse event, non-fatal	-	1

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Participants randomized to Part 1 could not participate in Part 2.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Participants randomized to Part 1 could not participate in Part 2.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Participants randomized to Part 1 could not participate in Part 2.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Participants randomized to Part 1 could not participate in Part 2.

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Participants randomized to Part 1 could not participate in Part 2.

[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Participants randomized to Part 1 could not participate in Part 2.

[7] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Participants randomized to Part 1 could not participate in Part 2.

[8] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Participants randomized to Part 1 could not participate in Part 2.

[9] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Participants randomized to Part 1 could not participate in Part 2.

[10] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Participants randomized to Part 1 could not participate in Part 2.

[11] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Participants randomized to Part 1 could not participate in Part 2.

[12] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Participants randomized to Part 1 could not participate in Part 2.

[13] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Participants randomized to Part 1 could not participate in Part 2.

Reporting group title	LNP023 10 mg BID
Reporting group description: 10 mg taken twice a day	
Reporting group title	LNP023 50 mg BID
Reporting group description: 50 mg taken twice a day	
Reporting group title	LNP023 100 mg BID - Part 2
Reporting group description: 100 mg taken orally twice a day	
Reporting group title	LNP023 200 mg BID
Reporting group description: 200 mg taken twice a day	
Reporting group title	Placebo
Reporting group description: Placebo identical to LNP023 taken orally twice a day	

	LNP023 10 mg BID	LNP023 50 mg BID	LNP023 100 mg BID - Part 2
Number of subjects	20	19	22
Age Categorical Units:			
18 years - <65 years	20	19	21
65 years - <85 years	0	0	1
Age Continuous Units: years			
arithmetic mean	39.2	36.6	36.0
standard deviation	± 12.42	± 8.42	± 13.15
Sex: Female, Male Units:			
Female	11	6	11
Male	9	13	11
Race/Ethnicity, Customized Units: Subjects			
Asian	10	9	12
White	10	9	10
Black or African American	0	1	0
American Indian or Alaska Native	0	0	0
Prior use of ACEi and/or ARB			
Prior use of angiotensin converting enzyme inhibitor and/or angiotensin receptor blocker			
Units: Subjects			
No prior use of ACEi/or ARB	1	0	0
Prior use of ACEi/ARB	19	19	22
Urine Protein to Creatinine Ratio (UPCR)			
From 24 hour urine collection			
Units: g/mol			
arithmetic mean	214.1	188.2	203.4

standard deviation	± 122.29	± 90.38	± 98.29
Estimated Glomerular Filtration Rate (eGFR) Units: mL/min/1.73m^2			
arithmetic mean	66.0	53.8	67.0
standard deviation	± 28.51	± 22.73	± 31.75
Supine Blood Pressure Units: mmHg			
arithmetic mean	134.4	122.6	125.0
standard deviation	± 11.65	± 12.15	± 11.30
Supine Blood Pressure Units: mmHg			
arithmetic mean	84.1	76.9	80.0
standard deviation	± 7.65	± 8.41	± 10.40

	LNP023 200 mg BID	Placebo	Total
Number of subjects	26	25	112
Age Categorical Units:			
18 years - <65 years	24	25	109
65 years - <85 years	2	0	3
Age Continuous Units: years			
arithmetic mean	42.5	39.4	
standard deviation	± 15.76	± 11.00	-
Sex: Female, Male Units:			
Female	11	7	46
Male	15	18	66
Race/Ethnicity, Customized Units: Subjects			
Asian	12	11	54
White	13	13	55
Black or African American	1	0	2
American Indian or Alaska Native	0	1	1
Prior use of ACEi and/or ARB			
Prior use of angiotensin converting enzyme inhibitor and/or angiotensin receptor blocker			
Units: Subjects			
No prior use of ACEi/or ARB	0	0	1
Prior use of ACEi/ARB	26	25	111
Urine Protein to Creatinine Ratio (UPCR)			
From 24 hour urine collection			
Units: g/mol			
arithmetic mean	151.0	146.6	
standard deviation	± 109.46	± 61.62	-
Estimated Glomerular Filtration Rate (eGFR) Units: mL/min/1.73m^2			
arithmetic mean	57.9	65.7	
standard deviation	± 28.92	± 32.60	-
Supine Blood Pressure Units: mmHg			

arithmetic mean	125.7	125.5	
standard deviation	± 11.65	± 11.37	-
Supine Blood Pressure			
Units: mmHg			
arithmetic mean	79.7	78.2	
standard deviation	± 7.62	± 7.32	-

Reporting group title	LNP023 10 mg BID
Reporting group description: 10 mg taken twice a day	
Reporting group title	LNP023 50 mg BID
Reporting group description: 50 mg taken twice a day	
Reporting group title	LNP023 100 mg BID - Part 2
Reporting group description: 100 mg taken orally twice a day	
Reporting group title	LNP023 200 mg BID
Reporting group description: 200 mg taken twice a day	
Reporting group title	Placebo
Reporting group description: Placebo identical to LNP023 taken orally twice a day	
Subject analysis set title	<9 rbc/hpf
Subject analysis set type	Full analysis
Subject analysis set description: Low-grade hematuria	
Subject analysis set title	>=9 to =<50 rbc/hpf
Subject analysis set type	Full analysis
Subject analysis set description: Intermediate-grade hematuria	
Subject analysis set title	>50 rbc/hpf
Subject analysis set type	Full analysis
Subject analysis set description: Higher-grade hematuria	
Subject analysis set title	Baseline
Subject analysis set type	Full analysis
Subject analysis set description: Categories of hematuria at baseline	
Subject analysis set title	<9 rbc/hpf
Subject analysis set type	Full analysis
Subject analysis set description: Low-grade hematuria	
Subject analysis set title	>=9 to =<50 rbc/hpf
Subject analysis set type	Full analysis
Subject analysis set description: Intermediate-grade hematuria	
Subject analysis set title	>50 rbc/hpf
Subject analysis set type	Full analysis
Subject analysis set description: Higher-grade hematuria	

End point title	MCP-Mod estimates of the ratio to baseline of urine protein to creatinine ratio (UPCR) (g/mol) - Parts 1 and 2 at Day 90

End point description:

For UPCR test, participants collected all of their urine over a 24-hour period. The change from baseline in log transformed (natural log, base of e) UPCR at multiple time points (baseline, day 30, and day 90) was analyzed using a Mixed Model of Repeated Measures (MMRM) model. • The model included treatment, time point (as study day relative to start of study treatment), study part (Part 1 or Part 2), and ancestry (Asian/non-Asian) as fixed effects, and baseline log UPCR as a fixed covariate. The existence of a dose-response relationship was assessed using Multiple Comparison Procedure (MCP-Mod) method. The lower the number of the ratio, the greater the reduction in proteinuria.

End point type	Primary

End point timeframe:

Baseline, Days 30 and 90

	LNP023 10 mg BID	LNP023 50 mg BID	LNP023 100 mg BID - Part 2	LNP023 200 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	19	22	26
Units: Ratio to baseline				
number (confidence interval 80%)	0.85 (0.77 to 0.93)	0.80 (0.73 to 0.87)	0.76 (0.70 to 0.81)	0.69 (0.61 to 0.77)

	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: Ratio to baseline				
number (confidence interval 80%)	0.88 (0.80 to 1.00)			

	10 mg vs Placebo
Comparison groups	Placebo v LNP023 10 mg BID
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Ratio of the UPCR ratio to placebo
Point estimate	0.99
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.86
upper limit	1

	50 mg vs Placebo
Comparison groups	LNP023 50 mg BID v Placebo
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Ratio of the UPCR ratio to placebo
Point estimate	0.94
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.76
upper limit	0.98

	100 mg vs Placebo
Comparison groups	LNP023 100 mg BID - Part 2 v Placebo
Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Ratio of the UPCR ratio to placebo
Point estimate	0.87
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.72
upper limit	0.96

	200 mg vs Placebo
Comparison groups	LNP023 200 mg BID v Placebo
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Ratio of the UPCR ratio to placebo
Point estimate	0.77
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.66
upper limit	0.92

	All doses vs placebo

Comparison groups	LNP023 10 mg BID v LNP023 50 mg BID v LNP023 100 mg BID - Part 2 v LNP023 200 mg BID v Placebo
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.038
Method	Multiple comparison procedure-modeling

End point title	Mixed Model of Repeated Measures (MMRM) of the change from baseline for Estimated Glomerular Filtration Rate (eGFR) - Parts 1 and 2 at Day 90

End point description:

eGFR was calculated according to the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI)

End point type	Secondary

End point timeframe:

Baseline, Days 8, 15, 30 and 90

	LNP023 10 mg BID	LNP023 50 mg BID	LNP023 100 mg BID - Part 2	LNP023 200 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	19	22	26
Units: mL/min/SSA				
arithmetic mean (standard error)	-0.06 (± 1.760)	2.49 (± 1.859)	0.23 (± 1.821)	2.42 (± 1.545)

	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: mL/min/SSA				
arithmetic mean (standard error)	-3.34 (± 1.606)			

	10 mg vs Placebo
Comparison groups	LNP023 10 mg BID v Placebo

Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Mean difference (final values)
Point estimate	3.28
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.21
upper limit	6.344

	50 mg vs Placebo
Comparison groups	LNP023 50 mg BID v Placebo
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Mean difference (final values)
Point estimate	5.83
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	2.642
upper limit	9.01

	100 mg vs Placebo
Comparison groups	LNP023 100 mg BID - Part 2 v Placebo
Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Mean difference (final values)
Point estimate	3.56
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.427
upper limit	6.7

	200 mg vs Placebo
Comparison groups	LNP023 200 mg BID v Placebo

Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Mean difference (final values)
Point estimate	5.76
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	2.882
upper limit	8.638

End point title	Shift table from baseline for Hematuria levels - Parts 1 and 2 at Day 90

End point description:

Hematuria levels were the number of erythrocytes/high-power-field (hpf) measured through microscopic examination. Levels considered in the analysis were: Low-grade hematuria: <9 rbc/hpf, Intermediate-grade hematuria: >= 9 to <=50 rbc/hpf and Higher-grade hematuria: >50 rbc/hpf.

End point type	Secondary

End point timeframe:

Baseline, Days 8, 15, 30 ,60 and 90

	<9 rbc/hpf	>=9 to =<50 rbc/hpf	>50 rbc/hpf	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	56	10	1	
Units: participants				
LNP023 10mg <9	7	1	0	
LNP023 10mg >=9 to =<50	1	3	0	
LNP023 10mg >50	0	0	0	
LNP023 50mg <9	13	0	0	
LNP023 50mg >=9 to =<50	1	1	0	
LNP023 50mg >50	0	0	0	
LNP023 100mg <9	6	0	0	
LNP023 100mg >=9 to =<50	4	0	0	
LNP023 100mg >50	2	1	0	
LNP023 200mg <9	6	0	0	
LNP023 200mg >=9 to =<50	6	2	0	
LNP023 200mg >50	0	0	0	
Placebo <9	6	2	0	
Placebo >=9 to =<50	4	0	1	
Placebo >50	0	0	0	

No statistical analyses for this end point

End point title	Mixed Model of Repeated Measures (MMRM) of the ratio to baseline in 24hour urine protein (UP) - Parts 1 and 2 to Day 90

End point description:

Participants collected all of their urine over a 24-hour period.

End point type	Secondary

End point timeframe:

Baseline, Days 30 and 90

	LNP023 10 mg BID	LNP023 50 mg BID	LNP023 100 mg BID - Part 2	LNP023 200 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	19	22	26
Units: Ratio to baseline				
geometric mean (confidence interval 80%)	0.80 (0.661 to 0.965)	0.89 (0.740 to 1.070)	0.61 (0.509 to 0.729)	0.70 (0.601 to 0.823)

	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: Ratio to baseline				
geometric mean (confidence interval 80%)	0.84 (0.713 to 0.987)			

	10 mg vs Placebo
Comparison groups	LNP023 10 mg BID v Placebo
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric mean ratio
Point estimate	0.95
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.742
upper limit	1.222

	50 mg vs Placebo
Comparison groups	LNP023 50 mg BID v Placebo
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric mean ratio
Point estimate	1.06
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.83
upper limit	1.356

	100 mg vs Placebo
Comparison groups	LNP023 100 mg BID - Part 2 v Placebo
Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric mean ratio
Point estimate	0.73
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.569
upper limit	0.928

	200 mg vs Placebo
Comparison groups	LNP023 200 mg BID v Placebo
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric mean ratio
Point estimate	0.84
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.669
upper limit	1.05

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End point title	Mixed Model of Repeated Measures (MMRM) of the ratio to baseline of 24 hour urine albumin (UA) - Parts 1 and 2 to Day 90
End point description: Participants collected all of their urine over a 24-hour period.	
End point type	Secondary
End point timeframe: Baseline, Days 30 and 90	

	LNP023 10 mg BID	LNP023 50 mg BID	LNP023 100 mg BID - Part 2	LNP023 200 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	19	22	26
Units: Ratio to baseline				
geometric mean (confidence interval 80%)	0.79 (0.648 to 0.964)	0.93 (0.763 to 1.122)	0.61 (0.504 to 0.734)	0.73 (0.623 to 0.865)

	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: Ratio to baseline				
geometric mean (confidence interval 80%)	0.82 (0.693 to 0.973)			

Comparison groups	LNP023 50 mg BID v Placebo
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric mean ratio
Point estimate	1.13
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.872
upper limit	1.458

	100 mg vs Placebo
Comparison groups	LNP023 100 mg BID - Part 2 v Placebo
Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric mean ratio
Point estimate	0.74
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.574
upper limit	0.957

	200 mg vs Placebo
Comparison groups	LNP023 200 mg BID v Placebo
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric mean ratio
Point estimate	0.89
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.706
upper limit	1.132

End point title	Mixed Model of Repeated Measures (MMRM) of the ratio to baseline in 24 hour urine albumin to creatinine (UACR) - Parts 1 and 2 to Day 90

End point description:	
Participants collected all of their urine over a 24-hour period.	
End point type	Secondary
End point timeframe:	
Baseline, Days 30 and 90	

	LNP023 10 mg BID	LNP023 50 mg BID	LNP023 100 mg BID - Part 2	LNP023 200 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	19	22	26
Units: Ratio to baseline				
geometric mean (confidence interval 80%)	0.85 (0.728 to 0.998)	0.89 (0.765 to 1.045)	0.66 (0.567 to 0.772)	0.74 (0.647 to 0.842)

	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: Ratio to baseline				
geometric mean (confidence interval 80%)	0.87 (0.756 to 0.998)			

	10 mg vs Placebo
Comparison groups	LNP023 10 mg BID v Placebo
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric mean ratio
Point estimate	0.98
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.794
upper limit	1.214

	50 mg vs Placebo
Comparison groups	LNP023 50 mg BID v Placebo

Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric mean ratio
Point estimate	1.03
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.835
upper limit	1.269

	100 mg vs Placebo
Comparison groups	LNP023 100 mg BID - Part 2 v Placebo
Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric mean ratio
Point estimate	0.76
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.616
upper limit	0.942

	200 mg vs Placebo
Comparison groups	LNP023 200 mg BID v Placebo
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric mean ratio
Point estimate	0.85
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.704
upper limit	1.027

End point title	Plasma Pharmacokinetics (PK) of Area Under the Curve at steady state (AUCtau,ss and AUClast,ss) at Day 30[1]

End point description:

AUClast,ss: the area under the plasma concentration-time curve from time zero to last quantifiable concentration at steady state AUCtau,ss: the area under the plasma concentration-time curve from time zero to the end of the dosing interval tau at steady state

End point type	Secondary

End point timeframe:

Baseline (0 hour), Day 30 (0, 0.25, 0.5, 1,2,4,6,8 hours)

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Plasma samples for participants receiving LNP023 treatment

	LNP023 10 mg BID	LNP023 50 mg BID	LNP023 100 mg BID - Part 2	LNP023 200 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	18	16	24
Units: hr*ng/mL				
arithmetic mean (standard deviation)				
AUClast,ss	5820 (± 1750)	13000 (± 2740)	18400 (± 6040)	27900 (± 9930)
AUCtau,ss	8010 (± 2550)	17700 (± 4250)	24700 (± 8030)	37100 (± 13500)

No statistical analyses for this end point

End point title	Plasma Pharmacokinetics (PK) of pre-dose trough at steady state (Ctrough,ss) and maximum concentrations (Cmax,ss) at Day 30[2]

End point description:

Cmax,ss: the observed maximum plasma concentration following drug administration at steady state (ng/mL) Ctrough,ss: the pre-dose plasma concentration observed during a dosing interval at steady state (ng/mL)

End point type	Secondary

End point timeframe:

Baseline (0 hour), Day 30 (0, 0.25, 0.5, 1, 2, 4, 6, 8 hours)

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Plasma samples for participants receiving LNP023 treatment

	LNP023 10 mg BID	LNP023 50 mg BID	LNP023 100 mg BID - Part 2	LNP023 200 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	18	16	24
Units: hr*ng/mL				
arithmetic mean (standard deviation)				
Ctrough,ss	515 (± 232)	1130 (± 348)	1510 (± 567)	2200 (± 964)
Cmax,ss	964 (± 264)	2150 (± 480)	3300 (± 1080)	4940 (± 1770)

No statistical analyses for this end point

End point title	Plasma Pharmacokinetics (PK) of time to maximum concentration at steady state (Tmax,ss) at Day 30[3]

End point description:

Tmax,ss: the time to reach the maximum concentration after drug administration at steady state (h)

End point type	Secondary

End point timeframe:

Baseline (0 hour), Day 30 (0, 0.25, 0.5, 1, 2, 4, 6, 8 hours)

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Plasma samples for participants receiving LNP023 treatment

	LNP023 10 mg BID	LNP023 50 mg BID	LNP023 100 mg BID - Part 2	LNP023 200 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	18	16	24
Units: hour				
median (full range (min-max))	2.00 (0.250 to 6.00)	2.00 (1.00 to 6.00)	2.00 (0.500 to 6.00)	2.00 (0.500 to 4.00)

No statistical analyses for this end point

End point title	Amount of LNP023 excreted into urine (Ae,ss) at Day 30[4]

End point description:

Ae,ss: the total cumulative urinary excretion at steady state

End point type	Secondary

End point timeframe:

Baseline and Day 30

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Samples for participants receiving LNP023 treatment

	LNP023 10 mg BID	LNP023 50 mg BID	LNP023 100 mg BID - Part 2	LNP023 200 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	14	14	22
Units: mg				
arithmetic mean (standard deviation)	1.72 (± 1.15)	11.7 (± 5.84)	30.9 (± 17.0)	60.3 (± 27.1)

No statistical analyses for this end point

End point title	Percent of LNP023 excreted into urine at Day 30[5]
End point description:	
Percent of drug excreted into the urine	
End point type	Secondary
End point timeframe:	
Baseline and Day 30	

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Samples for participants receiving LNP023 treatment

	LNP023 10 mg BID	LNP023 50 mg BID	LNP023 100 mg BID - Part 2	LNP023 200 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	14	14	22
Units: percent of dose				
arithmetic mean (standard deviation)	8.59 (± 5.77)	11.7 (± 5.84)	15.5 (± 8.50)	15.1 (± 6.77)

No statistical analyses for this end point

End point title	Renal clearance from plasma at steady state (CLr,ss) at Day
End point description:	
The renal clearance from plasma at steady state	
End point type	Secondary
End point timeframe:	
Baseline and Day 30	

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Plasma samples for participants receiving LNP023 treatment

	LNP023 10 mg BID	LNP023 50 mg BID	LNP023 100 mg BID - Part 2	LNP023 200 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	14	14	22
Units: L/hr				
arithmetic mean (standard deviation)	0.112 (± 0.0744)	0.348 (± 0.179)	0.719 (± 0.479)	0.942 (± 0.540)

No statistical analyses for this end point

End point title	Change from baseline in plasma levels of circulating fragment of Factor B (Bb) and soluble terminal complement complex (sC5b-9) biomarkers for Parts 1 and 2 to Day 90

End point description:

The complement AP biomarkers Bb and sC5b-9 were evaluated as potential pharmacodynamics and mode-of-action markers. Both biomarkers were measured using validated enzyme-linked immunosorbent assays (ELISAs).

End point type	Secondary

End point timeframe:

Baseline, Days 8, 15, 30, 60, 90

	LNP023 10 mg BID	LNP023 50 mg BID	LNP023 100 mg BID - Part 2	LNP023 200 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	19	22	26
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Day 8 - Bb, n=14,16,13,25,19	76.7 (± 22.89)	72.2 (± 22.86)	71.4 (± 30.66)	66.3 (± 28.15)
Day 15 - Bb, n=13,14,16,22,22	80.4 (± 32.59)	74.1 (± 23.30)	77.9 (± 33.28)	72.9 (± 20.47)
Day 30 - Bb, n=16,17,18,26,24	76.4 (± 18.32)	76.2 (± 23.62)	76.8 (± 34.00)	70.4 (± 28.96)
Day 60 - Bb, n=14,16,17,25,21	78.8 (± 20.26)	75.2 (± 19.05)	77.4 (± 35.23)	72.8 (± 23.97)
Day 90 - Bb, n=17,16,17,25,21	90.5 (± 25.57)	79.3 (± 22.47)	77.6 (± 35.42)	74.6 (± 23.91)
Day 8 sCB5b-9, n=12,16,13,22,17	80.6 (± 12.29)	69.6 (± 37.40)	65.9 (± 24.05)	75.8 (± 30.15)
Day 15 sCB5b-9, n=13,14,16,21,21	79.4 (± 27.60)	72.2 (± 33.86)	65.9 (± 24.05)	78.0 (± 32.06)
Day 30 sCB5b-9, n=16,17,18,25,24	85.8 (± 23.88)	68.6 (± 41.32)	76.4 (± 25.97)	69.8 (± 21.98)
Day 60 sCB5b-9, n=14,16,17,24,20	84.6 (± 27.37)	73.7 (± 31.99)	74.9 (± 29.65)	76.2 (± 29.80)
Day 90 sCB5b-9, n=16,16,17,23,19	89.6 (± 28.66)	73.8 (± 36.21)	79.0 (± 22.82)	75.0 (± 34.21)

	Placebo			

Subject group type	Reporting group			
Number of subjects analysed	25			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Day 8 - Bb, n=14,16,13,25,19	102.7 (± 19.78)			
Day 15 - Bb, n=13,14,16,22,22	108.6 (± 23.19)			
Day 30 - Bb, n=16,17,18,26,24	99.3 (± 22.07)			
Day 60 - Bb, n=14,16,17,25,21	102.9 (± 24.07)			
Day 90 - Bb, n=17,16,17,25,21	102.7 (± 22.01)			
Day 8 sCB5b-9, n=12,16,13,22,17	95.2 (± 22.01)			
Day 15 sCB5b-9, n=13,14,16,21,21	99.4 (± 25.40)			
Day 30 sCB5b-9, n=16,17,18,25,24	94.2 (± 24.96)			
Day 60 sCB5b-9, n=14,16,17,24,20	95.7 (± 30.11)			
Day 90 sCB5b-9, n=16,16,17,23,19	103.4 (± 21.52)			

No statistical analyses for this end point

End point title	Estimation of lowest dose providing maximal reduction of proteinuria

End point description:

The log transformation used refers to the natural log (base of e). Results are back-transformed and expressed as geometric means.

End point type	Secondary

End point timeframe:

Baseline up to Month 3

	LNP023 10 mg BID	LNP023 50 mg BID	LNP023 100 mg BID - Part 2	LNP023 200 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	19	22	26
Units: g/mol				
geometric mean (confidence interval 80%)	0.85 (0.77 to 0.93)	0.80 (0.73 to 0.87)	0.76 (0.70 to 0.81)	0.69 (0.61 to 0.77)

	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	25			

Units: g/mol				
geometric mean (confidence interval 80%)	0.88 (0.80 to 1.00)			

	10 mg vs Placebo
Comparison groups	LNP023 10 mg BID v Placebo
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Multiple Comparison Procedure (MCP-Mod)
Point estimate	0.99
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.86
upper limit	1

	50 mg vs Placebo
Comparison groups	LNP023 50 mg BID v Placebo
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Multiple Comparison Procedure (MCP-Mod)
Point estimate	0.94
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.76
upper limit	0.98

	100 mg vs Placebo
Comparison groups	LNP023 100 mg BID - Part 2 v Placebo
Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Multiple Comparison Procedure (MCP-Mod)
Point estimate	0.87
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.72
upper limit	0.96

	200 mg vs Placebo
Comparison groups	LNP023 200 mg BID v Placebo
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Multiple Comparison Procedure (MCP-Mod)
Point estimate	0.77
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.66
upper limit	0.92

End point title	Mixed Model of Repeated Measures (MMRM) of the change from baseline for Estimated Glomerular Filtration Rate (eGFR) - Part 2 up to Day 180

End point description:

eGFR; estimated by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI)

End point type	Secondary

End point timeframe:

Baseline, Days 8, 15, 30, 60, 90, 135 and 180

	LNP023 10 mg BID	LNP023 50 mg BID	LNP023 100 mg BID - Part 2	LNP023 200 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	10	19	11
Units: mL/min/SSA				
arithmetic mean (standard error)	0.78 (± 1.977)	-2.35 (± 1.995)	-2.91 (± 1.359)	-1.18 (± 1.798)

	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: mL/min/SSA				
arithmetic mean (standard error)	-3.17 (± 1.868)			

	10 mg vs Placebo
Comparison groups	LNP023 10 mg BID v Placebo
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Mean difference (final values)
Point estimate	3.95
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.42
upper limit	7.472

	50 mg vs Placebo
Comparison groups	LNP023 50 mg BID v Placebo
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Mean difference (final values)
Point estimate	0.82
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-2.747
upper limit	4.39

	100 mg vs Placebo
Comparison groups	LNP023 100 mg BID - Part 2 v Placebo
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Mean difference (final values)
Point estimate	0.26
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-2.745
upper limit	3.262

No statistical analyses for this end point

End point title	Mixed Model of Repeated Measures (MMRM) of the change from baseline in protein level urine using the urine protein-creatinine ratio (UPCR) from 24 hour urine collection - Part 2 up to Day 180
End point description: For UPCR test, participants collected all of their urine over a 24-hour period	
End point type	Secondary
End point timeframe: Baseline, Days 30, 90 and 180	

	LNP023 10 mg BID	LNP023 50 mg BID	LNP023 100 mg BID - Part 2	LNP023 200 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	10	19	11
Units: mg/d				
geometric mean (confidence interval 80%)	1.06 (0.803 to 1.394)	0.59 (0.452 to 0.779)	0.66 (0.540 to 0.798)	0.73 (0.568 to 0.940)

	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: mg/d				
geometric mean (confidence interval 80%)	0.91 (0.705 to 1.185)			

	10 mg vs Placebo
Comparison groups	LNP023 10 mg BID v Placebo

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric mean ratio
Point estimate	1.16
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.792
upper limit	1.692

	100 mg vs Placebo
Comparison groups	LNP023 100 mg BID - Part 2 v Placebo
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric mean ratio
Point estimate	0.72
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.518
upper limit	0.997

	200 mg vs Placebo
Comparison groups	LNP023 200 mg BID v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric mean ratio
Point estimate	0.8
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.558
upper limit	1.146

	50 mg vs Placebo
Comparison groups	LNP023 50 mg BID v Placebo

Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric mean ratio
Point estimate	0.65
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.446
upper limit	0.945

End point title	Mixed Model of Repeated Measures (MMRM) of the ratio to baseline in 24 hour urine albumin to creatinine (UACR) - Part 2 up to Day 180

End point description:

The 24-hour urine collection was started 1 day prior to the clinic visit, after participant urinated for the first time, than all urine was collected for the next 24 hours and refrigerated prior to clinic visit.

End point type	Secondary

End point timeframe:

Baseline, Days 30, 90 and 180

	LNP023 10 mg BID	LNP023 50 mg BID	LNP023 100 mg BID - Part 2	LNP023 200 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	10	19	11
Units: Ratio to baseline				
geometric mean (confidence interval 80%)	1.04 (0.779 to 1.392)	0.61 (0.454 to 0.808)	0.65 (0.526 to 0.792)	0.69 (0.533 to 0.902)

	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: Ratio to baseline				
geometric mean (confidence interval 80%)	0.91 (0.696 to 1.200)			

	10 mg vs Placebo
Comparison groups	LNP023 10 mg BID v Placebo

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric mean ratio
Point estimate	1.14
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.765
upper limit	1.699

	50 mg vs Placebo
Comparison groups	LNP023 50 mg BID v Placebo
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric mean ratio
Point estimate	0.66
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.446
upper limit	0.984

	100 mg vs Placebo
Comparison groups	LNP023 100 mg BID - Part 2 v Placebo
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric mean ratio
Point estimate	0.71
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.501
upper limit	0.995

	200 mg vs Placebo
Comparison groups	LNP023 200 mg BID v Placebo

Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric mean ratio
Point estimate	0.76
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.52
upper limit	1.107

End point title	Mixed Model of Repeated Measures (MMRM) of the change from baseline for Serum Creatine - Parts 1 and 2 at Day 90
End point description: Serum creatinine	
End point type	Secondary
End point timeframe: Baseline, Days 15, 30 ,60 and 90	

	LNP023 10 mg BID	LNP023 50 mg BID	LNP023 100 mg BID - Part 2	LNP023 200 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	19	22	26
Units: umol/L				
arithmetic mean (standard error)	-2.55 (± 3.488)	-2.60 (± 3.665)	0.76 (± 3.555)	-3.47 (± 3.043)

	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: umol/L				
arithmetic mean (standard error)	6.65 (± 3.150)			

	10 mg vs Placebo
Comparison groups	LNP023 10 mg BID v Placebo

Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Mean difference (final values)
Point estimate	-9.2
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-15.253
upper limit	-3.145

	50 mg vs Placebo
Comparison groups	LNP023 50 mg BID v Placebo
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Mean difference (final values)
Point estimate	-9.25
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-15.499
upper limit	-3

	100 mg vs Placebo
Comparison groups	LNP023 100 mg BID - Part 2 v Placebo
Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Mean difference (final values)
Point estimate	-5.89
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-12.04
upper limit	0.26

	200 mg vs Placebo
Comparison groups	LNP023 200 mg BID v Placebo

Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Mean difference (final values)
Point estimate	-10.12
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-15.763
upper limit	-4.471

End point title	Mixed Model of Repeated Measures (MMRM) of the ratio to baseline in 24 hour urine protein to creatinine (UPCR) from 1st morning void - Parts 1 and 2 at Day 90

End point description:

A midstream urine sample was obtained from the first morning void (FMV) on the visit day.

End point type	Secondary

End point timeframe:

Baseline, Days 30 and 90

	LNP023 10 mg BID	LNP023 50 mg BID	LNP023 100 mg BID - Part 2	LNP023 200 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	19	22	26
Units: Ratio to baseline				
geometric mean (confidence interval 80%)	0.77 (0.69 to 0.86)	0.74 (0.67 to 0.81)	0.71 (0.65 to 0.77)	0.66 (0.58 to 0.76)

	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: Ratio to baseline				
geometric mean (confidence interval 80%)	0.80 (0.71 to 0.95)			

	10 mg vs Placebo
Comparison groups	LNP023 10 mg BID v Placebo

Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric mean ratio
Point estimate	0.99
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.79
upper limit	1

	50 mg vs Placebo
Comparison groups	LNP023 50 mg BID v Placebo
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric mean ratio
Point estimate	0.95
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.74
upper limit	1

	100 mg vs Placebo
Comparison groups	LNP023 100 mg BID - Part 2 v Placebo
Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric mean ratio
Point estimate	0.9
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.71
upper limit	1

	200 mg vs Placebo
Comparison groups	LNP023 200 mg BID v Placebo

Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric mean ratio
Point estimate	0.81
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.66
upper limit	1.01

End point title	Mixed Model of Repeated Measures (MMRM) of the ratio to baseline in 24 hour urine protein to creatinine (UPCR) from 1st morning void - Part 2 up to Day 180
End point description:	
A midstream urine sample was obtained from the first morning void (FMV) on the visit day.	
End point type	Secondary
End point timeframe:	
Baseline, Days 8, 15, 30, 60, 90, 135 and 180	

	LNP023 10 mg BID	LNP023 50 mg BID	LNP023 100 mg BID - Part 2	LNP023 200 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	10	19	11
Units: Ratio to baseline				
geometric mean (confidence interval 80%)	0.81 (0.599 to 1.108)	0.72 (0.534 to 0.976)	0.63 (0.507 to 0.784)	0.72 (0.544 to 0.949)

	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: Ratio to baseline				
geometric mean (confidence interval 80%)	0.79 (0.590 to 1.047)			

	10 mg vs Placebo
Comparison groups	LNP023 10 mg BID v Placebo

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric mean ratio
Point estimate	1.04
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.68
upper limit	1.579

	50 mg vs Placebo
Comparison groups	LNP023 50 mg BID v Placebo
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric mean ratio
Point estimate	0.92
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.607
upper limit	1.39

	100 mg vs Placebo
Comparison groups	LNP023 100 mg BID - Part 2 v Placebo
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric mean ratio
Point estimate	0.8
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.558
upper limit	1.153

	200 mg vs Placebo
Comparison groups	LNP023 200 mg BID v Placebo

Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric mean ratio
Point estimate	0.91
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.614
upper limit	1.362

Timeframe for reporting adverse events:
Adverse events were reported from first dose of study treatment until end of study treatment plus 7 days post treatment, up to a maximum duration of 197 days.
Adverse event reporting additional description:
AE additional description

Assessment type	Systematic

Dictionary name	MedDRA
Dictionary version	24.0

Reporting group title	LNP023 10mg
Reporting group description:	
LNP023 10mg	
Reporting group title	LNP023 50mg
Reporting group description:	
LNP023 50mg	
Reporting group title	LNP023 100mg
Reporting group description:	
LNP023 100mg	
Reporting group title	LNP023 200mg
Reporting group description:	
LNP023 200mg	
Reporting group title	Placebo
Reporting group description:	
Placebo	

	LNP023 10mg	LNP023 50mg	LNP023 100mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 22 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19			

subjects affected / exposed

subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	10	0	0
Hypertension			
subjects affected / exposed	1 / 20 (5.00%)	1 / 19 (5.26%)	1 / 22 (4.55%)
occurrences (all)	1	1	1
Hypotension			
subjects affected / exposed	3 / 20 (15.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	3	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Chest pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Face oedema			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 20 (0.00%)	2 / 19 (10.53%)	1 / 22 (4.55%)
occurrences (all)	0	3	1
Feeling hot			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Influenza like illness			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Oedema			
subjects affected / exposed	1 / 20 (5.00%)	1 / 19 (5.26%)	0 / 22 (0.00%)
occurrences (all)	1	1	0
Oedema peripheral			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Pain			

subjects affected / exposed	2 / 20 (10.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Pyrexia			
subjects affected / exposed	0 / 20 (0.00%)	2 / 19 (10.53%)	1 / 22 (4.55%)
occurrences (all)	0	2	1
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Dyspnoea exertional			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Epistaxis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	2 / 22 (9.09%)
occurrences (all)	2	0	2
Oropharyngeal pain			
subjects affected / exposed	0 / 20 (0.00%)	2 / 19 (10.53%)	0 / 22 (0.00%)
occurrences (all)	0	2	0
Rhinitis allergic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Throat irritation			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	1 / 22 (4.55%)
occurrences (all)	2	0	1
Investigations			
Activated partial thromboplastin time prolonged			

subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Amylase increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Blood potassium increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Blood pressure increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Blood testosterone decreased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Blood triglycerides increased			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Coagulation test abnormal			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Cystatin C increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Lipase increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Pancreatic enzymes increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
SARS-CoV-2 test negative			
subjects affected / exposed	1 / 20 (5.00%)	1 / 19 (5.26%)	2 / 22 (9.09%)
occurrences (all)	1	2	2
Weight increased			

subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Skin abrasion			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Bundle branch block right			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Sinus bradycardia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Supraventricular extrasystoles			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Tachycardia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Wolff-Parkinson-White syndrome			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Dizziness			
subjects affected / exposed	2 / 20 (10.00%)	3 / 19 (15.79%)	1 / 22 (4.55%)
occurrences (all)	2	4	1
Dysaesthesia			

subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Epilepsy			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Head discomfort			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	2 / 20 (10.00%)	2 / 19 (10.53%)	2 / 22 (9.09%)
occurrences (all)	3	2	3
Migraine			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	4	0	0
Syncope			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Taste disorder			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Tremor			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Asthenopia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			

Abdominal discomfort			
subjects affected / exposed	0 / 20 (0.00%)	3 / 19 (15.79%)	2 / 22 (9.09%)
occurrences (all)	0	4	3
Abdominal pain			
subjects affected / exposed	1 / 20 (5.00%)	1 / 19 (5.26%)	1 / 22 (4.55%)
occurrences (all)	1	1	1
Abdominal pain lower			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	3	0	0
Abdominal pain upper			
subjects affected / exposed	2 / 20 (10.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Aphthous ulcer			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	0 / 20 (0.00%)	2 / 19 (10.53%)	1 / 22 (4.55%)
occurrences (all)	0	3	1
Dyspepsia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Epigastric discomfort			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Food poisoning			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Mouth haemorrhage			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Mouth ulceration			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1

Nausea			
subjects affected / exposed	3 / 20 (15.00%)	1 / 19 (5.26%)	0 / 22 (0.00%)
occurrences (all)	7	1	0
Toothache			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	3 / 20 (15.00%)	2 / 19 (10.53%)	0 / 22 (0.00%)
occurrences (all)	3	2	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Alopecia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Dermatosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Eczema			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Eczema nummular			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Pruritus			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Rash			

subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 22 (0.00%)
occurrences (all)	0	2	0
Vasculitic rash			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Haematuria			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Renal pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Renal vasculitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 19 (0.00%)	2 / 22 (9.09%)
occurrences (all)	2	0	3
Back pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	3 / 22 (13.64%)
occurrences (all)	1	0	3
Bursitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Joint swelling			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			

subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Musculoskeletal stiffness			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Plantar fasciitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Polyarthritis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Asymptomatic bacteriuria			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Bronchitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Gingivitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Hordeolum			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0

Influenza			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	2 / 20 (10.00%)	2 / 19 (10.53%)	0 / 22 (0.00%)
occurrences (all)	2	3	0
Norovirus infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Onychomycosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Oral herpes			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Otitis externa			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Otitis media			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Respiratory tract infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Tooth abscess			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Tracheobronchitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0

subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Iron deficiency			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Metabolic acidosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Vitamin B12 deficiency			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0

	LNP023 200mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 26 (53.85%)	17 / 25 (68.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Essential thrombocythaemia			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Polycythaemia vera			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Hypertension			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Hypotension			
subjects affected / exposed	2 / 26 (7.69%)	0 / 25 (0.00%)	
occurrences (all)	3	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	

Chest pain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Face oedema			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	0 / 26 (0.00%)	3 / 25 (12.00%)	
occurrences (all)	0	3	
Feeling hot			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Influenza like illness			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Oedema			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Oedema peripheral			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Pain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Pyrexia			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	1 / 26 (3.85%)	1 / 25 (4.00%)	
occurrences (all)	1	4	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Dyspnoea exertional			

subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Epistaxis			
subjects affected / exposed	0 / 26 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	2	
Oropharyngeal pain			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Rhinitis allergic			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Throat irritation			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Amylase increased			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Blood creatinine increased			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Blood potassium increased			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Blood pressure increased			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Blood testosterone decreased			

subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Blood triglycerides increased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Coagulation test abnormal			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Cystatin C increased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Lipase increased			
subjects affected / exposed	1 / 26 (3.85%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Pancreatic enzymes increased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
SARS-CoV-2 test negative			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Weight increased			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Skin abrasion			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Cardiac disorders			
Bundle branch block right			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Palpitations			

subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Sinus bradycardia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Supraventricular extrasystoles			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Tachycardia			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Wolff-Parkinson-White syndrome			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Dizziness			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Dysaesthesia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Epilepsy			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Head discomfort			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Headache			
subjects affected / exposed	2 / 26 (7.69%)	6 / 25 (24.00%)	
occurrences (all)	2	7	
Migraine			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	

Syncope			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Taste disorder			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Tremor			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	2	
Eye disorders			
Asthenopia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Abdominal pain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Abdominal pain lower			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Abdominal pain upper			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Aphthous ulcer			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	

Diarrhoea			
subjects affected / exposed	1 / 26 (3.85%)	3 / 25 (12.00%)	
occurrences (all)	1	3	
Dyspepsia			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Epigastric discomfort			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Food poisoning			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Mouth haemorrhage			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Mouth ulceration			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Nausea			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	2	
Toothache			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	1 / 26 (3.85%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Alopecia			

subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Dermatosis			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Dry skin			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Eczema			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Eczema nummular			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Erythema			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Pruritus			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Vasculitic rash			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Haematuria			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Renal pain			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	

Renal vasculitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Back pain			
subjects affected / exposed	1 / 26 (3.85%)	3 / 25 (12.00%)	
occurrences (all)	2	3	
Bursitis			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Flank pain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Joint swelling			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Muscle spasms			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Musculoskeletal stiffness			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Pain in extremity			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Plantar fasciitis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Polyarthritis			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			

Asymptomatic bacteriuria			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Bronchitis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
COVID-19			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Conjunctivitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Gastroenteritis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Gingivitis			
subjects affected / exposed	1 / 26 (3.85%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Hordeolum			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Influenza			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Nasopharyngitis			
subjects affected / exposed	1 / 26 (3.85%)	2 / 25 (8.00%)	
occurrences (all)	1	3	
Norovirus infection			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Onychomycosis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Oral herpes			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	

Otitis externa			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Otitis media			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Pharyngitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Respiratory tract infection			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Tonsillitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Tooth abscess			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Tracheobronchitis			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	
occurrences (all)	1	0	

subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Gout			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Hypercholesterolaemia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Hyperkalaemia			
subjects affected / exposed	1 / 26 (3.85%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Hypermagnesaemia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Hyperuricaemia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Hyponatraemia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Hypophosphataemia			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Iron deficiency			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Metabolic acidosis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	
Vitamin B12 deficiency			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	
occurrences (all)	0	0	

Were there any global substantial amendments to the protocol? Yes

31 March 2018	The purpose of this amendment was to include patients with a pulse rate <50 if the patient was otherwise in a physically good and stable condition without any other significant ECG abnormalities as judged by t.he investigator. The study stopping rules were adapted based on feedback by HA. Assessment schedule was updated for endocrine parameters to be checked on Day 15 and 30, additional pregnancy test on Day 90 for participating patients of child bearing potential.
30 September 2018	Amendment included changes to: number of 24h urine collections were reduced, inclusion criteria was modified: the urine protein level required was decreased from ≥1g/24h to ≥0.75g/24h from a 24h urine collection, or a urine protein to creatinine ratio (UPCR) ≥0.8g/g (90mg/mmol) from FMV sample, PK sampling, and PD and exploratory biomarkers were removed from Day 1 in the assessment schedule;
31 May 2019	The main purpose of this amendment was to increase the duration of treatment phase from 90 days to 180 days in Part 2 of the trial in order to gather information about longer term treatment effects and safety information for LNP023. In addition, the description and implementation of the planned adaptations to Part 2 of the trial was further clarified/modified.
30 April 2020	The main purpose of this amendment was to confirm the final number of patients to be recruited into Part 2 of the study and the doses to be investigated based on the results of the Part 1 interim analysis (IA1).
30 September 2020	The purpose of this amendment was to update the unblinding plan for the study. The update to this plan allowed sharing of unblinded group level results from IA1 and IA2 to support initiation of phase 3 IgAN study

Notes:

Were there any global interruptions to the trial? No

None reported