## SYNOPSIS

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| **Name of Sponsor / Company:**<br>LFB BIOTECHNOLOGIES | **INDIVIDUAL STUDY TABULAR FORMAT**<br>**Referring to Part of the dossier**<br>**Volume:**<br>**Page:** | **(For National Authority Use only)** |
| **Name of Finished Product:**<br>SEVENFACT® | | |
| **Name of Active substance:**<br>LR769, coagulation factor VIIa (recombinant) | | |

**Title of the study:** A Phase 3 Study of the Safety and Efficacy of Coagulation Factor VIIa (Recombinant) for the Prevention of Excessive Bleeding in Patients with Congenital Hemophilia A or B with Inhibitors to Factor VIII or IX Undergoing Elective Major Surgical Procedures – F7TG2202

Short title: SCOPE HIM

**Investigators:**

USA: **M. Escobar*** (coordinating investigator), R. Sidonio, M. Mazepa, M. Janbain
Malaysia: L. Wong Lee Lee, V. Selvaratnam,
Thailand: R. Natesirinikul, C. Chai-Adisaksopha
South Africa: **J. Mahlangu***
Türkiye: OB Zülfikar, AB Antmen, S. Aksu

***Patient enrolled**

**Study centers:**

12 activated sites, 2 sites enrolled 1 patient each:

USA: **Houston (TX)***, Atlanta (GA), Minneapolis (MN), New Orleans (LA)
Malaysia: Kota Kinabalu, Ampang
Thailand: Chiang Mai (2 sites)
South Africa: **Johannesburg***
Türkiye: Fatih/Istanbul, Seyhan/Adana, Altindağ/Ankara

***Patient enrolled**

**Publication (reference):** Not applicable

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| **Study period (years):** 2024 - 2025<br>**Date of first patient screening:** June 3, 2024<br>**Date of first patient enrollment:** July 15, 2024<br>**Date of last patient completed:** July 7, 2025 | **Clinical Phase:** 3 |

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**Objectives:**

The primary objective of this study was to assess the efficacy of LR769 in terms of achieving and maintaining hemostasis in hemophilia A or B patients with inhibitors to FVIII or FIX undergoing elective major surgical procedures.

The secondary objective of this study was to assess the safety of LR769.

**Methodology:** Interventional, prospective, international, multicenter, non-comparative, single-arm, phase 3, and sequential study

**Number of subjects (total and for each treatment / planned and analyzed):**

Planned: 19 patients for a minimum of 17 evaluable elective major surgical procedures

Enrolled: 2 patients

Analyzed: 2 patients for 2 evaluable procedures

Patient recruitment was discontinued on June 1st, 2025, due to difficulty in enrollment and feasibility considerations - namely, the extended timelines and significantly higher-than-anticipated costs required to complete recruitment.

**Diagnosis and main criteria for inclusion:**

Male patients, aged ≥12 years to ≤65 years, with hemophilia A or B with a current positive inhibitor test BU ≥5 or a history of high-responding inhibitors (BU ≥5) not further successfully treated by Immune Tolerance Induction or a condition precluding the use of FVIII or FIX products to treat or prevent bleeding such as a previous anamnestic response after exposure to factor concentrates or a previous failure to respond to FVIII or FIX concentrates, and undergoing elective major surgery. Patients also had to have a hemoglobin level of ≥12 g/dL.

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**Test product, dose, mode of administration, batch No.:**

LR769 was provided as lyophilized powder in single-use vials containing 5 mg of coagulation factor VIIa (recombinant)-jncw. After reconstitution with sterile water for injection, each milliliter contained 1 mg (1000 µg) of LR769.

LR769 was infused by intravenous at the following doses:

| **Inpatient dosing** | | |
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| **Day** | **Dose** | **Interval** |
| Immediately prior to surgical incision | 200 µg/kg | Initial dose (within 2 minutes prior to surgical incision) |
| Intra-operative period | 75 µg/kg | Every 2 hours (± 15 minutes) |
| Day 1 (wound closure) through Day 3 (72 hours from wound closure) | 75 µg/kg | Every 2 hours (± 15 minutes) |
| Day 4 (post 72-hour assessment) | 75 µg/kg | Every 2 hours (± 15 minutes) to 4 hours (± 15 minutes) |
| Days 5-6* | 75 µg/kg | Every 2 hours (± 15 minutes) to 6 hours (± 15 minutes) |
| Days 7+* | 75 µg/kg | Every 2 hours (± 15 minutes) to 8 hours (± 15 minutes) |
| **Outpatient dosing** | | |
| **Day** | **Dose** | **Interval** |
| From hospital discharge to last dose for peri-operative management** | 75 µg/kg | Every 2 hours (± 15 minutes) to 12 hours (± 15 minutes) |

**Dosing beyond D5 was optional*

***Hospital discharge was at the judgment of the investigator but did not occur until i) after the 120-hour efficacy assessment AND ii) the patient is successfully maintained at every 6 hours or greater dosing interval. Dosing frequency could be increased only with the investigator's recommendation in the outpatient setting as needed.*

Batch numbers of LR769 used during this study: CLI11871

**Duration of treatment:**

At least 5 days at hospital.

If the patient needed further treatment with LR769 after hospital discharge, the patient self-administered LR769 at home.

Then, the patient was followed until a follow-up phone call (i.e. end of study) 28 ± 2 days after the last visit occurring 48 ± 4 hours after the last dose of LR769.

**Reference therapy, dose, mode of administration, batch No.:**

Not applicable

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**Criteria for evaluation:**

**Efficacy**:

Primary endpoint

A successfully treated major procedure was defined by a good or excellent global hemostatic response. The global hemostatic response score is obtained by summing assigned scores from a defined 4-point hemostatic scale (excellent: score = 3, good: score = 2, moderate: score = 1, poor: score = 0) determined at wound closure (T0), at 24 hours, and at 120 hours after surgical wound closure.

The global hemostatic response was considered:

- Excellent if the aggregate score from the 3 timepoints is between 7 and 9 with no score <2 for any of the component score comprising the aggregate score
- Good if the aggregate score from the 3 timepoints is between 5 and 7 with scores <2 at T0 and at 120 hours after wound closure and no score <1 at 24 hours after wound closure
- Moderate if the aggregate score from the 3 timepoints is between 3 and 7 with no score <1 for any of the component score comprising the aggregate score or between 5 and 6 when including a score = 0 or missing (without a replacement score) for any of the component score comprising the aggregate score
- Poor if the aggregate score from the 3 timepoints is between 0 and 4 when including at least 1 score = 0 or missing (without a replacement score) for any of the component score comprising the aggregate score

Secondary endpoints

- Hemostasis rating at each time point (intra-operative period and, at 24 hours and 120 hours and daily until Day 15 post-surgery or discharge if earlier)
- Blood loss, hemoglobin levels and transfusion requirements
- Amount of LR769
- Bleeding episodes, surgical intervention/re-exploration
- Death attributed to ineffective hemostasis

Exploratory endpoint

- Number of days in intensive care unit (ICU) and hospital

**Safety:**

Safety was assessed based on treatment-emergent adverse events (TEAEs), vital signs, and clinical laboratory parameters.

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**Statistical methods:**

The planned primary null hypothesis to be tested for the proportion of major procedures successfully treated [i.e. defined by a good or excellent overall hemostatic response based on scores from a defined 4-point hemostatic scale during the intra-operative period and, at 24 hours and 120 hours after surgical wound closure] was a proportion of less than 0.55 against the alternative hypothesis that the proportion was at least 0.55.

The analyses of the secondary endpoints were planned to involve the calculation of a point estimate and the associated 95% confidence interval.

As only two patients were included, no statistical analysis was performed and the patient data were only described.

**SUMMARY - CONCLUSIONS:**

Due to enrollment difficulty and feasibility considerations, the study was discontinued on June 1st, 2025. Only two patients were enrolled.

**Efficacy results:**

Two severe hemophilia A patients with FVIII inhibitors, aged 33 and 35 years, were treated and completed the study. One patient was white, Hispanic or Latino, the other patient was black. One patient was obese (BMI of 34.3 $kg/m^2$), the other patient was overweight (BMI of 27.9 $kg/m^2$).

Overall, treatment dose was as recommended in the protocol.

The global hemostatic score was assessed as “excellent” for one patient who underwent left elbow open synovectomy. The score was based on the excellent rating obtained at each time point. The patient received RBCs and tranexamic acid for a traumatic bleeding episode after an accidental drain removal. Due to the accidental nature of this event, this bleeding was not included in the assessment.

The global hemostatic score was assessed as “poor” due to out of window assessments for the second patient who underwent total arthroplasty of the left knee. The investigator’s post-operative assessments at 24 hours and 120 hours were “good” and “excellent”, respectively, but were considered missing data because they were provided outside the time window. In addition, ratings performed by the surgeon (excellent) and the investigator (good and excellent) do not comply with the 4-point scale criteria, as the actual blood loss was >50% greater than the predicted blood loss. The investigator was asked to reassess the ratings and confirmed a good/excellent response.

Hemoglobin levels decreased in post-operative period in both patients, but this was not reported as clinically significant. There were no surgical complications and no use of rescue treatment.

The DMC concluded that both patients had an excellent hemostatic response.

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**Safety results:**

A total of 199 infusions of LR769 over 37 exposure days were administered to 2 patients. The infusion dose was 200 µg/kg for the initial dose, followed by doses of 75 µg/kg.

A total of 8 TEAEs were reported in the 2 patients enrolled and treated. None were serious, treatment-related, of special interest, or severe.

No clinically significant changes were reported in hematology, biochemistry, vital signs or physical examination.

**Conclusion:**

No conclusions can be drawn regarding the efficacy of LR769 in the context of major surgical procedures as the study was early terminated. However, the hemostatic response of the two patients enrolled in the study were evaluated as good/excellent by the investigators and DMC. A total of 199 infusions of LR769 at a dose of 200 µg/kg or 75 µg/kg were administered. No safety issues were observed.

**Date of report: 02 December 2025**