



## Clinical trial results:

### An Open Label, Intra-Subject Dose Escalation Study of CCX140-B in Subjects with Primary Focal Segmental Glomerulosclerosis (FSGS) and Nephrotic Syndrome

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2017-003022-32 |
| Trial protocol           | PL             |
| Global end of trial date | 24 June 2020   |

#### Results information

|                                |                                                                 |
|--------------------------------|-----------------------------------------------------------------|
| Result version number          | v2 (current)                                                    |
| This version publication date  | 14 September 2023                                               |
| First version publication date | 01 November 2022                                                |
| Version creation reason        | • Correction of full data set<br>additional clarification added |

#### Trial information

##### Trial identification

|                       |           |
|-----------------------|-----------|
| Sponsor protocol code | CL012_140 |
|-----------------------|-----------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03703908 |
| WHO universal trial number (UTN)   | -           |
| Other trial identifiers            | IND: 134007 |

Notes:

#### Sponsors

|                              |                                                                              |
|------------------------------|------------------------------------------------------------------------------|
| Sponsor organisation name    | ChemoCentryx, Inc.                                                           |
| Sponsor organisation address | 835 Industrial Road, San Carlos, United States, 94070                        |
| Public contact               | Clinical Trials Disclosure, ChemoCentryx,<br>clinicaltrials@chemocentryx.com |
| Scientific contact           | Clinical Trials Disclosure, ChemoCentryx,<br>clinicaltrials@chemocentryx.com |

Notes:

#### Paediatric regulatory details

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

Notes:

## Results analysis stage

|                                                      |                 |
|------------------------------------------------------|-----------------|
| Analysis stage                                       | Final           |
| Date of interim/final analysis                       | 27 January 2021 |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 24 June 2020    |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 24 June 2020    |
| Was the trial ended prematurely?                     | Yes             |

Notes:

## General information about the trial

Main objective of the trial:

The Primary Efficacy Objective is to evaluate the effect of CCX140-B on proteinuria in subjects with primary FSGS with nephrotic syndrome.

Protection of trial subjects:

The study was conducted in accordance with the Declaration of Helsinki and with all applicable laws and regulations of the locale and country where the study was conducted, and in compliance with Good Clinical Practice Guidelines. Only subjects that met all the study inclusion and none of the exclusion criteria were entered in the study. The rationale of the study, procedural details, and investigational goals were explained to each subject, along with potential risks and benefits. Each subject was assured of his/her right to withdraw from the study at any time.

Background therapy: -

Evidence for comparator: -

|                                                           |                   |
|-----------------------------------------------------------|-------------------|
| Actual start date of recruitment                          | 21 September 2018 |
| Long term follow-up planned                               | No                |
| Independent data monitoring committee (IDMC) involvement? | No                |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                  |
|--------------------------------------|------------------|
| Country: Number of subjects enrolled | Poland: 1        |
| Country: Number of subjects enrolled | United States: 4 |
| Worldwide total number of subjects   | 5                |
| EEA total number of subjects         | 1                |

Notes:

### Subjects enrolled per age group

|                                           |   |
|-------------------------------------------|---|
| In utero                                  | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days)                      | 0 |
| Infants and toddlers (28 days-23 months)  | 0 |
| Children (2-11 years)                     | 0 |
| Adolescents (12-17 years)                 | 0 |
| Adults (18-64 years)                      | 5 |
| From 65 to 84 years                       | 0 |

|                   |   |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

## Subject disposition

### Recruitment

Recruitment details:

17 subjects were screened and 10 (58.8%) subjects failed screening due to not meeting inclusion/exclusion criteria, and 2 (11.88%) failed due to other reasons (one per sponsor request and one due to the Coronavirus Disease Pandemic).

### Pre-assignment

Screening details:

The Screening Period was up to 28 days. Subjects visited the study centre during screening and on Day 1 (baseline), at pre-specified time points throughout Dose Escalation, and through Week 12.

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall Trial (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Not applicable                 |
| Blinding used                | Not blinded                    |

### Arms

|           |                              |
|-----------|------------------------------|
| Arm title | Escalation Study of CCX140 B |
|-----------|------------------------------|

Arm description:

All enrolled subjects will initially be treated with the active study medication CCX140-B at a dose of 5 mg twice daily. Dose will increase in a step-wise fashion up to 15 mg twice daily.

|                                        |            |
|----------------------------------------|------------|
| Arm type                               | Sequential |
| Investigational medicinal product name | CCX140-B   |
| Investigational medicinal product code |            |
| Other name                             |            |
| Pharmaceutical forms                   | Tablet     |
| Routes of administration               | Oral use   |

Dosage and administration details:

Eligible subjects started treatment with CCX140-B at 5 mg twice daily. CCX140-B was taken orally without food, at least 1 hour before a meal. The dose was increased in a stepwise manner to 15 mg twice daily.

| Number of subjects in period 1 | Escalation Study of CCX140 B |
|--------------------------------|------------------------------|
| Started                        | 5                            |
| Completed                      | 2                            |
| Not completed                  | 3                            |
| Consent withdrawn by subject   | 1                            |
| Progression of renal disease   | 1                            |
| Lack of efficacy               | 1                            |

## Baseline characteristics

### Reporting groups

|                                |               |
|--------------------------------|---------------|
| Reporting group title          | Overall Trial |
| Reporting group description: - |               |

| Reporting group values                             | Overall Trial | Total |  |
|----------------------------------------------------|---------------|-------|--|
| Number of subjects                                 | 5             | 5     |  |
| Age categorical                                    |               |       |  |
| Units: Subjects                                    |               |       |  |
| In utero                                           | 0             | 0     |  |
| Preterm newborn infants (gestational age < 37 wks) | 0             | 0     |  |
| Newborns (0-27 days)                               | 0             | 0     |  |
| Infants and toddlers (28 days-23 months)           | 0             | 0     |  |
| Children (2-11 years)                              | 0             | 0     |  |
| Adolescents (12-17 years)                          | 0             | 0     |  |
| Adults (18-64 years)                               | 5             | 5     |  |
| From 65-84 years                                   | 0             | 0     |  |
| 85 years and over                                  | 0             | 0     |  |
| Age continuous                                     |               |       |  |
| Units: years                                       |               |       |  |
| arithmetic mean                                    | 37.6          |       |  |
| standard deviation                                 | ± 18.65       | -     |  |
| Gender categorical                                 |               |       |  |
| Units: Subjects                                    |               |       |  |
| Female                                             | 1             | 1     |  |
| Male                                               | 4             | 4     |  |
| Race                                               |               |       |  |
| Units: Subjects                                    |               |       |  |
| White                                              | 4             | 4     |  |
| Other                                              | 1             | 1     |  |
| Ethnicity                                          |               |       |  |
| Units: Subjects                                    |               |       |  |
| Hispanic or Latino                                 | 2             | 2     |  |
| Not Hispanic or Latino                             | 3             | 3     |  |
| Country                                            |               |       |  |
| Units: Subjects                                    |               |       |  |
| Poland                                             | 1             | 1     |  |
| United States                                      | 4             | 4     |  |
| Podocyte effacement                                |               |       |  |
| Based on electron microscopy                       |               |       |  |
| Units: Subjects                                    |               |       |  |
| <30%                                               | 1             | 1     |  |
| ≥30%                                               | 4             | 4     |  |
| Glomeruli showing segmental lesions                |               |       |  |
| Units: Subjects                                    |               |       |  |
| ≤1                                                 | 1             | 1     |  |

|                                                                                                         |         |   |  |
|---------------------------------------------------------------------------------------------------------|---------|---|--|
| >1                                                                                                      | 4       | 4 |  |
| Concomitant use of glucocorticoids and/or immunosuppressive medications<br>Units: Subjects              |         |   |  |
| Yes                                                                                                     | 4       | 4 |  |
| No                                                                                                      | 1       | 1 |  |
| Concomitant use of ACE inhibitor or ARB                                                                 |         |   |  |
| ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker                                 |         |   |  |
| Units: Subjects                                                                                         |         |   |  |
| Yes                                                                                                     | 5       | 5 |  |
| No                                                                                                      | 0       | 0 |  |
| All calcineurin inhibitors combined                                                                     |         |   |  |
| Includes cyclosporin or tacrolimus                                                                      |         |   |  |
| Units: Subjects                                                                                         |         |   |  |
| Yes                                                                                                     | 2       | 2 |  |
| No                                                                                                      | 3       | 3 |  |
| Concomitant use of rituximab or other anti-CD20<br>Units: Subjects                                      |         |   |  |
| Yes                                                                                                     | 0       | 0 |  |
| No                                                                                                      | 5       | 5 |  |
| Age at diagnosis of FSGS                                                                                |         |   |  |
| FSGS= focal segmental glomerulosclerosis                                                                |         |   |  |
| Units: Years                                                                                            |         |   |  |
| arithmetic mean                                                                                         | 35.2    |   |  |
| standard deviation                                                                                      | ± 19.18 | - |  |
| Duration of FSGS                                                                                        |         |   |  |
| Duration of FSGS was calculated from the time of first diagnosis based on renal biopsy.                 |         |   |  |
| Units: Months                                                                                           |         |   |  |
| arithmetic mean                                                                                         | 29.4    |   |  |
| standard deviation                                                                                      | ± 16.32 | - |  |
| Baseline UPCR – morning void                                                                            |         |   |  |
| UPCR= urinary protein:creatinine ratio                                                                  |         |   |  |
| Units: g protein/g creatinine                                                                           |         |   |  |
| arithmetic mean                                                                                         | 5.71    |   |  |
| standard deviation                                                                                      | ± 1.563 | - |  |
| Baseline UPCR – 24-hour                                                                                 |         |   |  |
| Units: g protein/g creatinine                                                                           |         |   |  |
| arithmetic mean                                                                                         | 4.80    |   |  |
| standard deviation                                                                                      | ± 1.376 | - |  |
| Baseline UACR – morning void                                                                            |         |   |  |
| UACR= urinary albumin:creatinine ratio                                                                  |         |   |  |
| Units: g protein/g creatinine                                                                           |         |   |  |
| arithmetic mean                                                                                         | 4.12    |   |  |
| standard deviation                                                                                      | ± 1.394 | - |  |
| Baseline UACR – 24-hour                                                                                 |         |   |  |
| Units: g protein/g creatinine                                                                           |         |   |  |
| arithmetic mean                                                                                         | 3.24    |   |  |
| standard deviation                                                                                      | ± 1.316 | - |  |
| Baseline eGFR (CKD-EPI Creatinine-Cystatin C)                                                           |         |   |  |
| eGFR= estimated glomerular filtration rate; CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration |         |   |  |

|                                                                               |                   |   |  |
|-------------------------------------------------------------------------------|-------------------|---|--|
| Units: CKD-EPI Creatinine-Cystatin C<br>arithmetic mean<br>standard deviation | 50.60<br>± 23.923 | - |  |
| Baseline eGFR (MDRD Creatinine)                                               |                   |   |  |
| MDRD = Modification of Diet in Renal Disease                                  |                   |   |  |
| Units: MDRD Creatinine<br>arithmetic mean<br>standard deviation               | 54.40<br>± 26.245 | - |  |

## End points

### End points reporting groups

|                                                                                                                                                                                                                             |                              |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|
| Reporting group title                                                                                                                                                                                                       | Escalation Study of CCX140 B |
| Reporting group description:<br>All enrolled subjects will initially be treated with the active study medication CCX140-B at a dose of 5 mg twice daily. Dose will increase in a step-wise fashion up to 15 mg twice daily. |                              |

### Primary: Median Reduction from Baseline of Urine Protein to Creatinine Ratio (UPCR) of at least 20%

|                                                                                                                   |                                                                                                           |
|-------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------|
| End point title                                                                                                   | Median Reduction from Baseline of Urine Protein to Creatinine Ratio (UPCR) of at least 20% <sup>[1]</sup> |
| End point description:<br>Median reduction from baseline of UPCR of at least 20%, i.e., $\geq 20\%$ , by Week 12. |                                                                                                           |
| End point type                                                                                                    | Primary                                                                                                   |
| End point timeframe:<br>Baseline to week 12                                                                       |                                                                                                           |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analyses has been performed.

|                                      |                              |  |  |  |
|--------------------------------------|------------------------------|--|--|--|
| <b>End point values</b>              | Escalation Study of CCX140 B |  |  |  |
| Subject group type                   | Reporting group              |  |  |  |
| Number of subjects analysed          | 5                            |  |  |  |
| Units: g protein/g creatinine        |                              |  |  |  |
| arithmetic mean (standard deviation) | -1.3100 ( $\pm$ 3.76247)     |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Achievement of Partial Remission or Complete Remission of UPCR Through Week 12 and Through the End of Treatment

|                 |                                                                                                                 |
|-----------------|-----------------------------------------------------------------------------------------------------------------|
| End point title | Achievement of Partial Remission or Complete Remission of UPCR Through Week 12 and Through the End of Treatment |
|-----------------|-----------------------------------------------------------------------------------------------------------------|

End point description:

Partial and complete remission were defined as follows:

Partial remission (included all of the following):

Reduction from baseline by  $\geq 50\%$  in urine protein:creatinine ratio (UPCR)

Reduction in UPCR to a level that was  $< 3.5$  g/g

Subject could not have been a treatment failure

Complete remission (included all of the following):

Reduction in UPCR to  $< 0.3$  g/g

Serum albumin within normal range

For subjects with abnormal serum creatinine levels at baseline, return to normal levels

For subjects with normal serum creatinine levels at baseline, final value within 20% of baseline levels



Subject could not have been a treatment failure

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Baseline to week 12  |           |

|                                        |                              |  |  |  |
|----------------------------------------|------------------------------|--|--|--|
| <b>End point values</b>                | Escalation Study of CCX140 B |  |  |  |
| Subject group type                     | Reporting group              |  |  |  |
| Number of subjects analysed            | 5                            |  |  |  |
| Units: Participants                    |                              |  |  |  |
| Complete remission at Week 12          | 0                            |  |  |  |
| Complete remission at End of Treatment | 0                            |  |  |  |
| Partial remission at Week 12           | 1                            |  |  |  |
| Partial remission at End of Treatment  | 0                            |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in Urine Protein:Creatinine Ratio (UPCR) Over Time

|                                                                                |                                                                         |
|--------------------------------------------------------------------------------|-------------------------------------------------------------------------|
| End point title                                                                | Change From Baseline in Urine Protein:Creatinine Ratio (UPCR) Over Time |
| End point description:                                                         |                                                                         |
| Mean change from baseline in urinary protein:creatinine ratio (UPCR) over time |                                                                         |
| End point type                                                                 | Secondary                                                               |
| End point timeframe:                                                           |                                                                         |
| Baseline to week 12 and week 52                                                |                                                                         |

|                                      |                              |  |  |  |
|--------------------------------------|------------------------------|--|--|--|
| <b>End point values</b>              | Escalation Study of CCX140 B |  |  |  |
| Subject group type                   | Reporting group              |  |  |  |
| Number of subjects analysed          | 3 <sup>[2]</sup>             |  |  |  |
| Units: g protein/g creatinine        |                              |  |  |  |
| arithmetic mean (standard deviation) |                              |  |  |  |
| CCX140-B Week 52                     | -0.4985 (± 3.37926)          |  |  |  |
| CCX140-B Week 12                     | -1.3100 (± 3.76247)          |  |  |  |

Notes:

[2] - Week 12 = 3 subjects

Week 52 = 2 subjects

### Statistical analyses

No statistical analyses for this end point

### Secondary: Proportion of Subjects With Achievement of Complete Remission During the Treatment Period

|                                                                                                                                                                                                                       |                                                                                           |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                       | Proportion of Subjects With Achievement of Complete Remission During the Treatment Period |
| End point description:<br>Complete remission is defined as reduction in urine protein:creatinine ratio (UPCR) to <0.3 g/g, normal serum albumin, and normal serum creatinine levels or within 20% of baseline levels. |                                                                                           |
| End point type                                                                                                                                                                                                        | Secondary                                                                                 |
| End point timeframe:<br>Baseline to week 52                                                                                                                                                                           |                                                                                           |

|                                    |                              |  |  |  |
|------------------------------------|------------------------------|--|--|--|
| <b>End point values</b>            | Escalation Study of CCX140 B |  |  |  |
| Subject group type                 | Reporting group              |  |  |  |
| Number of subjects analysed        | 5                            |  |  |  |
| Units: Participants                |                              |  |  |  |
| Achieved complete remission        | 0                            |  |  |  |
| Did not achieve complete remission | 5                            |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Assessment of Time to and Proportion of Subjects With Achievement of Partial Remission during the treatment period

|                                                                                                                                                           |                                                                                                                    |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                           | Assessment of Time to and Proportion of Subjects With Achievement of Partial Remission during the treatment period |
| End point description:<br>Partial remission is defined as reduction from baseline by $\geq 50\%$ in UPCR, reduction in UPCR to a level that was <3.5 g/g. |                                                                                                                    |
| End point type                                                                                                                                            | Secondary                                                                                                          |
| End point timeframe:<br>Baseline to week 52                                                                                                               |                                                                                                                    |

|                             |                              |  |  |  |
|-----------------------------|------------------------------|--|--|--|
| <b>End point values</b>     | Escalation Study of CCX140 B |  |  |  |
| Subject group type          | Reporting group              |  |  |  |
| Number of subjects analysed | 0 <sup>[3]</sup>             |  |  |  |
| Units: Participants         |                              |  |  |  |

Notes:

[3] - Due to the small sample size and early termination of the study, no data was available

## Statistical analyses

No statistical analyses for this end point

### Secondary: Time to Rescue Therapy

|                 |                        |
|-----------------|------------------------|
| End point title | Time to Rescue Therapy |
|-----------------|------------------------|

End point description:

Based on Investigator or physician initiation of glucocorticoids or new immunosuppressive agents or new major treatment modalities (e.g. plasmapheresis, dialysis)

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to week 52

| End point values            | Escalation Study of CCX140 B |  |  |  |
|-----------------------------|------------------------------|--|--|--|
| Subject group type          | Reporting group              |  |  |  |
| Number of subjects analysed | 0 <sup>[4]</sup>             |  |  |  |
| Units: Participants         |                              |  |  |  |

Notes:

[4] - Due to the small sample size and early termination of the study, no data was available

## Statistical analyses

No statistical analyses for this end point

### Secondary: Mean Change From Baseline for the eGFR CKD-EPI Creatinine Equation Over Time

|                 |                                                                              |
|-----------------|------------------------------------------------------------------------------|
| End point title | Mean Change From Baseline for the eGFR CKD-EPI Creatinine Equation Over Time |
|-----------------|------------------------------------------------------------------------------|

End point description:

CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration; eGFR = estimated glomerular filtration rate

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 12 and Week 52

| End point values                       | Escalation Study of CCX140 B |  |  |  |
|----------------------------------------|------------------------------|--|--|--|
| Subject group type                     | Reporting group              |  |  |  |
| Number of subjects analysed            | 4                            |  |  |  |
| Units: mL/min/1.73m <sup>2</sup>       |                              |  |  |  |
| arithmetic mean (full range (min-max)) |                              |  |  |  |
| CCX140-B Week 12                       | -14.50 (-27.0 to -6.0)       |  |  |  |
| CCX140-B Week 52                       | -15.0 (-15.0 to -15.0)       |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Mean Change From Baseline for eGFR CKD-EPI Creatinine-Cystatin C Equation Over Time

|                 |                                                                                     |
|-----------------|-------------------------------------------------------------------------------------|
| End point title | Mean Change From Baseline for eGFR CKD-EPI Creatinine-Cystatin C Equation Over Time |
|-----------------|-------------------------------------------------------------------------------------|

End point description:

CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration; eGFR = estimated glomerular filtration rate

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 12 and Week 52

| End point values                       | Escalation Study of CCX140 B |  |  |  |
|----------------------------------------|------------------------------|--|--|--|
| Subject group type                     | Reporting group              |  |  |  |
| Number of subjects analysed            | 4                            |  |  |  |
| Units: mL/min/1.73 m <sup>2</sup>      |                              |  |  |  |
| arithmetic mean (full range (min-max)) |                              |  |  |  |
| CCX140-B Week 12                       | -2.25 (-18.0 to 13.0)        |  |  |  |
| CCX140-B Week 52                       | -8.0 (-8.0 to -8.0)          |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Mean Change From Baseline for the MDRD Creatinine Equation Over Time

|                 |                                                                      |
|-----------------|----------------------------------------------------------------------|
| End point title | Mean Change From Baseline for the MDRD Creatinine Equation Over Time |
|-----------------|----------------------------------------------------------------------|

End point description:

MDRD = Modification of Diet in Renal Disease. The mean eGFR (using the MDRD Creatinine equation) change from baseline to Week 12 and Week 52

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 12 and Week 52

| End point values                       | Escalation Study of CCX140 B |  |  |  |
|----------------------------------------|------------------------------|--|--|--|
| Subject group type                     | Reporting group              |  |  |  |
| Number of subjects analysed            | 4                            |  |  |  |
| Units: ml/min/1.73 m <sup>2</sup>      |                              |  |  |  |
| arithmetic mean (full range (min-max)) |                              |  |  |  |
| CCX140-B Week 12                       | -12.75 (-24.0 to -5.0)       |  |  |  |
| CCX140-B Week 52                       | -13.00 (-13.00 to -13.00)    |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Effect of CCX140-B Treatment on Quality of Life Endpoint SF-36V2

|                 |                                                                  |
|-----------------|------------------------------------------------------------------|
| End point title | Effect of CCX140-B Treatment on Quality of Life Endpoint SF-36V2 |
|-----------------|------------------------------------------------------------------|

End point description:

Summary of the Effect of CCX140-B Treatment on Quality of Life Endpoints SF-36V2 for the overall trial SF-36v2: Medical Outcomes Survey Short Form-36 version 2.

SF-36v2 measures each of the following eight health domains: Physical Functioning, Role-Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role-Emotional, and Mental Health. Scores on each item are summed and averaged. The SF-36v2 component domain scores range from 0 (worst health) to 100 (best health).

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 52

| End point values            | Escalation Study of CCX140 B |  |  |  |
|-----------------------------|------------------------------|--|--|--|
| Subject group type          | Reporting group              |  |  |  |
| Number of subjects analysed | 5 <sup>[5]</sup>             |  |  |  |
| Units: Score on a scale     | 0                            |  |  |  |

Notes:

[5] - No summary data collected for these results.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Effect of CCX140-B Treatment on Quality of Life Endpoint EQ-5D-5L for the Overall Trial

|                 |                                                                                         |
|-----------------|-----------------------------------------------------------------------------------------|
| End point title | Effect of CCX140-B Treatment on Quality of Life Endpoint EQ-5D-5L for the Overall Trial |
|-----------------|-----------------------------------------------------------------------------------------|

End point description:

Summary of the Effect of CCX140-B Treatment on Quality of Life Endpoint EQ-5D-5L for the overall trial  
EQ-5D-5L: EuroQuality of Life-5 Domains-5 Levels. The EQ-5D-5L consists of : the EQ-5D descriptive system. The descriptive system comprises five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has 5 levels: no problems, slight problems, moderate problems, severe problems and extreme problems. The answers given can be converted into an Index Score ranging from 0 for death to 1 for perfect health.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 52

|                             |                              |  |  |  |
|-----------------------------|------------------------------|--|--|--|
| End point values            | Escalation Study of CCX140 B |  |  |  |
| Subject group type          | Reporting group              |  |  |  |
| Number of subjects analysed | 5 <sup>[6]</sup>             |  |  |  |
| Units: Score on a scale     | 0                            |  |  |  |

Notes:

[6] - No summary data collected for these results

## Statistical analyses

No statistical analyses for this end point

### Secondary: Changes to Laboratory Parameters Related to Renal Function Including Serum Albumin, Creatinine, Cystatin C, Urinary Albumin:Creatinine Ratio, Total 24-hour Protein Excretion During the Trial

|                 |                                                                                                                                                                                                |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Changes to Laboratory Parameters Related to Renal Function Including Serum Albumin, Creatinine, Cystatin C, Urinary Albumin:Creatinine Ratio, Total 24-hour Protein Excretion During the Trial |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Changes to laboratory parameters related to renal function including serum albumin, creatinine, cystatin C, urinary albumin:creatinine ratio, total 24-hour protein excretion during the trial

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Day 57

| End point values            | Escalation Study of CCX140 B |  |  |  |
|-----------------------------|------------------------------|--|--|--|
| Subject group type          | Reporting group              |  |  |  |
| Number of subjects analysed | 0 <sup>[7]</sup>             |  |  |  |
| Units: Number of subjects   |                              |  |  |  |
| CCX140-B                    |                              |  |  |  |

Notes:

[7] - no patients were analysed

### Statistical analyses

No statistical analyses for this end point

### Secondary: Mean Change From Baseline for eGFR Using the CKD-EPI Cystatin C Equation Over Time

|                        |                                                                                                     |
|------------------------|-----------------------------------------------------------------------------------------------------|
| End point title        | Mean Change From Baseline for eGFR Using the CKD-EPI Cystatin C Equation Over Time                  |
| End point description: | eGFR-Estimated Glomerular Filtration Rate;CKD-EPI=Chronic Kidney Disease Epidemiology Collaboration |
| End point type         | Secondary                                                                                           |
| End point timeframe:   | Baseline to Week 12 and Week 52                                                                     |

| End point values                       | Escalation Study of CCX140 B |  |  |  |
|----------------------------------------|------------------------------|--|--|--|
| Subject group type                     | Reporting group              |  |  |  |
| Number of subjects analysed            | 4                            |  |  |  |
| Units: mL/min/1.73m <sup>2</sup>       |                              |  |  |  |
| arithmetic mean (full range (min-max)) |                              |  |  |  |
| CCX140-B Week 12                       | 7.50 (-11.0 to 37.0)         |  |  |  |
| CCX140-B Week 52                       | -2.00 (-2.0 to -2.0)         |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Time Taken of Subjects to Achieve Complete Remission During the Treatment Period

|                 |                                                                                  |
|-----------------|----------------------------------------------------------------------------------|
| End point title | Time Taken of Subjects to Achieve Complete Remission During the Treatment Period |
|-----------------|----------------------------------------------------------------------------------|

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End point description:

Complete remission is defined as reduction in urine protein:creatinine ratio (UPCR) to <0.3 g/g, normal serum albumin, and normal serum creatinine levels or within 20% of baseline levels.

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|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

---

End point timeframe:

Baseline to Week 52

---

|                             |                                    |  |  |  |
|-----------------------------|------------------------------------|--|--|--|
| <b>End point values</b>     | Escalation<br>Study of<br>CCX140 B |  |  |  |
| Subject group type          | Reporting group                    |  |  |  |
| Number of subjects analysed | 5 <sup>[8]</sup>                   |  |  |  |
| Units: Participants         | 0                                  |  |  |  |

Notes:

[8] - No subjects achieved complete remission

### Statistical analyses

---

No statistical analyses for this end point



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Day 1 to week 52

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 20.1 |
|--------------------|------|

### Reporting groups

|                       |                              |
|-----------------------|------------------------------|
| Reporting group title | Escalation Study of CCX140 B |
|-----------------------|------------------------------|

Reporting group description:

All enrolled subjects will initially be treated with the active study medication CCX140-B at a dose of 5 mg twice daily. Dose will increase in a step-wise fashion up to 15 mg twice daily.

| Serious adverse events                            | Escalation Study of<br>CCX140 B |  |  |
|---------------------------------------------------|---------------------------------|--|--|
| Total subjects affected by serious adverse events |                                 |  |  |
| subjects affected / exposed                       | 0 / 5 (0.00%)                   |  |  |
| number of deaths (all causes)                     | 0                               |  |  |
| number of deaths resulting from adverse events    | 0                               |  |  |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events                            | Escalation Study of<br>CCX140 B |  |  |
|-------------------------------------------------------|---------------------------------|--|--|
| Total subjects affected by non-serious adverse events |                                 |  |  |
| subjects affected / exposed                           | 4 / 5 (80.00%)                  |  |  |
| Investigations                                        |                                 |  |  |
| Amylase increased                                     |                                 |  |  |
| subjects affected / exposed                           | 1 / 5 (20.00%)                  |  |  |
| occurrences (all)                                     | 1                               |  |  |
| Blood creatine phosphokinase increased                |                                 |  |  |
| subjects affected / exposed                           | 1 / 5 (20.00%)                  |  |  |
| occurrences (all)                                     | 1                               |  |  |
| Blood potassium increased                             |                                 |  |  |
| subjects affected / exposed                           | 1 / 5 (20.00%)                  |  |  |
| occurrences (all)                                     | 1                               |  |  |
| Lipase increased                                      |                                 |  |  |

|                                                                                                                                                                                                                                                                     |                                                                           |  |  |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------|--|--|
| subjects affected / exposed<br>occurrences (all)                                                                                                                                                                                                                    | 1 / 5 (20.00%)<br>1                                                       |  |  |
| Injury, poisoning and procedural complications<br>Laceration<br>subjects affected / exposed<br>occurrences (all)                                                                                                                                                    | 1 / 5 (20.00%)<br>1                                                       |  |  |
| Nervous system disorders<br>Hypoaesthesia<br>subjects affected / exposed<br>occurrences (all)<br><br>Ophthalmoplegic migraine<br>subjects affected / exposed<br>occurrences (all)                                                                                   | 1 / 5 (20.00%)<br>1<br><br>1 / 5 (20.00%)<br>1                            |  |  |
| General disorders and administration site conditions<br>Fatigue<br>subjects affected / exposed<br>occurrences (all)<br><br>Oedema peripheral<br>subjects affected / exposed<br>occurrences (all)<br><br>Pyrexia<br>subjects affected / exposed<br>occurrences (all) | 1 / 5 (20.00%)<br>2<br><br>1 / 5 (20.00%)<br>1<br><br>1 / 5 (20.00%)<br>1 |  |  |
| Ear and labyrinth disorders<br>Vertigo<br>subjects affected / exposed<br>occurrences (all)                                                                                                                                                                          | 1 / 5 (20.00%)<br>1                                                       |  |  |
| Gastrointestinal disorders<br>Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all)<br><br>Nausea<br>subjects affected / exposed<br>occurrences (all)<br><br>Tongue discomfort                                                                   | 1 / 5 (20.00%)<br>1<br><br>1 / 5 (20.00%)<br>3                            |  |  |

|                                                                                                                                                                                                                                                                                                              |                                                                                              |  |  |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Vomiting</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                                                                                                      | <p>1 / 5 (20.00%)</p> <p>1</p> <p>1 / 5 (20.00%)</p> <p>3</p>                                |  |  |
| <p>Respiratory, thoracic and mediastinal disorders</p> <p>Dyspnoea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Nasal congestion</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                       | <p>1 / 5 (20.00%)</p> <p>1</p> <p>1 / 5 (20.00%)</p> <p>1</p>                                |  |  |
| <p>Renal and urinary disorders</p> <p>End stage renal disease</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Renal impairment</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                            | <p>1 / 5 (20.00%)</p> <p>1</p> <p>1 / 5 (20.00%)</p> <p>1</p>                                |  |  |
| <p>Musculoskeletal and connective tissue disorders</p> <p>Limb discomfort</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Muscular weakness</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Tendonitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 5 (20.00%)</p> <p>1</p> <p>1 / 5 (20.00%)</p> <p>1</p> <p>1 / 5 (20.00%)</p> <p>1</p> |  |  |
| <p>Infections and infestations</p> <p>Nasopharyngitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pulpitis dental</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                                     | <p>1 / 5 (20.00%)</p> <p>1</p> <p>1 / 5 (20.00%)</p> <p>1</p>                                |  |  |

|                                                                                       |                     |  |  |
|---------------------------------------------------------------------------------------|---------------------|--|--|
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 1 / 5 (20.00%)<br>2 |  |  |
| Metabolism and nutrition disorders                                                    |                     |  |  |
| Hyperkalaemia<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 5 (20.00%)<br>1 |  |  |
| Hyperlipidaemia<br>subjects affected / exposed<br>occurrences (all)                   | 1 / 5 (20.00%)<br>1 |  |  |
| Hyperphosphataemia<br>subjects affected / exposed<br>occurrences (all)                | 1 / 5 (20.00%)<br>1 |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date          | Amendment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|---------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 27 April 2018 | <p>Amendment 1.0</p> <p>Moved partial and complete remission from primary to secondary objectives and redefined them and evaluated median reduction of UPCR as primary efficacy</p> <p>Added several equations to calculate eGFR equations based on FDA recommendation in study CL011_140</p> <p>The full list of conditions for subjects being allowed to enter the extended treatment was provided</p> <p>Emphasis added on the importance of 24h urine collection</p> <p>Language added in Dose Modification Based on PK Exposure section</p> <p>Changes made to exclusion numbering as well as addition of exclusion Histological FSGS subtype of collapsing variant</p> <p>Addition of History of gastrointestinal conditions, and medications to exclusion criteria</p> <p>Additional information added for concomitant medications</p> <p>Updated guidelines for reporting of pregnancies and special situation reporting and updated contact information (Medpace) for SAE reporting</p> <p>Addition of Clinical Pharmacologist to SRC and Rescue Therapy</p> <p>Clarifications made throughout for:</p> <p>Dose and dose adjustments</p> <p>Dose modification rules for individual subjects</p> <p>Standardization of all titration requirements on day 43 or beyond, and extended treatment period with the initial treatment period.</p> <p>Adjustment from at least 30% to <math>\geq 20\%</math> reduction in UPCR</p> <p>The acronym ACTG-BPNS was changed to ACTG-BPNST</p> <p>Detail added onto primary FSGS factors</p> <p>Further clarification made on exclusions i.e. intended exclusion/use of calcineurin inhibitors, or other immunotherapy, Glucocorticoids, addition of international normalized ratio (INR) blood-clotting test, change of QTc to QTcF, two separate criteria for drug exclusion and medication exclusion and CYP3A4 inhibitors and inducers excluded.</p> <p>Removed references to the CTCAE in adverse event reporting</p> <p>Clarity added to the time and events table and footnotes</p> <p>As well as additional administrative and grammatical changes throughout.</p> |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was terminated early due to data from CL011\_140 study showing that CCX140-B didn't demonstrate a meaningful reduction in proteinuria relative to the control group after 12 weeks of blinded treatment.

Notes: