SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Agent, Injectable, Embolic

Device Trade Name: Lava™ Liquid Embolic System (Lava LES)

Device Procode: QVG

Applicant's Name and Address: BlackSwan Vascular, Inc.
709 Sandoval Way
Hayward, CA 94544

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P220020

Date of FDA Notice of Approval: April 4, 2023

II. INDICATIONS FOR USE

The Lava LES is indicated for embolization of arterial hemorrhage in the peripheral vasculature.

III. CONTRAINDICATIONS

Lava LES is not indicated for use in pregnant women, neonates or individuals with significant liver or kidney function impairment. Safety for these patient groups has not been evaluated.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Lava LES labeling.

V. DEVICE DESCRIPTION

The Lava Liquid Embolic System (Lava LES) consists of the Lava LES Kit and the Lava Mixing Kit.

The Lava liquid embolic (Lava) is an injectable, non-adhesive liquid embolic agent comprised of ethylene vinyl alcohol (EVOH) copolymer dissolved in dimethyl sulfoxide (DMSO) and suspended micronized tantalum powder to provide contrast for visualization under fluoroscopy. Lava liquid embolic agent (LES) is first mixed using the Lava Mixing Kit and then delivered to the target anatomy via a DMSO compatible microcatheter, as

identified in the instructions for use. Upon exposure to blood at the targeted location, Lava precipitates into a spongy, coherent mass or cast.

The Lava LES Kit comprises a sterile, sealed, serum vial containing the Lava liquid embolic agent (Lava), a sterile, sealed, serum vial containing DMSO, and a sterile, sealed pouch containing DMSO compatible syringes.

The Lava Mixing Kit comprises a sterile, sealed pouch containing a mixing manifold and two sterile, sealed pouches, each containing a single DMSO compatible mixing syringe.

The Lava LES Kit is available in two product formulations, Lava-18 (nominal viscosity of 20 centistokes), and Lava-34 (nominal viscosity of 33 centistokes). Due to its lower viscosity, Lava-18 will travel more distally and penetrate deeper into the vasculature compared to the Lava-34. Each product formulation of the Lava LES Kit is available in two volumes, 2mL and 6mL.

Lava LES is available in four product configurations (representing various permutations of viscosity and volume). The Lava Mixing Kit is available in two product configurations with the Lava Mixing Kit – 2 mL designed for use with the 2 mL Lava LES Kit configurations and the Lava Mixing Kit – 6 mL designed for use with the 6 mL Lava LES Kit configurations.

The details of each of the Lava LES Kit product configurations and the Lava Mixing Kit, and their associated Stock Keeping Units (SKUs), are provided in **Table 1** and **Table 2** and **Figure 1** and **Figure 2** below.

Table 1. Summary of Lava LES Kit Configurations

Lava LES Product Configurations(SKU)	Components	Quantity, Size
Lava-18, 2 mL (FG-00559-02)	Lava vial	1 each, 2 mL
	DMSO vial	1 each, 2 mL
	DMSO syringe	1 each, 1 mL
	Delivery syringe	2 each, 1 mL
Lava-18, 6 mL (FG-00559-03)	Lava vial	1 each, 6 mL
	DMSO vial	1 each, 2 mL
	DMSO syringe	1 each, 1 mL
	Delivery syringe	6 each, 1 mL
Lava-34, 2 mL (FG-00559-04)	Lava vial	1 each, 2 mL
	DMSO vial	1 each, 2 mL
	DMSO syringe	1 each, 1 mL
	Delivery syringe	2 each, 1 mL
Lava-34, 6 mL (FG-00559-05)	Lava vial	1 each, 6 mL
	DMSO vial	1 each, 2 mL
	DMSO syringe	1 each, 1 mL
	Delivery syringe	6 each, 1 mL

Table 2. Summary of Lava Mixing Kit Configurations

Lava Mixing Kit Product Configurations (SKU)	Components	Quantity, Size
Lava Mixing Kit – 2 mL (FG-00563-02) *Used with 2 mL Lava LES Kit configurations*	DMSO compatible mixing syringes	2 each, 3 mL
	Mixing manifold	1 each
Lava Mixing Kit – 6 mL (FG-00563-01) *Used with 6 mL Lava LES Kit configurations*	DMSO compatible mixing syringes	2 each, 6 mL
	Mixing manifold	1 each

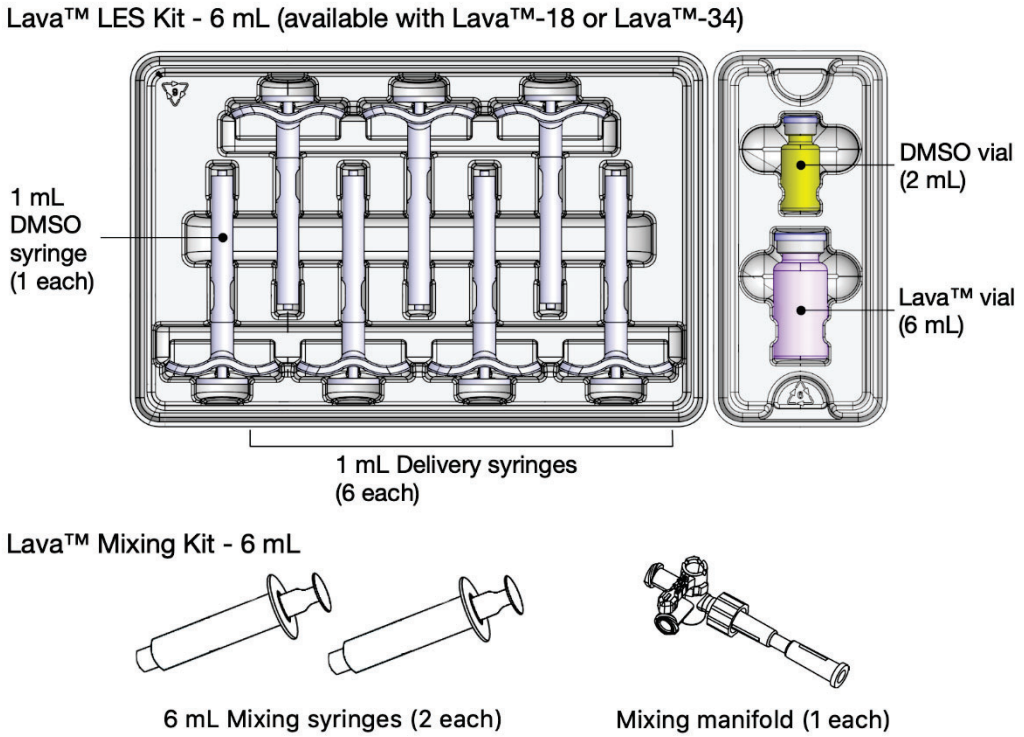

Figure 1. Lava™ LES – 6 mL Kit and Lava Mixing Kit – 6 mL

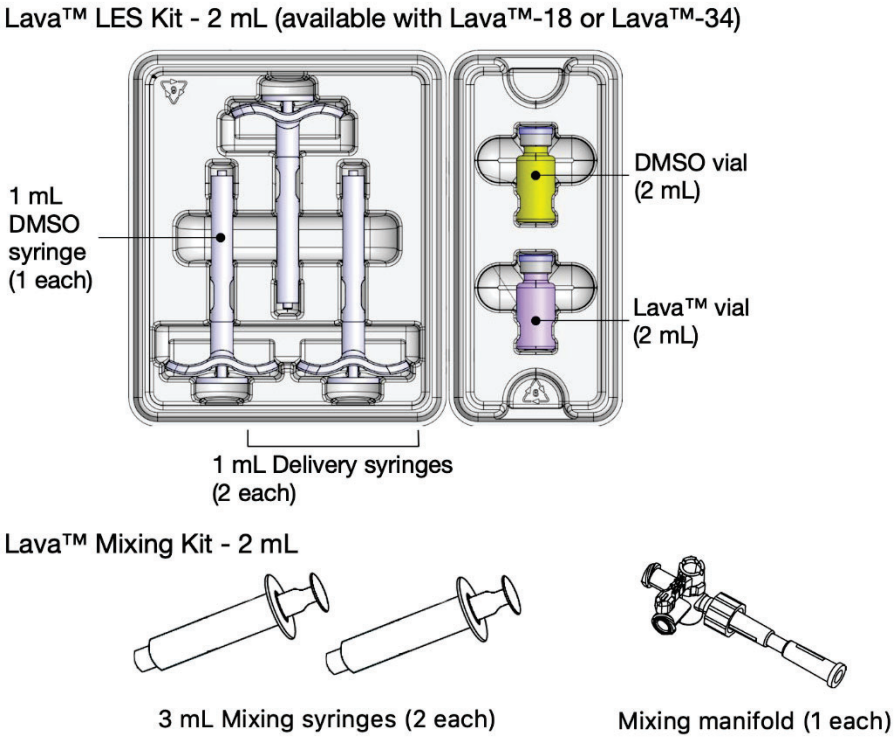

Figure 2. Lava™ LES – 2 mL Kit and Lava Mixing Kit – 2 mL

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the embolization of arterial hemorrhage in the peripheral vasculature. These include gelatin-based cubes, tris-acryl gelatin microspheres, and microcoil devices. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The Lava LES has not been marketed in the United States or any foreign country.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Potential adverse effects (e.g., complications) associated with the use of the device include:

- Non-target embolization
- Ischemia or infarction of the target territory
- Allergic reactions to device components
- Catheter breakage
- Catheter entrapment
- Inadvertent embolization of a non-target vessel or territory

- Embolization of device components
- Access site hematoma or ecchymosis
- Access site false aneurysm
- Pain at access site
- Arterial dissection
- Mural thrombus formation
- Vessel perforation
- Hemorrhage
- Recanalization
- Vessel perforation
- Arteriovenous fistula
- Distal atheroembolism
- Infection
- Sepsis
- Serous drainage
- Lymphorrhea
- Leg edema
- Leg pain
- Back pain

For the specific adverse events that occurred in the clinical study, please see **Section X** below.

IX. SUMMARY OF NONCLINICAL STUDIES

Physico-chemical, engineering, biocompatibility, animal studies, and sterilization testing were conducted on the Lava LES, as described below.

A. Physico-Chemical and Bench Testing

The tests described below in **Table 3** assessed the characterization and performance of Lava LES at baseline and the shelf life of 1 year.

Table 3. Physico-Chemical and Bench Testing

Study	Test method	Acceptance criteria	Results and Conclusions
Viscosity	ASTM D445	Lava-18 shall have a nominal viscosity of 20 centistoke. Lava-34 shall have a nominal viscosity of 33 centistoke	The viscosity of Lava-18 and Lava-34 met the acceptance criteria.
Solidification Time	No directly applicable Standard test method. Lava was precipitated in saline. At controlled intervals, the samples were monitored for evidence of DMSO elution. A sample was considered solidified when no DMSO could be observed eluting away from the sample.	The time of the onset of solidification of the liquid embolic must be ≤ 2 minutes after exposure of the embolic to saline. The time for complete solidification of the liquid embolic must be ≤ 8 minutes after exposure of the embolic to saline	The solidification time of Lava-18 and Lava-34 met the acceptance criteria.
Swelling	No directly applicable Standard test method. Lava was precipitated in saline. The diameter and length of the samples were measured at controlled intervals out to 7 days.	The Lava samples shall not swell or shrink substantially over the course of the testing.	The swelling of Lava-18 and Lava-34 met the acceptance criteria.
DMSO Stability	GC-MS analysis for impurities	The results shall not show trends that would be expected to negatively impact Lava performance	The DMSO stability of Lava-18 and Lava-34 met the acceptance criteria.
Tantalum Suspension / Duration of Suspension	No directly applicable Standard test method. Samples of Lava prepared per the instructions for use (IFU) were fluoroscopically examined against a marketed liquid embolic comparator	The homogeneity and duration of suspension of the Lava-18 and Lava-34 suspensions must be comparable to that of a marketed liquid embolic when prepared using the Lava Mixing Kit or when prepared using a minimum of 20 minutes of vortex agitation.	The tantalum suspension and duration of suspension of Lava-18 and Lava-34 met the acceptance criteria.

Study	Test method	Acceptance criteria	Results and Conclusions
Particulate Generation	No directly applicable Standard test method. Testing was conducted in alignment with Section IV.B.12 of the FDA guidance, "Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems," and Section 13 of "Certain Percutaneous Transluminal Coronary Angioplasty (PTCA) Catheters - Class II Special Controls Guidance for Industry and FDA."	The characteristics of particulate material (e.g., particle size distribution, morphology) of particulate generated during the deployment of Lava liquid embolic must be comparable to the characteristics of particulate generated by a marketed liquid embolic when prepared per their respective IFUs.	The particulate generation characteristics of Lava-18 and Lava-34 met the acceptance criteria.
Precipitate Morphology	Lava was deployed in a simulated use model and cross sections of the precipitated (i.e. solidified) samples were visually evaluated for appearance, color, and occlusion of the test vessel.	Characterization test – no acceptance criteria	All Lava-18 and Lava-34 samples display a uniformly distributed black color on cross section, and fully occluded the test segment. The precipitated liquid embolic appeared as a single coherent mass across all samples.
Infusion Pressure	Lava was infused into DMSO compatible microcatheters at a rate of 0.3 mL/minute. Peak pressure was recorded during each infusion	The peak pressure must be below the listed burst pressure of the DMSO compatible microcatheters	The infusion pressure of the Lava LES when injected through DMSO compatible microcatheters met the acceptance criteria.
Material Adhesion	No directly applicable Standard test method. The force required to extract various DMSO compatible microcatheters from a solidified Lava mass was measured.	The tensile force required to retract a microcatheter embedded in a fully solidified liquid embolic cast must be less than the minimum peak tensile force for catheters in ISO 10555-1	Both Lava-18 and Lava-34 met the acceptance criteria.
Simulated Use	Lava was deployed through DMSO compatible microcatheters into a simulated small diameter vessel under physiologically relevant conditions of temperature, pressure, flow, and pH.	Characterization test – no acceptance criteria	Both the Lava-18 and the Lava-34 successfully occluded the target location in a simulated vessel flow model and demonstrated that the precipitated embolic mass does not migrate after solidification.
Tensile Testing	No directly applicable Standard test method. Lava was precipitated in saline. The tensile strength of the samples were measured at controlled intervals out to 7 seven days.	Characterization test – no acceptance criteria	No statistically significant difference observed between tensile strength of the Lava-18 or Lava-34 liquid embolic precipitate samples from Day 0 and Day 7.

Study	Test method	Acceptance criteria	Results and Conclusions
Lava LES / Embolization Coil Compatibility Evaluation	Metal coils enlaced with synthetic fiber were incubated with DMSO to determine if the solvent could leach any chemical from the coils. The same fibered coils were used to conduct a simulated vessel occlusion in a flow model under physiologically relevant conditions of temperature, pressure, flow, and pH.	Characterization test – no acceptance criteria	HPLC evaluation revealed no substantial differences between neat DMSO and DMSO exposed to the fibered coils. Simulated use testing demonstrated no unexpected interactions between the representative embolic coil and Lava LES. Furthermore, there were no observations of migration of any coils and/or any combined coil/embolic mass samples.
Joint Tensile Strength (Mixing Manifold)	Testing was conducted in alignment with ISO 10555-1	The mixing manifold must withstand the tensile loads it is subjected to during use	The joint tensile strength performance of the Lava mixing manifold met the acceptance criteria.
Leak Pressure (Mixing Manifold)	Testing was conducted in alignment with ISO 10555-1	The mixing manifold must withstand the internal pressures it is subjected to during use	The liquid leak performance of the Lava mixing manifold met the acceptance criteria.
Shelf Life	The Lava LES products were evaluated per the testing listed above after real time aging for one year.	See the collective acceptance criteria used for baseline testing listed above	The results of product functionality and packaging validation testing support a 1-year shelf life for the Lava LES.

B. Biocompatibility Testing

Lava LES is a permanent (>30 days) blood-contact (circulating blood) implant device. The following tests and assessments were conducted in support of the biocompatibility of Lava LES:

- Bench and small animal biocompatibility testing per ISO 10993-1
- Systemic toxicity, implantation, and thrombogenicity assessments conducted in a chronic GLP swine model
- Chemical characterization and toxicological risk assessments

Biocompatibility testing per ISO 10993-1 is summarized in **Table 4**. The following tests were evaluated with a marketed control: complement activation (ISO-10993-4) and cytotoxicity (ISO-10993-5).

Table 4. Biocompatibility Evaluation

Description	Test Result			
Cytotoxicity (ISO-10993-5) MEM Elution, 72-hour extract @ 37°C. Serial dilutions of the neat liquid embolic solution were conducted with a marketed embolic agent as a comparator. See discussion below.	Lava LES		Comparator	
	Dilution	Ranking	Dilution	Ranking
	Neat	4/4/4	Neat	4/4/4
	1:2	3/3/3	1:2	3/3/3
	1:4	2/2/2	1:4	1/1/1
	1:8	0/0/0	1:8	0/0/0
Cytotoxicity (ISO-10993-5) MEM elution, 72-hour extract @ 37°C. Serial dilutions of a precipitated cast of the liquid embolic. See discussion below.	Dilution		Ranking	
	Neat		0/0/0	
	1:2		0/0/0	
	1:4		0/0/0	
	1:8		0/0/0	
Hemolysis (ASTM F756) ASTM Hemolysis (Direct Contact and Extract Methods), neat liquid embolic. See discussion below.	Direct contact: Hemolytic Extract: Non-hemolytic			
Hemolysis (ASTM F756) ASTM Hemolysis (Direct Contact Methods), precipitated cast of the liquid embolic. See discussion below.	Direct contact: Non-hemolytic			
Complement Activation (ISO-10993-4) Complement Activation (SC5b-9 only) of the neat liquid embolic solution with a marketed agent as a comparator.	• The test article and comparator induced more activation than the negative control. • The test article and comparator induced less activation than the positive control. • The test article induced more activation than the comparator.			
Sensitization (ISO-10993-10) Guinea pig maximization sensitization test, extracts of neat liquid embolic in normal saline and sesame oil	The normal saline extract and sesame oil extract of the test articles did not elicit a sensitization response.			
Irritation (ISO-10993-10) Intracutaneous irritation test, extracts of neat liquid embolic in normal saline and sesame oil.	The test article has met the requirements of the ISO intracutaneous reactivity test			
Pyrogenicity (ISO-10993-11) Materials mediated rabbit pyrogen, extracts of neat liquid embolic in normal saline	The test article is non-pyrogenic			

Cytotoxicity. Cytotoxicity testing showed that the Lava LES is more cytotoxic than the marketed comparator device at a 1:4 dilution after 72 hours of exposure to cells. However, testing of the precipitated Lava LES, showed no evidence of cytotoxicity with a cytotoxicity grade of 0 after 72 hours of exposure to cells.

Hemolysis. Both direct and indirect in vitro hemolysis tests were conducted per ASTM F756. Direct hemolysis testing showed that the Lava LES is hemolytic. Some hemolysis may be expected due to the presence of DMSO, which has been shown to induce hemolytic effects (X Yi et al, FEBS open bio 7(4): 485-495. 2017). However, indirect hemolysis testing showed that the Lava LES is non-hemolytic, and no significant concerns for hemocompatibility were noted in the chronic GLP animal studies. Finally, additional direct hemolysis evaluation using precipitated Lava as the test article reported the precipitated Lava to be non-hemolytic. These results indicate that the clinical risk of local hemolysis during the brief period between the introduction of the liquid embolic into the target vasculature and the precipitation of Lava is acceptable.

Complement activation. While SC5b-9 complement protein concentration was greater in the Lava LES than in the negative material control and comparator device control, it was much lower than in the positive control. In addition, no anaphylactic events were observed in the LAVA clinical study. These findings suggest that the clinical risk of the Lava LES acting as a major activator of the complement system and leading to anaphylactic events is low.

Systemic toxicity, implantation, and thrombogenicity observations that were included in the chronic swine (large animal) studies of the Lava LES following good laboratory practice (GLP). Lava LES implantation in relevant anatomical environments provided the following findings:

1. Systemic toxicity was not observed in the examined organs or tissue lesions observed during necropsy (heart, kidneys, liver, lungs, brain, spleen, downstream distal tibial and gastrocnemius muscles or coronary bands). No adverse effects or clinical signs pointing to systemic toxicity were elicited for the treatments with Lava-18 and Lava-34 in this swine model at 3, 28, 90, and 180 days.

2. After implantation of Lava LES, histological changes seen in the embolized target arteries and surrounding tissues were expected changes secondary to artery embolization with chronic occlusion of the target arteries, minimal to mild inflammation, and tissue remodeling at 3, 28, and 90 days. At 180 days, chronic thrombus resulting from target vessel embolization consisted of Lava LES embolic material surrounded by generally minimal-to-moderate granulomatous (foreign body reaction) inflammation and fibroplasia/fibrosis, with attenuation of typical vascular mural architecture due to incorporation into the vascular wall with chronic intravascular thrombus remodeling. The intravascular remodeling of the thrombus material was considered typical and appropriate (i.e., the presence of

Lava LES embolic material did not appear to affect typical intravascular healing/remodeling responses expected at 180 days). The mature appearance of the microscopic findings (mature tissue morphologic features and modest to negligible inflammation and absence of acute inflammatory features) reflected a stabilized/quiescent tissue response at this late time point.

3. No evidence of thrombogenicity (as assessed by lack of observed non-target embolization) for all Lava-18 and Lava-34 cases during post-embolization angiography. Histopathological evidence of thromboembolism or thromboembolic events was not seen in the brain, heart, kidneys, lungs, spleen, downstream distal tibial and gastrocnemius muscles or coronary bands.

Exhaustive chemical extraction of the Lava LES per ISO10993-18:2020 and a toxicological risk assessment per ISO10993-17:2002 were conducted. The toxicological risk assessment concluded that the current risk assessment supports that there is negligible genotoxicity risk, and thus negligible carcinogenicity risk. Moreover, all MOS values for identified polar and non-polar extractables were determined to be acceptable, so there is also no concern for systemic toxicity.

C. Animal Studies

Two GLP chronic studies were conducted in support of the safety and effectiveness of the Lava LES. The first study was a GLP study of the performance, efficacy, chronic safety, thrombogenicity and systemic toxicity of the Lava LES in the vascular anatomy of a swine model at 3 days, 28 days, and 90 days. The second study was a GLP study of the performance, efficacy, chronic safety, thrombogenicity and systemic toxicity of the Lava™ LES in the vascular anatomy of a Swine Model at 180 days. The studies utilized vessels of the hepatic, lower limb and pelvis, and the rete mirabile vascular systems of the domestic pig. The studies investigated and reported results for both low and high viscosity Lava LES (Lava-18 LES and Lava-34 LES, respectively).

Overall, Lava-18 and Lava-34 are well tolerated in all vascular beds. The time course of radiographic, clinical, clinical-pathologic, and pathologic findings mirrored the knowledge about other similar products. Consistent with the clinical and non-clinical findings of liquid embolic polymers, the administration of Lava-18 or Lava-34 in the rete mirabile and peripheral vessels of animal subjects is associated with a pathophysiologic response characterized by non-serious transient acute mild/moderate regional inflammation with occasional transient clinical manifestations of procedural discomfort. Except for one pig with extreme rete mirabile embolization, all remaining animals rapidly recovered from the procedure, gained weight, and had normal clinical chemistry values.

Specifically, the terminal angiographic findings demonstrated acceptable clinical outcomes for vascular embolization. Macroscopic findings of perivascular bruising early in the time course in peripheral vessels of the lower limb is consistent with the mechanism of action of necrosing embolized vessels. Microscopic findings at later timepoints indicate acceptable regional and downstream tolerability. Inflammatory scoring at all time points was non-reactive low. Rare instances of microscopic embolized particles were expected

findings indicating normal early necrosis and healing of the embolized vessels and were not associated with granulomatous or other adverse microscopic, clinical, or angiographic findings.

The cumulative Lava LES GLP Chronic animal study outcomes demonstrated the progression of vascular healing. At 180 days in this study, the mature appearance of the microscopic findings (mature tissue morphologic features and modest to negligible inflammation and absence of acute inflammatory features) reflected a stabilized/ quiescent tissue response to both Lava-18 and Lava-34 and are supportive of chronic safety of both formulations of the device.

D. Sterilization

All components of the Lava LES product are sterilized using conventional terminal sterilization processes at approved contract sterilization facilities as follows: Dry Heat process (for liquid embolic and DMSO serum vials), Ethylene Oxide process (for pouched syringe trays), or Electron Beam irradiation process (for Lava mixing manifolds), each of which has been validated per applicable Standards to achieve a Probability of a Non-Sterile Unit (PNSU) or Sterility Assurance Level (SAL) of 10^{-6} or better.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of the Lava LES for embolization of arterial hemorrhage in the peripheral vasculature in the US under IDE #G190291. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

The first subject was treated on April 14, 2021, and the database for this PMA reflected data collected through the last patient visit on August 17, 2022. The study included 113 patients at 19 investigational sites.

The Liquid Embolization of Arterial Hemorrhages in the Peripheral Vasculature Study or LAVA Study was a multicenter, prospective, single-arm trial of the Lava LES in patients with peripheral arterial bleeding in need of treatment. Subjects were followed for 30 days post procedure.

The objective of this study was to evaluate the safety and effectiveness of Lava LES embolotherapy for the treatment of hemorrhage from peripheral arteries.

Safety was evaluated by assessing freedom from 30-day Major Adverse Events (MAE), a composite endpoint that includes those complications that occur at the site of catheter insertion, along the pathway for access to the target arteries, and at the site of administration in the target territory or those non-target arterial beds where embolic agent was inadvertently administered. The MAE rate is compared to the rates reported in the literature after treatment with other modalities currently used to treat peripheral artery hemorrhage.

The study was powered for the primary effectiveness endpoint of Clinical Success, as defined by assessing the absence of bleeding in the treated target lesion after embolization with the Lava LES, without the need for reintervention through 30 days after the index procedure. Based upon a one sided 97.5% exact binominal test using a significance level of 0.025, the literature-derived performance goal of 72%, and an anticipated observed success rate of 84%, the required sample size to achieve a level of 80% power was 101 Target Lesions. Assuming a 10% attrition rate through 30 days, a total of 113 subjects were needed to be enrolled. For the primary safety endpoint, success was determined if the lower limit of one-sided 97.5% confidence interval was greater than 82%.

A core laboratory was used for independent central assessment of angiographic endpoints. The study also utilized a Data Safety Monitoring Board (DSMB) and an independent Clinical Events Committee (CEC) for adjudication of clinical events and clinical endpoints in the study.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the LAVA Study was limited to patients who met the following inclusion criteria.

- Age ≥18 years;
- Active arterial bleeding in the peripheral vasculature, documented on a suitable imaging study;
- Subject or subject's legally authorized representative is able and authorized to provide written informed consent for the procedure and the study;
- Subject is willing and able to comply with the specified follow-up evaluation schedule;
- Life expectancy >30 days;
- No prior embolization in the target territory.

Patients were not permitted to enroll in the LAVA Study if they met any of the following exclusion criteria:

- Pregnancy or breast feeding. A woman who, in the Investigator's opinion, is of child-bearing potential must have a negative pregnancy test within 7 days before the index procedure;
- Coexisting signs of peritonitis or other active infection;
- Participation in an investigational study of a new drug, biologic or device that has not reached its primary endpoint at the time of study screening;
- Uncorrectable coagulopathies such as thrombocytopenia <40,000/μL, international normalization ratio (INR) >2.0;
- Contraindication to angiography or catheterization, including untreatable allergy to iodinated contrast media;
- Anatomic arterial unsuitability such that, in the Investigator's opinion, the delivery catheter cannot gain access to the selected position for safe and intended embolization;

- Known allergy or other contraindication to any components of Lava LES including dimethyl sulfoxide (DMSO ;
- More than 4 Target Lesions will require embolization, in the Investigator's opinion after performance of diagnostic angiography or another suitable imaging study.

2. Follow-up Schedule

All enrolled subjects were evaluated at hospital discharge and followed to 30 days after the index procedure. A schedule of assessments is provided in **Table 5** below:

Table 5. Schedule of Assessments

Assessment	Screening/ Baseline	Index Procedure	Hospital Discharge	30 days ± 7 days*	Unscheduled Visits
Informed consent	<24 hours before the IP				
Medical history	<24 hours before the IP				
Verification eligibility criteria	<24 hours before the IP	X			
Pregnancy testing	<7 days before the IP				
Physical Examination†	<24 hours before the IP	X	X		X
Diagnostic Angiography		X	X‡		X‡
Embolic Therapy with Lava LES		X			
Adverse event assessment		X	X	X	X
Concomitant medications		X	X	X	X
Laboratory testing§	<24 hours before the IP		X		X

IP- Index procedure

** This assessment could have been performed via telephone with a member of the investigational site's research staff or with an in-person visit with the Investigator.*

† Physical examination included vital signs and an examination of the target territory (as appropriate, e.g. the subject's limb) pre-procedure. Physical examination also included an examination of the access site and target territory at the conclusion of the index procedure and at in-person scheduled or unscheduled follow-up visits. Abnormalities of the vascular system prompted a duplex ultrasound or another appropriate imaging study to exclude false aneurysm, hematoma, arteriovenous fistula, dissection, or deep venous thrombosis.

‡ Diagnostic angiography was repeated after the index procedure for continued bleeding or rebleeding, at the Investigator's discretion.

§ The following laboratory tests were required to be reported: the lowest hemoglobin reported during the current bleeding episode, the last hemoglobin, platelet count, and international normalized ratio (INR) prior to the index procedure, and the hemoglobin, platelet count and INR at discharge and at any unscheduled visits.

3. Clinical Endpoints

With regards to safety, the primary safety endpoint was freedom from 30-day Major Adverse Events (MAEs) after enrollment, which include the following events as

adjudicated by an independent CEC:

1. Ischemia or infarction of the target territory.
2. Non-target embolization: The target territory or territories were specified by the Investigator at the time of enrollment; embolization to a non-target territory was defined as unintentional administration of Lava to a vascular bed outside of a target territory.
3. Allergic reactions to Lava.
4. Catheter breakage: refers to defects in the luminal continuity of the microcatheter used to deliver Lava, but not to other catheters that may be used in other aspects of the procedure separate from the administration of Lava. Catheter kinks without defects in luminal continuity did not trigger the endpoint.
5. Catheter entrapment defined as the inability to withdraw the catheter refers to the catheter with which Lava is administered and is defined by the need for endovascular or open surgical procedures to remove the catheter or portions thereof. Retained portions of the catheter trigger the endpoint, irrespective of whether additional endovascular or open surgical procedures were performed.

With regards to effectiveness, the primary effectiveness endpoint was clinical success and is defined as absence of bleeding from a target lesion after embolization with the Lava LES, without the need for emergency surgery, re-embolization, or other target lesion reinterventions within 30 days of the index procedure. Absence of bleeding is defined as no BARC (Bleeding Academic Research Consortium) Type 3 or greater bleeding occurring after the index procedure, either persistent or recurrent. The ascertainment of persistent or recurrent BARC Type 3 or greater bleeding does not include bleeding that occurred prior to the conclusion of the index procedure.

Regarding the study success/failure criteria, the study was considered a success if both the primary effectiveness and primary safety hypotheses were met.

B. Accountability of PMA Cohort

In total, 113 subjects were enrolled (successful arterial access established to the Target Lesion) at 19 sites. **Table 6** presents subject follow-up compliance. A total of 103 subjects were eligible at the 30-day follow-up visit and 10 were not eligible due to 9 who died prior to the 30-day visit and 1 who withdrew consent on post-procedure day 32.

Table 6. Subject Follow-up Compliance

Subject Compliance Characteristics	Lava LES (N=113 Subjects)
Subjects at 30-Days	
Eligible Subjects[a]	103
Not Eligible Subjects	10
Reason not Eligible	
Not Past Due	0
Withdrew Consent	1

Subject Compliance Characteristics	Lava LES (N=113 Subjects)
Investigator Withdrew Subject	0
Lost to Follow-up	0
Death	9
Other	0
Follow-up Not Done in Eligible Subjects	0
Follow-up visit within window[b]	86
Follow-up visit out of window[b]	17
Follow-up Compliance (%)[c]	84

[a] *Eligible subjects are all subjects who are enrolled by snapshot date and either complete the study, have a follow-up visit form or are past due for their follow-up (beyond upper limit of window on study and did not exit the study before the upper limit of the window)*
[b] *Within window visits are defined as: 30 days ± 7 days;*
[c] *Percentage based on number of subjects who had follow-up visit within window divided by total number of eligible subjects*
Site reported data.

All 113 patients were considered as part of the Intention-to-Treat (ITT) and Completed Cases (CC) Populations. The ITT population includes all consented subjects in whom the Lava LES study device entered the vasculature, irrespective of adherence with the entry criteria, treatment received, subsequent withdrawal, or deviation from the Protocol. The CC population includes all ITT subjects who completed 30-day follow-up. The CC population also includes ITT subjects who experienced failure of the primary effectiveness endpoint prior to the beginning of the 30-day follow-up timepoint, irrespective of their length of follow-up.

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for an embolization study for peripheral bleeding performed in the US. **Table 7** presents baseline demographics and medical history of the study population. Subjects were more frequently male (72; 63.7%), with a mean age of 57.4 years (range 18-93), average BMI of 28.9 ± 6.88 kg/m^2 and had comorbidities including hypertension (66; 58.4%), hyperlipidemia (36; 31.9%), renal insufficiency (32; 28.3%) and diabetes 28; 24.8%). Sixteen subjects (14.2%) had prior surgery at the target lesion.

Table 7. Baseline Demographic and Medical History

Subject Characteristics	Lava LES (N=113 Subjects)
Age (years)	
N	113
Mean ± SD	57.4 ± 18.00
Sex	
Female	36.3% (41/113)
Male	63.7% (72/113)
Ethnicity Hispanic or Latino	19.2% (20/104)
Race	
Asian	9.3% (10/108)

Subject Characteristics	Lava LES (N=113 Subjects)
Black or African-American	14.8% (16/108)
Native Hawaiian or other Pacific Islander	0.9% (1/108)
White	58.3% (63/108)
Other	16.7% (18/108)
BMI (kg/m^2)	
N	113
Mean ± SD	28.9 ± 6.88
History of Diabetes	24.8% (28/113)
Prior Myocardial Infarction	7.1% (8/113)
Cardiac Valve Disorder	8.0% (9/113)
Hypertension	58.4% (66/113)
Coronary Artery Disease	18.6% (21/113)
Congestive Heart Failure	12.4% (14/113)
Chronic Obstructive Pulmonary Disease	8.0% (9/113)
Atrial Arrythmia	15.9% (18/113)
Ventricular Arrythmia	2.7% (3/113)
Collagen Vascular Disease	0.9% (1/113)
Aortic Aneurysm	1.8% (2/113)
Hyperlipidemia	31.9% (36/113)
Deep Venous Thrombosis	8.0% (9/113)
Pulmonary Embolism	6.2% (7/113)
Neurological Disorder	15.9% (18/113)
Cerebrovascular Disease	2.7% (3/113)
Stroke or Transient Ischemic Attack (TIA)	6.2% (7/113)
Renal Insufficiency	28.3% (32/113)
Prior Surgery at Target Lesion	14.2% (16/113)
Bleeding Disorder	5.3% (6/113)
Peripheral vascular disease	7.1% (8/113)
Current Smoker	19.5% (22/113)

Numbers are % (counts/sample size) unless otherwise stated.

Table 8 summarizes baseline clinical characteristics. The most frequently encountered bleeding territories in the 113 subjects were gastrointestinal in 21 subjects (18.6%) and visceral (non-intestinal) in 41 subjects (36.3%). Among the subjects with visceral bleeding, the most common organs were the spleen 14, 34.1%) and the liver (12; 29.3%). The two most common etiologies were traumatic, non-iatrogenic (32; 28.3%) and iatrogenic 29; 25.7%).

Table 8. Baseline Clinical Characteristics

Subject Bleed Characteristics	Lava LES (N=113 Subjects)
Target Bleed Territory	
Upper GI	9.7% (11/113)
Lower GI	8.8% (10/113)
Non-GI Visceral	36.3% (41/113)
Extremity	7.1% (8/113)
Pulmonary	0.0% (0/113)
Other	38.1% (43/113)
Upper GI Subset (N=11)	

Subject Bleed Characteristics	Lava LES (N=113 Subjects)
Esophageal	0.0% (0/11)
Gastric	54.5% (6/11)
Duodenal	45.5% (5/11)
Lower GI Subset (N=10)	
Small Intestine	30.0% (3/10)
Colon	70.0% (7/10)
Rectal	0.0% (0/10)
Non-GI Subset (N=41)	
Splenic	34.1% (14/41)
Hepatic	29.3% (12/41)
Adrenal	2.4% (1/41)
Pancreas	7.3% (3/41)
Prostate	0.0% (0/41)
Bladder	0.0% (0/41)
Uterus	2.4% (1/41)
Other	24.4% (10/41)
Extremity Territory	
Right Arm	0.0% (0/8)
Left Arm	12.5% (1/8)
Right Leg	12.5% (1/8)
Left Leg	75.0% (6/8)
Etiology of Bleeding	
Traumatic, non-iatrogenic	28.3% (32/113)
Iatrogenic	25.7% (29/113)
Ulcer	4.4% (5/113)
Benign Neoplasm	0.9% (1/113)
Malignant Neoplasm	4.4% (5/113)
Mallory Weiss Tear	0.0% (0/113)
Congenital Vascular Lesion	0.0% (0/113)
Unknown	5.3% (6/113)
Other	31.0% (35/113)
Currently Taking Antiplatelet Agents	9.4% (9/96)
Currently Taking Anticoagulant Agents	8.9% (8/90)

Numbers are % (counts/sample size) unless otherwise stated.

D. Safety and Effectiveness Results

1. Safety Results

The analysis of the primary safety endpoint was based on the 101 subjects available for the 30-day follow-up period. Of the 113 subjects, 12 subjects exited the study prior to the 30-day follow-up window (23 days post-procedure) and did not have a reported event prior to exit (8 subjects died and 4 exited early), leaving 101 evaluable subjects. All evaluable subjects 100%; 101/101) had Freedom from MAE at 30 Days. The primary safety endpoint was met with the lower limit of the one-sided 97.5% confidence interval being 96.4%, which was greater than the 82% performance goal. As shown in **Table 9** below, no subjects experienced major adverse events through 30 days based on data adjudicated by an independent CEC. The details of the Secondary Safety Endpoints at 30 Days are as follows:

- No subjects presented with symptomatic ischemia in the target territory that did not require intervention.
- All-cause mortality rate was 8.3% (9/109) through the 30-day follow-up timepoint. The denominator for the all-cause mortality rate excluded 4 subjects that exited the study before the 30-day follow-up visit without death. Of the 9 deaths, 8 were CEC adjudicated as being related to the procedure since they occurred within 30 days of the index procedure (cardiac arrest, end stage liver disease, septic shock (2), complications following nephrectomy, respiratory failure, pancytopenia, metastatic renal cancer). Of these, 2 subject deaths were also CEC adjudicated as related to the device (end stage liver disease complicated by spontaneous hemorrhagic rupture of the gall bladder, cardiac arrest following complications from a Whipple procedure for advanced pancreatic carcinoma).
- Bleeding-related mortality that was attributable to the target territory was 1.9% (2/103).
- No subjects 0%; 0/101) required open surgical conversion for persistent or recurrent bleeding.
- Device-related Serious Adverse Events occurred in 4.9% (5/103) of subjects
- Procedure-related Serious Adverse Event occurred in 23.1% (25/108) of subjects
- No subjects (0%; 0/101) had access site hematoma >5cm in longest axis based on core-laboratory determined assessment of bleeding.
- No subjects (0%; 0/101) developed access site false aneurysms.

Table 9. Major Adverse Events and Secondary Safety Endpoints at 30 Days

Complications	**Lava LES (N=113 Subjects)**
Major Adverse Events Composite	0.0% (0/101)
Non-target Embolization	0.0% (0/101)
Ischemia or Infarction of the Target Territory	0.0% (0/101)
Allergic Reactions to Lava	0.0% (0/101)
Catheter Breakage	0.0% (0/101)
Catheter Entrapment	0.0% (0/101)
Secondary Safety Endpoints at 30 Days	
Symptomatic Ischemia in the Target Territory not Requiring Intervention	0.0% (0/101)
All-cause Mortality	8.3% (9/109)
Bleeding-related Mortality	1.9% (2/103)
Open Surgical Conversion[a]	0.0% (0/101)
Device-related Serious Adverse Events	4.9% (5/103)
Procedure-related Serious Adverse Events	23.1% (25/108)
Access Site Hematoma (>5cm in longest axis)[b]	0.0% (0/101)
Access Site False Aneurysm[b]	0.0% (0/101)

Complications	Lava LES (N=113 Subjects)
Endpoint Definitions: *The Major Adverse Event (MAE) endpoint is defined as a composite safety endpoint, triggered by any of the following through 30 days following the index procedure:* *• Ischemia or Infarction of the Target Territory* *• Non-target Embolization defined as unintentional administration of Lava to a vascular bed outside of a target territory* *• Allergic Reactions to Lava* *• Catheter Breakage defined as defects in the luminal continuity of the microcatheter used to deliver Lava* *• Catheter Entrapment defined as the inability to withdraw the Lava administration catheter requiring the need for endovascular or open surgical procedures to remove the catheter or portions thereof.* *Denominators are number of subjects who had the event before 23 days or had last contact date after 23 days.* *[a]Site reported data.* *[b]Core Lab reported data.* *Other endpoints were CEC adjudicated.*	

Serious adverse events (SAE) by System-Organ Class (SOC) are summarized in **Table 10**. A total of 50 SAEs occurred in 35.4% (40/113) of subjects with 4.9% (5/103) that were device-related and 23.1% (25/108) that were procedure-related. The most frequent SAEs were vascular disorders (9.7%; 11/113), gastrointestinal disorders (5.3%; 6/113), blood and lymphatic system disorders (4.4%; 5/113) and general disorders and administration site conditions 4.4%; 5/113 .

Table 10. Number of Subjects with One or More Serious Adverse Events by MedDRA System-Organ Class and Preferred Term

Adverse Event	Lava LES (N=113 Subjects)
Subjects with one or more SAE	35.4% (40/113)
Blood and lymphatic system disorders[a]	4.4% (5/113)
Anaemia	2.7% (3/113)
Chronic myeloid leukaemia	0.9% (1/113)
Thrombocytopenia	0.9% (1/113)
Cardiac disorders[a]	3.5% (44/113)
Atrial fibrillation	1.8% (2/113)
Cardiac arrest	0.9% (1/113)
Chest pain	0.9% (1/113)
Gastrointestinal disorders[a]	5.3% (6/113)
Abdominal pain	1.8% (2/113)
Haematochezia	0.9% (1/113)
Ileus	0.9% (1/113)
Melaena	1.8% (2/113)
Small intestinal perforation	0.9% (1/113)
General disorders and administration site conditions[a]	4.4% (5/113)
Death	2.7% (3/113)
Flank pain	1.8% (2/113)

Adverse Event	Lava LES (N=113 Subjects)
Hepatobiliary disorders[a]	1.8% (2/113)
Cholangitis infective	0.9% (1/113)
Gallbladder rupture	0.9% (1/113)
Infections and infestations[a]	3.5% (4/113)
Sepsis	3.5% (4/113)
Injury, poisoning and procedural complications[a]	1.8% (2/113)
Vascular pseudoaneurysm	1.8% (2/113)
Metabolism and nutrition disorders[a]	1.8% (2/113)
Acute respiratory failure	0.9% (1/113)
Respiratory failure	0.9% (1/113)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)[a]	1.8% (2/113)
Adenocarcinoma	0.9% (1/113)
Endometrial cancer	0.9% (1/113)
Renal and urinary disorders[a]	1.8% (2/113)
Acute kidney injury	0.9% (1/113)
Nephrolithiasis	0.9% (1/113)
Respiratory, thoracic and mediastinal disorders[a]	1.8% (2/113)
COVID-19	0.9% (1/113)
Pleural effusion	0.9% (1/113)
Surgical and medical procedures[a]	0.9% (1/113)
Colectomy	0.9% (1/113)
Vascular disorders[a]	9.7% (11/113)
Cardiogenic shock	0.9% (1/113)
Epistaxis	0.9% (1/113)
Extravasation blood	2.7% (3/113)
Haematoma infection	0.9% (1/113)
Hepatic haemorrhage	0.9% (1/113)
Hypotension	0.9% (1/113)
Pulmonary embolism	0.9% (1/113)
Retroperitoneal haematoma	0.9% (1/113)
Septic shock	0.9% (1/113)
Shock haemorrhagic	0.9% (1/113)

[a]*Event verbatim terms are reported by sites. The events listed in this table are then coded using MedDRA version 24 and then stratified by System-Organ Class (SOC) and Preferred Term. Patients may be counted in this table more than once by Preferred Term but are only counted once in each SOC summary line.*
Numbers are % (counts/sample size) unless otherwise stated.
Site reported and MedDRA coded data.

2. Effectiveness Results

The analysis of effectiveness was based on 113 evaluable patients and 148 lesions at 30 days. Of the 148 lesions treated with Lava LES, 141 of these lesions were evaluable. A total of six subjects with these seven lesions were not included in the effectiveness analysis because they died prior to 23 days post-procedure and did not have an event to be considered as a failure prior to the death. The primary effectiveness endpoint (Clinical Success at 30 Days) was achieved in 94.3% (133/141) of lesions (**Table 11**).

The primary effectiveness endpoint was met with the lower limit of the one-sided 97.5% confidence interval bound of 89.1%, which was greater than the 72% performance goal. There were 8 lesions that had a bleed from the Target Lesion within 30 days. No subjects required emergency surgery or re-embolization. There were 2 lesions that required target lesion reintervention through 30-day follow-up.

Table 11. Clinical Success at 30 Days

Parameter	Lava LES (N=113 Subjects, n=148 Lesions)
Clinical Success at 30 Days	94.3% (133/141)
Absence of Bleeding from Target Lesion	94.3% (133/141)
No Emergency Surgery	100% (141/141)
No Re-embolization	100% (141/141)
No Target Lesion Reintervention	98.6% (139/141)

Endpoint Definitions:
Clinical Success is defined as:
• Absence of bleeding from the target lesion defined as no BARC Type 3 or greater bleeding, either persistent or recurrent after embolization with the Lava LES.
• Without the need for emergency surgery, re-embolization, or other target lesion reinterventions within 30 days of the index procedure.
Numbers are % (counts/sample size) unless otherwise stated.
Site/Core Laboratory reported and Clinical Events Committee adjudicated data.

The secondary effectiveness endpoints of: (1) technical success, defined as absence of angiographic evidence of bleeding from target lesion at the conclusion of the index procedure was 97.3% (144/148) of lesions and (2) successful delivery of Lava and intact retrieval of the microcatheter was achieved in all 141 (100%) evaluable lesions.

3. Subgroup Analyses

A subgroup analyses was conducted based on gender (**Table 12**.). Males accounted for 72 subjects and 95 lesions compared to 41 female subjects and 53 lesions. Clinical Success at 30 Days was significant between the genders with greater clinical success in the male population. Freedom from MAE at 30 Days was the same at 100% in both populations. Other notable differences were all-cause mortality rate being higher in females (M: 5.8%; 4, F: 12.5%; 5) and both Device and Procedure related SAEs being higher in the female population (Device – M: 3.1%, F: 7.9%, Procedure – M: 17.4%, F: 33.3%). All other characteristics were similar including Technical Success and Successful Delivery of Lava. Univariate analyses were done between the male and female subjects to evaluate any baseline differences that might explain the different results by sex. There were no significant differences in the age, race, BMI of the subjects, or etiology of the lesions. There were more males with hypertension, coronary artery disease and history of atrial arrythmias. The only baseline differences found were a higher frequency of non-GI visceral target lesions (35.8% vs. 28.4%) and upper GI target lesions (20.8% vs. 6.3%) in females. Whether the lesion location was causally

associated with the sex differences remains undetermined.

Parameter	Male (N=72 Subjects, n=95 Lesions)	Female (N=41 Subjects, n=53 Lesions)
Primary Effectiveness Endpoint		
Clinical Success at 30 Days	98.9% (89/90)	86.3% (44/51)
P-value*	0.003	
Primary Safety Endpoint		
Freedom from MAE at 30 Days	100% (65/65)	100% (36/36)
Secondary Effectiveness Endpoints		
Technical Success	96.8% (92/95)	98.1% (52/53)
Successful Delivery of Lava and Intact Retrieval of the Microcatheter	100% (92/92)	100% (49/49)
Secondary Safety Endpoints		
Major Adverse Events Composite at 30 Days	0.0% (0/65)	0.0% (0/36)
Non-target Embolization	0.0% (0/65)	0.0% (0/36)
Ischemia or Infarction of the Target Territory	0.0% (0/65)	0.0% (0/36)
Allergic Reactions to Lava	0.0% (0/65)	0.0% (0/36)
Catheter Breakage	0.0% (0/65)	0.0% (0/36)
Catheter Entrapment	0.0% (0/65)	0.0% (0/36)
Symptomatic Ischemia in the Target Territory not Requiring Intervention at 30 Days	0.0% (0/65)	0.0% (0/36)
All-cause Mortality at 30 Days	5.8% (4/69)	12.5% (5/40)
Bleeding-related Mortality at 30 Days	0.0% (0/65)	5.3% (2/38)
Open Surgical Conversion at 30 Days	0.0% (0/65)	0.0% (0/36)
Device-related Serious Adverse Events at 30 Days	3.1% (2/65)	7.9% (3/38)
Procedure-related Serious Adverse Events at 30 Days	17.4% (12/69)	33.3% (13/39)
Access Site Hematoma (>5cm in longest axis) at 30 Days	0.0% (0/65)	0.0% (0/36)
Access Site False Aneurysm at 30 Days	0.0% (0/65)	0.0% (0/36)

**Statistical hypothesis testing will be conducted to assess the similarity of the primary effectiveness endpoint across each sub-group using a Fisher's exact test and a significance level of 0.15.*

4. Pediatric Extrapolation

In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population.

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included twenty (20) principal investigators of which none were full-time or part-time employees of the sponsor and four (4) had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: Four (4)
- Significant payment of other sorts: None
- Proprietary interest in the product tested held by the investigator: None
- Significant equity interest held by investigator in sponsor of covered study: None

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were conducted to determine whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data.

XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

Effectiveness of the device was demonstrated in terms of clinical success, technical success, and successful device delivery. The primary effectiveness endpoint of clinical success at 30 Days, as defined as the absence of bleeding from a target lesion after embolization with the Lava LES, without the need for emergency surgery, re-embolization, or other target lesion reinterventions within 30 days of the index procedure, was achieved in 94.3% (133/141) of lesions. Therefore, the primary effectiveness endpoint was met with the lower limit of the one-sided 97.5% confidence interval bound of 89.1%, which was greater than the 72% performance goal. Technical Success, defined as absence of angiographic evidence of bleeding from target lesion at the conclusion of the index procedure, was achieved in 97.3% (144/148) of lesions and successful delivery of Lava and Intact Retrieval of the Microcatheter was 100% (141/141).

B. Safety Conclusions

The risks of the device are based on the results of the non-clinical and pre-clinical animal study as wells as data collected in the clinical study conducted to support PMA approval as described above. With respect to clinical evaluation, the primary safety endpoint of freedom from MAE at 30 Days was achieved in all evaluable subjects (100%; 101/101). Therefore, the primary safety endpoint was met with the lower limit of the one-sided 97.5% confidence interval bound of 96.4%, which was greater than the 82% performance goal. No subjects experienced an MAE through 30-day follow-up and there were also no cases of symptomatic ischemia in the target territory not requiring intervention, access site

hematomas nor access site false aneurysms through 30-days. There were 9 deaths resulting in a 30-day all-cause mortality rate of 8.3% (9/109) and bleeding related mortality of 1.9% (2/103). Two deaths were adjudicated as being related to the device and 8 of the 9 deaths were adjudicated as procedure related. The deaths are not unexpected given the underlying medical conditions and do not raise device safety concerns. There were no unanticipated adverse device effects.

C. Benefit-Risk Determination

The probable benefits of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. Arterial hemorrhage is life-threatening and requires emergency care to control. The data presented in this study of the Lava LES demonstrates the device is of clinical benefit in arresting hemorrhage, minimizing associated ischemic complications, and preventing the recurrence of bleeding through 30 days.

The probable risks of the device are also based on data collected in the clinical study to support PMA approval as described above. The use of the Lava LES did not present any unknown risks that have not been previously described, including death and bleeding. The other adverse events reported in the first 30 days of follow-up were not unexpected, neither in rate nor occurrence.

1. Patient Perspective

   This submission either did not include specific information on patient perspectives or the information did not serve as part of the basis of the decision to approve or deny the PMA for this device.

In conclusion, given the available information above, the data support that for embolization of arterial hemorrhage in the peripheral vasculature, the probable benefits outweigh the probable risks when used according to its labeling.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The results from the clinical study support the conclusion that the Lava LES is safe and effective for embolization of arterial hemorrhage in the peripheral vasculature when used in accordance with device labeling and the instructions for use (IFU).

XIII. CDRH DECISION

CDRH issued an approval order on April 4, 2023. The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.