Inclusion Criteria (cont'd):	4. At initial screening assessment and at last qualifying assessment during screening period prior to baseline, FSGS subjects must have a urine protein creatinine ratio (UPCR) of ≥2.0 mg/mg. Subjects can be treatment-naïve or receiving steroid treatment (oral or IV) for FSGS. Subjects taking steroids must show signs of improvement in proteinuria, defined as at least a 20% improvement in UPCR from initiation of steroids to the last stability assessment prior to baseline. Subjects who have discontinued steroid treatment due to poor tolerability may be considered for the study. Subjects should also have a serum albumin level of ≤3.2 g/dL at screening and at the last qualifying assessment prior to baseline; subjects with serum albumin >3.2 g/dL may be included following review to confirm primary FSGS and after discussion with the Medical Monitor. 5. All subjects should be treated with angiotensin converting enzyme inhibitors (ACEIs) and/or angiotensin receptor blockers (ARBs) unless they have documented intolerance or contraindication to these medications. Doses of these agents must be stable for at least 2 weeks prior to baseline, with blood pressure (BP) ≤150/90 mmHg at the baseline visit (Visit 2). a) Subjects with nephrotic edema may be treated with diuretics during the screening period. Volume status should be optimized based on the clinical judgment of the Investigator and the doses of diuretics must be stable for at least 2 weeks prior to baseline. b) At the discretion of the Investigator, subjects with hyperlipidemia may be treated with lipid-lowering agents (e.g., statins) in accordance with standard clinical practice. Doses must be stable for at least 2 weeks prior to baseline. 6. Stable proteinuria, renal function, and BP for at least 2 weeks prior to baseline, as assessed by the Investigator. Changes in UPCR, estimated glomerular filtration rate (eGFR), and/or BP during the screening period may be due to treatments administered (e.g., ACEIs and ARBs); and, therefore, may interfere with study assessments or outcomes, or may place the subject at increased risk. All subjects must be discussed with the Medical Monitor prior to initiation of study treatment. 7. Women of childbearing potential must have a negative serum pregnancy test prior to dispensing study treatment. Two effective forms of contraception must be used simultaneously unless abstinence is the chosen method. Subjects must use effective contraception during the study.
Exclusion Criteria:	1. Subjects unable or unwilling to give written informed consent and/or to comply with study procedures. 2. Clinical or histologic evidence of secondary FSGS. 3. Histologic evidence of collapsing variant FSGS. 4. eGFR as calculated by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation of ≤30 mL/minute/1.73 m^2 at initial screening assessment or ≤45 mL/minute/1.73 m^2 at last qualifying assessment during screening period prior to baseline.

1 Stability assessments to occur at 14-day intervals (± 3 days) with first assessment approximately 2 weeks after the screening visit. Stability assessments 1 and 2 are mandatory; assessments 3 and 4 are optional if additional time is required for the subject's clinical status to stabilize. Note that the laboratory assessments and FMV results of the last stability assessment will be used as the qualifying values for eligibility. Enrollment of eligible subjects must occur within 1 week of the final stability assessment.

2 If a subject has not had a recent renal biopsy, one may be performed to assess eligibility for the study provided informed consent has been given. The biopsy must have been performed 6 months prior to the screening visit. Biopsy results over 6 months prior to screening may be permitted following review with the Medical Monitor to confirm eligibility. Repeat renal biopsies may be done at Week 24 in a subset of subjects at selected sites.

3 Complete physical exam at screening; abbreviated exam at all other visits.

4 BP, pulse, temperature, weight, and height. Height included at initial screening assessment only. At stability assessments, BP only will be included.

5 In the event that a subject is noted to have a QTcF value exceeding 500 msec, or an increase of >60 msec from baseline, the ECG should be repeated within 24 hours. Further details provided in the study protocol.

6 Laboratory assessments will be performed according to the schedule in the study protocol. Subjects must be fasting for at least 8-12 hours at Baseline and at end of study/early termination visit.

7 Pharmacokinetic assessments will be done at Weeks 4 and 24. PK samples will be drawn prior to study treatment dosing (trough sample), and at 1, 2 and 4 hours post-dose. In the event a subject experiences an SAE or requires a dose modification or is withdrawn from treatment, a voclosporin sample should be taken, with a trough sample preferred.

8 The UPCR will be calculated both from the FMV and from standard urinalysis results. If the FMV is for some reason not available, then standard urinalysis from a 24-hour urine collection may be substituted as an exception but only after agreement is reached with the Medical Monitor.

9 24-hour urine collection should begin 2 days prior to the scheduled study visit in order not to coincide with the FMV sampling due on the day of the study visit.

10 Patient Reported Outcome Measurement Information system (PROMIS) and Kidney Disease Quality of Life-Short Form (KDQOL-SF™).

11 Serum pregnancy test to be evaluated at central laboratory at Screening and Week 24; urine pregnancy test will be performed locally at all other visits as applicable.

12 If screening visit occurs on the same day as informed consent, any findings are to be recorded as Medical History. Any change since the date of signed consent and/or during the screening period would be considered an AE.

13 Subjects in Cohort 1, will be contacted by telephone at the end of Week 1 as a reminder to increase their dose to 2 capsules (15.8 mg) BID for 1 week, starting at Week 2. Subjects will be contacted again by telephone at the end of Week 2 as a reminder to increase their dose to 3 capsules (23.7 mg) BID, starting at Week 3, for the remainder of the treatment period. Subjects in Cohort 2, will also be contacted at the end of each week (as required) up to Week 4, as a reminder to increase their dose to the maximum selected for Cohort 2.

14 Compliance only.

15 First dose of study medication should occur in the morning the day after dispensing.

Notes: Subjects who discontinue therapy will be requested to attend their regularly scheduled study visits to the end of the study.
AE = Adverse event; BID = Twice daily; BP = Blood pressure; Disc. = Discontinuation; ECG = Electrocardiogram; FMV = First morning void; Min = Minimum; QoL = Quality of life; QTcF = QT interval duration corrected for heart rate using method of Fridericia; SAE = Serious adverse event; Wk= Week.

GMP	Good Manufacturing Practice
HIV	Human immunodeficiency virus
HR	Heart rate
IB	Investigator's Brochure
ICF	Informed consent form
ICH	International Council for Harmonisation
IEC	Independent Ethics Committee
IRB	Institutional Review Board
ISA247	Voclosporin
ITT	Intent-to-treat
IV	Intravenous
KDIGO	Kidney Disease: Improving Global Outcomes
KDQOL-SF™	Kidney Disease Quality of Life-Short Form
LN	Lupus nephritis
MMF	Mycophenolate mofetil
NSAID	Non-steroidal anti-inflammatory drug
OR	Odds ratio
PD	Pharmacodynamic
P-gp	P-glycoprotein
PK	Pharmacokinetic
PO	Orally
PPS	Per-protocol set
PROMIS	Patient Reported Outcome Measurement Information System
QoL	Quality of life
QTcF	QT interval duration corrected for heart rate using method of Fridericia
SAE	Serious adverse event
SAP	Statistical analysis plan
SD	Standard deviation
$t_{1/2}$	Terminal elimination half-life

- Change from baseline in UPCR at each time point
- Proportion of subjects with a confirmed >30% decrease from baseline in eGFR (utilizing the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula) at each time point
- Proportion of subjects with a confirmed >30% increase in eGFR from the final visit (Week 24 or last on-treatment visit, for subjects who discontinue prematurely) to the second Safety Follow-up visit (Visit 10)
- Change in UPCR from the final visit (Week 24 or last on-treatment visit, for subjects who discontinue prematurely) to the second Safety Follow-up visit (Visit 10)
- Change in eGFR from the final visit (Week 24 or last on-treatment visit, for subjects who discontinue prematurely) to the second Safety Follow-up visit (Visit 10)
- Change from baseline in serum creatinine, serum albumin, and eGFR at each time point
- Quality of life (QoL) assessments
  - Mean change in Patient Reported Outcome Measurement Information System (PROMIS) measures at Week 24
  - Change from baseline in Kidney Disease Quality of Life-Short Form (KDQOL-SF^{TM}) score at Week 24
- Safety and tolerability over 24 weeks
- Renal biopsy: descriptive analyses of changes in histopathology will be evaluated in post-treatment (24 weeks) renal biopsies in a subset of patients
- Change from baseline to Week 4 and 24 in the following biomarkers:
  - Urine nephrin
  - Urine synaptopodin
  - Serum TGF-β

will be assessed as well. For subject withdrawal procedures and criteria, see Section 5.5, Withdrawal of Subjects.

4.2 Duration of Subject Participation and Study

The expected duration of subject participation is up to 36 weeks. The duration of the screening period will be approximately 4 weeks to 10 weeks (allowing for visit windows) and the treatment duration is 24 weeks, with further Safety Follow-up visits at 1 and 2 weeks after last dose (completion or withdrawal).

is discontinued due to an AE, the event should be followed by the Investigator through contact with the subject until resolution or stabilization has occurred. All AEs should be followed until resolution, stabilization or the subject is lost to follow-up and cannot be contacted.

Test Type	Test Parameters	Collection at Visits
Coagulation	Coagulation Activated partial thromboplastin time (aPTT) Prothrombin time (PT) Partial thromboplastin time (PTT)	Screening
Blood Chemistry	Alanine aminotransferase (ALT) Albumin Alkaline phosphatase (ALP) Aspartate aminotransferase (AST) Bicarbonate Bilirubin (direct and total) Blood urea nitrogen (BUN) Calcium Chloride	All
	Cholesterol (total, HDL, and LDL) & triglycerides Creatine kinase	Day 1 and Week 24
	Creatinine Gamma-glutamyl transferase (GGT) Glucose	All
	Glycosylated hemoglobin (HbA1c)	Day 1 and Week 24
	Lactic dehydrogenase (LDH) Magnesium	All
	Phosphorous, inorganic	Day 1 and Week 24
	Potassium Protein, total Sodium	All
Urinalysis and urine microscopy	Complete urinalysis (to include urine protein, creatinine, blood, urine microscopy).	All except for stability assessment visits during the screening period
FMV urine collection	FMV will be performed to analyze UPCR.	All
24-hour urine	UPCR	Day 1, Week 12 and Week 24 Note that 24-hour urine collection should be scheduled so as not to coincide with the FMV sampling due on the day of the study visit

9.1.3 Vital Signs

The following vital signs will be measured in accordance with the Schedule of Events:

- Resting BP (systolic and diastolic)
- Resting heart rate (HR)
- Body temperature (°C or °F)
- Weight (kg)
- Height (cm)

To avoid variability, the same method of obtaining body temperature should be used throughout the study.

At stability assessments, BP only will be included.

Height will be recorded at the initial screening assessment only.

9.1.3.1 Blood Pressure Management

Blood pressure and HR will be measured with the subject in a sitting position after 5 minutes of rest. The procedure for standardized measurement of BP is detailed in Appendix 2.

If the mean BP measure is >130/80 mmHg (determined by the mean of the second and third repeats of 3 readings), the subject's BP will be managed per local practice. If the BP remains uncontrolled with the maximal doses of first- and second-line antihypertensive therapies referenced in Appendix 1, then the Investigator should contact the Medical Monitor to consider dose adjustment of the study treatment. See Section 7.7, Increased Blood Pressure for management of increased BP.

9.1.4 Standard 12-lead Electrocardiogram

The electrocardiogram (ECG) will be a standard 12-lead tracing performed at the investigational site, assessed by a qualified physician at the investigational site, and retained as a source document. Any abnormalities will be recorded in the eCRF. Electrocardiograms will be recorded after the subject has been in a resting, supine position for at least 5 minutes. Abnormal ECG tracings can be reviewed by the Medical Monitor. Significant abnormalities, including findings that may prompt discontinuation of study treatment, must be discussed with the Medical Monitor.

Electrocardiograms will be measured at the initial screening assessment, Day 1, and Week 24.

schedule back on track in order to avoid large variances in treatment exposure or to avoid delaying overall study timelines.

9.2.1 Screening Visit and Stability Assessment Procedures

The duration of the screening period will be approximately 4 weeks to 10 weeks (allowing for visit windows) and will consist of an initial screening assessment and 2 to 4 stability assessments to ensure that subjects meet eligibility criteria.

The initial screening assessment will include provision of informed consent; complete physical examination; medical history (including FSGS history); vital signs measurements, including weight and height; 12-lead ECG; blood and urine sample collection for central laboratory assessments, urinalysis, and urine microscopy; FMV urine collection (for determination of UPCR); a serum pregnancy test (for women of childbearing potential); and review of prior and concomitant medications and entry criteria. Following these assessments and if clinically indicated, subjects receiving steroids may start reducing their steroid dose as described in the corticosteroid dosing guidelines (see Section 7.1.2.2, Corticosteroids). Any AEs which occur after informed consent will be recorded.

Stability assessments will occur at 14-day intervals (±3 days) with the first assessment approximately 2 weeks after the initial screening assessment visit. Stability assessments 1 and 2 are mandatory; assessments 3 and 4 are optional if additional time is required for the subject's clinical status to stabilize. These stability assessment visits will include BP determination; blood sample collection for central laboratory assessments; FMV urine collection (for determination of UPCR); a serum pregnancy test (for women of childbearing potential); review of any AEs; and review of concomitant medications and entry criteria.

These renal disease stability assessments will be evaluated to ensure eligibility with respect to entry criteria for UPCR and eGFR.

Note that the laboratory assessments and FMV results of the last stability assessment will be used as the qualifying values for eligibility.

FMV urine samples (for determination of UPCR) will be collected at all visits during the screening period and must be returned and the results evaluated prior to Baseline/Day 1. If the FMV is for some reason not available at Day 1, Week 12 or Week 24, standard urinalysis from a 24-hour urine collection may be substituted as an exception but only after agreement is reached with the Medical Monitor.

Blood samples will be drawn according to Table 1.

If the subject is from an area where TB is endemic or whose history suggests an increased personal risk, e.g., from contact with people with TB or travel to areas with endemic TB, the subject will be carefully evaluated for latent or active TB.

10. EVALUATION, RECORDING AND REPORTING OF AEs AND SAEs

10.1 Definitions

10.1.1 Adverse Event

Any untoward medical occurrence in a subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment is an AE. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product.

10.1.2 Adverse Drug Reaction

In the pre-approval clinical experience with a new medical product or its new usages, particularly as the therapeutic dose(s) may not be established, all unintended responses to a medicinal product related to any dose should be considered adverse drug reactions (ADRs). The phrase "responses to a medicinal product" means that a causal relationship between a medicinal product and an AE is at least a reasonable possibility, i.e., the relationship cannot be ruled out.

10.1.3 Serious Adverse Event

An SAE (experience) or reaction is an untoward medical occurrence that at any dose meets one or more of the following criteria:

- Results in death (Note: death is an outcome, not an event)
- Is life-threatening (Note: the term "life-threatening" refers to an event in which the subject was at immediate risk of death at the time of the event; it does not refer to an event which could hypothetically have caused a death had it been more severe)
- Requires in-patient hospitalization or prolongation of existing hospitalization
- Results in persistent or significant disability/incapacity
- Results in a congenital anomaly/birth defect
- Is a medically important event or reaction

The definitions and reporting requirements of International Council for Harmonisation (ICH) Guidelines for Clinical Safety Data Management, Definitions, and Standards for Expedited Reporting, Topic E2 will be adhered to.

Medical and scientific judgment must be exercised in deciding whether expedited reporting is appropriate in other situations, such as important medical events that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the subject or may require intervention to prevent one of the other outcomes listed in the definition above. These events will also usually be considered serious.

Hospitalizations that have been scheduled prior to the subject signing the informed consent form (ICF), although not recorded as SAEs, must be documented in the subject's source documents. A renal biopsy performed as part of the study to verify eligibility will not be considered an SAE. Any complication experienced during a renal biopsy procedure resulting in hospitalization or a prolongation of the hospitalization requires SAE reporting.

10.1.4 Suspected Unexpected Serious Adverse Reaction

Any ADR that is both serious and unexpected (per the IB) that, based on the opinion of the Investigator or Aurinia, is felt to have a reasonable suspected causal relationship to a medicinal product is a suspected unexpected serious adverse reaction.

10.2 Adverse Event Descriptors

10.2.1 Intensity/Severity Categorization

The term "severe" is often used to describe the intensity (severity) of a specific event (as in mild, moderate, or severe myocardial infarction); however, the event itself may be of relatively minor medical significance (such as severe headache). This is not the same as "serious," which is based on subject/event outcome or action criteria usually associated with events that pose a threat to a subject's life or ability to function. Seriousness (not severity) serves as a guide for defining regulatory reporting obligations.

In general, the intensity of a particular AE to be recorded is the worst intensity experienced by the subject during the course of the event. The medical assessment of intensity will be determined by using the following definitions:

Mild: The AE is easily tolerated and does not interfere with usual activity.

Moderate: The AE interferes with daily activity, but the subject is still able to function.

Severe: The AE is incapacitating and the subject is unable to work or complete usual activity.

10.2.2 Causal Relationship Categorization

An Investigator who is qualified in medicine must make the determination of relationship to the study treatment for each AE and SAE. The Investigator must decide whether, in his or her medical judgment, there is a reasonable possibility that the event may have been caused by the

study treatment. If there is no valid reason for suggesting a relationship, then the AE/SAE must be classified as not related. Otherwise, if there is any valid reason, even if undetermined or untested, for suspecting a cause-and-effect relationship between the study treatment and the occurrence of the AE/SAE, then the AE/SAE will be considered related. For SAEs, the Investigator must provide a brief comment explaining the rationale of his/her assessment of causal relationship on the SAE reporting form.

The following additional guidance may be helpful:

Term	Relationship	Definition
Related	Yes	The temporal relationship of the clinical event to study treatment administration indicates a causal relationship, and other drugs, therapeutic interventions or underlying conditions do not provide a sufficient explanation for the observed event.
Not related	No	The temporal relationship of the clinical event to study treatment administration does not indicate a causal relationship, or other drugs, therapeutic interventions or underlying conditions provide a sufficient explanation for the observed event.

If the causal relationship between an AE/SAE and the study treatment is determined to be "related", the event will be considered to be related to study treatment for the purposes of expedited regulatory reporting. In circumstances where the Investigator has not yet provided his/her assessment about the relationship, the event will be considered as "related" and qualify for expedited regulatory reporting.

10.2.3 Outcome Categorization

Outcome may be classified as recovered without sequelae; recovered with sequelae; improved; worsened; ongoing; ongoing at end of study; fatal; or unknown. If the outcome is reported as recovered with sequelae for an SAE, the Investigator should specify the kind of sequelae on the SAE reporting form. SAEs that are ongoing at the time of death will have an outcome of "unknown" recorded. SAEs resulting in a fatal outcome will have an outcome of "fatal" recorded.

10.2.4 Clinical Laboratory Evaluations

A change in the value of a safety laboratory investigation can represent an AE if the change is clinically relevant in the opinion of the Investigator or if, during treatment with the study treatment, a shift of a parameter is observed from a normal value to a pathological value, or a further worsening of an already pathological value.

If, at the end of the treatment phase, there are pathological laboratory values which were not present at baseline, further clinical or laboratory investigations will be performed until the values return to within reference range or until a plausible explanation (e.g., concomitant disease) is found for the pathological laboratory values.

If the Investigator considers such an AE as serious it must be reported as an SAE.

10.2.5 Abuse, Misuse, Overdose and Medication Error

All AEs of special interest such as study drug abuse, misuse, overdose, and medication error have to be documented in the subject's eCRF and source documentation. If any occurrence of abuse, misuse, overdose, or medication errors leads to any event that fulfils any seriousness criteria, the event has to be reported as an SAE.

10.3 Reporting Procedure for AEs, SAEs, and Pregnancy

10.3.1 Adverse Events

All AEs observed from time of signing of the ICF will be recorded in the subject's source documentation. This applies to all AEs regardless of presumed relationship to the study drug. For screen failure subjects, any AEs and SAEs occurring during the screening period (after informed consent) will be recorded in the subject's source documentation only and will not be collected on the eCRF. Adverse events leading to discontinuation of study drug must be collected.

If any AE is reported, the date of onset, relationship to study treatment, relationship to disease under study, any action taken, date of resolution (or the fact that it is still continuing or has become chronic), outcome, and whether the AE is serious or not, will be recorded. Use of colloquialisms and abbreviations should be avoided. Only one AE term should be recorded in the event field on the AE eCRF. Where possible, the Investigator should report a diagnosis rather than signs and symptoms or abnormal laboratory values. However, if a constellation of signs and/or symptoms cannot be medically characterized as a single diagnosis or syndrome at the time of reporting, each individual event should be recorded on the AE eCRF. If a diagnosis is subsequently established, all previously reported AEs based on signs and symptoms should be nullified and replaced by one AE report based on the single diagnosis, with a starting date that corresponds to the starting date of the first symptom of the eventual diagnosis.

The AE reporting period begins at the time the ICF is signed by the subject. Note that for screen failure subjects, any AEs and SAEs occurring during the screening period will be recorded in the subject's source documentation only. For enrolled subjects (i.e., those who successfully complete screening), the AE reporting period ends at the second Safety Follow-up visit (Visit 10). Adverse events persisting at the time of study completion will be followed by the Investigator through contact with the subject until resolution or stabilization has occurred (or the subject is lost to follow-up and cannot be contacted) and recorded in the source documents. If the subject reports an AE, it is the Investigator's responsibility to acquire sufficient information in order to assess causality. This may require additional laboratory testing, physical examinations, telephone contacts, etc. In circumstances where the Investigator is unable to make contact with the subject, the Investigator must provide a written statement to Aurinia confirming that the subject is lost to follow-up.

In order to avoid bias in eliciting AEs, subjects should be asked a non-leading question, such as "How are you feeling?" It is also important to question the subject in a non-leading way about changes in their health or concomitant medication usage since their last visit. This information should be collected prior to completion of assessments at all study visits. In addition, any symptoms/conditions reported during assessments and deemed to be clinically significant by the Investigator will be considered AEs.

10.3.2 Serious Adverse Events

For screen failure subjects, any SAEs occurring during the screening period (after informed consent) will be recorded in the subject's source documentation only and will not be collected on the eCRF.

For enrolled subjects (i.e., those who successfully complete screening), all SAEs occurring after the signing of the ICF will be reported to [redacted] within 24 hours of the Investigator, designee, or site staff's knowledge of the event regardless of relationship to study drug or relationship to disease under study. For enrolled subjects, all SAEs will be recorded in the AE section of the subject's eCRF and source documentation.

In the event that the site experiences a temporary disruption of the EDC system a back-up paper SAE Reporting Form will be available for site staff to complete.

- Site staff will complete the paper SAE report form and e-mail it within 24 hours to the following address: [redacted]
- Only in cases where the email system is unavailable, site staff will send the SAE by fax to: [redacted].

If notification is made via email or fax, site staff must enter the SAE information into the EDC system as soon as the system becomes available.

All SAEs, regardless of causality, will be reported from the time the ICF is signed until 30 days following the last study visit or 30 days after last study treatment administration, whichever is longer. No formal study visit is required but Investigators must report any SAEs that occur during this 30-day period using the SAE reporting form provided; these will be entered into the safety database only. If the Investigator has not seen the subject at a clinic visit at the end of the reporting period, the Investigator must make reasonable efforts to contact the subject to inquire about SAEs.

All recorded SAEs, regardless of relationship to study treatment or relationship to disease under study, will be followed up until resolution, stabilization, or the subject is lost to follow-up and cannot be contacted. In circumstances where the Investigator is unable to make contact with the subject, the Investigator must provide a written statement to Aurinia confirming that the subject is lost to follow-up.

Any SAE considered to have a causal relationship (i.e., "related") to the study treatment and discovered by the Investigator at any time after the study will be reported. A rationale for the assessment of a causal relationship must be provided by the Investigator. Any safety information that is obtained after the Follow-up Visit (Visit 9) will be documented in the safety database only.

A death occurring during the study or which comes to the attention of the Investigator within 30 days after the last study visit (including the Follow-up Visit) or until 30 days after the last study treatment administration, whichever is longer, whether considered drug-related or not, must be reported to Aurinia. If the subject died, the SAE report should include the cause of death as the event term and whether or not the death was related to study treatment, as well as the autopsy findings, if available. Preliminary reports will be followed by detailed descriptions which will include copies of hospital case reports, autopsy reports/certificates and other documents when requested and applicable.

Additional follow-up information must be reported in the eCRF within 24 hours of awareness following Investigator (or site) awareness of the information. The Investigator should not delay reporting an SAE in order to obtain additional information. Additional information, when available, should be reported to [redacted] by the reporting procedures described above.

The Investigator is encouraged to discuss with the study Medical Monitor when the issue of seriousness is unclear or questionable.

An investigator who receives an investigator safety report describing an SAE or other specific safety information (e.g., summary or listing of SAE) from the sponsor will file it along with the IB and will notify the Institutional Review Board (IRB)/Ethics Committee (EC)/Independent Ethics Committee (IEC), if appropriate according to local requirements.

The sponsor or its representative will be responsible for determining and, in turn, reporting SAEs to regulatory authorities according to the applicable regulatory requirements.

10.3.3 Pregnancy

Pregnancy occurring in a female subject or in the partner of a male subject should be reported to [redacted] within 24 hours of becoming aware of the event using the pregnancy eCRF. The Investigator should counsel the subject, and in the case of a male subject, the subject's partner, discuss the risks of continuing with the pregnancy and the possible effects on the fetus. A female subject must immediately inform the Investigator if she becomes pregnant during the study. Monitoring of the pregnancy in a female subject should continue until conclusion of the pregnancy. In case of a pregnancy in the partner of a male subject, the Investigator should obtain informed consent of the pregnant partner prior to monitoring of the pregnancy.

12. DATA AND SAFETY MONITORING BOARD PROCEDURES

Not applicable.

- Time to first occurrence of partial remission of proteinuria
- Time to first occurrence of 50% reduction in UPCR from baseline
- Duration of UPCR <0.3 mg/mg
- Change from baseline in UPCR at each time point
- Proportion of subjects with a confirmed >30% decrease from baseline in eGFR (utilizing the CKD-EPI formula) at each time point (Baseline eGFR is defined as the last assessment prior to first dose of study treatment)
- Proportion of subjects with a confirmed >30% increase in eGFR from the final visit (Week 24 or last on-treatment visit, for subjects who discontinue prematurely) to the second Safety Follow-up visit (Visit 10)
- Change in UPCR from the final visit (Week 24 or last on-treatment visit, for subjects who discontinue prematurely) to the second Safety Follow-up visit (Visit 10)
- Change in eGFR from the final visit (Week 24 or last on-treatment visit, for subjects who discontinue prematurely) to the second Safety Follow-up visit (Visit 10)
- Change from baseline in serum creatinine, serum albumin, and eGFR at each time point
- QoL assessments
  - Mean change in PROMIS measures at Week 24
  - Change from baseline in KDQOL-SF^{TM} score at Week 24
- Safety and tolerability over 24 weeks
- Renal biopsy: descriptive analyses of changes in histopathology will be evaluated in post-treatment (24 weeks) renal biopsies in a subset of patients
- Change from baseline to Week 4 and 24 in the following biomarkers:
  - Urine nephrin
  - Urine synaptopodin
  - Serum TGF-β

- AE profile and routine biochemical and hematological safety parameters
- Vital signs (BP, HR, temperature) at specific time points and change from baseline
- Standard 12-lead ECGs change from baseline
- Discontinuations from treatment
- Concomitant medications

Laboratory values, vital signs, and other safety parameters providing numeric data will be summarized by visit, and as change from baseline.

Adverse events and diseases will be coded using the latest available version of the Medical Dictionary for Regulatory Activities, the version of which will be provided in the clinical study report.

Treatment-emergent adverse events will be summarized by treatment arm, System Organ Class, and Preferred Term. SAEs, SAEs that led to death, and SAEs/AEs that led to withdrawal will also be summarized and listed.

Only AEs which started on or after the date of first dose of study treatment and up until 14 days after last dose will be considered TEAEs, though all AEs after informed consent will be recorded. SAEs occurring at any time after informed consent and prior to first study medication will be listed.

All prior and concomitant medications will be summarized using preferred terms and ATC Level 2.

Details of these and other analyses will be provided in the SAP.

All study data analyses involving laboratory values will be based on results from the central laboratory.

13.11 Interim Analyses

There will be no full interim analysis.

13.12 Other Evaluations

13.12.1 Pharmacokinetics

Estimates of voclosporin exposure derived from this analysis will be examined for possible relationship to measures of efficacy and safety. Full details will be described in a separate analysis plan.

14. ETHICAL CONDUCT OF THE STUDY

The study will be conducted according to the principles of the World Medical Association's Declaration of Helsinki [28] and the ICH guidelines for GCP [29]. Aurinia will ensure that the study complies with all local, federal, and country regulatory requirements.

The Investigator must ensure the confidentiality of all subjects participating in the study.

All anonymous data remains the property of Aurinia.

14.1 Informed Consent

The ICF used for the study must comply with the Declaration of Helsinki, federal regulations, and ICH guidelines; and must have been approved by the IRB/EC/IEC prior to use. The Investigator or an authorized associate must explain the nature of the study and the treatment in such a manner that the subject is aware of potential benefits and risks. Subjects must also be informed that participation is voluntary and that they may withdraw from the study at any time, without prejudice. Subjects must be provided sufficient time to consider participation, including discussion with family members prior to signing the ICF. Documentation of the discussion and the date of informed consent must be recorded in the source documentation. After signing the ICF, subjects will be enrolled into the study and assigned a subject identification number that will be used on all subject documentation.

The informed consent can be signed up to 30 days before the screening Visit 1. If more than 30 days elapses between date of consent and the screening Visit 1, the subject should be asked to re-sign and date the consent form to confirm continued interest in study participation.

14.2 Institutional Review Board or EC/IEC

The protocol, any protocol amendments and consent form for the proposed clinical study and any other documents required by the local IRB/EC/IEC must be submitted by the Investigator for review and approval to the IRB/EC/IEC. The Investigator must also ensure that the IRB/EC/IEC reviews the progress of the study on a regular basis and, if necessary, renews its approval of the study per local requirements.

Appendix 3 Classification of FSGS

The epidemiology, classification and pathogenesis of FSGS has been reviewed by Reiser et al, 2017 [33].

According to this review, FSGS "is a histologic lesion, rather than a specific disease entity, that is commonly found to underlie the nephrotic syndrome in adults and children, particularly in the United States, Brazil, and many other countries. FSGS is characterized by the presence of sclerosis in parts (segmental) of some (focal) glomeruli on light microscopic examination of a kidney biopsy specimen."

According to this review, FSGS can be classified into the following etiologies, based upon the known and/or postulated causes of this histologic pattern:

- "Primary or idiopathic FSGS, which most often presents with the nephrotic syndrome."
- "Secondary FSGS, which most often presents with non-nephrotic proteinuria and, commonly, some degree of renal insufficiency. This category most commonly refers to FSGS that develops as an adaptive response to glomerular hypertrophy or hyperfiltration. This includes disorders associated with a reduced renal mass and/or renal vasodilation, such as unilateral renal agenesis. In addition, a nonspecific pattern of secondary FSGS can result from scarring produced by a previous injury (due to a variety of conditions, including active IgA nephropathy, vasculitis, and LN). Other secondary causes of FSGS include drugs and toxins (including heroin, interferon, and pamidronate) and viral infections (particularly HIV)."
- "Genetic causes of FSGS, which may present early in childhood with massive proteinuria and nephrotic syndrome or in adolescence or adulthood with less massive proteinuria."

Biopsy and diagnosis: According to Reiser et al, "precise quantification of sclerotic glomeruli requires three-dimensional morphometric analysis of entire glomeruli and the examination of sufficient glomeruli to ensure that the biopsy specimen is representative of glomeruli in the whole kidney. Kidney biopsies with few glomeruli (i.e., fewer than 15) cannot confidently exclude the diagnosis of FSGS, and, due to sampling error, some cases will be misclassified as minimal change disease."

"In patients who are found to have a FSGS lesion by light microscopy, the following approach can be used to distinguish between those with primary and secondary FSGS:

Exclusion Criteria (cont'd):	5. Currently taking or expected to require any of the prohibited medications listed in the protocol at screening or during the study. This includes prior use of cytotoxic or other immunosuppressant treatment for FSGS. Subjects who have discontinued steroid treatment due to lack of response are excluded from the study. 6. Currently requiring renal dialysis (hemodialysis or peritoneal dialysis) or expected to require dialysis during the study period. 7. A previous renal transplant or planned renal transplant during the study. 8. Body mass index >40 kg/m^2 at last stability assessment. 9. Family history of nephrotic syndrome. 10. Any known hypersensitivity or contraindication to cyclosporine, or components of any cyclosporine drug product. 11. Current or medical history of: • Congenital or acquired immunodeficiency. • In the opinion of the Investigator, clinically significant drug or alcohol abuse within 2 years prior to screening. • Malignancy within 5 years of screening, with the exception of basal and squamous cell carcinomas treated by complete excision. Subjects with cervical dysplasia that is cervical intraepithelial neoplasia 1, but have been treated with conization or loop electrosurgical excision procedure and have had a normal repeat Papanicolaou test are allowed. • Current or past lymphoproliferative disease or previous total lymphoid irradiation. • Severe viral infection (e.g., cytomegalovirus, hepatitis B virus, hepatitis C virus) within 3 months of screening, or known HIV infection. Severe viral infection is defined as active disease requiring antiviral therapy. • Active tuberculosis (TB) or known history of TB/evidence of old TB if not taking prophylaxis with isoniazid. 12. Other clinically significant active medical conditions, such as: • Severe cardiovascular disease including congestive heart failure, history of cardiac dysrhythmia or congenital long QT syndrome. Subjects with QT interval duration corrected for heart rate using method of Fridericia exceeding 480 msec in the presence of a normal QRS interval (<110 msec) at time of screening are excluded. • Liver dysfunction: aspartate aminotransferase, alanine aminotransferase, or bilirubin ≥2.5 times the upper limit of normal at last qualifying assessment during screening period prior to baseline. • Chronic obstructive pulmonary disease or asthma requiring oral steroids.

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TB	Tuberculosis
TEAE	Treatment-emergent adverse event
TGF-β	Transforming growth factor beta
UPCR	Urine protein creatinine ratio

4. INVESTIGATIONAL PLAN

4.1 Overall Study Design

This is a Phase 2, open-label, multicenter, prospective, 24-week, exploratory cohort study to assess the efficacy and safety of two dose levels of voclosporin in achieving complete or partial remission of proteinuria in subjects with biopsy-confirmed primary FSGS. Subjects who have provided a signed and dated informed consent will be screened into the study. Subjects will be assigned a unique subject number which will be used to identify them throughout the study. The duration of the screening period will be approximately 4 weeks to 10 weeks (allowing for visit windows (14±3 days) for each stability assessment) to ensure that subjects meet eligibility criteria, including renal disease stability assessments. If a subject has not had a renal biopsy within the 6-month (prior to screening) required timeframe for study eligibility, one may be performed to assess eligibility into the study, provided the subject has given consent and provided the results can be obtained and reviewed before baseline; biopsy results over 6 months prior to screening may be permitted following review with the Medical Monitor. Subjects who meet all of the inclusion criteria and none of the exclusion criteria will be eligible to receive treatment with voclosporin. Up to 10 subjects will be enrolled into Cohort 1, at a starting dose of 7.9 mg BID for Week 1, 15.8 mg BID for Week 2, and a target dose of 23.7 mg BID for Weeks 3 to 24. The first dose of study treatment should occur in the morning on Day 2, the day after dispensing. Subjects will be contacted by telephone at the end of Week 1 and Week 2 to be reminded to increase their dose as per Section 7.1.2.1, Voclosporin Study Treatment.

Evaluable safety and tolerability from 12 weeks of treatment in the first 5-6 subjects from Cohort 1 are required in order to determine the dose level for Cohort 2. The dose selected may be higher or lower than 23.7 mg BID. The maximum dose possible for Cohort 2 will be 39.5 mg (5 capsules) BID. Dosing in this group will follow the same cautious approach as Cohort 1, with at a starting dose of 7.9 mg BID for Week 1, 15.8 mg BID for Week 2, 23.7 mg BID for Week 3 and a maximum dose of 39.5 mg BID for Weeks 4 to 24.

Doses and dose increments smaller than anticipated or an intermediate dose may be proposed for Cohort 2 based on the safety and tolerability results from the Cohort 1.

All subjects will return for assessment of efficacy and safety at Weeks 2, 4, 8, 12, 18, and 24. See Schedule of Events, for detailed information regarding visits.

All subjects, completed or withdrawn from the study, will complete the End of Treatment/Early Termination assessments (Visit 8) at Week 24, or at the time of withdrawal, and should attend two Safety Follow-up visits at 1 and 2 weeks after completion of treatment (i.e., at Week 25 (Visit 9) and Week 26 (Visit 10)) (or 7 and 14 days, respectively, following withdrawal) to collect any new AEs and concomitant medications. At the follow-up visit, UPCR and eGFR

5. SELECTION, WITHDRAWAL OF SUBJECTS AND PERMANENT DISCONTINUATION OF DRUG

5.1 Number of Subjects

It is anticipated that approximately 20 subjects will be recruited in this study.

5.2 Inclusion Criteria

The following inclusion criteria must be met for each subject:

1. Written informed consent before any study-specific procedures are performed.

2. Male or female subjects with a minimum age of 18 years (or legal age of consent if >18 years) to 75 years of age, inclusive, at the time of consent.

3. Primary FSGS diagnosed by renal biopsy within 6 months prior to the screening visit. Biopsy results over 6 months prior to screening may be permitted following review with the Medical Monitor to confirm eligibility (see Appendix 3).

4. At initial screening assessment and at last qualifying assessment during screening period prior to baseline, FSGS subjects must have a urine protein creatinine ratio (UPCR) of ≥2.0 mg/mg. Subjects can be treatment-naïve or receiving steroid treatment (oral or intravenous (IV)) for FSGS. Subjects taking steroids must show signs of improvement in proteinuria, defined as at least a 20% improvement in UPCR from initiation of steroids to the last stability assessment prior to baseline. Subjects who have discontinued steroid treatment due to poor tolerability may be considered for the study. Subjects should also have a serum albumin level of ≤3.2 g/dL at screening and at the last qualifying assessment prior to baseline; subjects with serum albumin >3.2 g/dL may be included following review to confirm primary FSGS and after discussion with the Medical Monitor.

5. All subjects should be treated with ACEIs and/or ARBs unless they have documented intolerance or contraindication to these medications. Doses of these agents must be stable for at least 2 weeks prior to baseline, with BP ≤150/90 mmHg at the baseline visit (Visit 2).

    a) Subjects with nephrotic edema may be treated with diuretics during the screening period. Volume status should be optimized based on the clinical judgment of the Investigator and the doses of diuretics must be stable in the 2 weeks prior to baseline.

    b) At the discretion of the Investigator, subjects with hyperlipidemia may be treated with lipid-lowering agents (e.g., statins) in accordance with standard clinical practice. Doses must be stable in the 2 weeks prior to baseline.

6. RANDOMIZATION, BLINDING AND UNBLINDING PROCEDURES

Not applicable.

Test Type	Test Parameters	Collection at Visits
Pregnancy Test	For females of childbearing potential.	Serum pregnancy test to be evaluated at central laboratory at Screening, and Week 24; urine pregnancy test will be performed locally at all other applicable visits.
Serology	Cytomegalovirus Hepatitis A, B, and C Hepatitis B surface antigen (HBsAg)	Screening (including stability assessments)
Special Tests	Estimated glomerular filtration rate (eGFR)	All
Biomarkers	Urine nephrin Urine synaptopodin Serum TGF-β	Day 1, Week 4 and Week 24

Notes: FMV = First morning void; HDL = High-density lipoprotein; LDL = Low-density lipoprotein; UPCR = Urine protein creatinine ratio.

The total amount of blood that will be collected during the study from an individual subject is approximately 200 mL over 34 weeks.

For details on whether laboratory abnormalities should be reported as AEs and on the follow-up required in such cases, see Section 10.2.4, Clinical Laboratory Evaluations.

9.1.1.1 Evaluation of Biomarkers

Samples for biomarker assessments will be obtained in blood/urine and stored (frozen) for future analysis for subjects who consent to have their leftover samples retained.

9.1.2 Physical Examinations

Physical examinations will be performed in accordance with the Schedule of Events.

The physical examination will include a review of FSGS-related manifestations which will also be recorded. A complete physical examination will be conducted at the initial screening assessment, and an abbreviated physical will be performed at all other visits as per the Schedule of Events. The abbreviated examination will consist of checking the normality or abnormality of the following body systems: general appearance, cardiovascular system, and pulmonary system. Any abnormalities will be recorded in the eCRF and reported as an AE. Because the investigational medication is an immunosuppressant, physical examination will include clinical examination for tumors.

9.1.4.1 Procedures to Manage a Treatment-Emergent Increase in QTcF

In the event that a subject has a corrected QT interval duration corrected for heart rate using method of Fridericia (QTcF) value exceeding 500 msec, or an increase >60 msec from baseline, the Medical Monitor must be informed. The subject will be asked to return for an unscheduled visit within 24 hours and the ECG will be repeated (confirmed), in triplicate (i.e., three 10-second ECGs in rapid succession within 1 minute). If the repeat measurements confirm that the QTcF is >500 msec or >60 msec from baseline, study treatment will be discontinued and the subject followed until the QTcF value either returns to baseline or until, in the judgment of the Investigator, further evaluation is not clinically indicated.

If study treatment is discontinued, the subject should continue in the study for all remaining scheduled study visits.

9.1.5 QoL Assessments

Assessments for QoL will be conducted at Day 1, Week 24, Week 25 and Week 26.

The PROMIS assesses physical function, pain interference, and fatigue. See Appendix 7.

The KDQOL-SF™ survey is a kidney disease-specific measure of QoL that assesses general health, kidney disease and its effects on daily life, and satisfaction with care. See Appendix 8.

9.1.6 Voclosporin Pharmacokinetic and Biomarker Assessment

Blood samples for PK assessments will be taken at Week 4 and Week 24. PK samples will be drawn prior to study treatment dosing (trough sample), and at 1, 2 and 4 hours post-dose. These samples will be analyzed for voclosporin. Should a subject experience a serious adverse event (SAE), require a dose modification or be withdrawn from treatment, a blood PK sample will be taken (with a trough sample preferred) for later determination of drug level. If a subject has discontinued from study treatment, further PK samples are not required.

Blood and urine samples for biomarker assessments will be taken at Day 1, Week 4 and Week 24, samples will be collected prior to study treatment dosing.

9.2 Schedule of Assessments

A detailed schedule of assessments (including all protocol-required assessments, visits, and visit windows) is located on the Schedule of Events. No study-related assessments will be performed (including changes to current medications to meet study eligibility) until the subject has provided signed and dated informed consent. Every effort will be made to keep the subject within the requested visit schedule. If a subject is seen outside of the visit window listed on the Schedule of Events, the reason must be clearly documented in the source notes. The Investigator (or designee) should contact Aurinia for assistance with getting the subject's

Women of childbearing potential must have a negative serum pregnancy test result before baseline.

If a subject has not met the requirements in Inclusion Criteria #3 due to not having renal biopsy result within the required time frame, a renal biopsy can be performed as per local procedures, after signing the study consent, provided the results can be obtained and reviewed prior to baseline.

9.2.2 Treatment Procedures

Only subjects who meet all of the inclusion and none of the exclusion criteria will be eligible for study treatment.

Study medication will be dispensed per the Schedule of Events, beginning on Day 1. Subjects will take their first dose of study medication on Day 2. Women of childbearing potential must have a negative serum pregnancy test during Screening and a negative urine pregnancy test result on Day 1 prior to dispensing of study treatment.

Subjects in Cohort 1, will be contacted by telephone at the end of Week 1 as a reminder to increase their dose to 2 capsules (15.8 mg) BID for 1 week, starting at Week 2. Subjects will be contacted again by telephone at the end of Week 2 as a reminder to increase their dose to 3 capsules (23.7 mg) BID, starting at Week 3, for the remainder of the treatment period (see Section 7.1.2.1, Voclosporin).

Subjects in Cohort 2, will also be contacted by telephone at the end of each week, as required up to the end of Week 3, as a reminder to increase their dose of study medication to the maximum dose selected for the second cohort.

Subjects will complete all assessments per the Schedule of Events at Day 1 and at Weeks 2, 4, 8, 12 and 18.

Adverse events and concomitant medication will be recorded prior to the conduct of other study assessments at each visit.

Assessments at visits during the treatment period include:

- PROMIS and KDQOL-SF™ QoL questionnaires will be answered by the subject, as first study procedure, at Day 1/Baseline.
- Abbreviated physical examination at Day 1.
- Vital signs including weight.
- Standard 12-lead ECG at Day 1.

Women who have a positive pregnancy test during the study will be withdrawn from the study treatment and the procedures for withdrawal will be completed. The Medical Monitor must be contacted immediately.

All pregnancies, subject or partner of a subject, that occur during the study or come to the attention of the Investigator within 30 days after the last study visit (including the Follow-up Visit) or until 30 days after last study treatment administration, whichever is longer, must be reported to [redacted] by the reporting procedures described above.

The outcome of all such pregnancies (including normal births) should be followed up and documented, even if the subject was withdrawn from the study. Every effort should be made to gather information regarding the pregnancy outcome until 90 days (or otherwise as appropriate) post-partum. It will be the responsibility of Aurinia, together with the appropriate support of the Investigator, to obtain this information.

Complications of pregnancy such as abortion (spontaneous or induced), premature birth, or congenital abnormality are considered SAEs and should be reported following the reporting procedures as outlined in Section 10.3.2, Serious Adverse Events. In the event that the site experiences a temporary disruption of the EDC system, a back-up paper Pregnancy Reporting Form will be available for site staff to complete.

13. STATISTICAL ANALYSIS

13.1 Statistical Methods

Complete details of the statistical and analytical methods will be provided in a formal Statistical Analysis Plan (SAP), which will be finalized prior to the database lock. A general description of the planned methods is provided below. Any deviation from the SAP will be noted and explained in the clinical study report.

13.2 Sample Size and Power Calculations

The total sample size will be approximately 20 subjects, with up to 10 subjects in Cohort 1 and at least 10 subjects in Cohort 2.

As this is an exploratory study, sample size calculations are not required. Descriptive statistics will be used and the results will only be hypothesis-generating.

13.3 Populations

13.3.1 Intent-to-Treat Set

The intent-to-treat (ITT) set will consist of all enrolled subjects (non-screening failures) and will be used for all efficacy analyses.

13.3.2 Safety Set

The safety set will consist of all subjects who have taken at least 1 dose of study treatment.

13.3.3 Per-protocol Set

The per-protocol set (PPS) will consist of all subjects eligible from the ITT set who do not have any major protocol violations. Major protocol violations will be defined in the SAP.

13.4 Datasets

Assessments taken at each visit will be analyzed using 2 different datasets. The first will be the observed cases dataset whereby all values collected will contribute to the dataset. A second dataset will be used for summaries and analyses incorporating data carried forward from a subject's last known value. This dataset will be referred to as the last observation carried forward dataset and as such, all subjects with any post-baseline efficacy assessment will contribute to the Week 24 analyses.

13.5 Background and Demographic Characteristics

Demographic and clinical disease characteristics will be summarized.

13.9 Statistical and Analytical Methods

All statistical analyses relating to the primary and secondary objectives will be undertaken at study closure and will incorporate all available data.

In order to aid dose decisions for Cohort 2, an analysis of the first 5 or 6 subjects in Cohort 1 will be undertaken once the 5th or 6th subject reaches Week 12.

Given the small sample size, all analyses will be descriptive in nature.

Binary remission endpoints will be summarized using counts and proportions while continuous data will be summarized using means, SDs, medians, minimums and maximums. Kaplan-Meier methodology will be used for the analysis of time-to endpoints. Confidence intervals for proportions may be calculated but it is recognized that such intervals, being based on 20 patients, will be very wide. As an example, the 95% Clopper-Pearson CI for a proportion of 30% based on 20 patients is (11.9%, 54.3%).

The analysis of the primary endpoint, complete or partial remission of proteinuria at Week 24, will be conducted on the ITT set and confirmed with the PPS (if applicable). Remission of proteinuria will be summarized and an exact 2-sided 95% CI for the remission rate will be calculated.

The analyses of the secondary endpoints will incorporate the use of 2-sided 95% CIs and are described below:

- Binary endpoints will be summarized using counts and proportions along with exact 2-sided 95% CIs.

- Endpoints measured as a time-to-event will be displayed using Kaplan-Meier methodology. Median time-to-event along with 2-sided 95% CIs will be displayed.

- Other endpoints will be summarized by visit. Absolute values and differences between baseline and each time point up to and including Week 24 will be summarized using means and 2-sided 95% CIs. Changes between last on treatment value and post treatment follow-up will also be summarized.

Given the nature of the study, additional exploratory analysis will be undertaken as appropriate. This may include the reporting of individual case studies.

13.10 Safety Evaluations

Specific safety endpoints are as follows:

- Biochemical (including liver function tests) and hematological laboratory tests

15. QUALITY CONTROL AND QUALITY ASSURANCE

The Investigator must ensure that all study-related site source data, study-related documents, and reports will be available, and that the provision of direct access for monitoring and auditing by Aurinia or its designees will be permitted. In addition, the Investigator must ensure that all study-related site source data, study-related documents, and reports will be made available for inspection by the appropriate Regulatory Authority and review by the IRB/EC/IEC.

The Investigator is responsible for notifying Aurinia in advance of an impending regulatory inspection. He/she may request that Aurinia provide support for preparation, if necessary. The Investigator is required to provide updates to Aurinia on the ongoing activities during the inspection, respond to any citations/objectionable findings (i.e., U.S. Food and Drug Administration Form 483) and to share any follow-up responses from the Regulatory Authority.

Accurate and reliable data collection will be assured by verification and cross-check of the eCRFs against the Investigator's records by the Study Monitor (source document verification). The Monitor will also review the Investigator's drug accountability records to ensure that the drug supplies are stored and dispensed appropriately. A comprehensive validation program will verify the data and queries will be generated for resolution by the Investigator. Throughout the study, Aurinia or its designates may review data as deemed necessary.

- Patients who present with nephrotic syndrome (ie, urine protein excretion >3.5 g/day and hypoalbuminemia), who exhibit extensive foot process effacement (≥80 percent) on EM [electron microscopic] examination, and who have no identifiable risk factors associated with secondary FSGS (eg, viral infection, drugs) most likely have primary FSGS, although genetic forms of FSGS lesions cannot always be excluded with confidence. Thus, primary FSGS is always a diagnosis of exclusion.

- Patients who present with subnephrotic (ie, <3.5 g/day in an adult) or nephrotic-range proteinuria and a normal serum albumin concentration (ie, without nephrotic syndrome) and segmental foot process effacement (<80 percent) on EM [electron microscopic] examination most likely have secondary FSGS."