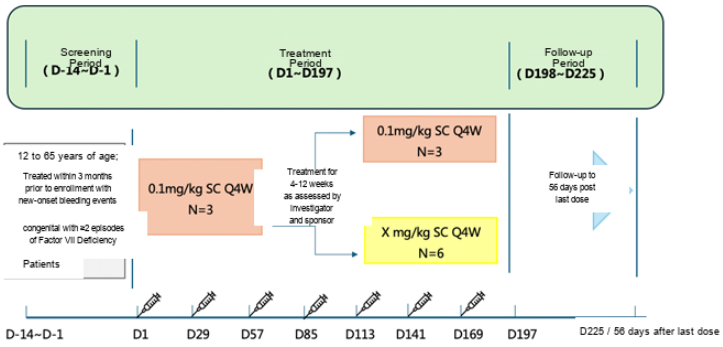
# PROTOCOL SUMMARY

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| **Study Title** | An Open-Label, Multicenter, Phase II Clinical Trial to Evaluate the Efficacy, Safety, and Pharmacokinetic Characteristics of SR604 Injection in Patients with Congenital Coagulation Factor VII Deficiency |
| **Study Drug** | SR604 Injection |
| **Protocol Number** | LS-SR604-VII-II01 |
| **Version/Date** | Ver 1.0 / May 25, 2026 |
| **Sponsor** | Shanghai RAAS Blood Products Co., Ltd. |
| **Study Sites** | Approximately 4-6 centers are planned to be selected as clinical trial sites |
| **Study Phase** | Phase II |
| **Study Population** | Patients with Congenital Coagulation Factor VII Deficiency |
| **Study Objectives** | **Primary Objective:** To evaluate the efficacy of multiple doses of SR604 in patients with congenital coagulation Factor VII deficiency.<br><br>**Secondary Objective:** To evaluate the safety, additional efficacy, and pharmacokinetic characteristics of multiple doses of SR604 in patients with congenital coagulation Factor VII deficiency. |
| **Study Design** | This is an open-label, multicenter, exploratory Phase II clinical trial designed to evaluate the efficacy, safety, and pharmacokinetic characteristics of SR604 Injection in patients with congenital coagulation Factor VII deficiency.<br><br>The trial consists of a screening period, treatment period, and follow-up period. The screening period is 14 days, extendable up to 42 days. The trial includes 0.1 mg/kg Q4W or other doses, comprising two dose groups. The 0.1 mg/kg Q4W dose group will first enroll 3 subjects; after 4 weeks (D29) to 12 weeks (D85) of treatment, the investigator and sponsor will jointly assess subject safety and efficacy to determine the next dose group (0.2 mg/kg Q4W, 0.05 mg/kg Q4W, or other dose). The plan is to ultimately enroll 6 patients per group, totaling 12 patients. The treatment period is 28 weeks with 7 doses administered. The last follow-up visit will be completed 56 days after the last dose, with the follow-up period extending to 56 days post-last dose. This is an exploratory trial; based on the indication, clinical needs, and product characteristics, the trial design—including sample size, dose, dosing frequency, and follow-up duration—will be adjusted in a timely manner based on interim results to support expedited regulatory filing.<br><br>The study design diagram is shown below:<br><br><br><br>Figure 3-1 Study Design Diagram |
| **Sample Size** | This trial plans to enroll 12 patients, divided into 2 dose groups with 6 patients each. |

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| **Study Duration** | From the screening of the first subject to the last visit of the last subject, the estimated study duration is 18 months. |
| **Subject Participation Duration** | From the signing of the informed consent form to the completion of all protocol-specified visits, the maximum expected duration for each subject is approximately 270 days. |
| **Subject Selection** | **Inclusion Criteria:**<br><br>1. Age ≥12 years and ≤65 years at the time of signing the informed consent form; both genders eligible;<br><br>2. Clinically diagnosed with congenital coagulation Factor VII deficiency, with historical or screening FVII activity <10%, and ≥2 treated new-onset bleeding events within 3 months prior to enrollment;<br><br>3. No active bleeding symptoms prior to first administration of SR604 Injection;<br><br>4. The subject and/or legal representative and impartial witness have signed the informed consent form, indicating voluntary agreement to participate in this trial, to provide biological samples for testing as required by the protocol, and to comply with the planned study visits;<br><br>5. Female subjects (post-menarche) must have a negative serum pregnancy test (HCG) during the screening period; subjects with childbearing potential (females post-menarche or males post-spermarche) must agree to use highly effective contraceptive measures throughout the study period.<br><br>**Exclusion Criteria:**<br><br>1. Known history of hypersensitivity to the study drug formulation or any of its components;<br><br>2. Intolerance to subcutaneous injection or other local skin abnormalities or dermatoses that may affect drug administration or safety assessment;<br><br>3. Meeting any one of the following criteria during screening:<br>a. Hemoglobin <60 g/L;<br>b. Platelet count <100×10⁹/L;<br>c. Abnormal hepatic or renal function: alanine aminotransferase (ALT) or aspartate aminotransferase (AST) ≥2.5× upper limit of normal (ULN), or total bilirubin ≥1.5× ULN; or serum creatinine (Cr) ≥1.5× ULN;<br>d. Positive for anti-human immunodeficiency virus (HIV) antibodies.<br><br>4. Any bleeding disorder other than congenital Factor VII deficiency, or other conditions causing significantly abnormal coagulation parameters (e.g., hemophilia A or B, von Willebrand disease, platelet disorders, vitamin K deficiency, etc.);<br><br>5. Protein C deficiency or Protein S deficiency;<br><br>6. History of thrombosis, family history of thrombosis, or history of thrombophilia;<br><br>7. Intracranial hemorrhage within 2 years prior to signing the informed consent form; |

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| | 8. Severe cardiac disease, such as unstable angina, congestive heart failure (New York Heart Association class ≥III), serious arrhythmia (QTc interval >450 ms, corrected by Fridericia formula), uncontrolled hypertension (systolic blood pressure ≥160 mmHg or diastolic blood pressure ≥100 mmHg), etc.;<br><br>9. Female patients with menstrual abnormalities caused by organic gynecological conditions (e.g., uterine fibroids, endometriosis, adenomyosis, etc.);<br><br>10. Received Factor VII-containing products within 48 hours prior to first administration of SR604 Injection; received whole blood or plasma transfusion within 2 weeks prior to first administration of SR604 Injection;<br><br>11. Used any anticoagulants, antifibrinolytics, or agents affecting platelet function (including chemical drugs, biological products, or traditional Chinese medicine), including aspirin, within 1 week prior to screening, or required use of such agents during the treatment period;<br><br>12. Underwent major surgery (defined as Grade III or IV surgery) within 1 month prior to signing the informed consent form, or planned to undergo surgery during the study period;<br><br>13. Enrolled in other clinical trials within 1 month prior to signing the informed consent form;<br><br>14. Miscarriage or pregnancy termination within 3 months prior to signing the informed consent form; pregnant or breastfeeding women;<br><br>15. Mental illness or significant psychiatric disorder, or incapacity or lack of cognitive ability due to other causes;<br><br>16. Other conditions deemed by the investigator to be unsuitable for enrollment, such as alcoholism, anticipated poor subject compliance preventing completion of dosing and study follow-up, poorly controlled comorbid chronic diseases, or serious systemic diseases. |
| **Dose Rationale** | In vitro inhibition studies showed that in human coagulation factor-deficient plasma at concentrations of 0.303–0.445 μg/mL, and in normal monkey plasma and human plasma at concentrations of 0.455 and 0.439 μg/mL respectively, the inhibition rate for Protac APTT reached approximately 90%.<br><br>In a separate pharmacokinetic study in PROC+/+F8-/- mice, SR604 concentrations at 24 h after subcutaneous injection of 0.05 and 0.2 mg/kg were 0.506 μg/mL and 1.36 μg/mL, respectively. The SR604 concentration of 0.506 μg/mL associated with the 0.05 mg/kg dose in mice is considered the minimum relevant SR604 trough level required to provide a clinically relevant pharmacodynamic response in humans.<br><br>Based on the above nonclinical pharmacodynamic results and nonclinical PK data, the minimum effective concentration of SR604 was set at 0.506 μg/mL (close to the in vitro 90% inhibition concentration). Modeling and simulation predicted that after a single subcutaneous injection of 0.05 mg/kg in hemophilia patients, the peak concentration would reach the predicted minimum effective concentration; after a single subcutaneous injection of 0.1 mg/kg, the concentration could be maintained at or above the minimum |

effective level for approximately 16 days; and after a single subcutaneous injection of 0.2 mg/kg, for approximately 29 days.

An ongoing Phase I/II clinical trial of SR604 in hemophilia A/B and congenital Factor VII deficiency patients was used for quantitative pharmacological analysis and simulation of different doses based on available clinical data (see Figure 3-2). Multiple dosing from 0.1 mg/kg Q4W to 0.8 mg/kg Q4W all achieved concentrations above the effective threshold (510 ng/mL), while 0.8 mg/kg Q4W exceeded the maximum safe concentration (4650 ng/mL).

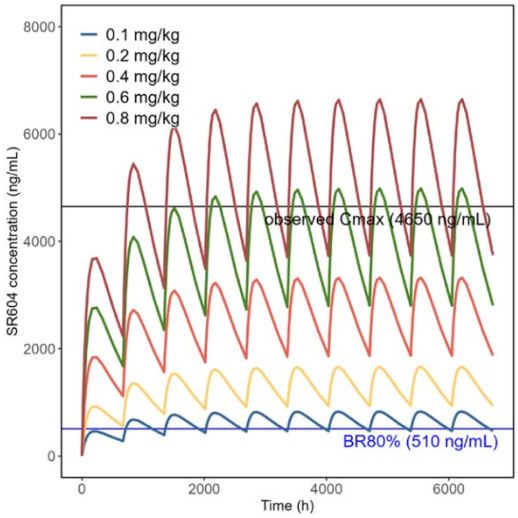



Figure 3-2 Simulated SR604 Concentration-Time Profile with Q4W Dosing

Phase IIa clinical trial (Protocol No. LS-SR604-I01) has enrolled one patient with congenital Factor VII deficiency in the 0.05 mg/kg dose group: male, 30 years old, diagnosed on March 4, 2018. Screening FVII activity <1.0%, severe, no history of FVII inhibitor positivity or family history of FVII inhibitors. Laparoscopic cholecystectomy in 2022. Comorbidities: periodontitis and renal calculi. On-demand treatment with recombinant human Factor VIIa (rFVIIa) was used in the 3 months prior to enrollment, with a pre-enrollment ABR of 32 events/year. After 24 weeks of SR604 Injection treatment (0.05 mg/kg Q2W, loading dose), no bleeding events occurred. During the trial, 8 AE episodes occurred (Grade 1 or 2), all resolved; no withdrawal due to AEs; no SAEs; no thromboembolic events; no ADRs; the safety profile was favorable. PK data for this patient after multiple dosing are shown in Table 3-1: Cmax,ss = 1040 ng/mL, AUC0-τ,ss = 304.31 h·μg/mL, Cmin,ss = 656 ng/mL, Cav,ss = 905.68 ng/mL, DF = 42.40%, Swing = 0.59, Tmax,ss = 2.00 days, AUC0-t = 304.12 h·μg/mL, CLss/F = 0.17 mL/h/kg, t1/2z = 15.35 days, λz = 0.0021/h.

Based on completed Phase I/II trial results, SR604 Injection demonstrated excellent safety and tolerability with single dosing (6 dose groups, 0.025–0.8 mg/kg), multiple dosing Phase IIa (2 dose groups: 0.05 mg/kg and 0.1 mg/kg, Q2W), and Phase IIb (3 groups: 0.4 mg/kg Q4W/Q6W/Q8W). A total of 76 subjects were enrolled; only the 0.05 mg/kg multiple-dose group had 4 subjects (5.3%) reporting 6 ADR episodes, 1 subject (1.3%) with 1 injection site reaction, and 2 subjects (2.6%) with 2 SAEs. No serious ADRs or thromboembolic events occurred.

Based on available Phase IIa PK data from 2 dose groups (0.05 mg/kg and 0.1 mg/kg, Q2W) — see table below — 1 subject in the 0.05 mg/kg group was excluded from

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| | analysis due to ADA and NAb positivity after D29, resulting in BQL drug concentrations from D57 onward; thus the actual number of subjects was 11.<br><br>Table 3-1 Summary of SR604 Multiple-Dose PK Parameters (Part B)<br><br>[PK Parameter Table inserted below]<br><br>Based on simulation results and data from the enrolled congenital Factor VII deficiency patient (0.05 mg/kg Q2W), while also considering the thrombotic risk in these patients, this trial selected the 0.1 mg/kg Q4W dose group to first enroll 3 subjects. After 4 weeks (D29) to 12 weeks (D85) of treatment, the investigator and sponsor will jointly assess safety and efficacy to determine the next dose group (0.2 mg/kg Q4W, 0.05 mg/kg Q4W, or other dose). The plan is to ultimately enroll 6 patients per group, totaling 12 patients. |
| **Study Drug** | Name: SR604 Injection<br><br>Strength: 30 mg/mL<br><br>Composition: SR604; excipients mainly include: histidine, histidine hydrochloride, trehalose, arginine hydrochloride, polysorbate 80<br><br>Storage Conditions: Store and transport at 2–8°C, protected from light<br><br>Supplier: Shanghai RAAS Blood Products Co., Ltd. |
| **Dosing Regimen** | Administration:<br><br>Administer by slow subcutaneous injection at the labeled dose, completing the injection within 5 minutes at a pace comfortable for the subject. Injection sites may include the thigh (anterior mid-region), abdomen (excluding a 5 cm radius around the umbilicus), or the lateral upper arm. Different injection sites should be selected for each injection within a 1-month period, at least 2.5 cm from the previous injection site. Avoid areas that may rub against belts or waistbands. Do not inject into areas with moles, scars, or bruises. Do not inject into areas that are tender, erythematous, indurated, or damaged. Abdominal administration is recommended.<br><br>Dosage:<br><br>The dose is calculated based on the subject's body weight and assigned dose group: Dose (mg) = Dose level (mg/kg) × Body weight (kg); subcutaneous injection once every 4 weeks. If the study drug is not administered within the planned dosing window, it should be given as soon as possible; if more than 14 days have elapsed without dosing, the drug should be administered on the next scheduled dosing day, with the regular dosing schedule resumed thereafter.<br><br>The injection volume is calculated based on the labeled strength. If the injection volume does not exceed 1 mL, the volume should be precise to 0.01 mL (rounded). If the injection volume exceeds 1 mL, the volume should be precise to 0.1 mL (rounded). |
| **Study Procedures** | The trial includes a screening period, treatment period, and follow-up period.<br><br>Screening Period:<br><br>After signing the informed consent form, patients enter the screening period, during which screening examinations and assessments will be completed per the visit schedule. The screening period shall not exceed 14 days (if the patient requires drug treatment for |

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<tr><td></td><td>bleeding events, or if a 14-day screening period cannot encompass one menstrual cycle for menstruating females, the screening period may be extended up to a maximum of 42 days). Subjects meeting all inclusion criteria and none of the exclusion criteria will enter the trial.<br><br>Treatment Period:<br><br>Eligible subjects enter a 28-week treatment period with dosing every 4 weeks, for a total of 7 doses. Specific dosages are detailed in the dosing regimen section. Subjects will complete efficacy and safety assessments, immunogenicity assessments, and PK blood sample collection per the visit schedule.<br><br>When bleeding events requiring treatment occur during the treatment period, the occurrence and treatment details will be collected. The investigator will select appropriate treatment medications and measures based on the subject's specific condition, including recombinant human Factor VIIa, human prothrombin complex concentrate, fresh plasma, and antifibrinolytic agents; other anti-hemorrhagic agents may also be selected as appropriate.<br><br>Follow-up Period:<br><br>The investigator will select appropriate treatment medications and measures based on the subject's specific condition, including recombinant human Factor VIIa, human prothrombin complex concentrate, fresh plasma, and antifibrinolytic agents; other anti-hemorrhagic agents may also be selected as appropriate.<br><br>On Day 56 after the last dose or at any time of withdrawal, the investigator must perform safety assessments including vital signs, physical examination, adverse event assessment, laboratory tests (complete blood count, urinalysis, blood chemistry, coagulation function, FDP), serum pregnancy test (females of childbearing potential only), 12-lead ECG, anti-SR604 antibody (ADA), and neutralizing antibody testing. Bleeding events and their treatment, adverse events, and concomitant medications/non-drug treatments will be recorded. Abnormal safety parameters must be followed up until normalization, clinically insignificant abnormality, stabilization, or return to baseline.</td></tr>
<tr><td>Pharmacokinetics (PK)</td><td>Biological Sample Collection:<br><br>All subjects enrolled in this trial are required to collect biological samples at specified time points for PK analysis, per the preliminary sampling schedule (see table below). Biological sample collection will be performed by authorized or trained research personnel in accordance with the requirements of the testing laboratory.<br><br>Collected blood samples will be centrifuged and stored at -60°C or below. Samples for testing will be transported to the central laboratory by a professional cold-chain logistics company. Backup samples will be temporarily stored at the clinical trial site or transported by a professional cold-chain company to a third-party facility designated by the sponsor and stored at -60°C or below.<br><br>PK Sampling Time Points and Windows<br><br>
<table>
<tr><th>Dosing Visit</th><th>Collection Time Point</th><th>PK Sample</th><th>Allowed Deviation</th></tr>
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| | 1st Dose | D1 (within 1h pre-dose) | ✓ | Within 1h pre-dose |
| | | D2 (24h post-dose) | ✓ | ±4h |
| | | D3 (48h post-dose) | ✓ | ±4h |
| | | D5 (96h post-dose) | ✓ | ±4h |
| | | D8 (168h post-dose) | ✓ | ±4h |
| | | D11 (240h post-dose) | ✓ | ±4h |
| | | D15 (336h post-dose) | ✓ | ±4h |
| | 2nd Dose | D29±3d (672h after 1st dose) | ✓ | Within 1h pre-dose |
| | 3rd Dose | D57±3d (within 1h pre-dose) | ✓ | Within 1h pre-dose |
| | 4th Dose | D85±3d (within 1h pre-dose) | ✓ | Within 1h pre-dose |
| | | 24h post-dose | ✓ | ±4h |
| | | 48h post-dose | ✓ | ±4h |
| | | 96h post-dose | ✓ | ±4h |
| | | 168h post-dose | ✓ | ±4h |
| | | 240h post-dose | ✓ | ±4h |
| | | 336h post-dose | ✓ | ±4h |
| | 5th Dose | D113±3d (672h after 4th dose) | ✓ | Within 1h pre-dose |
| | 6th Dose | D141±3d (within 1h pre-dose) | ✓ | Within 1h pre-dose |
| | Last Dose | 672h post-dose | ✓ | ±3d |
| | | 1008h post-dose | ✓ | ±3d |
| | | 1344h post-dose | ✓ | ±3d |

Biological Sample Analysis:

All PK biological samples collected from patients will be shipped to the central laboratory. Specific requirements will be followed in accordance with the standard operating procedures established by the central laboratory and the testing requirements.

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| **Primary Efficacy Endpoint** | Treated overall Annualized Bleeding Rate (ABR) over 28 weeks of treatment.<br><br>Calculated using the following formula over 28 weeks of treatment:<br>Total number of treated bleeding events during 28 weeks / 28-week bleeding exposure time × 365.25.<br><br>Note: Total bleeding includes spontaneous and traumatic bleeding. Treated bleeding refers to bleeding events for which drug treatment was administered (events managed without medication or treated only by physical methods are not counted). |
| **Secondary Efficacy Endpoints** | 1. Treated spontaneous annualized bleeding rate over 28 weeks of treatment;<br><br>2. Treated overall annualized joint bleeding rate over 28 weeks of treatment; |

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| | 3. Overall annualized bleeding rate over 28 weeks of treatment, including treated and untreated bleeding events;<br><br>4. Annualized menorrhagia bleeding rate over 28 weeks of treatment (menstruating females only);<br><br>5. Change in PBAC score from baseline over 28 weeks of treatment (menstruating females only);<br><br>6. Change in EQ-5D-5L health index score from pre-treatment over 28 weeks of treatment;<br><br>7. Change in EQ-VAS score from baseline over 28 weeks of treatment;<br><br>8. Subject overall satisfaction score with treatment efficacy over 28 weeks of treatment. |
| **PK Endpoints** | Single-dose PK parameters:<br><br>Tmax, Cmax, AUC0-t, etc.; if data permit, t1/2z, AUC0-∞, CLz/F, Vz/F, MRT, λz, etc. will be calculated.<br><br>Multiple-dose PK parameters:<br><br>Tmax,ss, Cmax,ss, AUC0-t, CLss/F, Cmin,ss, Cav,ss, AUC0-τ,ss, and degree of fluctuation (DF), etc.; if data permit, t1/2z, AUC0-∞, Vz/F, MRT, λz, etc. will be calculated.<br><br>AUC0-t and other parameters will be normalized by dosing interval when necessary. |
| **Safety and Immunogenicity Endpoints** | Safety Endpoints: Incidence of AE/SAE/AESI assessed through clinical signs and symptoms, vital signs, physical examination, laboratory tests (complete blood count, urinalysis, and blood chemistry), coagulation function [prothrombin time (PT), thrombin time (TT), international normalized ratio (INR), fibrinogen (FIB), activated partial thromboplastin time (APTT), D-dimer], FDP, 12-lead ECG, injection site reactions, hypersensitivity/allergic reactions, and thrombotic events; incidence of drug-related AE/SAE/AESI.<br><br>Immunogenicity Endpoints: Anti-drug antibody (ADA) and neutralizing antibody (NAb) — number of subjects and incidence rate. |
| **Statistical Software and General Requirements** | Detailed statistical methods will be provided in the statistical analysis plan.<br><br>Pharmacokinetic analysis will be performed using Phoenix WinNonlin (version 8.3 or above); all other analyses will be performed using SAS software (version 9.4 or above). |