NOVARTIS

Clinical Trial Results Website

Sponsor

Novartis Pharmaceuticals

Generic Drug Name

CLNP023 (iptacopan)

Trial Indication(s)

Pharmacokinetics, Pharmacodynamics, Safety and Tolerability of LNP023

Protocol Number

CLNP023X2202

Protocol Title

An open-label, non-randomized study on efficacy, pharmacokinetics, pharmacodynamics, safety and tolerability of LNP023 in two patient populations with C3 glomerulopathy

Clinical Trial Phase

Phase 2

Phase of Drug Development

Phase 2

Study Start/End Dates

Study Start Date: February 20, 2019 (Actual)
Primary Completion Date: April 23, 2021 (Actual)
Study Completion Date: April 23, 2021 (Actual)

Study Design/Methodology

The study was a non-confirmatory, open-label, two Cohort, single-arm, non-randomized study evaluating the efficacy, safety, tolerability, pharmacokinetics, pharmacodynamics and dose/biomarker relation of LNP023 in two patient populations:

- Non-transplanted C3G patients with reduced C3 serum levels (<0.90 x lower limit of the lab normal range), enrolled in Cohort A Patients who have undergone kidney transplant and have C3G recurrence, enrolled in Cohort B. Cohort B started in parallel to Cohort A

Number of patients (planned and analyzed):

- Cohort A: 15 patients were planned and 16 were enrolled and analyzed.
- Cohort B: 12 patients were planned and 11 were enrolled and analyzed.

Centers

9 centers in 6 countries: Spain(2), United Kingdom(2), France(2), Italy(1), Germany(1), United States(1)

Objectives:

Primary objective:

- Cohort A: To evaluate the efficacy of LNP023 in reducing proteinuria at Week 12
- Cohort B: To assess histopathological changes in kidney biopsies at Week 12

Secondary objective:

- All Cohorts: To assess the relationship between LNP023 dose and pharmacodynamic biomarkers
- All Cohorts: To assess the relationship between LNP023 dose and proteinuria
- All Cohorts: To assess the effect of LNP023 on renal function
- All Cohorts: To assess the effect of LNP023 on alternative complement pathway hyperactivity
- All Cohorts: To assess the safety and tolerability of LNP023
- All Cohorts: To assess the plasma and urine pharmacokinetics of LNP023 in patients with C3G
- Cohort B: To evaluate the efficacy of LNP023 in reducing proteinuria at Week 12

Test Product (s), Dose(s), and Mode(s) of Administration

The investigational drug, LNP023 as 5 mg, 25 mg and 100 mg oral capsules

Statistical Methods

Cohort A: The log ratio to baseline in UPCR, was analyzed using a mixed model repeated measures (MMRM), the analysis included all data up to and including Week 12. Additional analyses, were made considering subgroup with baseline UPCR 24hr <200g/mol and ≥ 200g/mol.
Cohort B: The Wilcoxon signed rank test was used for C3 Deposit Score data at Week 12 timepoint to compare the median difference of change from baseline between periods. The Hodges-Lehmann estimate and two-sided 80% confidence interval for the median difference was provided.

For each secondary variable (apart from hematuria, Bb and C3 biomarker) a similar statistical model was used as described for the primary variable. Additionally, for Cohort B only, the log ratio to baseline in UPCR and UACR derived from 24-h urine collection were analyzed with the same MMRM model.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria for Cohort A and B:
- Written informed consent must be obtained before any assessment is performed
- Male and female patients between the ages of 18 to 65 (inclusive) at screening
- C3G patients wit proteinuria
- Able to communicate well with the investigator, to understand and comply with the requirements of the study
- At screening and baseline visits, patients must weigh at least 35 kg
- Supine vital signs should be within the following ranges :
oral body temperature between 35.0-37.5 °C systolic blood pressure, 80-170 mm Hg diastolic blood pressure, 50-105 mm Hg pulse rate, 45 - 100 bpm
.

Inclusion Criteria for Cohort A:
- Estimated GFR (using the CKD-EPI formula) or measured GFR ≥30 mL/min per 1.73 m2 for patients on a maximum recommended or maximum tolerated dose of an angiotensin converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB)

- UPCR ≥ 100 mg/mmol (equivalent to ≥ 1 g/24h total urinary protein excretion)
- Prior to entry, all patients must have been on supportive care including a maximally tolerated dose of ACEi or ARB for at least 30 days.

Inclusion Criteria for Cohort B:
- No histological/laboratory/clinical signs of allorejection
- If applicable, induction treatment after allotransplantation needs to be completed >30 days before inclusion.
- Transplantation of a kidney allograft >90 days before inclusion
- Patients need to be on a stable dose of immunsuppressive regimen prior to inclusion. Any approved treatments are allowed for this purpose.

Exclusion Criteria for Cohort A and B:
- Use of other investigational drugs at the time of enrollment, or within 5 half-lives of randomization, or within 30 days, whichever is longer; or longer if required by local regulations
- A history of clinically significant ECG abnormalities,
- Known family history or known presence of long QT syndrome or Torsades de Pointes
- Use of agents known to prolong the QT interval unless they can be permanently discontinued for the duration of the study
- Pregnant or nursing (lactating) women, where pregnancy is defined as the state of a female after conception and until the termination of gestation, confirmed by a positive hCG laboratory test.
- Women of child bearing potential, defined as all women physiologically capable of becoming pregnant, unless they are using highly effective methods of contraception during dosing and for 1 week after stopping of investigational drug.
- History of immunodeficiency diseases, or a positive HIV test result.
- Chronic infection with Hepatitis B (HBV) or Hepatitis C (HCV).
- Patients who cannot receive vaccinations against N. meningitidis, S. pneumoniae, or H. influenzae

Participant Flow Table

Run-in Phase

	Cohort A: Run-In Phase	Cohort B: Run-In Phase	Cohort A: Dose Escalation/LNP023 Treatment 200 mg b.i.d	Cohort B - Dose Escalation/LNP023 Treatment 200 mg b.i.d	Total
Arm/Group Description	Cohort A: No kidney transplant. C3G patients who have	Cohort B: kidney transplant. C3G patients who have	Cohort A - no kidney transplant C3G patients who have not received a kidney	Cohort B - kidney transplant C3G patients who have	

	not received a kidney transplant and have reduced C3 blood levels	received a kidney transplant and have C3G recurrence	transplant and have reduced C3 blood levels	received a kidney transplant and have C3G recurrence	
Started	16	11	0	0	27
Completed	16	11	0	0	27
Not Completed	0	0	0	0	0

Dose Escalation/200mg b.i.d treatment

	Cohort A: Run-In Phase	**Cohort B: Run-In Phase**	**Cohort A: Dose Escalation/LNP023 Treatment 200 mg b.i.d**	**Cohort B - Dose Escalation/LNP023 Treatment 200 mg b.i.d**	**Total**
Arm/Group Description	Cohort A: No kidney transplant. C3G patients who have not received a kidney transplant and have reduced C3 blood levels	Cohort B: kidney transplant. C3G patients who have received a kidney transplant and have C3G recurrence	Cohort A - no kidney transplant C3G patients who have not received a kidney transplant and have reduced C3 blood levels	Cohort B - kidney transplant C3G patients who have received a kidney transplant and have C3G recurrence	
Started	0	0	16	11	27
Completed	0	0	16	11	27
Not Completed	0	0	0	0	0

Baseline Characteristics

	Cohort A - no kidney transplant	**Cohort B - kidney transplant**	**Total**
Arm/Group Description	C3G patients who have not received a kidney transplant and have reduced C3 blood levels.	C3G patients who have received a kidney transplant and have C3G recurrence.	

Number of Participants [units: participants]	16	11	27
Baseline Analysis Population Description	For all analysis sets, patients were analyzed according to study drug received for Cohort A and B. Safety analysis set included all patients that received any study drug. PK analysis set included all patients with available PK data and no protocol deviations with relevant impact on PK data.		
Age, Customized (units: Years) Description: Age in Years Analysis Population Type: Participants Median (Full Range)			
	22.0 (18 to 59)	31.0 (18 to 70)	24.0 (18 to 70)
Sex: Female, Male (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)			
Female	6	3	9
Male	10	8	18
Race/Ethnicity, Customized (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)			
American Indian or Alaska	0	1	1
Black or African American	0	1	1
White	16	9	25
Hispanic or Latino	0	1	1
Not Hispanic or Latino	16	8	24
Not Reported	0	2	2

Primary Outcome Result(s)

1.1 Cohort A: Change from baseline in Urine Protein to Creatinine concentration Ratio (UPCR)

Description	Change in proteinuria assessed by ratio to baseline of UPCR derived from 24h urine collection
Time Frame	Week 12
Analysis Population Description	Pharmacodynamics (PD) Analysis Set 1: number of patients included in the analysis with at least one post-baseline value of the outcome variable

	Cohort A - no kidney transplant
Arm/Group Description	C3G patients who have not received a kidney transplant and have reduced C3 blood levels.
Number of Participants Analyzed [units: participants]	16
Cohort A: Change from baseline in Urine Protein to Creatinine concentration Ratio (UPCR) (units: ratio)	**Geometric Mean (80% Confidence Interval)**
Week 12: Day 84	0.55 (0.46 to 0.65)

1.2 Statistical Analysis

Groups	Cohort A - no kidney transplant
Type of Statistical Test	Other
Non-Inferiority/Equivalence Test	Log Ratio to Baseline
P Value	0.0003
Method	Other Mixed Model Repeated Measures (MMRM)

Mean Difference (Final Values)	0.55
80 % Confidence Interval 2-Sided	0.46 to 0.65

1.3 Cohort B: Change from baseline in C3 Deposit

Description	Histopathological changes in kidney biopsies as assessed by change from baseline in C3 Deposit Score (based on immunofluorescence microscopy)
Time Frame	Week 12
Analysis Population Description	Pharmacodynamics (PD) Analysis Set 1: number of patients included in the analysis with at least one post-baseline value of the outcome variable

	Cohort B - kidney transplant
Arm/Group Description	C3G patients who have received a kidney transplant and have C3G recurrence.
Number of Participants Analyzed [units: participants]	7
Cohort B: Change from baseline in C3 Deposit (units: Percentage change)	**Median** **(80% Confidence Interval)**
Week 12: Day 84	-2.50 (-3.75 to -0.75)

1.4 Statistical Analysis

Groups	Cohort B - kidney transplant
Type of Statistical Test	Other
P Value	0.0313

Method	Wilcoxon (Mann-Whitney)
Median Difference (Final Values)	-2.50
80 % Confidence Interval 2-Sided	-3.75 to -0.75

Secondary Outcome Result(s)

1.5 Change from baseline in Urine Protein Creatinine Concentration Ratio (UPCR)

Description	Ratio to baseline UPCR derived from 24 hour urine collection
Time Frame	Week 12: Day 84
Analysis Population Description	Pharmacodynamics (PD) Analysis Set 1: number of patients included in the analysis with at least one post-baseline value of the outcome variable

	Cohort A - no kidney transplant	**Cohort B - kidney transplant**
Arm/Group Description	C3G patients who have not received a kidney transplant and have reduced C3 blood levels.	C3G patients who have received a kidney transplant and have C3G recurrence.
Number of Participants Analyzed [units: participants]	16	7
Change from baseline in Urine Protein Creatinine Concentration Ratio (UPCR) (units: ratio)	**Geometric Mean** **(80% Confidence Interval)**	**Geometric Mean** **(80% Confidence Interval)**
Week 12: Day 84	0.55 (0.46 to 0.65)	0.79 (0.49 to 1.28)

1.6 Statistical Analysis

Groups	Cohort A - no kidney transplant	Day 84
Type of Statistical Test	Other	
P Value	0.0003	
Method	Other Mixed Model Repeated Measures (MMRM)	
Mean Difference (Final Values)	0.55	
80 % Confidence Interval 2-Sided	0.46 to 0.65	

1.7 Statistical Analysis

Groups	Cohort B - kidney transplant	Day 84
Type of Statistical Test	Other	
P Value	0.4766	
Method	Other Mixed Model Repeated Measures (MMRM)	
Mean Difference (Final Values)	0.79	
80 % Confidence Interval 2-Sided	0.49 to 1.28	

1.8 Statistical Analysis

Groups	Cohort A - no kidney transplant, Cohort B - kidney transplant	Overall- Day 84

Type of Statistical Test	Other
P Value	0.0002
Method	Other Mixed Model of Repeated Measures (MMRM)
Mean Difference (Final Values)	0.59
80 % Confidence Interval 2-Sided	0.51 to 0.69

1.9 Change from baseline in Urine Protein (UP) Excretion

Description	Ratio to baseline UP excretion derived from 24 hour urine collection
Time Frame	Week 12: Day 84
Analysis Population Description	Pharmacodynamics (PD) Analysis Set 1: number of patients included in the analysis with at least one post-baseline value of the outcome variable

	Cohort A - no kidney transplant	**Cohort B - kidney transplant**
Arm/Group Description	C3G patients who have not received a kidney transplant and have reduced C3 blood levels.	C3G patients who have received a kidney transplant and have C3G recurrence.
Number of Participants Analyzed [units: participants]	16	9
Change from baseline in Urine Protein (UP) Excretion (units: ratio)	**Geometric Mean (80% Confidence Interval)**	**Geometric Mean (80% Confidence Interval)**
Week 12: Day 84	0.57 (0.47 to 0.68)	1.00 (0.75 to 1.33)

1.10 Statistical Analysis

Groups	Cohort A - no kidney transplant	Day 84
Type of Statistical Test	Other	
P Value	0.0011	
Method	Other Mixed Model Repeated Measures (MMRM	
Mean Difference (Final Values)	0.57	
80 % Confidence Interval 2-Sided	0.47 to 0.68	

1.11 Statistical Analysis

Groups	Cohort B - kidney transplant	Day 84
Type of Statistical Test	Other	
P Value	0.9998	
Method	Other Mixed Model Repeated Measures (MMRM)	
Mean Difference (Final Values)	1.00	
80 % Confidence Interval 2-Sided	0.75 to 1.33	

1.12 Statistical Analysis

Groups	Cohort A - no kidney transplant, Cohort B - kidney transplant	Overall- Day 84

Type of Statistical Test	Other
P Value	0.0016
Method	Other Mixed Model Repeated Measures (MMRM)
Mean Difference (Final Values)	0.66
80 % Confidence Interval 2-Sided	0.56 to 0.77

1.13 Change from baseline in Urine Albumin Creatinine concentration Ratio (UACR) Excretion

Description	Ratio to baseline UACR excretion derived from 24 hour urine collection
Time Frame	Week 12: Day 84
Analysis Population Description	Pharmacodynamics (PD) Analysis Set 1: number of patients included in the analysis with at least one post-baseline value of the outcome variable

	Cohort A - no kidney transplant	**Cohort B - kidney transplant**
Arm/Group Description	C3G patients who have not received a kidney transplant and have reduced C3 blood levels.	C3G patients who have received a kidney transplant and have C3G recurrence.
Number of Participants Analyzed [units: participants]	16	7
Change from baseline in Urine Albumin Creatinine concentration Ratio (UACR) Excretion (units: ratio)	**Geometric Mean** **(80% Confidence Interval)**	**Geometric Mean** **(80% Confidence Interval)**
Week 12: Day 84	0.55 (0.47 to 0.64)	0.61 (0.30 to 1.27)

1.14 Statistical Analysis

Groups	Cohort A - no kidney transplant	Day 84
Type of Statistical Test	Other	
P Value	<0.0001	
Method	Other Mixed Model Repeated Measures (MRM)	
Mean Difference (Final Values)	0.55	
80 % Confidence Interval 2-Sided	0.47 to 0.64	

1.15 Statistical Analysis

Groups	Cohort B - kidney transplant	Day 84
Type of Statistical Test	Other	
P Value	0.3707	
Method	Other Mixed Model Repeated Measures (MMRM)	
Mean Difference (Final Values)	0.61	
80 % Confidence Interval 2-Sided	0.30 to 1.27	

1.16 Statistical Analysis

Groups	Cohort A - no kidney transplant, Cohort B - kidney transplant	Overall- Day 84

Type of Statistical Test	Other
P Value	0.0002
Method	Other Mixed Model Repeated Measures (MMRM)
Mean Difference (Final Values)	0.60
80 % Confidence Interval 2-Sided	0.51 to 0.71

1.17 Change from baseline change in Urinary Albumin (UA) Excretion

Description	Ratio to baseline UA excretion derived from 24 hour urine collection
Time Frame	Week 12: Day 84
Analysis Population Description	Pharmacodynamics (PD) Analysis Set 1: number of patients included in the analysis with at least one post-baseline value of the outcome variable

	Cohort A - no kidney transplant	**Cohort B - kidney transplant**
Arm/Group Description	C3G patients who have not received a kidney transplant and have reduced C3 blood levels.	C3G patients who have received a kidney transplant and have C3G recurrence.
Number of Participants Analyzed [units: participants]	16	9
Change from baseline change in Urinary Albumin (UA) Excretion (units: ratio)	**Geometric Mean (80% Confidence Interval)**	**Geometric Mean (80% Confidence Interval)**
Week 12: Day 84	0.57 (0.47 to 0.70)	0.81 (0.67 to 0.98)

1.18 Statistical Analysis

Groups	Cohort A - no kidney transplant	Day 84
Type of Statistical Test	Other	
P Value	0.0018	
Method	Other Mixed Model Repeated Measures (MMRM)	
Mean Difference (Final Values)	0.57	
80 % Confidence Interval 2-Sided	0.47 to 0.70	

1.19 Statistical Analysis

Groups	Cohort B - kidney transplant	Day 84
Type of Statistical Test	Other	
P Value	0.1632	
Method	Other Mixed Model Repeated Measures (MMRM)	
Mean Difference (Final Values)	0.81	
80 % Confidence Interval 2-Sided	0.67 to 0.98	

1.20 Statistical Analysis

Groups	Cohort A - no kidney transplant, Cohort B - kidney transplant	Overall- Day 84

Type of Statistical Test	Other
P Value	0.0040
Method	Other Mixed Model Repeated Measure (MMRM)
Mean Difference (Final Values)	0.67
80 % Confidence Interval 2-Sided	0.57 to 0.79

1.21 Change from baseline in estimated glomerular filtration rate (eGFR)

Description	Effect of LNP023 on estimated glomerular filtration rate (eGFR)
Time Frame	Day 84
Analysis Population Description	Pharmacodynamics (PD) Analysis Set 1: number of patients included in the analysis with at least one post-baseline value of the outcome variable

	Cohort A - no kidney transplant	**Cohort B - kidney transplant**
Arm/Group Description	C3G patients who have not received a kidney transplant and have reduced C3 blood levels.	C3G patients who have received a kidney transplant and have C3G recurrence.
Number of Participants Analyzed [units: participants]	16	9
Change from baseline in estimated glomerular filtration rate (eGFR) (units: ml/min)	**Mean** **(80% Confidence Interval)**	**Mean** **(80% Confidence Interval)**
Week 12: Day 84	2.59 (0.12 to 5.06)	-0.61 (-3.36 to 2.15)

1.22 Statistical Analysis

Groups	Cohort A - no kidney transplant	Day 84
Type of Statistical Test	Other	
P Value	0.1795	
Method	Other Mixed Model of Repeated Measures (MMRM)	
Mean Difference (Final Values)	2.59	
80 % Confidence Interval 2-Sided	0.12 to 5.06	

1.23 Statistical Analysis

Groups	Cohort B - kidney transplant	Day 84
Type of Statistical Test	Other	
P Value	0.7763	
Method	Other Mixed Model Repeated Measures (MMRM)	
Mean Difference (Final Values)	-0.61	
0.7763 % Confidence Interval 2-Sided	-3.36 to 2.15	

1.24 Statistical Analysis

Groups	Cohort A - no kidney transplant, Cohort B - kidney transplant	Overall- Day 84

Type of Statistical Test	Other
P Value	0.3754
Method	Other Mixed Model Repeated Measures (MMRM)
Mean Difference (Final Values)	1.32
80 % Confidence Interval 2-Sided	-0.59 to 3.22

1.25 Change from baseline in serum creatinine

Description	The effect of LNP023 on renal function - serum creatinine
Time Frame	Week 12: Day 84
Analysis Population Description	Pharmacodynamics (PD) Analysis Set 1: number of patients included in the analysis with at least one post-baseline value of the outcome variable

	Cohort A - no kidney transplant	**Cohort B - kidney transplant**
Arm/Group Description	C3G patients who have not received a kidney transplant and have reduced C3 blood levels.	C3G patients who have received a kidney transplant and have C3G recurrence.
Number of Participants Analyzed [units: participants]	16	9
Change from baseline in serum creatinine (units: mmol/L)	**Mean** **(80% Confidence Interval)**	**Mean** **(80% Confidence Interval)**
Week 12: Day 84	-5.04 (-9.36 to -0.72)	7.17 (-1.79 to 16.13)

1.26 Statistical Analysis

Groups	Cohort A - no kidney transplant	Day 84
Type of Statistical Test	Other	
P Value	0.1364	
Method	Other Mixed Model Repeated Measuers (MMRM)	
Mean Difference (Final Values)	-5.04	
80 % Confidence Interval 2-Sided	-9.36 to -0.72	

1.27 Statistical Analysis

Groups	Cohort B - kidney transplant	Day 84
Type of Statistical Test	Other	
P Value	0.3038	
Method	Other Mixed Model Repeated Measures (MMRM)	
Mean Difference (Final Values)	7.17	
80 % Confidence Interval 2-Sided	-1.79 to 16.13	

1.28 Statistical Analysis

Groups	Cohort A - no kidney transplant, Cohort B - kidney transplant	Overall- Day 84

Type of Statistical Test	Other
P Value	0.8352
Method	Other Mixed Model Repeated Measures (MMRM)
Mean Difference (Final Values)	-0.77
80 % Confidence Interval 2-Sided	-5.56 to 4.01

1.29 Change from baseline in creatinine clearance

Description	The effect of LNP023 on renal function - creatinine clearance
Time Frame	Week 12: Day 84
Analysis Population Description	Pharmacodynamics (PD) Analysis Set 1: number of patients included in the analysis with at least one post-baseline value of the outcome variable

	Cohort A - no kidney transplant	**Cohort B - kidney transplant**
Arm/Group Description	C3G patients who have not received a kidney transplant and have reduced C3 blood levels.	C3G patients who have received a kidney transplant and have C3G recurrence.
Number of Participants Analyzed [units: participants]	16	8
Change from baseline in creatinine clearance (units: mL/min)	**Geometric Mean** **(80% Confidence Interval)**	**Geometric Mean** **(80% Confidence Interval)**
Week 12: Day 84	1.07 (0.99 to 1.17)	1.20 (0.83 to 1.72)

1.30 Statistical Analysis

Groups	Cohort A - no kidney transplant	Day 84
Type of Statistical Test	Other	
P Value	0.2752	
Method	Other Mixed Model Repeated Measures (MMRM)	
Mean Difference (Final Values)	1.07	
80 % Confidence Interval 2-Sided	0.99 to 1.17	

1.31 Statistical Analysis

Groups	Cohort B - kidney transplant	Day 84
Type of Statistical Test	Other	
P Value	0.476	
Method	Other Mixed Model Repeated Measures (MMRM)	
Mean Difference (Final Values)	1.20	
80 % Confidence Interval 2-Sided	0.83 to 1.72	

1.32 Statistical Analysis

Groups	Cohort A - no kidney transplant, Cohort B - kidney transplant	Overall- Day 84

Type of Statistical Test	Other
P Value	0.1963
Method	Other Mixed Model Repeated Measures (MMRM)
Mean Difference (Final Values)	1.10
80 % Confidence Interval 2-Sided	1.00 to 1.20

1.33 Number of patients with hematuria

Description	The effect of LNP023 on renal function - hematuria
Time Frame	Week 12: Day 84
Analysis Population Description	Pharmacodynamics (PD) Analysis Set 1: number of patients included in the analysis with at least one post-baseline value of the outcome variable. n: number of patients in the respective baseline category and post-baseline time point.

	Cohort A - no kidney transplant	**Cohort B - kidney transplant**
Arm/Group Description	C3G patients who have not received a kidney transplant and have reduced C3 blood levels.	C3G patients who have received a kidney transplant and have C3G recurrence.
Number of Participants Analyzed [units: participants]	16	9
Number of patients with hematuria (units: participants)	**Count of Participants** **(Not Applicable)**	**Count of Participants** **(Not Applicable)**
Week 12: Day 84: <9 rbc/hpf n (%)	10 (62.5%)	3 (33.33%)
Week 12: Day 84: >= 9 to =<50 rbc/hpf n (%)	0 (%)	0 (%)
Week 12: Day 84: >50 rbc/hpf n (%)	0 (%)	0 (%)

1.34 Change from baseline in Urine Protein to Creatinine Concentration Ratio (UPCR) First Morning Void

Description	Ratio to baseline of UPCR reduction derived from total cumulative urinary excretion first morning void
Time Frame	Week 9: Day 64
Analysis Population Description	Pharmacodynamics (PD) Analysis Set 1: number of patients included in the analysis with at least one post-baseline value of the outcome variable

	Cohort A - no kidney transplant	**Cohort B - kidney transplant**
Arm/Group Description	C3G patients who have not received a kidney transplant and have reduced C3 blood levels.	C3G patients who have received a kidney transplant and have C3G recurrence.
Number of Participants Analyzed [units: participants]	15	7
Change from baseline in Urine Protein to Creatinine Concentration Ratio (UPCR) First Morning Void (units: ratio)	**Geometric Mean (80% Confidence Interval)**	**Geometric Mean (80% Confidence Interval)**
Week 9: Day 64	0.56 (0.48 to 0.65)	0.99 (0.76 to 1.28)

1.35 Statistical Analysis

Groups	Cohort A - no kidney transplant	Day 64
Type of Statistical Test	Other	
P Value	<0.0001	
Method	Other Mixed Model Repeated Measures (MMRM)	

Mean Difference (Final Values)	0.56
80 % Confidence Interval 2-Sided	0.48 to 0.65

1.36 Statistical Analysis

Groups	Cohort B - kidney transplant	Day 64
Type of Statistical Test	Other	
P Value	0.9544	
Method	Other Mixed Model Repeated Measures (MMRM)	
Mean Difference (Final Values)	0.99	
80 % Confidence Interval 2-Sided	0.76 to 1.28	

1.37 Statistical Analysis

Groups	Cohort A - no kidney transplant, Cohort B - kidney transplant	Overall- Day 64
Type of Statistical Test	Other	
P Value	<.0001	
Method	Other Mixed Model Repeated Measures (MMRM)	
Mean Difference (Final Values)	0.64	

80 % Confidence Interval 2-Sided	0.56 to 0.72

1.38 Change from baseline in Urine Albumin to Creatinine Concentration Ratio (UACR) First Morning Void

Description	UACR reduction derived from total cumulative urinary excretion first morning void
Time Frame	Week 9: Day 64
Analysis Population Description	Pharmacodynamics (PD) Analysis Set 1: number of patients included in the analysis with at least one post-baseline value of the outcome variable

	Cohort A - no kidney transplant	**Cohort B - kidney transplant**
Arm/Group Description	C3G patients who have not received a kidney transplant and have reduced C3 blood levels.	C3G patients who have received a kidney transplant and have C3G recurrence.
Number of Participants Analyzed [units: participants]	15	7
Change from baseline in Urine Albumin to Creatinine Concentration Ratio (UACR) First Morning Void (units: g/mol)	**Geometric Mean (80% Confidence Interval)**	**Geometric Mean (80% Confidence Interval)**
Week 9: Day 64	0.59 (0.50 to 0.69)	0.87 (0.60 to 1.26)

1.39 Statistical Analysis

Groups	Cohort A - no kidney transplant	Day 64
Type of Statistical Test	Other	
P Value	<.0001	

Method	Other Mixed Model Repeated Measures (MMRM)
Mean Difference (Final Values)	0.59
80 % Confidence Interval 2-Sided	0.50 to 0.69

1.40 Statistical Analysis

Groups	Cohort B - kidney transplant	Day 64
Type of Statistical Test	Other	
P Value	0.6209	
Method	Other Mixed Model Repeated Measures (MMRM)	
Median Difference (Final Values)	0.87	
80 % Confidence Interval 2-Sided	0.60 to 1.26	

1.41 Statistical Analysis

Groups	Cohort A - no kidney transplant, Cohort B - kidney transplant	Overall- Day 64
Type of Statistical Test	Other	
P Value	0.0002	
Method	Other Mixed Model Repeated Measures (MMRM)	
Mean Difference (Final Values)	0.63	

80
% Confidence Interval 0.54 to 0.73
2-Sided

1.42 Pharmacokinetics of LNP023 Area under the Plasma-concentration-time curve AUClast (AUC)

Description	The area under the plasma concentration-time curve calculated from time zero to the last quantifiable concentration point (hr*ng/mL)
Time Frame	Day 7, Day 14, Day 21, Day 28 (pre-dose, 0.5h, 1h, 2h, 4h, 6h, 8h post dose) and Day 36, Day 64 and Day 84 (pre-dose)
Analysis Population Description	PK Analysis Set: all patients with available PK data and no protocol deviations with relevant impact on PK data.

	Cohort A - no kidney transplant - LNP023 10mg b.i.d.	**Cohort A - no kidney transplant - LNP023 25 mg b.i.d.**	**Cohort A -no kidney transplant - LNP023 100 mg b.i.d.**	**Cohort A -no kidney transplant - LNP023 200 mg b.i.d.**	**Cohort B - kidney transplant - LNP023 10mg b.i.d.**	**Cohort B - kidney transplant - LNP023 25 mg b.i.d.**	**Cohort B - kidney transplant - LNP023 100 mg b.i.d.**	**Cohort B - kidney transplant - LNP023 200 mg b.i.d.**
Arm/Group Description	C3G patients who have not received a kidney transplant and have reduced C3 blood levels. Patients received 10 mg b.i.d.of LNP023 during the first treatment week (Week 1) of the dose escalation phase	C3G patients who have not received a kidney transplant and have reduced C3 blood levels. Patients received 25 mg b.i.d.of LNP023 during the second treatment week (Week 2) of the dose escalation phase	C3G patients who have not received a kidney transplant and have reduced C3 blood levels. Patients received 100 mg b.i.d. of LNP023 during the third treatment week (Week 3) of the dose escalation phase	C3G patients who have not received a kidney transplant and have reduced C3 blood levels. Patients received 200 mg b.i.d. of LNP023 during the fourth treatment week (Week 4) of the dose escalation phase, and continued receiving	C3G patients who have received a kidney transplant and have C3G recurrence. Patients received 10 mg b.i.d.of LNP023 during the first treatment week (Week 1) of the dose escalation phase	C3G patients who have received a kidney transplant and have C3G recurrence. Patients received 25 mg b.i.d.of LNP023 during the second treatment week (Week 2) of the dose escalation phase	C3G patients who have received a kidney transplant and have C3G recurrence. Patients received 100 mg b.i.d.of LNP023 during the third treatment week (Week 3) of the dose escalation phase	C3G patients who have received a kidney transplant and have C3G recurrence. Patients received 200 mg b.i.d.of LNP023 during the fourth treatment week (Week 4) of the dose escalation phase and continued receiving 200

				200 mg b.i.d. for additional 8 weeks (Patients received 200 mg b.i.d. of LNP023 a total of 9 weeks).				mg b.i.d. for additional 8 weeks (Patients received 200 mg b.i.d. of LNP023 a total of 9 weeks).
Number of Participants Analyzed [units: participants]	15	16	16	15	11	11	11	9
Pharmacokinetics of LNP023 Area under the Plasma-concentration-time curve AUClast (AUC) (units: hr*ng/mL)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
	3690 ± 693	5790 ± 1630	13200 ± 4410	20300 ± 8180	4560 ± 2060	7880 ± 3830	19600 ± 12100	28100 ± 15900

1.43 Pharmacokinetics of LNP023 Area under the Plasma-concentration-time curve AUCtau (AUC)

Description	The area under the plasma concentration-time curve calculated to the end of the dosing interval (hr*ng/mL)
Time Frame	Day 7, Day 14, Day 21, Day 28 (pre-dose, 0.5h, 1h, 2h, 4h, 6h, 8h post dose) and Day 36, Day 64 and Day 84 (pre-dose)
Analysis Population Description	PK Analysis Set: all patients with available PK data and no protocol deviations with relevant impact on PK data.

	Cohort A - no kidney transplant - LNP023 10mg b.i.d.	**Cohort A - no kidney transplant - LNP023 25 mg b.i.d.**	**Cohort A -no kidney transplant - LNP023 100 mg b.i.d.**	**Cohort A -no kidney transplant - LNP023 200 mg b.i.d.**	**Cohort B - kidney transplant - LNP023 10mg b.i.d.**	**Cohort B - kidney transplant - LNP023 25 mg b.i.d.**	**Cohort B - kidney transplant - LNP023 100 mg b.i.d.**	**Cohort B - kidney transplant - LNP023 200 mg b.i.d.**

Arm/Group Description	C3G patients who have not received a kidney transplant and have reduced C3 blood levels. Patients received 10 mg b.i.d.of LNP023 during the first treatment week (Week 1) of the dose escalation phase	C3G patients who have not received a kidney transplant and have reduced C3 blood levels. Patients received 25 mg b.i.d.of LNP023 during the second treatment week (Week 2) of the dose escalation phase	C3G patients who have not received a kidney transplant and have reduced C3 blood levels. Patients received 100 mg b.i.d. of LNP023 during the third treatment week (Week 3) of the dose escalation phase	C3G patients who have not received a kidney transplant and have reduced C3 blood levels. Patients received 200 mg b.i.d. of LNP023 during the fourth treatment week (Week 4) of the dose escalation phase, and continued receiving 200 mg b.i.d. for additional 8 weeks (Patients received 200 mg b.i.d. of LNP023 a total of 9 weeks).	C3G patients who have received a kidney transplant and have C3G recurrence. Patients received 10 mg b.i.d.of LNP023 during the first treatment week (Week 1) of the dose escalation phase	C3G patients who have received a kidney transplant and have C3G recurrence. Patients received 25 mg b.i.d.of LNP023 during the second treatment week (Week 2) of the dose escalation phase	C3G patients who have received a kidney transplant and have C3G recurrence. Patients received 100 mg b.i.d.of LNP023 during the third treatment week (Week 3) of the dose escalation phase	C3G patients who have received a kidney transplant and have C3G recurrence. Patients received 200 mg b.i.d.of LNP023 during the fourth treatment week (Week 4) of the dose escalation phase and continued receiving 200 mg b.i.d. for additional 8 weeks (Patients received 200 mg b.i.d. of LNP023 a total of 9 weeks).
Number of Participants Analyzed [units: participants]	15	16	16	15	11	11	11	9
Pharmacokinetics of LNP023 Area under the Plasma-concentration-time curve AUCtau (AUC) (units: hr*ng/mL)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**

	5020 ± 1110	7970 ± 2250	17800 ± 5800	26900 ± 10900	6300 ± 3000	10700 ± 5310	26600 ± 16500	37700 ± 22000

1.44 Observed maximum concentration after drug administration (Cmax)

Description	The observed maximum plasma concentration (ng/mL)
Time Frame	Day 7, Day 14, Day 21, Day 28 (pre-dose, 0.5h, 1h, 2h, 4h, 6h, 8h post dose) and Day 36, Day 64 and Day 84 (pre-dose)
Analysis Population Description	PK Analysis Set: all patients with available PK data and no protocol deviations with relevant impact on PK data.

	Cohort A - no kidney transplant - LNP023 10mg b.i.d.	**Cohort A - no kidney transplant - LNP023 25 mg b.i.d.**	**Cohort A -no kidney transplant - LNP023 100 mg b.i.d.**	**Cohort A -no kidney transplant - LNP023 200 mg b.i.d.**	**Cohort B - kidney transplant - LNP023 10mg b.i.d.**	**Cohort B - kidney transplant - LNP023 25 mg b.i.d.**	**Cohort B - kidney transplant - LNP023 100 mg b.i.d.**	**Cohort B - kidney transplant - LNP023 200 mg b.i.d.**
Arm/Group Description	C3G patients who have not received a kidney transplant and have reduced C3 blood levels. Patients received 10 mg b.i.d.of LNP023 during the first treatment week (Week 1) of the dose escalation phase	C3G patients who have not received a kidney transplant and have reduced C3 blood levels. Patients received 25 mg b.i.d.of LNP023 during the second treatment week (Week 2) of the dose escalation phase	C3G patients who have not received a kidney transplant and have reduced C3 blood levels. Patients received 100 mg b.i.d. of LNP023 during the third treatment week (Week 3) of the dose escalation phase	C3G patients who have not received a kidney transplant and have reduced C3 blood levels. Patients received 200 mg b.i.d. of LNP023 during the fourth treatment week (Week 4) of the dose escalation phase, and continued receiving 200	C3G patients who have received a kidney transplant and have C3G recurrence. Patients received 10 mg b.i.d.of LNP023 during the first treatment week (Week 1) of the dose escalation phase	C3G patients who have received a kidney transplant and have C3G recurrence. Patients received 25 mg b.i.d.of LNP023 during the second treatment week (Week 2) of the dose escalation phase	C3G patients who have received a kidney transplant and have C3G recurrence. Patients received 100 mg b.i.d.of LNP023 during the third treatment week (Week 3) of the dose escalation phase	C3G patients who have received a kidney transplant and have C3G recurrence. Patients received 200 mg b.i.d.of LNP023 during the fourth treatment week (Week 4) of the dose escalation phase and continued receiving 200

				mg b.i.d. for additional 8 weeks (Patients received 200 mg b.i.d. of LNP023 a total of 9 weeks).				mg b.i.d. for additional 8 weeks (Patients received 200 mg b.i.d. of LNP023 a total of 9 weeks).
Number of Participants Analyzed [units: participants]	15	16	16	15	11	11	11	9
Observed maximum concentration after drug administration (Cmax) (units: ng/mL)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
	637 ± 97.1	941 ± 278	2270 ± 805	3600 ± 1230	713 ± 292	1280 ± 552	3250 ± 1790	4700 ± 2200

1.45 Observed minimum concentration after drug administration (Ctrough)

Description	The concentration that is just prior to the beginning of, or at the end, of a dosing interval (ng/mL)
Time Frame	Day 7, Day 14, Day 21, Day 28 (pre-dose, 0.5h, 1h, 2h, 4h, 6h, 8h post dose) and Day 36, Day 64 and Day 84 (pre-dose)
Analysis Population Description	PK Analysis Set: all patients with available PK data and no protocol deviations with relevant impact on PK data.

	Cohort A - no kidney transplant - LNP023 10mg b.i.d.	**Cohort A - no kidney transplant - LNP023 25 mg b.i.d.**	**Cohort A -no kidney transplant - LNP023 100 mg b.i.d.**	**Cohort A -no kidney transplant - LNP023 200 mg b.i.d.**	**Cohort B - kidney transplant - LNP023 10mg b.i.d.**	**Cohort B - kidney transplant - LNP023 25 mg b.i.d.**	**Cohort B - kidney transplant - LNP023 100 mg b.i.d.**	**Cohort B - kidney transplant - LNP023 200 mg b.i.d.**
Arm/Group Description	C3G patients who have not received a	C3G patients who have not received a	C3G patients who have not received a	C3G patients who have not received a	C3G patients who have received a	C3G patients who have received a	C3G patients who have received a	C3G patients who have received a

	kidney transplant and have reduced C3 blood levels. Patients received 10 mg b.i.d.of LNP023 during the first treatment week (Week 1) of the dose escalation phase	kidney transplant and have reduced C3 blood levels. Patients received 25 mg b.i.d.of LNP023 during the second treatment week (Week 2) of the dose escalation phase	kidney transplant and have reduced C3 blood levels. Patients received 100 mg b.i.d. of LNP023 during the third treatment week (Week 3) of the dose escalation phase	kidney transplant and have reduced C3 blood levels. Patients received 200 mg b.i.d. of LNP023 during the fourth treatment week (Week 4) of the dose escalation phase, and continued receiving 200 mg b.i.d. for additional 8 weeks (Patients received 200 mg b.i.d. of LNP023 a total of 9 weeks).	kidney transplant and have C3G recurrence. Patients received 10 mg b.i.d.of LNP023 during the first treatment week (Week 1) of the dose escalation phase	kidney transplant and have C3G recurrence. Patients received 25 mg b.i.d.of LNP023 during the second treatment week (Week 2) of the dose escalation phase	kidney transplant and have C3G recurrence. Patients received 100 mg b.i.d.of LNP023 during the third treatment week (Week 3) of the dose escalation phase	kidney transplant and have C3G recurrence. Patients received 200 mg b.i.d.of LNP023 during the fourth treatment week (Week 4) of the dose escalation phase and continued receiving 200 mg b.i.d. for additional 8 weeks (Patients received 200 mg b.i.d. of LNP023 a total of 9 weeks).
Number of Participants Analyzed [units: participants]	15	16	16	15	11	11	11	9
Observed minimum concentration after drug administration (Ctrough) (units: ng/mL)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
	314 ± 133	519 ± 133	1090 ± 408	1480 ± 653	417 ± 237	644 ± 325	1650 ± 1010	2180 ± 1610

1.46 Time to reach the maximum plasma concentration (Tmax)

Description	The time to reach peak or maximum concentration (hr)
Time Frame	Day 7, Day 14, Day 21, Day 28 (pre-dose, 0.5h, 1h, 2h, 4h, 6h, 8h post dose) and Day 36, Day 64 and Day 84 (pre-dose)
Analysis Population Description	PK Analysis Set: all patients with available PK data and no protocol deviations with relevant impact on PK data.

	Cohort A - no kidney transplant - LNP023 10mg b.i.d.	Cohort A - no kidney transplant - LNP023 25 mg b.i.d.	Cohort A -no kidney transplant - LNP023 100 mg b.i.d.	Cohort A -no kidney transplant - LNP023 200 mg b.i.d.	Cohort B - kidney transplant - LNP023 10mg b.i.d.	Cohort B - kidney transplant - LNP023 25 mg b.i.d.	Cohort B - kidney transplant - LNP023 100 mg b.i.d.	Cohort B - kidney transplant - LNP023 200 mg b.i.d.
Arm/Group Description	C3G patients who have not received a kidney transplant and have reduced C3 blood levels. Patients received 10 mg b.i.d.of LNP023 during the first treatment week (Week 1) of the dose escalation phase	C3G patients who have not received a kidney transplant and have reduced C3 blood levels. Patients received 25 mg b.i.d.of LNP023 during the second treatment week (Week 2) of the dose escalation phase	C3G patients who have not received a kidney transplant and have reduced C3 blood levels. Patients received 100 mg b.i.d. of LNP023 during the third treatment week (Week 3) of the dose escalation phase	C3G patients who have not received a kidney transplant and have reduced C3 blood levels. Patients received 200 mg b.i.d. of LNP023 during the fourth treatment week (Week 4) of the dose escalation phase, and continued receiving 200 mg b.i.d. for additional 8 weeks (Patients	C3G patients who have received a kidney transplant and have C3G recurrence. Patients received 10 mg b.i.d.of LNP023 during the first treatment week (Week 1) of the dose escalation phase	C3G patients who have received a kidney transplant and have C3G recurrence. Patients received 25 mg b.i.d.of LNP023 during the second treatment week (Week 2) of the dose escalation phase	C3G patients who have received a kidney transplant and have C3G recurrence. Patients received 100 mg b.i.d.of LNP023 during the third treatment week (Week 3) of the dose escalation phase	C3G patients who have received a kidney transplant and have C3G recurrence. Patients received 200 mg b.i.d.of LNP023 during the fourth treatment week (Week 4) of the dose escalation phase and continued receiving 200 mg b.i.d. for additional 8 weeks (Patients

				received 200 mg b.i.d. of LNP023 a total of 9 weeks).				received 200 mg b.i.d. of LNP023 a total of 9 weeks).
Number of Participants Analyzed [units: participants]	15	16	16	15	11	11	11	9
Time to reach the maximum plasma concentration (Tmax) (units: hr)	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**
	2.00 (0.800 to 6.00)	2.00 (0.900 to 4.00)	2.00 (0.500 to 4.00)	2.00 (1.00 to 4.00)	2.00 (1.00 to 4.00)	2.00 (1.00 to 6.00)	2.00 (1.00 to 4.00)	2.00 (1.00 to 4.00)

1.47 Summary of Change from Baseline Complement C3 biomarker in serum

Description	To assess the effect of LNP023 on alternative complement pathway hyperactivity.
Time Frame	Baseline, Day 1, Day 7, Day 14, Day 21, Day 28, Day 36, Day 64, Day 84
Analysis Population Description	PD Analysis Set 2: included all patients with available Pharmacodynamics (PD) data and no protocol deviations with relevant impact on PD data. At each timepoint only subjects with a value at both baseline and that timepoint were included.

	Cohort A - no kidney transplant	**Cohort B - kidney transplant**
Arm/Group Description	C3G patients who have not received a kidney transplant and have reduced C3 blood levels.	C3G patients who have received a kidney transplant and have C3G recurrence.
Number of Participants Analyzed [units: participants]	16	10
Summary of Change from Baseline Complement C3 biomarker in serum (units: g/L)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**

Day 1 pre-dose	0.0 ± 0.06	0.0 ± 0.12
Day 7 - pre-dose	0.1 ± 0.10	0.2 ± 0.22
Day 14 - pre-dose	0.3 ± 0.17	0.4 ± 0.29
Day 21 - pre-dose	0.5 ± 0.25	0.4 ± 0.33
Day 28 - pre-dose	0.5 ± 0.29	0.4 ± 0.27
Day 36 - pre-dose	0.6 ± 0.28	0.4 ± 0.32
Day 64 - pre-dose	0.6 ± 0.27	0.4 ± 0.26
Day 84 - pre-dose	0.6 ± 0.30	0.5 ± 0.26

1.48 Ratio to baseline summary of Plasma Bb

Description	To assess the relationship between LNP023 dose and pharmacodynamic biomarker levels of blood Bb
Time Frame	Baseline, Day 1, Day 7, Day 14, Day 21, Day 28, Day 36, Day 64, Day 84
Analysis Population Description	PD Analysis Set 2: included all patients with available Pharmacodynamics (PD) data and no protocol deviations with relevant impact on PD data. At each timepoint only subjects with a value at both baseline and that timepoint were included

	Cohort A - no kidney transplant	**Cohort B - kidney transplant**
Arm/Group Description	C3G patients who have not received a kidney transplant and have reduced C3 blood levels.	C3G patients who have received a kidney transplant and have C3G recurrence.
Number of Participants Analyzed [units: participants]	16	10
Ratio to baseline summary of Plasma Bb (units: Ratio of plasma Bb)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
Day 1 pre-dose	101.8 ± 45.18	109.7 ± 34.08
Day 7 pre-dose	102.4 ± 40.47	83.6 ± 27.73
Day 14 pre-dose	104.4 ± 43.35	81.8 ± 39.34

Day 21 pre-dose	97.0 ± 58.06	66.4 ± 22.95
Day 28 pre-dose	90.2 ± 46.24	71.5 ± 29.52
Day 36 pre-dose	102.5 ± 54.06	65.9 ± 31.20
Day 64 pre-dose	116.8 ± 59.76	73.2 ± 29.62
Day 84 pre-dose	116.6 ± 57.85	76.3 ± 35.84

Safety Results

All-Cause Mortality

	Cohort A - Run-in Phase N = 16	Cohort A - Dose Escalation Phase N = 16	Cohort A - LNP023 200mg b.i.d N = 16	Cohort B - Run-in Phase N = 11	Cohort B - Dose Escalation Phase N = 11	Cohort B - LNP023 200mg b.i.d N = 11
Arm/Group Description	No Kidney Transplant- C3G patients who have not received a kidney transplant and have reduced C3 blood levels	No Kidney Transplant- C3G patients who have not received a kidney transplant and have reduced C3 blood levels	No Kidney Transplant- C3G patients who have not received a kidney transplant and have reduced C3 blood levels	Kidney Transplant- C3G patients who have received a kidney transplant and have C3G recurrence	Kidney Transplant- C3G patients who have received a kidney transplant and have C3G recurrence	Kidney Transplant- C3G patients who have received a kidney transplant and have C3G recurrence
Total Number Affected	0	0	0	0	0	0
Total Number At Risk	16	16	16	11	11	11

Serious Adverse Events by System Organ Class

	Cohort A - Run-in Phase N = 16	Cohort A - Dose Escalation	Cohort A - LNP023 200mg	Cohort B - Run-in Phase N = 11	Cohort B - Dose Escalation	Cohort B - LNP023 200mg

		Phase N = 16	b.i.d N = 16		Phase N = 11	b.i.d N = 11
Arm/Group Description	No Kidney Transplant- C3G patients who have not received a kidney transplant and have reduced C3 blood levels	No Kidney Transplant- C3G patients who have not received a kidney transplant and have reduced C3 blood levels	No Kidney Transplant- C3G patients who have not received a kidney transplant and have reduced C3 blood levels	Kidney Transplant- C3G patients who have received a kidney transplant and have C3G recurrence	Kidney Transplant- C3G patients who have received a kidney transplant and have C3G recurrence	Kidney Transplant- C3G patients who have received a kidney transplant and have C3G recurrence
Total # Affected by any Serious Adverse Event	0	0	0	0	0	2
Total # at Risk by any Serious Adverse Event	16	16	16	11	11	11
Injury, poisoning and procedural complications						
Overdose	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)
Metabolism and nutrition disorders						
Hyperkalaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)

Other Adverse Events by System Organ Class

Frequent Event Reporting Threshold 5%

	Cohort A - Run-in Phase N = 16	Cohort A - Dose Escalation Phase N = 16	Cohort A - LNP023 200mg b.i.d N = 16	Cohort B - Run-in Phase N = 11	Cohort B - Dose Escalation Phase N = 11	Cohort B - LNP023 200mg b.i.d N = 11
Arm/Group Description	No Kidney Transplant- C3G patients who have	No Kidney Transplant- C3G patients who have	No Kidney Transplant- C3G patients who have	Kidney Transplant- C3G patients who have	Kidney Transplant- C3G patients who have	Kidney Transplant- C3G patients who have

	not received a kidney transplant and have reduced C3 blood levels	not received a kidney transplant and have reduced C3 blood levels	not received a kidney transplant and have reduced C3 blood levels	received a kidney transplant and have C3G recurrence	received a kidney transplant and have C3G recurrence	received a kidney transplant and have C3G recurrence
Total # Affected by any Other Adverse Event	0	6	8	0	5	6
Total # at Risk by any Other Adverse Event	16	16	16	11	11	11
Blood and lymphatic system disorders						
Anaemia	0 (0.00%)	1 (6.25%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Normochromic normocytic anaemia	0 (0.00%)	0 (0.00%)	1 (6.25%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cardiac disorders						
Palpitations	0 (0.00%)	0 (0.00%)	1 (6.25%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Endocrine disorders						
Hypothyroidism	0 (0.00%)	1 (6.25%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Eye disorders						
Conjunctival hyperaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)
Gastrointestinal disorders						
Abdominal pain upper	0 (0.00%)	1 (6.25%)	1 (6.25%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dyspepsia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)
Nausea	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)
Vomiting	0 (0.00%)	1 (6.25%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)
General disorders and administration site conditions						
Chest pain	0 (0.00%)	0 (0.00%)	1 (6.25%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Oedema peripheral	0 (0.00%)	0 (0.00%)	1 (6.25%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infections and infestations						
COVID-19	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)
Hordeolum	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)
Influenza	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)
Nasopharyngitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)
Respiratory tract infection viral	0 (0.00%)	1 (6.25%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urinary tract infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)
Injury, poisoning and procedural complications						
Contusion	0 (0.00%)	1 (6.25%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Investigations						
Blood creatine phosphokinase increased	0 (0.00%)	1 (6.25%)	1 (6.25%)	0 (0.00%)	0 (0.00%)	1 (9.09%)
Blood luteinising hormone increased	0 (0.00%)	1 (6.25%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Body temperature increased	0 (0.00%)	0 (0.00%)	1 (6.25%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Lipase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)
Metabolism and nutrition disorders						
Dyslipidaemia	0 (0.00%)	0 (0.00%)	1 (6.25%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gout	0 (0.00%)	0 (0.00%)	1 (6.25%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypercholesterolaemia	0 (0.00%)	1 (6.25%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hyperkalaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (18.18%)
Iron deficiency	0 (0.00%)	0 (0.00%)	1 (6.25%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Musculoskeletal and connective tissue disorders						
Back pain	0 (0.00%)	0 (0.00%)	1 (6.25%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
Skin papilloma	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)
Nervous system disorders						
Anosmia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)
Dysgeusia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)
Headache	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (18.18%)	0 (0.00%)
Migraine	0 (0.00%)	0 (0.00%)	1 (6.25%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Syncope	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)
Psychiatric disorders						
Adjustment disorder with depressed mood	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)
Intentional self-injury	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)
Renal and urinary disorders						
Proteinuria	0 (0.00%)	0 (0.00%)	1 (6.25%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Skin and subcutaneous tissue disorders						
Skin discolouration	0 (0.00%)	0 (0.00%)	1 (6.25%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vascular disorders						
Hypertension	0 (0.00%)	0 (0.00%)	1 (6.25%)	0 (0.00%)	1 (9.09%)	0 (0.00%)
Spider vein	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)

Conclusion:

Treatment with LNP023 200 mg b.i.d. in patients with native kidneys or recurrent C3G was well tolerated. LNP023 200mg b.i.d. resulted in statistically significant and clinically important reduction of urinary protein excretion (UPCR), overall normalization of serum C3 levels and stabilization of renal function (eGFR) in patients with native kidney C3G (Cohort A). In addition, LNP023 at 200 mg b.i.d. significantly reduced the histologic C3 Deposit Score in patients with recurrent C3G after kidney transplantation (Cohort B).

All secondary pharmacodynamic endpoints were consistent with a treatment benefit in both native kidney and recurrent C3G Cohorts. A trend to improvement in symptomatic fatigue was also observed in native kidney C3G patients through the FACIT-F patient reported outcome measurement. The pharmacokinetics of LNP023 in C3G patients was consistent with that established in healthy volunteers.

Date of Clinical Trial Report

03-March-2022