



## Evaluating the Safety and Efficacy of Mesire BRS™ Drug-Eluting Bioresorbable Sinus Scaffold System in a Porcine Model

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### Abstract

This preclinical study evaluated the safety and performance of the Mesire BRS™ Drug-Eluting Bioresorbable Sinus Scaffold System (Meril Medical Innovations Pvt. Ltd., Vapi, Gujarat, India) was conducted in accordance with applicable ISO and FDA guidance documents, including BS EN ISO 14630 for general implant safety, ISO 10993 series for biocompatibility, ISO 13781 for bioresorbable polymers, and relevant FDA guidelines on combination products and drug-eluting implantables. Animal studies were designed following ISO 10993-2 and CPCSEA guidelines for ethical use and welfare compliance when implanted in the frontal sinus of Porcine. The primary objective was to assess the device's ability to maintain sinus patency, elicit local tissue response, and follow its biodegradation profile over two observation periods—Day 43 and Day 88. The secondary objective was to evaluate any adverse effects such as infection, inflammation, or tissue damage, and to assess the structural integrity and degradation rate of the device.

Two healthy female Porcine, weighing 58.6 kg and 48.8 kg on Day 0, were used. The test item (8x15 mm) was implanted bilaterally in the frontal sinus under endoscopic guidance. No intraoperative complications occurred, and the device demonstrated excellent ease of deployment. The animals were monitored for clinical signs, body weight, and pain throughout the study. Mild pain was observed until Day 4, resolving by Day 5. No morbidity, mortality, or abnormal clinical signs were noted during the study period.

Plasma samples collected at predefined intervals showed Mometasone levels below the quantification limit, indicating negligible systemic drug exposure. However, localized sinus tissue analysis at termination revealed detectable Mometasone concentrations of 42.21 ng/g (Day 43, P1) and 85.49 ng/g (Day 88, P2), confirming drug retention at the implant site. Hematological and biochemical parameters remained within normal limits throughout the study.

Endoscopic examinations had confirmed sinus patency, and postmortem evaluations had revealed no gross pathological changes or device remnants. Histopathological analysis had shown minimal inflammatory response, likely due to surgical trauma. No foreign body reactions or tissue overgrowth had been observed.

Overall, the Mesire BRS™ (Drug-Eluting Bioresorbable Sinus Scaffold System) device exhibited a favorable safety and performance profile, with excellent local tolerability, controlled drug release, and no significant systemic or local adverse effects in the porcine model. These findings supported further clinical evaluation.

**Keywords:** Mesire BRS™(Drug-Eluting Bioresorbable Sinus Scaffold System),LC-MS/MS Analysis, Mometasone Furoate, Porcine Model, Histopathology.

## Introduction

This study is conducted to evaluate the safety and performance of the Mesire BRS™ (Drug-Eluting Bioresorbable Sinus Scaffold System) after implantation in the frontal sinus of porcine. Sinus infections occur when fluid accumulates in the air-filled pockets of the face (sinuses), creating an environment for microbial growth. In such conditions, one or more sinuses become inflamed, leading to symptoms such as congestion and nasal discharge. [8]

The Mesire BRS™ (Drug-Eluting Bioresorbable Sinus Scaffold System) is designed to maintain sinus patency following surgery by functioning as a temporary, self-absorbing implant. It delivers the corticosteroid Mometasone Furoate locally to the sinus mucosa for 30 days and then gradually degrades. The purpose of the device is to minimize the need for postoperative interventions such as scar-tissue removal or systemic steroid administration. It is intended for adult patients (18 years and older) who have undergone ethmoid or frontal sinus surgery. [9]

In this study, a porcine model was used because its sinus anatomy and physiological characteristics closely resemble those of humans. The nasal tissues, mucociliary clearance mechanisms, and healing responses in porcine models are comparable to human physiology, making them suitable for evaluating device safety, performance, and biodegradation. The anatomical size of the porcine sinuses also allows precise scaffold placement and effective endoscopic monitoring. [4]

Additionally, the bioresorption of the scaffold's polymeric components—Mometasone Furoate (0.521 kDa), PEG 6000 (5.5 kDa), PLG 50:50 (45 kDa), and PLG 10:90 (100 kDa)—was evaluated to confirm

complete or near-complete degradation during the study period.

The primary objective of this study is to assess the ability of the device to maintain sinus opening, evaluate local tissue response, and examine the biodegradation profile at specified time points (Day 43 and Day 88). The study also aims to identify any potential adverse effects such as infection, inflammation, or tissue damage, and to assess device integrity and degradation inside the sinus.

Two healthy female porcine weighing 58.6 kg and 48.8 kg were included. On Day 0, under general anesthesia, a small opening was created in the frontal bone to access the sinus, and the BRS™ Drug-Eluting Bioresorbable Sinus Scaffold System (8 × 15 mm) was implanted into both left and right sinuses using a delivery system under endoscopic visualization. Proper placement was confirmed, and the surgical site was closed. The animals were monitored throughout the study for clinical signs, body weight changes, and any abnormal responses.

To study how the drug spreads in the body, blood samples were collected at predefined intervals and analyzed using a validated liquid chromatography–tandem mass spectrometry (LC-MS/MS) method. At the end of the study, sinus tissues were also examined to confirm localized drug release. Gross pathology and microscopic (histopathological) evaluations were performed to assess tissue reactions, implant degradation, and any remaining material. This study helps generate important data on the safety, tissue compatibility, and local effects of the Mesire BRS™ in a controlled research setting.

## Materials And Methods

### Medication Details

This section delineates the drugs administered to the animals prior to, during, and following surgery.

**Table 1: Details of medications used in the study.**

Drug name	Manufactured by	Batch / Lot No.	Expiry date
Ketamine	Themis Medicare Ltd	KME24002	Sep 2026
Xylazine	IIL India	FHK24005	Feb 2027

Isoflurane	Troikaa Pharmaceuticals Ltd	I30250	July 2027
Tramadol	Neon Lab	KP949131	Nov 2025
Atropine Sulphate	Pentagon Labs Ltd	23GAS002	Jun 2026
Thiopentone sodium	Neon Lab	173288	Feb 2026

**Table 2: Animal P1 and P2 Clinical signs.**

Animal Number	Acclimatization phase		Experiment Phase	
	07532	07527	P1	P2
Sex	Female	Female	Female	Female
Day of Observations	Mortality/ Incidences		Mortality/ Incidences	
Acclimatization Phase (Day -1 to -3)	0/2		--	
Experiment Phase (Day 0 - 43)	--		0/1	--
Experiment Phase (Day 0 - 88)	--		--	0/1

### Device Description:

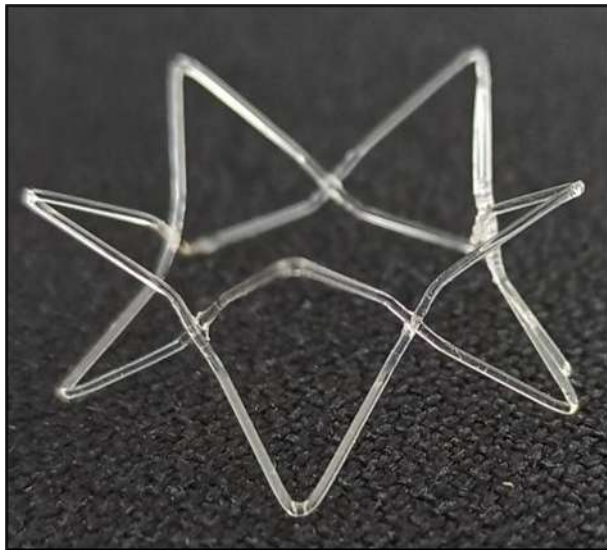
Mesire BRS™ Drug Eluting Bioresorbable Sinus Scaffold System is a temporary, self absorbing implant designed to keep the spaces within and around the sinuses during open sinus surgery. It consists of, a. Mometasone Furoate USP Drug Eluting Bioresorbable Sinus Scaffold b. Delivery system Accessories/ loading tools – funnel and pusher The drug is embedded in a bioabsorbable polymer matrix containing poly-(DL-lactide-coglycolide) and polyethylene glycol (inactive ingredients) which provides for gradual release of the drug The scaffold delivers sustained release of Mometasone furoate directly to the sinus mucosa over a 30 day period prior to dissolving. A delivery system is supplied to access the sinus ostium and deploy the scaffold. The accessories/ loading tools; a funnel and pusher are supplied to load scaffold into delivery system. The product images are shown below in Figure 1, Figure 2 and Figure 3.

### Product Image:

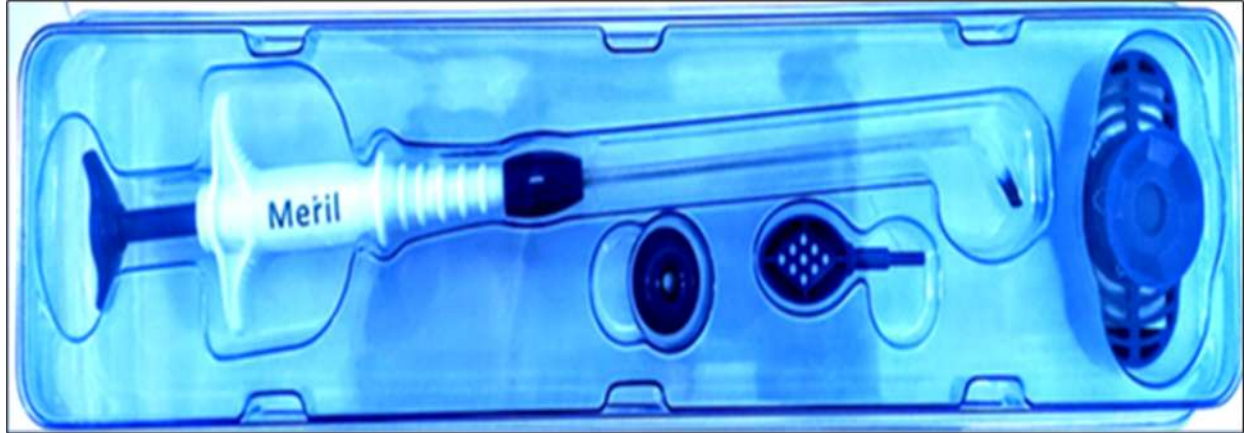
**Figure 1: Crimped Sinus Scaffold**



**Figure 2: Mesire BRS™ (Drug-Eluting Bioresorbable Sinus Scaffold System).**



**Figure 3 : Bioresorbable sinus scaffold system**



**Experimental Procedures**

**Fasting:**

Feed was withdrawn overnight prior to the procedure (Day 0) and on follow up days. On these days, animals were anesthetized, and food was further withheld for a period of 6 hr after recovery of the animals from anaesthesia.

**Animal Preparation included:**

Animal was prepared and draped for aseptic procedure. The animal was weighed and anesthetized using preanesthetic, Atropine at the dose level of 0.05 mg/kg (IM), Xylazine 2.5 mg/kg (IM), Ketamine 15 mg/kg (IM) followed by inhalation anesthesia 1-4% through facemask. Tramadol (4 mg/Kg IM) as an analgesic was administered to the animal once prior to procedure.

Animal hair was clipped free of hair on the electrode placing sites, neck region, chest and flank area. Once the glottis reflexes were checked, animal was intubated with endotracheal tube. Weight of the animals is illustrated in table no 3

**Table 4: Animal P1 and P2 body weights (Day 0 to Day 88)**

Animal Number	Body weights (kg)		
	Day 0	Day 43	Day 88
P1	58.6	63.4	--
P2	48.8	--	54.1

**Experimental Design Or Animal Trial**

**Day when procedure is performed can be said as 0 day:**

On Day 0, the animal was prepared for the surgical procedure and placed in a sternal recumbence position. A horizontal incision was made on the frontal bone along a line connecting the external commissars of both eyes, and this incision was extended downward along the supraorbital grooves. The skin flap and underlying soft tissue were carefully separated to enhance visualization of the surgical field. Using a bone drilling machine, a small opening was created on the bone flap, and an endoscope was inserted to access and visualize the sinus cavity for stent deployment. The test item, a sinus stent (8x15 mm), was gently introduced into the frontal sinus through the opening using a stent delivery system under endoscopic guidance. The stent was deployed in both

the right and left sinus cavities, ensuring proper placement to maintain patency while avoiding obstruction of natural sinus drainage. Endoscopic verification confirmed correct positioning without stent deformation or misplacement. The sinus membrane was intentionally left open to facilitate proper stent function. The bone flap was then repositioned and secured using bone wax, and the overlying soft tissue and skin were closed in layers with absorbable and non-absorbable sutures. The animal was monitored closely until full recovery from anesthesia.

**Procedural Images :**

**Figure 4: Animal P1, Day 0 - Incision site and creation of opening on bone flap**



**Figure 5: Animal P1, Day 0 – Sinus stents before deploying on Left and Right side**



**Endoscopy Images Day 0 :**



**Figure 6:** Animal P1, Day 0 - Left Side Endoscopy Image (Pre-Implantation of stent)



**Figure 7:** Animal P1, Day 0 - Left Side Endoscopy Image (Post-deployment of stent)



**Figure 8:** Animal P1, Day 0 - Right Side Endoscopy Image (Pre-Implantation of stent)



**Figure 9:** Animal P1, Day 0 - Right Side Endoscopy Image (Post-deployment of stent)



**Figure 10:** Animal P1, Day 0 - Closing of implantation site using bone wax

**Procedural Images : Animal No - Porcine -2**

**Figure 4:** Animal P1, Day 0 - Incision site and creation of opening on bone flap



## OBSERVATION

During the course of the study, both animals showed normal weight gain. Body weights were recorded on the acclimatization start day, procedural day (Day 0), and on the respective terminal days (Day 43 for P1 and Day 88 for P2), with additional weekly monitoring for feed calculation. No mortality or morbidity was observed at any stage. Clinical signs, including pain assessment and general health status, were monitored twice daily (once daily on holidays) during all phases of the study—acclimatization, pre-operative, and post-operative. Mild pain was noted in both animals from Day 0 to Day 4, which resolved by Day 5. No other abnormal clinical signs were observed during the remaining study duration. Intra-operative monitoring of ECG, heart rate, respiratory rate, and oxygen saturation confirmed stable physiological status during surgical implantation.

The test item, Mesire BRS™, demonstrated excellent ease and accuracy of deployment in both animals, with no evidence of migration or malposition. On terminal days, the biodegradation profile observed at two interval points Day 43 (P1) and Day 88 (P2) showed that the implant was no longer visible during endoscopic or gross examination, indicating complete or near-complete bioresorption of its polymeric components, including Mometasone Furoate (0.521 kDa), PEG6000 (5.5kDa), PLG50:50 (45kDa), PLG10:90 (100kDa). No abnormal tissue overgrowth or occlusion was observed at the implantation sites. Plasma bioanalysis for Mometasone showed levels below the quantification limit at all evaluated time points, indicating negligible systemic exposure. In contrast, tissue analysis confirmed localized drug presence at the sinus implantation site, with Mometasone concentrations of 42.21 ng/g (Day 43, P1) and 85.49 ng/g (Day 88, P2). Hematological and clinical biochemistry parameters remained within normal ranges at both baseline and terminal evaluations, suggesting no systemic adverse effects due to the implant.

Following humane euthanasia with thiopental sodium (100 mg/kg IV), both animals underwent complete necropsy. No gross pathological lesions were observed in any major organs, and there were no visible remnants of the implanted device. Histopathological examination of the sinus tissues revealed minimal inflammatory responses at the implantation sites, attributed to the surgical procedure. There were no signs of adverse tissue reactions or foreign body responses. These findings collectively support the local biocompatibility and favorable safety profile of the Mesire BRS™ device in the porcine model.

## Pathology

Clinical pathology assessments were conducted to evaluate the systemic safety of the implanted *Mesire BRS™* device. Blood samples were collected from both animals on Day 0 (pre-implantation) and on their respective terminal days (Day 43 for P1 and Day 88 for P2). Hematology parameters were analyzed using the Siemens Advia 2120i analyzer, while clinical biochemistry was performed using the Beckman Coulter AU480 analyzer. Electrolyte levels were determined using the Starlyte 3/ABG electrolyte analyzer in plasma mode. The hematological evaluation included red and white blood cell counts, hemoglobin levels, hematocrit, platelet counts, reticulocyte percentage, and differential leukocyte counts. Clinical chemistry parameters assessed liver and kidney function, glucose levels, lipid profile, and electrolyte balance. All evaluated parameters were found to be within normal physiological ranges, indicating no systemic toxicity or treatment-related abnormalities.

Euthanasia was performed at designated time points using thiopental sodium (100 mg/kg, IV), and death was confirmed by observing a-systolic ECG and absence of oxygen saturation. A detailed gross necropsy was conducted post-euthanasia, which included examination of the surgical site and all major organs. No macroscopic abnormalities or pathological lesions were observed in either animal. Furthermore, no visible remnants of the implanted scaffold were identified at the nasal sinus implantation sites, suggesting complete or near-complete bioresorption of the device.

For histopathological examination, the sinus tissues from both animals were collected and preserved in 10% neutral buffered formalin. The tissues were processed using resin embedding, and sectioned at a thickness of approximately 100–200 microns using a Secotom cutting system. The sections were further polished with a Bainpol VTD polishing unit to the desired thickness, stained with Hematoxylin and Eosin (H&E), and evaluated

under a light microscope. Histopathological analysis revealed minimal inflammatory responses at the implantation sites in both animals, consistent with normal post-surgical healing. No evidence of adverse tissue reaction, necrosis, or foreign body response was observed. These findings confirm the local biocompatibility of the *Mesire BRS™* device and support its safe use in the porcine model

### Morbidity and Mortality

There was no morbidity/mortality observed during the procedure, and throughout the study duration from day 0 till termination day (P1-Day 43, P2-Day 88) detailed in Table no 6.

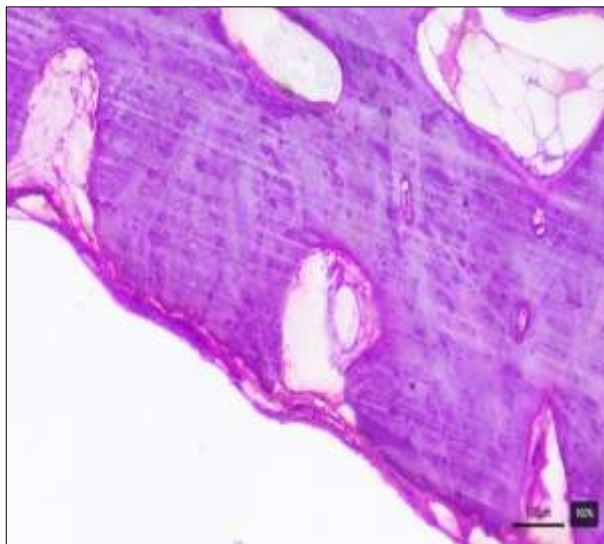
Table 6: Animal P1, P2 Mortality observation on Day 0 to Termination Day

Animal Number	Acclimatization phase		Experiment Phase	
	07532	07527	P1	P2
Sex	Female	Female	Female	Female
Day of Observations	Mortality/ Incidences		Mortality/ Incidences	
Acclimatization Phase (Day -1 to -3)	0/2		--	
Experiment Phase (Day 0 - 43)	--		0/1	--
Experiment Phase (Day 0 - 88)	--		--	0/1

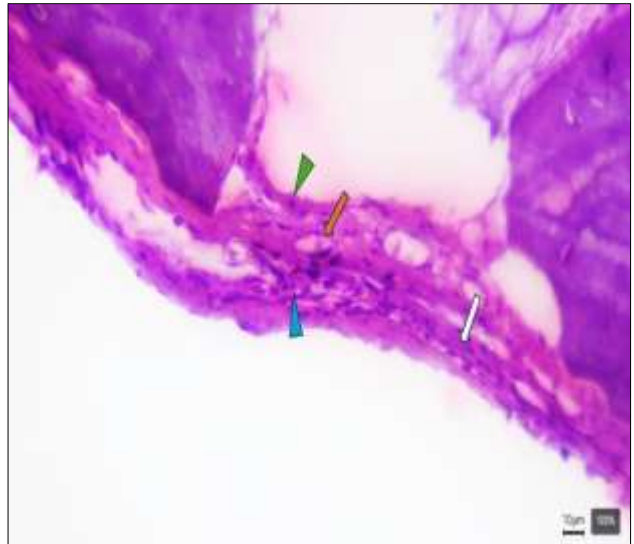
### Histopathology

At the scheduled termination time points (P1 on Day 43 and P2 on Day 88), the animals were humanely euthanized using an overdose of thiopental sodium. A detailed gross pathological examination was conducted, and the nasal sinus implantation sites of the *Mesire BRS™* (Drug-Eluting Bioresorbable Sinus Scaffold System) were collected and fixed in 10% neutral buffered formalin. The tissues were processed for resin embedding, sectioned at a thickness of 100–200 microns using a Secotom Cutting Machine, and further polished using a Bainpol VTD Polishing Machine to achieve optimal section thickness. The sections were stained with Haematoxylin and Eosin (H&E) and examined under a light microscope by the study pathologist. Histopathological evaluation of the nasal sinus (implanted sites) showed minimal inflammatory response, with lymphocytes, macrophages, and fibrosis each scoring 1 (rare; 1–5 cells per high-power field) in both P1 and P2 animals. Neovascularization, also scored 1, was observed only in the P1 animal. The overall tissue response scores were 6 for P1 and 5 for P2. No visible remnants of the implanted *Mesire BRS™* scaffold were observed at the implantation sites in either animal.

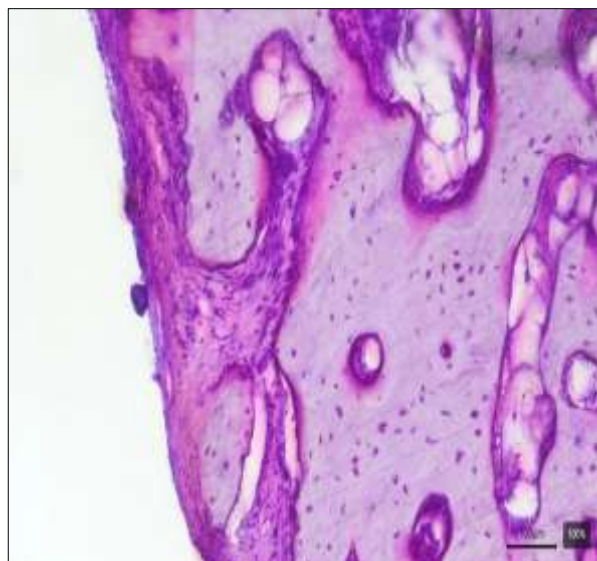
### Histopathology Images



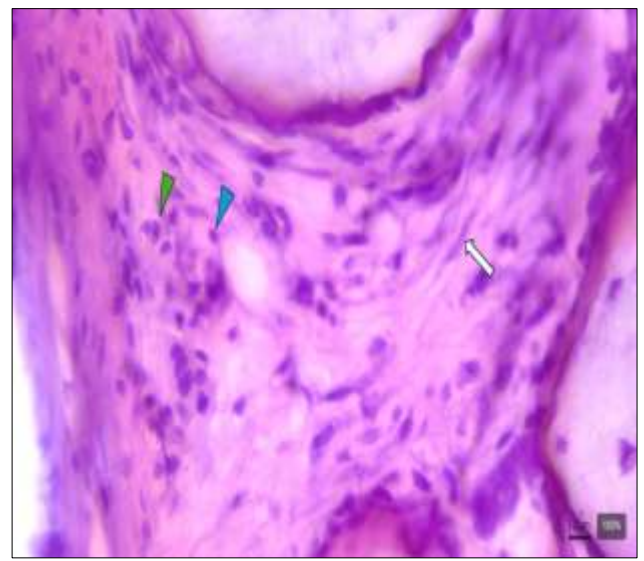
**Figure 26: Animal No. Porcine -1 (Mesire BRS™), H&E100X**







**Figure 27: Animal No. Porcine -2 (Mesire BRS™), H&E 400X**



**Figure 28: Animal No. Porcine -2 (Mesire BRS™), H&E 100X**



**Figure 29: Animal No. Porcine -2 (Mesire BRS™), H&E 400X**

**Keys.**  - Macrophages,  - Lymphocytes,  - Neovascularisation,  - Fibrosis

### Discussion

The primary objective of this study is to evaluate the safety and performance of the Mesire BRS™ (Drug-eluting Bioresorbable Sinus Scaffold System) when implanted in the frontal sinus of Porcine. The study aims to assess the device's ability to maintain sinus patency, the extent of local tissue response, and its

biodegradation profile over a specified period (Day 43 and Day 88). The secondary objective is to evaluate potential adverse effects such as infection, inflammation, or tissue damage, as well as the stent's structural integrity and degradation rate in the porcine model.

Two female Porcine weighing 58.6 kg and 48.8 kg on Day 0 are included in the study. On the procedural day, the animals are anesthetized and administered analgesics. The frontal bone is exposed, and an opening is created using a mechanical drill to visualize the frontal sinus cavities. The test item (8x15 mm Mesire BRS™) is introduced into both left and right sinuses using the delivery system under endoscopic guidance, with positioning confirmed endoscopically. The bone flap is sealed with bone wax, and the skin is sutured in layers. The animals recover uneventfully and are returned to their cages.

No mortality is observed during the study. The animals gain weight normally and show no abnormal clinical signs from Day 0 to the end of the study. Both animals exhibit mild pain from Day 0 to Day 3, which resolves by Day 4. Hematology and clinical biochemistry parameters remain within normal ranges at baseline and at termination. On Day 0, the stent is deployed accurately and smoothly. At termination (Day 43 for P1 and Day 88 for P2), the implant is not visible in the sinus cavity, and no tissue overgrowth is observed.

Plasma samples collected at predefined intervals show Mometasone levels below the quantification limit, indicating negligible systemic exposure. However, sinus tissue samples show localized Mometasone concentrations of 42.21ng/g (P1) and 85.49ng/g (P2), confirming drug retention at the implantation site. No pathological lesions or remnants of the device are observed during necropsy. Minimal inflammatory responses noted at the implant sites are comparable between animals and are attributed to the surgical procedure.

#### Some limitation for using Porcine model

- **Lack of Disease Model:** Healthy Porcine do not exhibit chronic sinus conditions such as inflammation or scarring, limiting assessment in clinically relevant scenarios<sup>[6]</sup>.
- **No Symptom Evaluation :** Clinical symptoms like nasal congestion or discomfort cannot be assessed in animals, limiting interpretation to anatomical and histological parameters.
- **Translatability Concerns:** Results obtained from porcine models may not fully predict human clinical outcomes due to interspecies variability<sup>[7]</sup>.

#### Conclusion

The Mesire BRS™ (Drug-Eluting Bioresorbable Sinus Scaffold System) demonstrates favorable safety and performance when implanted in the frontal sinus of Porcine. The device deploys easily and accurately without intraoperative complications. Both animals maintain normal weight gain, stable clinical parameters, and show no signs of morbidity or mortality throughout the study period. Systemic exposure to Mometasone remains negligible, while localized sinus tissue levels confirm effective drug retention at the implantation site. No abnormal clinical signs, tissue overgrowth, or pathological lesions are observed at termination. Histopathological evaluation shows only minimal inflammatory responses, with no visible remnants of the device, indicating proper biodegradation. Overall, the findings suggest that Mesire BRS™ is well-tolerated, biocompatible, and does not produce significant adverse effects, supporting its potential for safe use in sinus-related clinical applications.

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