MASTER INFORMED CONSENT FORM

Protocol Title:
A phase 1, multicenter, nonrandomized, open-label, parallel-group study to evaluate the pharmacokinetics, safety, and tolerability of S-892216-PO in participants with varying degrees of renal impairment and matched control participants with normal renal function

Protocol Number: 2420T1614

Sponsor:
Shionogi Inc.
400 Campus Drive, Florham Park, NJ 07932 USA

Document date: 21-Oct-2025

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400 Campus Drive, Florham Park, NJ 07932 USA

The sponsor is the company responsible for arranging and paying for the study.

Study Doctor: [redacted]

Please read this Informed Consent Form (ICF) carefully

You are invited to take part in a research study of an experimental medication called S-892216--PO that is being developed for the treatment of COVID-19. The sponsor of this study is Shionogi Inc. The plan for this study was reviewed and approved by an Institutional Review Board (IRB), which is a group of scientific and non-scientific people who protect the rights and wellbeing of people who take part in research studies.

Before you decide whether to take part in the study, we would like you to understand why this research study is being performed and what it will involve for you.

One of our study staff will go through this informed consent form (ICF) with you and answer any questions you have. If you would like more information, or if there is anything you do not understand, please speak to the study doctor or study staff before signing this ICF. You may take an unsigned copy of this form home with you to read in your own time. Take your time to think and talk about the study with your family, friends, and/or your regular doctor before making your decision. If you decide to participate in the study, the study doctor or study staff will ask you to sign and date this ICF. You will receive a copy of the signed and dated form.

Key Information

The purpose of this research is to test an experimental drug, called S-892216-PO, that is being developed for the treatment of COVID-19. The study will evaluate the safety and the pharmacokinetics (the way that the body handles the experimental medication [i.e., absorbs, circulates, breaks down, and eliminates it]) of S-892216-PO in participants with renal impairment (some on hemodialysis [HD]) and volunteers with normal renal function.

Up to 40 participants will take part in the study at approximately 5 study sites in the United States (US). This study will enroll 8 participants with severe renal impairment (Group A), 8 participants with severe renal impairment on HD (Group B) and 8 volunteers with normal renal function (Group C). Eight participants with moderate renal impairment (Group D) and 8 participants with mild renal impairment (Group E) may be added based on the results of Groups A and C.

The study duration for each participant will vary by Group. For participants with severe, moderate, or mild impairment and normal renal function (Groups A, C, D, and E), the screening

period will last up to 35 days, and the study will last up to 25 days from the admission to the clinical research unit (CRU) to the final follow-up visit and involve a stay of 15 nights and 16 days, and 1 follow up outpatient visit.

For participants on HD (Group B), the screening period will last up to 35 days, and the study will last up to 42 days from the admission to the CRU to the follow-up visit and involve 2 stays (first stay: 15 nights and 16 days, second stay: 4 nights and 5 days) and 2 follow-up outpatient visits.

You will have physical examinations, laboratory tests, vital signs, and electrocardiograms (ECGs).

You will need to avoid certain foods such as grapefruit, grapefruit juice, Seville orange juice, caffeine-containing products (e.g., coffee, green tea, black tea, cola beverages, other caffeinated beverages, or chocolate) and alcohol or alcohol-containing products during the study (details are listed in the section “WHAT WILL I BE ASKED TO DO IF I DECIDE TO TAKE PART?”).

All medical treatments involve risks, including side effects, reactions, and discomfort. You may experience side effects from taking S-892216-PO. Details on what type of side effects are possible when taking these medications are described in the section “WHAT ARE THE POSSIBLE DISADVANTAGES AND RISKS OF TAKING PART?”. You will not benefit from being in this study. However, the information learned from this study may help others in the future. You decide if you want to take part or not take part in this study. No matter what you decide, your decision will not affect the medical care or any benefits you are entitled to.

This is not a treatment study. Your alternative is to not participate.

The rest of this document will explain more about the research study. Members of the study team will talk with you about the information in this document. Feel free to ask any questions and discuss this study with study doctor, staff, family, friends, and personal healthcare providers to help you make your decision.



1. WHAT IS THE PURPOSE OF THE STUDY?

This research study is being performed to evaluate the safety and the pharmacokinetics (the way that the body handles the experimental medication [i.e., absorbs, circulates, breaks down and eliminates it]) of S-892216-PO in participants with renal impairment (some on HD) and volunteers with normal renal function.

S-892216-PO is an experimental drug being developed for the treatment of COVID-19. The experimental drug will be tested in this and other clinical studies and has not been approved for use by the US Food and Drug Administration (FDA).

2. DO I HAVE TO TAKE PART? WHAT WILL HAPPEN IF I DON'T WANT TO CARRY ON WITH THE STUDY?

Taking part in this study is up to you. Even if you agree to take part in the study, you are free to leave the study at any time, without giving any reason. Leaving the study will not affect your care or any benefit you should receive, now or in the future.

If you decide to stop the study early, please tell the study doctor or study staff immediately. You may be asked to return to the study doctor to have final tests completed. Tell the study doctor or study staff if you have any side effects up to your follow-up visit (approximately 21 days after you stop taking the study drug). The study doctor or study staff may add that information to your study record.

If you withdraw your consent from the study, the sponsor can use the data collected up to your withdrawal. You can withdraw your permission for the data or samples collected to be used by requesting this in writing to your study doctor. However, it will not be possible to delete your data from analyses that have already been completed at the time of your request.

3. HOW MANY PARTICIPANTS WILL BE INVOLVED, WHERE WILL THE STUDY TAKE PLACE, AND HOW LONG WILL IT LAST?

Up to 40 participants will take part in the study at approximately 5 study sites in the US. This study will enroll 8 participants with severe renal impairment not on hemodialysis (HD) (Group A), 8 participants with severe renal impairment on HD (Group B), and 8 volunteers with normal renal function (Group C). Eight participants with moderate renal impairment (Group D) and 8 participants with mild renal impairment (Group E) may be added based on the results of Groups A and C.

Group		Dose of S-892216-PO	Study Period(s)	Number of Participants
A	Severe renal impairment not on HD	40-mg tablet	1	8
B	Renal impairment on HD		1 and 2	8
C	Normal renal function		1	8
D	Moderate renal impairment		1	8
E	Mild renal impairment		1	8

HD = hemodialysis

The study duration for each participant will vary by group.

For participants with severe, moderate, or mild impairment and those with normal renal function (Groups A, C, D, and E), the screening period will last up to 35 days, and the study will last up to 25 days from the admission to the CRU to the final follow-up visit and involve a stay of 15 nights and 16 days, and 1 follow-up outpatient visit.

[redacted]

For participants on HD (Group B), the screening period will last up to 35 days, and the study will last up to 42 days from the initial admission to the CRU to the last follow-up visit and involve 2 stays (first stay: 15 nights and 16 days, second stay: 4 nights and 5 days) and 2 follow-up outpatient visits.

4. WHAT WILL I BE ASKED TO DO IF I DECIDE TO TAKE PART?

If you decide to take part in this study, you will be asked to:

- Sign and date this ICF before you can be evaluated for participation.
- Tell the study doctor or study staff if you have been in another study in the past 28 days or are currently in another study.
- Give the study doctor permission to contact your regular doctor, if you are being treated by another doctor, to let him/her know that you are taking part in this study.
- Follow the instructions given to you by the study doctor or study staff.
- Do not take part in any other study while you are in this study.
- Give correct and accurate information about your past and current medical conditions.
- Do not take certain medications (including over-the-counter [OTC] or prescription medicines, recreational drugs, vitamins, minerals, Chinese medicines, vaccines, dietary supplements etc.) as discussed by the study doctor.
- Tell the study doctor or study staff about any changes in the way you feel, your health, or your diet during this study.
- Tell the study doctor or study staff about any changes to or additional medicine or medication (including prescription, OTC, and “natural” treatments) you take during the study.
- Be available for the required study visits and overnight clinic stay periods.
- Allow the study doctor or study staff to contact you and ask how you are doing.
- During your overnight clinic stay, take meals and beverages prepared at our clinic at the predetermined time.
- Do not eat or drink caffeine-containing products (eg, coffee, green tea, black tea, cola beverages, other caffeinated beverages, or chocolate) from 24 hours prior to admission to the study completion.
- Do not eat or drink alcohol or alcohol-containing products from 72 hours prior to admission to the study completion.
- Do not use cannabis (medical or recreational) from 1 month prior to the screening to the study completion.
- If you are a smoker, do not use more than 10 cigarettes, e-cigarettes or cigars per day and do not use other tobacco-, or nicotine-containing products from the screening to the study completion.
- Do not eat or drink grapefruit, grapefruit juice, Seville orange juice or food or beverages containing them, from 7 days prior to admission to the study completion.
- Avoid intensive exercise that could cause muscle aches or injury, including contact sports or heavy lifting from the screening visit to the study completion
- If you are a woman of child-bearing potential, agree to use acceptable methods of birth control. The study doctor will explain acceptable birth control methods to you (also refer to "Pregnancy risks" in Section 7).



- If you or your partner become pregnant before you have completed the study, please tell the study doctor or study staff. Your pregnant partner may be asked to sign a separate consent form to allow collection of data about the health of your baby. If your pregnant partner agrees, your pregnant partner will be followed up until the pregnancy is over. The study doctor will share this information with the sponsor.
- Information you learn from taking part in this study contains confidential and personal information. Please refrain from telling such information to a third party (posting it on the internet, etc.), with the exception of when you use it to consult with your family and your regular doctor.

5. WHAT WILL HAPPEN TO ME IF I TAKE PART?

If you are a participant with renal impairment not on HD, or a participant with normal renal function (Groups A, C, D and E)

This study is made up of the following periods:

- Screening period: Up to 35 days before you take the study drug
- Clinic stay during the treatment period: Remain in the clinic for 15 nights and 16 days, including 1 day (day 1) on which you take the study drug
- Follow-up visit/end of study: Visit clinic on day 22 (± 3 days)
    - For participants who discontinued from the study before day 15, visit clinic 7 days after discharge (± 2 days)

The table below will provide you with a summary of what will happen at each visit:

Study Period	Days (Visit)	Planned Evaluations/Assessments
Screening Period	Days -35 to -2	• Sign the informed consent form • Undergo a physical examination (including height and body weight) • Provide your demographic information (age, sex at birth, ethnicity, and other) • Undergo drug, alcohol, cotinine, and cannabis screening tests and confirm you are not consuming any tobacco (more than 10 cigarettes, e-cigarettes or cigars per day or other tobacco-, or nicotine-containing products), caffeine, or cannabis products • Provide your medical and medication history • Have blood drawn to check if you are positive for syphilis or viral diseases (hepatitis B, hepatitis C or HIV) • Undergo a SARS-CoV-2 (COVID-19) screening test • For female participants, undergo a urine pregnancy test • Have blood drawn and urine collected to perform safety assessments and other assessments to check the status of your body systems • For female participants, have blood drawn to check your levels of follicle stimulating hormone (FSH) to confirm female study participant's postmenopausal status if there is no available documentation confirming postmenopausal status • Undergo electrocardiogram (ECG) test to check electrical activity of your heart • Have your vital signs collected (blood pressure, pulse rate, body temperature, and respiratory rate) • Report any side effects or physical abnormalities that you may experience • Confirm any prescription or OTC medication you are taking

[redacted]

Study Period	Days (Visit)	Planned Evaluations/Assessments
Clinic stay during the treatment period	Day -1 (Admission)	Based on the screening assessments, if you qualify for the study, you will be admitted to the study clinic. The following procedures will occur: • Undergo a physical examination and have your vital signs collected (blood pressure, pulse rate, body temperature, and respiratory rate) • Undergo drug, alcohol, cotinine, and cannabis screening tests • Undergo a SARS-CoV-2 (COVID-19) screening test • For female participants, undergo a urine pregnancy test • Have blood drawn and urine collected to perform safety assessments and other assessments to check the status of your body systems • Undergo ECG test to check electrical activity of your heart • Report any side effects or physical abnormalities that you may experience • Confirm any prescription or OTC medication you are taking
Clinic stay during the treatment period	Days 1 to 15	The study drug will be administered by qualified study staff on day 1. The following procedures will occur: • Daily monitoring of your physical well-being to determine if you are developing symptoms that could be related to the study drug or procedures (days 1 to 14) • Undergo a physical examination (day 15) • Have blood drawn and urine collected to perform safety assessments and other assessments to check the status of your body systems (days 2, 3, 4, 6, 9, 12 and 15) • Undergo ECG test to check electrical activity of your heart (days 1, 2, 3, 4, 6, 9, 12 and 15) • Have your vital signs collected daily (blood pressure, pulse rate, body temperature, and respiratory rate) (days 1 to 15) • Report any side effects or physical abnormalities daily that you may experience (days 1 to 15) • Confirm any prescription or OTC medication you are taking (days 1 to 15) • For female participants, undergo a urine pregnancy test (day 15) • Have blood drawn for pharmacokinetics measurements (days 1, 2, 3, 4, 6, 9, 12 and 15) and for protein binding measurements (days 1 and 2) • Have urine collected for pharmacokinetic measurements (throughout days 1 to 15) For participants who discontinue from the study before day 15, the discharge visit assessments will be conducted. For the exact schedule, please contact the study doctor or study staff.
Follow-up Early termination	Day 22 (± 3 days) 7 days after discharge (± 2 days)	• Undergo a physical examination and have your vital signs collected (blood pressure, pulse rate, body temperature, and respiratory rate) • For female participants, undergo a urine pregnancy test • Have blood drawn and urine collected to perform safety assessments and other assessments to check the status of your body systems • Undergo ECG test to check electrical activity of your heart • Report any side effects or physical abnormalities that you may experience • Confirm any prescription or OTC medication you are taking • Have blood drawn for pharmacokinetics measurements

If you are a participant with renal impairment on HD (Group B)

[redacted]

This study is made up of the following periods:

- Screening period: Up to 35 days before you take the study drug
- Period 1:
    - Clinic stay during the treatment: Remain in the clinic for 15 nights and 16 days, including 1 day (day 1) on which you take the study drug
    - Follow-up visit: Visit clinic on day 22 (± 3 days)
        - For participants who discontinued from the study before day 15 in Period 1, visit clinic 7 days after discharge (± 2 days)
- Washout Period:
    - Period between the end of Period 1 and the start of Period 2. This period is to make sure that the study drug administered on day 1 has been sufficiently excreted from your body. During this period, HD will continue to be conducted according to your HD schedule.
- Period 2
    - Clinic stay during the treatment: Remain in the clinic for 4 nights and 5 days, including 1 day (day 29) on which you take the study drug

      Clinic stay during the treatment for Period 2 can be conducted 28 days or more after day 1 in Period 1. This is based on your schedule.
- Follow-up visit/end of study: Visit clinic on day 39 (± 3 days)
    - This follow-up visit will occur 10 days after your start of clinic stay for Period 2. This is also based on your schedule.
    - For participants who discontinued from the study before day 32 in Period 2, visit clinic 7 days after discharge (± 2 days)

The table below will provide you with a summary of what will happen at each visit:

Study Period	Days (Visit)	Planned Evaluations/Assessments
Screening Period	Days -35 to -2	• Sign the informed consent form • Undergo a physical examination (including height and body weight) • Provide your demographic information (age, sex at birth, ethnicity and other) • Undergo drug, alcohol, cotinine, and cannabis screening tests and confirm you are not consuming any tobacco (more than 10 cigarettes, e-cigarettes or cigars per day or other tobacco-, or nicotine-containing products), caffeine, or cannabis products • Provide your medical and medication history including any other drugs you might be taking/using • Have blood drawn to check if you are positive for syphilis or viral diseases (hepatitis B, hepatitis C or HIV) • Undergo a SARS-CoV-2 (COVID-19) screening test • For female participants, undergo a pregnancy test • Have blood drawn and urine collected to perform safety assessments and other assessments to check the status of your body systems • For female participants, have blood drawn to check your levels of follicle stimulating hormone (FSH) to confirm female study participant's postmenopausal status if there is no available documentation confirming postmenopausal status

[redacted]

Study Period	Days (Visit)	Planned Evaluations/Assessments
		• Undergo electrocardiogram (ECG) test to check electrical activity of your heart • Have your vital signs collected (blood pressure, pulse rate, body temperature, and respiratory rate) • Report any side effects or physical abnormalities that you may experience • Confirm any prescription or OTC medication you are taking
Period 1		
Clinic stay during the treatment period	Day -1 (Admission)	Based on the screening assessments, if you qualify for the study, you will be admitted to the study clinic. The following procedures will occur: • Undergo a physical examination and have your vital signs collected (blood pressure, pulse rate, body temperature, and respiratory rate) • Undergo drug, alcohol, cotinine, and cannabis screening tests • Undergo a SARS-CoV-2 (COVID-19) screening test • For female participants, undergo a pregnancy test • Have blood drawn and urine collected to perform safety assessments and other assessments to check the status of your body systems • Undergo ECG test to check electrical activity of your heart • Report any side effects or physical abnormalities that you may experience • Confirm any prescription or OTC medication you are taking
Clinic stay during the treatment period	Days 1 to 15	The study drug will be administered by qualified study staff on day 1. **In Period 1, the study drug will be administered 2 hours before your scheduled start of hemodialysis.** The following procedures will occur: • Daily monitoring of your physical well-being to determine if you are developing symptoms that could be related to the study drug or procedures (days 1 to 14) • Undergo a physical examination (day 15) • Have blood drawn and urine collected to perform safety assessments and other assessments to check the status of your body systems (days 2, 3, 4, 6, 9, 12 and 15) • Undergo ECG test to check electrical activity of your heart (days 1, 2, 3, 4, 6, 9, 12 and 15) • Have your vital signs collected daily (blood pressure, pulse rate, body temperature, and respiratory rate) (days 1 to 15) • Report any side effects or physical abnormalities daily that you may experience (days 1 to 15) • Confirm any prescription or OTC medication you are taking (days 1 to 15) • For female participants, undergo a pregnancy test (day 15) • Have blood drawn for pharmacokinetics measurements (days 1, 2, 3, 4, 6, 9, 12 and 15) and for protein binding measurements (day 1). On day 1, pooled HD aliquot, and arterial and venous blood samples from HD port will also be collected. • Have urine collected for pharmacokinetics measurements (throughout days 1 to 15) (for participants able to produce urine) For participants who discontinue from the study before day 15, the discharge visit assessments will be conducted.

[redacted]

Study Period	Days (Visit)	Planned Evaluations/Assessments
		Assessments must be conducted before the participant is discharged (provided consent has been withdrawn). For the exact schedule, please contact the study doctor or study staff.
Follow-up Early termination	Day 22 (± 3 days) 7 days after discharge (± 2 days)	• Undergo a physical examination and have your vital signs collected (blood pressure, pulse rate, body temperature, and respiratory rate) • For female participants, undergo a pregnancy test • Have blood drawn and urine collected to perform safety assessments and other assessments to check the status of your body systems • Undergo ECG test to check electrical activity of your heart • Report any side effects or physical abnormalities that you may experience • Confirm any prescription or OTC medication you are taking • Have blood drawn for pharmacokinetics measurements
Washout Period		
Period 2		
Clinic stay during the treatment period	Day 28 (Admission)	On Day 28, the following assessments will be done to confirm you are eligible to receive your second dose of study drug. If the results of any assessment indicate you are no longer eligible to receive the second dose of study drug, the study doctor or study staff will inform you if you should return to the clinic to be reassessed at a later date or proceed directly to the Early Termination Visit. • Undergo a physical examination and have your vital signs collected (blood pressure, pulse rate, body temperature, and respiratory rate) • Undergo drug, alcohol, cotinine, and cannabis screening tests • Undergo a SARS-CoV-2 (COVID-19) screening test • For female participants, undergo a pregnancy test • Have blood drawn and urine collected to perform safety assessments and other assessments to check the status of your body systems • Undergo ECG test to check electrical activity of your heart • Report any side effects or physical abnormalities that you may experience • Confirm any prescription or OTC medication you are taking
Clinic stay during the treatment period	Days 29 to 32	The study drug will be administered by qualified study staff on day 29. **In Period 2, the study drug will be administered after you return from the hemodialysis center.** The following procedures will occur: • Daily monitoring of your physical well-being to determine if you are developing symptoms that could be related to the study drug or procedures (days 29 to 31) • Undergo a physical examination (day 32) • Have blood drawn and urine collected to perform safety assessments and other assessments to check the status of your body systems (days 30, 31 and 32) • Undergo ECG test to check electrical activity of your heart (days 29, 30, 31 and 32) • Have your vital signs collected daily (blood pressure, pulse rate, body temperature, and respiratory rate) (days 29 to 32) • Report any side effects or physical abnormalities daily that you may experience (days 29 to 32) • Confirm any prescription or OTC medication you are taking (days 29 to 32)

[redacted]

Study Period	Days (Visit)	Planned Evaluations/Assessments
		• For female participants, undergo a pregnancy test (day 32) • Have blood drawn for pharmacokinetics measurements (days 29 to 32) and for protein binding measurements (days 29 and 30) • Have urine collected for pharmacokinetics measurements (for participants able to produce urine) For participants who discontinue from the study before day 32, the discharge visit assessments will be conducted. For the exact schedule, please contact the study doctor or study staff.
Follow-up	Day 39 (± 3 days)	• Undergo a physical examination and have your vital signs collected (blood pressure, pulse rate, body temperature, and respiratory rate) • For female participants, undergo a pregnancy test • Have blood drawn and urine collected to perform safety assessments and other assessments to check the status of your body systems • Undergo ECG test to check electrical activity of your heart • Report any side effects or physical abnormalities that you may experience • Confirm any prescription or OTC medication you are taking • Have blood drawn for pharmacokinetics measurements
Early termination	7 days after discharge (± 2 days)	

[redacted]

Schedule of Activities - Participants Not on Hemodialysis (Groups A, C, D, and E)

Procedure	Screening Period (days -35 to −2)	Treatment Period (Day)															Follow-up Visit (day 22 ± 3)
		Admission to CRU (day –1)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Discharge from CRU (day 15)	
Informed consent	X																	
Inclusion and exclusion criteria	X	X																
Renal function assessment	X	X																
Demography	X																	
Medical history	X	X																
Drug, alcohol, cotinine, and cannabis screen	X	X																
Serological tests	X																	
SARS-CoV-2 screening test	X	X																
Urine pregnancy test	X	X															X	X
FSH test	X																	
Laboratory assessments	X	X		X	X	X		X			X			X			X	X
Full physical examination including height, weight, and BMI	X	X															X	X
Symptom-focused physical examination			X	X	X	X	X	X	X	X	X	X	X	X	X	X		
ECG	X	X	X	X	X	X		X			X			X			X	X
Vital signs	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Study intervention			X															
PK blood samples			X	X	X	X		X			X			X			X	X
Protein binding blood samples			X	X														
PK urine samples			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Adverse events review	X	◄———															———►	
Concomitant medication review		◄———															———►	

BMI = body mass index, CRU = clinical research unit, ECG = electrocardiography/electrocardiogram, FSH = follicle-stimulating hormone, PK = pharmacokinetic(s)

[redacted]

Schedule of Activities – Participants on Hemodialysis (Group B)

Procedure	Screening Period (days -35 to −2)	Treatment Period 1 (Day)															Follow-up (day 22 ± 3)	Washout period	Treatment Period 2 (Day)					Follow-up Visit (day 39 ± 3)
		Admission to CRU (day –1)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Discharge from CRU (day 15)			Admission to CRU (at least day 28)	29	30	31	Discharge from CRU (day 32)	
Informed consent	X																								
Inclusion and exclusion criteria	X	X																		X					
Renal function assessment	X	X																		X					
Demography	X																								
Medical history	X	X																		X					
Drug, alcohol, cotinine, and cannabis screen	X	X																		X					
Serological tests	X																								
SARS-CoV-2 screening test	X	X																		X					
Pregnancy test	X	X															X	X		X				X	X
FSH test	X																								
Laboratory assessments	X	X		X	X	X		X			X			X			X	X		X		X	X	X	X
Full physical examination including height, weight, and BMI	X	X															X	X		X				X	X
Symptom-focused physical examination			X	X	X	X	X	X	X	X	X	X	X	X	X	X					X	X	X		
ECG	X	X	X	X	X	X		X			X			X			X	X		X	X	X	X	X	X
Vital signs	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X
Study intervention			X																		X				
PK blood samples			X	X	X	X		X			X			X			X	X			X	X	X	X	X

[redacted]

Procedure	Screening Period (days -35 to −2)	Treatment Period 1 (Day)															Follow-up (day 22 ± 3)	Washout period	Treatment Period 2 (Day)					Follow-up Visit (day 39 ± 3)
		Admission to CRU (day –1)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Discharge from CRU (day 15)			Admission to CRU (at least day 28)	29	30	31	Discharge from CRU (day 32)	
Protein binding blood samples			X																		X	X			
PK urine samples*			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X				X	X	X	X	
HD			X			◄	—	—	—	—	—	—	—	—	—	—	►		X		X			◄	— ►
PK HD Samples (pooled HD aliquot, and arterial and venous blood samples from HD port)			X																						
Adverse events review	X	◄	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	►
Concomitant medication review		◄	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	►

BMI = body mass index, CRU = clinical research unit, ECG = electrocardiography/electrocardiogram, FSH = follicle-stimulating hormone, HD = hemodialysis, PK = pharmacokinetic(s)

*For participants able to produce urine.

[redacted]

6. WHAT WILL HAPPEN TO THE SAMPLES I GIVE?

For participants not on HD (Groups A, C, D, and E), about 237 milliliters of blood (about 1 ¼ cups) will be collected over the course of the study. The blood is collected every day during the clinic stay period and at follow up visit(s).

For participants on HD (Group B), about 392 milliliters of blood (about 2 cups) will be collected over the course of the study. The blood is collected every day during the clinic stay period and at follow-up visit(s).

Below is a breakdown of the number of blood draws and volume of blood per occurrence:

Participants not on hemodialysis (Groups A, C, D and E)

Contents	Blood sampling volume	Maximum frequency of blood sampling	Total volume of blood sampling
Hepatitis B, Hepatitis C, HIV, and syphilis	11 mL (about 2 tsp)	1 time (screening only)	11 mL (about 2 tsp)
Laboratory tests (hematology, blood chemistry, coagulation, and endocrinology)	16 mL (about 3 tsp)	10 times	160 mL (about ¾ cup)
Measurement of S-892216 concentration	3 mL (about ½ tsp)	20 times	60 mL (about 11 tsp)
Measurement of protein binding	3 mL (about ½ tsp)	2 times	6 mL (about 1 tsp)
Total		33 times	237 mL (about 1 ¼ cup)

tsp = teaspoon

Participants on hemodialysis (Group B)

Contents	Blood sampling volume	Maximum frequency of blood sampling	Total volume of blood sampling
Hepatitis B, Hepatitis C, HIV, and syphilis	11 mL (about 2 tsp)	1 time (screening only)	11 mL (about 2 tsp)
Laboratory tests (hematology, blood chemistry, coagulation, and endocrinology)	16 mL (about 3 tsp)	15 times	240 mL (about 1 cup)
Measurement of S-892216 concentration	3 mL (about ½ tsp)	35 times	105 mL (about ½ cup)
Measurement of protein binding	3 mL (about ½ tsp)	4 times	12 mL (about 1 tsp)
Measurement of S-892216 concentration (Arterial port)	3 mL (about ½ tsp)	4 times	12 mL (about 1 tsp)
Measurement of S-892216 concentration (Venous port)	3 mL (about ½ tsp)	4 times	12 mL (about 1 tsp)
Total		55 times	392 mL (about 2 cup)

tsp = teaspoon

The sponsor will use any blood and urine samples collected from you for the purposes of this research study. To protect your privacy, your samples will be labelled with a unique identifier (also known as your participant ID).

The sponsor may wish to use your samples for research purposes outside of this study. If the sponsor wishes to use your samples for a purpose outside of what is outlined in this ICF, the sponsor will ask you to sign another ICF.

Your samples will be stored up to 15 years after the study ends. Your samples will be destroyed after this period.

7. WHAT ARE THE POSSIBLE DISADVANTAGES AND RISKS OF TAKING PART?

During the study, you may have discomforts and risks from the study drugs and from the study procedures. Discomforts and risks may vary from person to person. Everyone taking part in the study will be observed carefully for side effects; however, doctors do not know all the discomforts and risks that may happen. There is always the possibility that unknown risks or side effects may occur. **If any discomforts or symptoms occur, you must tell your study doctor or study staff right away.**

Possible risks and side effects of S-892216-PO

As of 07 Aug 2025, 212 healthy adult and elderly participants have received the study drug.

Three mild events and 1 severe event were reported as related to the study drug. These events resolved on their own. No deaths or serious side effects have been reported.

Also, in a study with male and female beagle dogs given S-892216 daily for 4-weeks (higher than doses expected to be used in humans), some male and female dogs had possible signs of reproductive organ changes (testicular hyperplasia [small nodules in the testicles] and ovarian cysts). These changes returned to normal. These changes were not observed in non-clinical studies using other species. In the same study, changes in electrocardiograms (irregular heart rhythm) were observed. Although similar findings have not been seen in healthy people thus far, you will be closely monitored throughout the study.

If you are a participant with renal impairment, the metabolism of S-892216-PO in your body might be altered due to your medical condition, resulting in new, unknown risks. Please tell the study doctor or study staff immediately if you have any discomforts or symptoms.

Pregnancy risks:

The effects of S-892216-PO on an unborn child are currently not known.

If you or your partner becomes pregnant before you have completed the study, please tell the study doctor or study staff. You or your pregnant partner may be asked to sign a separate consent form to allow collection of data about the health of your baby. If you or your pregnant partner agrees, you or your pregnant partner will be followed up until the pregnancy is over. The study doctor will share this information with the sponsor.

Blood pressure measurement:

The blood pressure cuff used to take your blood pressure may cause discomfort or bruising to the upper arm.

Blood sample collection:
During this study, samples of your blood will be taken (most often by inserting a needle into a vein). You might experience the following side effects of having blood drawn. If you feel dizzy or faint, tell the study doctor or study staff immediately.

- Fainting
- Dizziness
- Redness
- Pain



- Swelling
- Bruising
- Bleeding
- Infection
- Nerve injury

Electrocardiogram:

The ECG is a procedure that requires you to lie still for a few minutes while electrodes are attached to your chest to record the activity of your heart. There is generally no risk with having an ECG. The sticky patches may cause slight discomfort when removing from your skin by pulling your skin, or cause redness or itching. If the patches trouble you when pulling them off, you could remove them easier with water (such as when in the shower or with a wet paper towel).

Unknown risks:

It is possible that you could have side effects from S-892216-PO that nobody knows about yet.

It is possible that taking S-892216-PO with your regular medications or supplements may change how your regular medications or your regular supplements work.

Risks of stopping your regular medication:

If you have to stop your regular medication(s) to participate in the study, your symptoms might come back or get worse. Please tell the study doctor or study staff immediately if you have any problems when you stop your regular medication(s).

To help keep you safe during the study, it is very important that you get medical help and contact the study doctor or study staff if you have any of these side effects or any other side effects during the study. If you do not understand what any of these side effects mean, please ask the study doctor or study staff to explain these terms to you.

8. WHAT ARE THE POSSIBLE ADVANTAGES OR BENEFITS OF TAKING PART IN THE STUDY?

There is no direct benefit to you for participating in this clinical study. However, by taking part in this study, you will be contributing to the development of a drug for the treatment of COVID-19, particularly by providing evidence that will help recommend dosing in renally-impaired individuals.

9. WHAT ARE THE ALTERNATIVE OPTIONS FOR TREATMENT?

This study only accepts participants that are COVID-19 negative, therefore alternative options for treatments are not applicable. The study doctor will answer any questions you may have.

10. WHAT HAPPENS WHEN THE STUDY STOPS?

The study doctor, the IRB, the US FDA, and the sponsor have the right to remove you from the study at any time (early termination), with or without your agreement. This decision will be made if:

- You do not follow instructions
- The study is terminated by the sponsor
- It is in your best medical interest to stop your participation, such as if you have an adverse (bad) reaction to the study drug
- You do not consent to any testing or examination required in this study



- You cannot attend planned clinic visits or commit to the planned clinic stay period
- You withdraw your consent to disclose your protected health information (PHI) (refer to "How will my personal information be used, shared, and protected?" in Section 16)
- We find out that you enrolled or are participating in another study at the same time
- For participants in Group B, you are found to be ineligible to receive your second dose of study drug.

If the study is discontinued during your participation, the study doctor will explain the reason. You will be asked to complete a final study visit for the study doctor to assess your health and well-being at the time of study stop/discontinuation.

If you decide to withdraw consent and stop the study early, please tell the study doctor or study staff immediately. Tell the study doctor or study staff if you have any side effects. The study doctor may add that information to your study record.

11. WILL THE STUDY DRUG BE AVAILABLE AFTER I HAVE FINISHED THE STUDY?

S-892216-PO is an experimental medication and will not be available after the study.

12. WHAT IF NEW RELEVANT INFORMATION BECOMES AVAILABLE?

Sometimes the sponsor and the study doctor will get new information about the study drugs. If this happens, the study doctor will tell you about this new information and discuss whether you should continue in the study. If you decide not to continue in the study, tell the study doctor or study staff immediately. If you decide to continue in the study, the study doctor will ask you to sign an updated ICF reflecting any new information about the study requirements.

13. WILL I RECEIVE ANY PAYMENT FOR TAKING PART IN THE STUDY?

You will be compensated for your participation in this study. In addition, during the overnight clinic stay period, your meals will be provided at no cost to you.

Payment received as a study participant may be taxable income to you. If payments are more than $600 in any 1 calendar year, the Institution is required to report this information to the Internal Revenue Service (IRS). An IRS Form 1099 (Miscellaneous Income) will be sent to you and a copy will be sent to the IRS.

14. WILL IT COST ME ANYTHING TO BE IN THE STUDY?

All costs connected with the study, including the costs for study drugs, tests, examinations, and procedures needed only for the study, will be provided free of charge to you.

If you receive medical care unrelated to the study and it includes the cost of an overnight clinic stay and any procedures, you or your insurance will be responsible for the cost of that medical care. Since some insurance companies will not cover costs when you are in a clinical study, you will need to call your insurance company and make sure your insurance coverage is not affected by your participation in this study.

15. WHAT IF SOMETHING GOES WRONG?

To help keep you safe during the study, it is very important you follow all study directions. If you have any unusual symptoms or believe you have an illness or injury, please contact the study doctor or study staff immediately at the phone number listed on the cover of this ICF. If you believe



you need urgent medical attention, please go to your nearest emergency room, call 911 or use your nurse call button to notify hospital/medical practice staff if you are hospitalized. If you see another doctor during the study, please inform him/her that you are taking part in this research study.

In case of study-related injury:

The sponsor will cover the reasonable medical expenses necessary to treat an illness or injury that occurred as a direct result of your use of the study drug, or a test performed only for the purposes of the study, so long as the study procedures have been followed and you have followed the instructions given to you by the study doctor or study staff. The sponsor may not pay if the sponsor and the study doctor do not agree that your injury resulted from your taking part in this study. Unless you are covered by Medicare, this payment by the sponsor applies only to costs that are not covered by your health insurance policy or by any other third party. If you are covered by Medicare, the sponsor will pay the costs of the medical care related to these injuries. There are no plans for payment for lost wages or other expenses.

Federal law requires the sponsor to inform the Centers for Medicare & Medicaid Services (the agency responsible for administration of the Medicare program) when the sponsor is going to pay for treatment of an injury to a Medicare beneficiary. The sponsor or its representatives may need to collect certain personal information about you such as your name, date of birth, gender, social security number, and Medicare identification number (if you have one). The sponsor needs this information in order to comply with a Medicare reporting obligation. This information may be collected directly from you or from researchers, physicians, or other healthcare providers who treated your problem or injury. This information and also information about your injury or other health problem may be shared with others, including sponsor representatives, sponsor's insurance company, and the Centers for Medicare & Medicaid Services.

Legal rights:

Nothing in this ICF limits or excludes any of your legal rights or remedies or releases the study doctor, sponsor, or healthcare institution from liability arising out of their negligence.

16. HOW WILL MY PERSONAL INFORMATION BE USED, SHARED, AND PROTECTED?

This study may only be performed by collecting, using, and sharing the personal information of study participants as described in this ICF, and you may therefore only participate in this study if you agree to this.

Information about your participation in the study such as the study doctor medical evaluation reports, test results, and any other that is needed will be collected via paper, electronically, or a combination of both.

The study sponsor, Shionogi Inc., will be responsible for safeguarding the personal information about you that is collected and used for the study and for using it properly. Your hospital/medical practice [redacted] will have a similar responsibility with respect to use of your existing medical records.

This research is covered by a Certificate of Confidentiality (CoC) from the [redacted] Administration for Strategic Preparedness and Response (ASPR), a US Federal Government entity under the Department of Health and Human Services (HHS).

This means that the staff of [redacted] cannot share or give to any other person not connected with this

[redacted]

research your name, information about you, documents, or samples that may identify you in any action or suit unless you say it is okay.

A CoC protects your private information from all legal proceedings. Your information can't be used as evidence even if there is a court subpoena. All copies of your information are immune from the legal process, and cannot, be admitted as evidence or used for any purpose in any action, suit, or other judicial, legislative, or administrative proceeding unless you say it is okay.

The information about you CAN be shared for other research if it is allowed by Federal regulations. We will let you know beforehand if this is something we will do.

The CoC DOES NOT stop the reporting that federal, state or local laws require. Some examples are laws that require reporting of child or elder abuse, some communicable diseases, and threats to harm yourself or others. The CoC CANNOT BE USED to stop a US federal or state government agency from checking records or evaluating programs. The CoC DOES NOT stop disclosures required by the US FDA.

You should understand that a CoC does not keep you from voluntarily releasing information about yourself or your involvement in this research. It also does not prevent you from having access to your own information. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide specific consent to allow the researchers to release it.

Before the study doctor shares your study data with the study sponsor, it will be coded. This means your name will be replaced with a coded reference number. The study doctor and your hospital/medical practice will keep the code list linking your name to the coded reference number confidential. The code list will not be shared with the study sponsor.

The study sponsor may share the coded study data with selected individuals from the sponsor’s company, its group companies, its vendors and partners, and/or US and foreign regulators.

With your consent, the study sponsor will use your coded study data for scientific research purposes, including to carry out and evaluate this study, to understand the study drug and the condition, and advance scientific research and medical discovery.

The study sponsor will also use your coded study data to meet its legal obligations, for example, in relation to clinical trials and the safety of its products, to seek approval to market its medicines and to inform decisions from regulatory authorities on access and reimbursement of new treatments for the benefit of participants.

The study sponsor may transfer the coded study data to its group companies, vendors, and partners located in other countries which may not be regarded as providing the same level of protection to personal information as the laws of your home country (such as the US, Japan, the United Kingdom, and the Netherlands). The study sponsor will ensure that adequate safeguards are implemented to protect your coded data, as required under applicable data protection legislation.

The hospital/medical practice will keep the code list and the study data for at least 25 years after the study has ended. At the end of the study, the study sponsor will archive the coded study data for the same duration or longer (for example, when used in applications for marketing approval of new products).

If you have questions, comments or concerns about how your personal information is being handled in this study, you should contact the study doctor. They will coordinate with the study sponsor as necessary.



17. AT THE END OF THE STUDY, WHERE ARE THE SUMMARY RESULTS POSTED AND HOW WILL THE CODED STUDY DATA BE SHARED FOR FUTURE SCIENTIFIC RESEARCH?

Information about this study and result summaries in an easy-to-read language will be publicly available on the website of “SHIONOGI CLINICAL TRIAL DATA”:

https://www.shionogi.com/global/en/innovation/randd/clinical-development/clinical-trial-data.html

and the following clinical trial registries:

US Clinical Trials Register: http://www.ClinicalTrials.gov

This information is disclosed to other national clinical trial registries or databases according to industry guidance and regulatory requirements. You can search these websites/public registries at any time. You will not be able to be identified from any summary results, reports, or publications produced at the end of the study.

At the end of the study, the study sponsor may make coded participant-level study data available to qualified researchers for approved future scientific research to be conducted in your country or abroad. The researchers may belong to the study sponsor’s group companies or to independent third parties such as publicly funded healthcare bodies, universities, and/or pharmaceutical companies. Where possible, the study sponsor will anonymize the coded study data before it is shared securely for future scientific research. Data sharing requests will be subject to formal approval processes and safeguards will be put in place to control access and protect your privacy.

The responsible sharing of clinical trial research data for future scientific research maximizes the value of the data and helps to advance scientific knowledge and public health. The data will be used for future scientific research only and will not be used to make future decisions about your healthcare. **If you do not want your coded study data to be used for future scientific research, you can object to this at any time by notifying the study doctor.** However, in some cases, national laws may restrict that right to preserve the scientific integrity of the data. If you object, your coded study data will not be used for further scientific research, but this will not affect any research activities already undertaken.

18. WHO HAS REVIEWED THIS STUDY?

An IRB is a group of scientific and nonscientific people who perform the initial and ongoing ethical review of the clinical study with the study participant’s rights and welfare in mind. This study has been reviewed and approved by [redacted] and the US FDA.

19. FURTHER INFORMATION AND CONTACT DETAILS

If you have questions, concerns, or complaints about this study or to report a study-related injury, contact your study team, listed below:

	Study Doctor	Study Coordinator
Name:		
Telephone number:		
24-hour contact number(s):		

If you have any questions or concerns about your rights as a study participant or want to discuss a problem, get information, or offer input, you may contact the IRB at [redacted]

[redacted]

Thank you for reading this and considering taking part in this study.
If you decide to take part, you will receive a copy of this signed and dated ICF to keep.

SIGNATURE FORM

Protocol Title: A phase 1, multicenter, nonrandomized, open-label, parallel-group study to evaluate the pharmacokinetics, safety, and tolerability of S-892216-PO in participants with varying degrees of renal impairment and matched control participants with normal renal function

Study Doctor: [redacted]

STATEMENT OF CONSENT

I have read and understood the statements in this ICF.

I have had the chance to ask questions, and I am satisfied with the answers given to me.

I understand that this study may only be performed by collecting and using my health data. Therefore, by signing this ICF, I specifically give permission for my data to be checked, transferred, and processed as follows:

- The authorized representatives of BARDA and/or SHIONOGI, the IRB, and inspectors for regulatory authorities may review my health data by directly accessing my health records.
- Study data, including my coded health data, may be used and shared for legitimate study and scientific purposes.

I agree to take part in this study of my own free will.

I understand that I will receive a copy of this signed and dated written ICF.

_____
Printed name of participant, in full

_____
Signature of participant Date (dd-MON-yyyy)

Person Obtaining Consent

I have presented the study and answered the participant's questions.

I will give the participant a copy of this signed and dated ICF.

_____
Printed name of person obtaining consent (investigator or designee)

_____

[redacted]

Signature of person obtaining consent (investigator or designee)	Date (dd-MON-yyyy)

Printed name of investigator if different from the person obtaining consent

Signature of investigator if different from the person obtaining consent	Date (dd-MON-yyyy)

[redacted]

HIPAA Authorization to Use and Disclose Protected Health Information [redacted]

The US government has issued a privacy rule to protect the privacy rights of patients. This rule was issued under a law called the "Health Insurance Portability and Accountability Act" of 1996 (HIPAA) and describes how PHI may be used, disclosed (shared), and made accessible to you. This privacy rule is designed to protect the confidentiality of PHI. Please read this Authorization carefully, as it describes your rights regarding the use or disclosure of your PHI.

You are being asked to allow the use of your PHI because this study may be performed only by collecting and using this information. Your study records will be kept confidential as described in this form. Only a number and initials will be used to identify you in the study data sent to others, and you will not be personally identified in any reports or publications that may result from this clinical study. The information about you that will be reviewed by the study doctor and study staff for the study may allow you to be identified by your name, address, telephone number, social security number, health plan number, study number, date of birth, dates relating to various (different) medical surgeries, or other identifying information.

Because of the research goals of this study, your study records cannot be kept completely confidential. The following sections provide a specific description of how your PHI will be used and disclosed if you take part in this research study. If you decide to take part in the study, you will be asked to authorize (allow) those uses and disclosures by signing this Authorization. If you choose not to allow these uses and sharing of your PHI, you will not be able to take part in the study.

Information that may be given to others by the study doctor and/or study staff:

- Past and present medical records
- Research records, including records of study visits and telephone calls about the study
- Information collected for this study from:
    - Physical examinations
    - Laboratory and other test results, including tests for reportable infectious diseases
    - Study questionnaires
    - Records about the study drug you received
    - Records about the diagnosis and treatment of any mental health condition(s)
    - Information about your (or your partner's) pregnancy and its outcome, should you (or your partner) get pregnant during participation in the study

Your information may be used or shared with others for the following purposes:

- To conduct and oversee research
- To support the development and testing of the investigational rapid diagnostic tests that may be used in the study
- To ensure the research meets legal, institutional, and accreditation requirements
- To conduct public health activities (including reporting of adverse events or situations where you or others may be at risk of harm)
- To perform future research
- Researchers may need to discuss your health care with your regular physician when appropriate to maintain the quality of your treatment
- When required by law
- To make sure the research was performed correctly

For the purposes described immediately above, your information may be shared with:

- The sponsor and its representatives and vendors providing services for this study
- Outside individuals or entities that have a need to access this information to perform functions on behalf of the hospital and its affiliates, for example, data storage companies, insurers, or legal advisors
- Other research doctors and medical centers participating in this research or in your treatment

outside the study
- The US FDA
- The US Department of Health and Human Services (DHHS)
- Other federal and state agencies and government agencies in other countries
- IRB overseeing this study
- Hospital accrediting agencies

Your anonymized data may be shared with certain vendors and/or other researchers for the purpose of conducting future or additional research focused on the improvement of public health and the advancement of science and medicine. However, once your study information is shared as authorized, it may no longer be protected by federal law and there is a chance it may be re-disclosed without your permission. The sponsor will ensure that those vendors and/or researchers are required to hold your information as confidential.

If you do not give permission to use and give out your health information, you will not be able to take part in this study. While the study is in progress, you will not have access to your study records. You will be able to access your information when the clinical study is completed. After the study is completed, you have the right to see and copy the health information collected from you during the course of the study for as long as that information is maintained (kept) by the study staff and other entities according to federal privacy regulation (law). You have the right to request corrections of incorrect data (information) if needed.

You may withdraw your permission for us to use and give out your health information at any time. To do this, a written withdrawal notice must be submitted to your study doctor at the following address:

[redacted]

If you withdraw from the study and withdraw your Authorization, no new information will be collected for study purposes unless the information concerns an adverse event (a bad effect) related to the study. If an adverse event occurs, your entire medical record may be reviewed. All information that has already been collected for study purposes, and any new information about an adverse event related to the study, will be sent to the sponsor.

If you withdraw your Authorization, you will not be able to stay in the study. After you withdraw your Authorization, no new health information identifying you will be gathered. However, information already gathered may be used and given to others. If you withdraw from the study but do not withdraw your Authorization, new personal health information may be collected until this study ends.

This Authorization does not have an expiration date. If you do not withdraw this Authorization in writing, it will remain in effect indefinitely. [redacted] This Authorization will expire 31 December 2050, unless you withdraw it in writing before then.

Your study doctor will keep this Authorization for at least 6 years.

If you do not sign this Authorization, you cannot take part in this clinical study or receive study-related treatment. If you withdraw this Authorization while you are in the study, you will no longer be able to take part in this study. Your decision to withdraw your Authorization, or not to take part in the study, will not involve any penalty or loss of access to treatment or other benefits to which you are entitled.

[redacted]

AUTHORIZATION

By signing this Authorization, I give permission to [redacted] to use or disclose (release) my PHI as explained above. I have been told that I will receive a signed and dated copy of this Authorization for my records.

Printed Name of Participant

Signature of Participant **Date (dd-MON-yyyy)**

[redacted]