SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Implant, Gastroesophageal Reflux System

Device Trade Name: RefluxStop® Device and RefluxStop® Deployment Tool

Device Procode: LEI (Implant, Anti-Gastroesophageal Reflux)

Applicant's Name and Address: Implantica CE Reflux Ltd.
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Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P250018

Date of FDA Notice of Approval: August 20, 2026

II. INDICATIONS FOR USE

RefluxStop® is an implantable sterile medical device intended to treat acid and non-acid reflux in patients diagnosed with gastroesophageal reflux disease (GERD). The device ensures maintenance of a normal physiological situation for the gastroesophageal junction (GEJ) in a defined intra-abdominal position, allowing a natural physiological function of the lower esophageal sphincter (LES), thereby reducing or eliminating acid and non-acid reflux.

The RefluxStop® Deployment Tool is indicated for patients diagnosed with Gastroesophageal Reflux Disease (GERD), defined by abnormal impedance pH and/or pH testing, and indicated for RefluxStop® implantation.

III. CONTRAINDICATIONS

The RefluxStop® System is contraindicated in patients with:

- Known sensitivities or allergies to the device materials (medical grade silicone [NusilMED-4860] and barium sulphate [$BaSO_4$ powder]);
- Intraoperative findings determined by the operating surgeon that may result in

unfavorable conduct of the procedure.

- Known sensitivities or allergies to the device materials (Stainless Steel AISI 316L and medical-grade silicone ML-154).

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the RefluxStop® and RefluxStop® Deployment Tool labeling.

V. DEVICE DESCRIPTION

The RefluxStop® System consists of the RefluxStop® Device and the RefluxStop® Deployment Tool.

The RefluxStop® device is an implantable, single-use sterile device that is implanted into the abdominal cavity at a predetermined place at the fundus of the stomach during a laparoscopic procedure. Based on its placement outside the stomach fundus wall fixated only by the created pouch, the RefluxStop® device ensures maintenance of the gastro esophageal junction (GEJ) in an intra-abdominal position, allowing a normal function of the LES thereby reducing or eliminating acid and weak acid gastric reflux.

The RefluxStop® Deployment Tool (RS-300), an accessory of the RefluxStop® System, is a reusable medical device that is designed exclusively for use with the RefluxStop® device (RS-A1) and helps facilitate the introduction of the device into the abdominal cavity.

The RefluxStop® Device consists of an assembly of five components, supplied sterile, that engage to form a rounded cuboid. Each of the five components contain recesses and protrusions that are designed to fit with each other (**Figure 1**). The components are to be pre-mounted with a resorbable suture (2-0 Vicryl Plus, 70cm) holding the pieces together (**Figure 2**).
The RefluxStop® Device is manufactured from an **MR Safe** material consisting of a mixture of medical grade silicone (90-95% NusilMED-4860) and barium sulphate (5-10% BaSO4 powder). The barium sulphate contained is a manufacturing additive to enable visibility of the device under x-ray imaging.

Figure 1. RefluxStop® Device Assembled (left) and in an Exploded View (right)

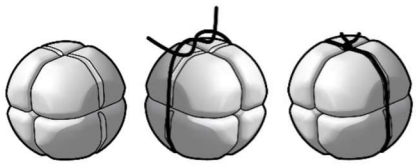

Figure 2. Assembly of the RefluxStop® Device with the Resorbable Suture

The RefluxStop® Deployment Tool consists of four subassemblies as depicted in **Figure 3**:

- The Trocar is used to create a port into the abdominal cavity.
- The Insertion Tool holds the assembled RefluxStop® Device during advancement into the abdominal cavity.
- The Compression Parts allow the RefluxStop® Device to be inserted into the Pipe of the Ejector Device.
- The Ejector Device will house the RefluxStop® Device in a compressed state while inserted into the abdominal cavity.

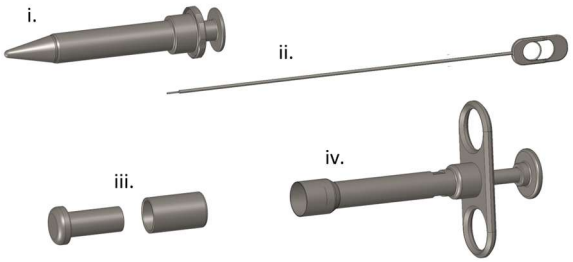

Figure 3. Subassemblies of the RefluxStop® Deployment Tool

i. **Trocar**: Obturator, Cannula, Cross Slit Valve, Lid Nut
ii. **Insertion Tool**: Tube, Wire, Insertion Handle
iii. **Compression Parts**: Insert Device and Funnel
iv. **Ejector Device**: Pipe, Handle, Ejector Tube

When the LES is temporarily or permanently positioned above the diaphragm or positioned too close to the hiatus opening of the diaphragm, it is unable to function properly as there is not sufficient pressure to close. Rather than adhering to the esophagus itself, the RefluxStop® Device is placed freely in a pouch created on the outside of the stomach fundus by stomach to stomach sutures and acts as a mechanical stop against the diaphragm preventing the LES from moving upwards to the diaphragm and into the thorax (**Figure 4**). Through the creation of a mechanical stop, the RefluxStop® Device ensures that the LES remains sufficiently below the diaphragm and therefore experiences enough pressure to function normally and close on its own.

The RefluxStop® procedure restores the flap valve and the angle of His – essential for a good functioning LES, and restores the hiatus opening. Thus, the RefluxStop® Device restores a fully normal anatomic state in the GEJ, thereby treating the cause of acid reflux without encircling and putting pressure on the food passageway, which is especially advantageous in patients with weak peristalsis, with the goal of reducing side effects, such as dysphagia.

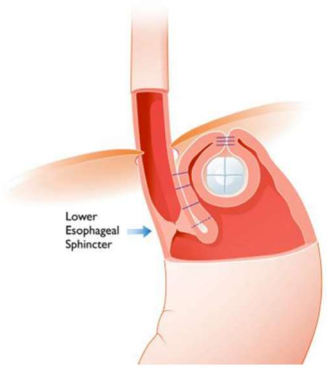

Figure 4. RefluxStop® System

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the treatment of GERD. These include lifestyle changes, drug treatment, and surgical intervention. 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.

Simple lifestyle or dietary modifications are often recommended as part of the initial therapy for mild GERD symptoms and may include:

- weight loss;
- sleeping patterns;
- avoidance of carbonated beverages;
- abstinence from smoking;
- reducing alcohol and caffeine intake;
- avoiding "trigger" foods (spicy foods, citrus, or acidic foods);
- maintaining a low-fat diet;
- avoiding eating or drinking several hours before going to bed; and
- elevating the head of the bed at night

Patients whose GERD symptoms persist after behavioral and lifestyle changes may respond well to one or more drug treatment options:

- antacids;
- H_2-receptor antagonists (H_2RAs); and

- proton pump inhibitors (PPIs)

It is important to note that the medications do not stop the occurrence of reflux of stomach content but instead reduce the amount of acid in the gastric fluid, thus relieving (or even, in some cases, eliminating) symptoms; however, about 40% are not helped by the most effective and common medication PPIs[i]. Long-term PPI therapy is associated with serious side effects[ii].

Patients who experience inadequate or incomplete relief of GERD symptoms following lifestyle changes/drug treatment or who do not tolerate / want to take the risk of the side effects of PPIs will be recommended for surgical intervention. There are currently only three primary surgical options available in the United States for GERD treatment:

- fundoplication, a surgical technique;
- endoscopic suturing/plication; and
- the LINX Reflux Management System, a surgical implantation of a medical device.

Surgical options currently involve stomach tissue or a medical device to encircle the esophagus. 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 RefluxStop® System was granted CE mark approval in August 2018 and has been successfully marketed in the EU, Switzerland, and the UK since that time. The RefluxStop® System has not been withdrawn from the market in any country.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the RefluxStop® System:

Adverse events that may be related to the use of the RefluxStop® Device include, but are not limited to, those that are commonly associated with general anesthesia, abdominal laparoscopic surgery, and those that are associated with the RefluxStop® Device or procedure. These may be serious and even cause death. Potential adverse events related to general anesthesia and abdominal surgery in general comprise of, but are not limited to: abdominal abscess, abdominal pain, adverse reactions to anesthesia (dizziness, headache, nausea, sore throat, teeth damage, visual complications), allergic shock, anaphylactic shock, atrial arrhythmia or fibrillation, cardiac arrhythmia or arrest, fever, hemorrhage, heart attack, hypotension, hypoxemia, ileus, incisional herniation, infection, perforation, peritonitis, pneumonia, pneumothorax, pulmonary embolism, respiratory distress, septic shock, septicemia, stroke, thrombophlebitis, thrombosis, urinary retention, urinary tract infection, visceral adhesions, weight loss, and wound dehiscence.

Possible risks related to anti-reflux surgery in general, which may apply to the RefluxStop® surgical procedure, may include, but are not limited to: intraoperative complications, reinterventions, respiratory complications also comprising atelectasis, pleurisy and pneumothorax, flatulence, retching, vomiting, bloating, hiccups, reherniation of the fundus including the device, bleeding especially hemorrhage from the short gastrics, risks to the spleen including spleen extirpation, gastric or esophageal perforation, dysphagia including need for esophagus dilatation, odynophagia, recurrence of GERD symptoms such as heartburn, regurgitation, crus sutures damaging/cutting through the crus muscles due to retching/heaving/vomiting, esophageal sutures cutting through the wall of the esophagus with retching or vomiting resulting in tearing of the esophagus, pain, ileus, esophageal widening due to poor esophageal emptying, narrowing or stenosis, or infection including peritonitis and abscess, gas bloating, inability to belch or vomit, diarrhea, vomiting and delayed gastric emptying, and hiatal repair performed too tightly causing dysphagia.

Finally, there are also possible adverse events related to the RefluxStop® Device. Potential adverse events comprise of but are not limited to: lack of treatment effect or regain of reflux symptoms, device removal or re-operation, device erosion early and long-term. Early erosion could occur due to surgery-related hampered blood supply to the stomach wall or surgically induced damage on the stomach wall serosa. Blood supply may be affected due to too tight of an invagination, causing too much pressure on the stomach wall. Too tight of an invagination not causing erosion may theoretically instead cause a mucosal ulcer to form at the device position due to a reduced blood supply (not verified). Fundoplication sutures may also come loose, causing relapse of reflux symptoms. Not closing the pouch may cause device slippage. Re-herniation may occur, but often the re-herniated fundus could be restored with the device intact in its fundal pouch. This risk is greater in patients with larger hernia before surgery.

The device hangs in a teardrop shape into the stomach cavity surrounded by single stomach wall, with double stomach wall sutured together most cranial of the pouch. This surgical technique of placing the device in a pouch, and the design of the device in smaller pieces, are performed to reduce the risk of erosion of the device. This said, an eroded device could theoretically end up anywhere.

Adverse events that may be related to the use of the RefluxStop® Deployment Tool include, but are not limited to, those that are commonly associated with general anesthesia, abdominal laparoscopic surgery, and those that are associated with the RefluxStop® Deployment Tool. These may be serious and even cause death. Potential adverse events relating to general anesthesia and abdominal laparoscopic surgery are similar to those described in the implant section of this document.

Additionally, like other laparoscopic procedures, there are foreseeable adverse events related to careless handling of an instrument and also off-label use of the RefluxStop® Deployment Tool could result in damage to tissue or organs, especially the spleen if not handled with care. An accidental impact or unintentional displacement of the tool could have severe consequences.

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

IX. SUMMARY OF NON-CLINICAL STUDIES

Nonclinical studies were completed to evaluate the RefluxStop® System, including non-clinical bench testing, biocompatibility, sterilization, packaging, and shelf-life studies. These are described in detail in the following sections.

A. **Laboratory & Shelf Life Studies**

The integrity and performance of the RefluxStop® System was evaluated through the testing summarized below.

Table 1. Summary of Laboratory & Shelf Life Testing on the RefluxStop® Device (RS-A1)

Timepoint	Test Performed	Acceptance Criteria	Test Results
T=0 T=5-year Accelerated Aging T=5-year Real Time Aging	Visual Inspection	No extraneous matter or surface defects	Pass
	Static Force	The implant shall withstand a force of 50N without gross damage.	Pass
	Separation Force	The outer segments of the RefluxStop® Device implant must separate from the inner core in the absence of a suture with minimal force.	Pass
	Lifetime Simulation (equivalent to 104 implant years)	The implant shall maintain its structural integrity and shall be free from wear and damage.	Pass
	Simulated Use: Implant Compression	Confirm that RefluxStop® Device is successfully compressed and protrudes slightly from the Pipe (approximately 5 mm)	Pass
	Simulated Use: Implant Ejection	The RefluxStop® Device can successfully be ejected from the pipe by the user. The RefluxStop® Device remains intact with all 5 components held together by the suture.	Pass
	Simulated Use: Implant Release	RefluxStop® Device implant can be released from the wire of the Deployment Tool by the user. The RefluxStop® Device remains intact with all 5 components held together by the suture.	Pass
T=0	Magnetic Resonance Imaging Safety	Confirm that the product is electrically nonconductive and nonmagnetic.	Pass
	Radiopacity Assessment	Visible under x-ray and comparable to a reference specimen when placed under a body mimic per ASTM F640-23.	Pass
	Thermogravimetric analysis (TGA)	. The purpose of this test is to quantify the amount of $BaSO_4$ in each RefluxStop® Device and confirm it is uniformly distributed. This is accomplished via laboratory technique to measure changes in physical and chemical properties as a function of increasing temperature or as a function of time.	The thermogravimetric analysis showed that the Barium Sulphate was distributed evenly across the two batches of material, with no statistical difference between the residual material in each batch.

Table 2. Summary of Laboratory & Shelf Life Testing on the RefluxStop® Deployment Tool (RS-300)

Timepoint	Test Performed	Acceptance Criteria	Test Results
T=0 T=200 Reprocessing Cycles (SS)	Visual Inspection	No extraneous matter or surface defects	Pass
	Simulated Use: Implant Compression	Confirm that RefluxStop® Device is successfully compressed by the user.	Pass
	Simulated Use: Implant Ejection	The RefluxStop® Device can successfully be ejected from the pipe by the user.	Pass
	Simulated Use: Implant Release	RefluxStop® Device implant can be released from the wire of the Deployment Tool by the user.	Pass
	Corrosion Testing (Boil Test)	No visual signs of corrosion.	Pass
T=0 T=50 Reprocessing Cycles	Pressure Leak Test	No gross leak through the Trocar as well as the assembled RefluxStop® Deployment Tool.	Pass
T=0	Corrosion Testing (Copper Sulphate Test)	No visual signs of copper plating.	Pass

SS = Stainless Steel Components; CSV = Silicone Cross Slit Valve Component

B. Biocompatibility Studies

In alignment with ISO 10993-1, Implantica has assessed and conducted relevant biocompatibility testing for both devices in the RefluxStop® System:

- The RefluxStop® Device (RS-A1) consists of five (5) components that are manufactured from a medical-grade silicone (Nusil MED-4860) mixed with $BaSO_4$. All components are classified as implant, direct tissue/bone contact with long-term exposure/permanent duration (> 30 days).
- The RefluxStop® Deployment Tool (RS-300) consists of twelve components. Eleven (11) of these components are manufactured from Stainless Steel AISI 316L and the final component is an off-the-shelf component manufactured from medical-grade silicone. RS-300 is considered an externally communicating medical device. Six (6) of the stainless steel components are classified as direct tissue or direct body fluid (peritoneal fluid) contact with limited exposure (≤ 24 hours). The remaining components are considered non-contacting. The devices tested underwent 200+ reprocessing cycles in alignment with the use stated in the IFU.

Table 3. Summary of Biocompatibility Testing on the RefluxStop® System

Test Performed	Test Description	Implant	Tool	Test Results
Cytotoxicity	L929 MEM Elution	X	X	Non-cytotoxic
Sensitization	Guinea Pig Maximization	X	X	Non-sensitizing
Irritation / Intracutaneous Reactivity	Intracutaneous Injection Test in Rabbits	X	X	Non-irritating
Material-Mediated Pyrogenicity	Rabbit Pyrogen Study (Material-Mediated)	X	X	Non-pyrogenic
Acute Systemic Toxicity	Acute Systemic Toxicity Study in Mice	X	X	Non-toxic
Subacute Systemic Toxicity	4-week Subacute Systemic Toxicity Study in Rats	X	X*	Non-toxic
Subchronic Systemic Toxicity	Chemical Characterization/ Toxicological Risk Evaluation	X	N/A	Non-toxic
Chronic Systemic Toxicity	26-week Chronic Systemic Toxicity Study in Rats	X	X*	Non-toxic
Implantation	4 and 13-week Muscle Implantation Study in Rabbits	X	N/A	Non-irritant
Genotoxicity	AMES & Mouse Lymphoma Assay	X	N/A	Non-mutagenic
Carcinogenicity	Chemical Characterization/ Toxicological Risk Evaluation	X	N/A	Non-carcinogenic
Biodegradation	Biological Risk Assessment	X	N/A	No biodegradation risks
Reproductive/Developmental Toxicity	Biological Risk Assessment	X	N/A	Non-toxic
Immunotoxicity	Biological Risk Assessment	X	N/A	Non-toxic

** To fully evaluate the biocompatibility profile of the RS-A1 device and the required materials to perform the RefluxStop® implantation procedure, Implantica has conducted subacute (4 week) systemic toxicity testing as well as chronic (26 week) toxicity testing in accordance with ISO 10993-11 utilizing a test article "system". This test article "system" consisted of the RS-A1 implant (to be marketed by Implantica) as well as the absorbable suture and lubricant (both of which are to be acquired by the implanting physician per the IFU). Additionally, the test was designed to deploy the Test Article "System" through one (1) final, finished RefluxStop® Deployment Tool (RS-300) to simulate setup/use per the IFU. To ensure all potential residuals were considered, the RS-300 device underwent six (6) reprocessing cycles prior to use. Only the implant was implanted in the study.*

C. Sterilization and Packaging Studies

The RefluxStop® Device is supplied disassembled and sterile (gamma irradiated, 25-38 kGy). The five components of the device are enclosed in two thermally-welded pouches, one sealed inside the other, creating a double sterile barrier system. The sterilization testing conducted supports that the RefluxStop® Device (RS-A1) meets the requirements of ISO 11137-1 and ISO 11137-2 and confirms that the documented routine sterilization procedures with ≥25 kGy ensures a Sterility Assurance Level (SAL) of 10^{-6}.

Additionally, the RefluxStop® Device (RS-A1) has undergone bench testing (**Table 1**) following exposure to this maximum dose to confirm that the device and its packaging continues to meet its specified functional requirements throughout its defined lifetime. Furthermore, the packaging validation demonstrated the ability of the packaging to protect the product and maintain a sterile barrier through shipping and shelf life. Based on this testing, a 5-year shelf life has been established for both the device and its packaging.

The RefluxStop® Deployment Tool is supplied disassembled and non-sterile. Before first time use and after each re-use, the device is to be cleaned, packaged, and sterilized by the user using autoclave sterilization. Per the labeling, the product can be reprocessed up to a pre-defined number of cycles (200 cycles for stainless steel components, 50 cycles for the silicone component). The cleaning and sterilization validation testing conducted supports that the RefluxStop® Deployment Tool (RS-300) may be safely and effectively reprocessed using either the manual or automated cleaning instructions as well as the sterilization parameters provided in the IFU. Refer to the RefluxStop® Deployment Tool IFU for specific information on the end-user cleaning and sterilization parameters.

Additionally, the RefluxStop® Deployment Tool (RS-300) has undergone bench testing (

Table 2) following exposure to these maximum reprocessing cycles to confirm that the device continues to meet its specified functional requirements throughout its defined lifetime. Furthermore, the packaging validations demonstrated the ability of the different packaging configurations to protect the product through shipping.

X. SUMMARY OF PRIMARY CLINICAL STUDY(IES)

The applicant performed a clinical study to support the safety and effectiveness of the RefluxStop® System in the treatment of acid and non-acid reflux in patients diagnosed with GERD. Data from this 5-year clinical study were the basis for the PMA approval decision. A summary of this pivotal clinical study is presented below, the results of which have been published in two papers in Surgical Endoscopy:

- The 5-year results have been published in Surgical Endoscopy 2025[iii]: https://link.springer.com/article/10.1007/s00464-025-11979-9

- In addition, the 5-year data relating to food passageway-related sequelae has been published in Surgical Endoscopy 2025[iv]: https://link.springer.com/article/10.1007/s00464-025-11818-x

A. Study Design

Patients were treated between December 7, 2016, and December 22, 2023. The database for this PMA reflected data collected through December 22, 2023, and included 50 patients. There were 4 investigation sites.

The study was a prospective, open-label, multi-center, single-arm, treatment-only trial conducted to evaluate the safety and effectiveness of RefluxStop® Device, an implantable, single-use, non-active medical device indicated for the treatment of GERD. The study population consisted of adult subjects between 18 and 75 years of age with documented typical GERD symptoms for >6 months, daily use of PPIs as anti-GERD medication, and proven GERD as determined by 24-hour pH monitoring. The study investigated the effects of the device implant on GERD symptoms, PPI usage, lower esophageal acid exposure, and health-related quality of life (HRQL). The device was investigated in 50 subjects over a period of 5 years.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the RXI001 study was limited to patients who met the following key inclusion criteria.

- Subject's age ≥18 years and ≤75 years;
- Subject has documented typical GERD symptoms present for >6 months which respond to PPIs as anti-GERD medication. Typical symptom of GERD is defined as heartburn, which is a burning epigastric or substernal pain;
- Subject requires daily PPI anti-GERD medication;
- Subject has a 24-hour pH monitoring-proven GERD, performed taken off any anti-reflux medication or after discontinuation for at least 7 days prior to testing. Total distal esophageal pH must be <4 for ≥4.5% of time during a 24-hour monitoring;
- Subject was able to undergo general anesthesia and was suitable laparoscopic surgical candidate;
- Subject was willing and able to participate;
- Subject provided written informed consent after being informed of the study procedures and risks prior to any study-related events.

Patients were not permitted to enroll in the RXI001 study if they met any of the following key exclusion criteria:

- Subject has a history or a suspicion of esophageal or gastric cancer;

- Presence of a para-esophageal hernia or sliding hernia > 3 centimeters determined on endoscopy;
- Subject has a body mass index (BMI) >35 kg/m^2;
- Female subjects that are pregnant or nursing;
- Known sensitivity or allergies to silicone materials;
- Intra-operative findings that may preclude conduct of the study procedures;
- Subject was participating in another study involving investigational drugs or devices;
- Subject had a history of gastroesophageal surgery, anti-reflux, or bariatric procedure;
- Subject had a history of endoscopic anti-reflux intervention;
- Subject had a history of major psychiatric disorder;
- Presence of an esophagitis grade C or D according to the Los Angeles classification;
- Presence of esophageal dysmotility disorder such as but not limited to scleroderma, achalasia, Nutcracker esophagus;
- Presence of esophageal stricture or stenosis;
- Presence of delayed gastric emptying;
- Presence of esophageal or gastric varices;
- Subjects who were unable to comply with the protocol requirements;
- Subjects with limited life expectancy (<3 years).

2. Follow-up Schedule

All subjects were followed for 5 years or until study exit and follow-up examinations were scheduled at week 6, month 3, month 6, and years 1-5 post-device implantation.

Preoperatively, subjects were screened to verify eligibility with baseline assessments including medical history, previous medications for GERD and other diseases, GERD-HRQL questionnaire and individual questions from the Foregut questionnaire, EGD endoscopy, 24-h pH monitoring, contrast swallow x-ray and a gastric emptying test.

Postoperatively, at each follow-up visit, subjects completed the GERD-HRQL questionnaire, individual questions from the Foregut questionnaire and a question on PPI use. Objective parameters were measured by 24-hour pH monitoring at 6 months and 5 years, contrast swallow x-ray to verify device location was performed at hospital stay, 6 weeks, 6 months, and 5 years and EGD Endoscopy was performed at 6 months. Furthermore, if subject's GERD-HRQL was <50% improved from baseline or regular daily PPIs were used, an additional 24-hour pH monitoring and contrast swallow x-ray were performed at least once to verify whether subject symptoms were due to acid reflux. Adverse events and complications were recorded at all visits.

The key timepoints are shown below in the tables summarizing safety and effectiveness.

3. Clinical Endpoints

Primary Safety Endpoint

The incidence of serious adverse device effects (SADEs) and procedure-related serious adverse events (SAEs) at 6 months.

Secondary Safety Endpoint

The incidence of SADEs and procedure-related SAEs at all time points other than 6 months. The incidence of ADEs and procedure-related AEs during the entire 5 years after device implantation.

Primary Effectiveness Endpoint

The percent reduction from Baseline of GERD symptoms based on the total GERD HRQL score measured at 6 months. These data were also presented as the number of subjects obtaining at least 50% improvement from baseline figures with success defined as 60% of the subjects reaching such score improvement. Thus, the aim of this analysis was to show that the lower limit of the confidence interval (CI) exceeded 60%.

Secondary Effectiveness Endpoints

The secondary effectiveness endpoints consisted of:

- 24-hour pH monitoring to objectively measure acid reflux at 6 months and 5 years
- Contrast swallow x-ray to assess the device position and reherniation
- EGD endoscopy to assess improvement in esophagitis
- Regular daily PPI usage as a predictor of potential return of GERD
- GERD-HRQL questionnaire completion to measure subjective symptom recurrence and total score at all time points other than 6 months (primary endpoint)
- Regurgitation existence based on individual question from Foregut questionnaire
- Inability to belch and vomit to measure potential side effects of acid reflux procedure
- Possible therapy failures (defined as subjects with <50% improvement in GERD-HRQL score since baseline or regular daily PPI usage) were assessed with additional examinations including 24-hour pH monitoring and contrast-swallow x-ray to determine if their symptoms were confirmed to be due to GERD

B. Accountability of PMA Cohort

At the time of database lock, there were 74 subjects enrolled in the study. Of these, 50 subjects received the device implant and 44 (88%) subjects were available for analysis at the completion of the study during the 5-year follow-up post-operative visit. **Table 4** describes subject enrollment and follow-up at the different timepoints in the study as well as the sample sizes across the analysis population. As shown in **Table 4**, the sample size is the same for the Safety Analysis Set, Full Analysis Set (FAS), and PP (Per Protocol Analysis Set) populations (N=50). Three (3) additional subjects are included in the Full Intention-to-Treat (ITT) Analysis Set population but are excluded from the other analysis populations because they underwent surgery but did not receive the RefluxStop® Device. The three subjects fulfilled the exclusion criterion of intra-operative findings that may preclude conduct of the study procedures, namely due to a short esophagus (two subjects) and severe esophagitis with a Brachy esophagus (one subject), in which all findings occurred during surgery.

Table 4. Subject Enrollment and Follow-up at Different Timepoints

	Total	**Total** ***Excluding COVID Deaths (2) and Bedbound with long-COVID (1)***	**Total** ***Excluding Additional Patients who Terminated the Study (3)***
Number of Subjects			
Enrolled	74	-	-
Eligible	55	-	-
Surgery performed - ITT	53*	-	-
Received the device implant (Study subjects) †	50 (94.3%)	-	-
Number of Study Subjects			
Completed 6 weeks visit‡	50 (100.0%)	-	-
Completed 3 months visit‡	49 (98.0%)	-	Terminated (n=1)**
Completed 6 months visit‡	48 (96.0%)	-	Terminated (n=2)**
Completed 1-year follow-up‡	46 (92.0%)	-	-

Table 4. Subject Enrollment and Follow-up at Different Timepoints

	Total	**Total** ***Excluding COVID Deaths (2) and Bedbound with long-COVID (1)***	**Total** ***Excluding Additional Patients who Terminated the Study (3)***
Completed 2-year follow-up‡	47 (94.0%)	-	-
Completed 3-year follow-up‡	47 (94.0%)	-	-
Completed 4-year follow-up‡,¥	46 (92.0%)	46 (**93.9%**) (n=1)	46 (**100%**) (n=4)
Completed 5-year follow-up‡,¥	44 (88.0%)	44 (**93.6%**) (n=3)	44 (**100%**) (n=6)
Analysis Sets			
Safety analysis set	50	-	-
Full analysis set	50	-	-
Per-protocol analysis set	50	-	-
Full intention-to-treat analysis set	53		

**Three of the study subjects fulfilled exclusion criterion of intra-operative findings that may preclude conduct of the study procedures, due to short esophagus.*

*** None of the three subjects that terminated early was a verified failure and no-one took PPI.*

†*Percentages are based on the number of subjects that underwent surgery. Additional columns exclude COVID "deaths" and study termination.*

‡ *Percentages are based on the number of subjects that received the device implant.*

¥*Two of the study subjects died of covid infection (one between Year 3 and 4 and one be tween Year 4 and 5)* and one subject bedbound by long-COVID. *ITT = Intention to treat*

During the 5-year study period, one (1) subject withdrew from the study at 3 months, two (2) subjects refused to consent for follow-up beyond 6 months, two subjects (2) died from COVID-19 after the 3- and 4-year follow-ups, respectively, and one (1) bedbound subject suffered from long COVID-19 and was unable to further participate in the study after the 4-year follow-up. Therefore, a total of 44 subjects completed the follow-up at 5 years.

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a GERD study performed in the U.S. As evidenced in the peri-operative assessments and medical history in **Table 5**, the baseline demographic characteristics of the subjects in the study are comparable to those of the U.S. GERD patient population and, therefore, the results of this study can be generalized.

Table 5. RXI001 Demographics Before Surgery, Safety Analysis Set (n=50)

Variable	Min	Q25	Median	Q75	Max	Mean	SD	N (%)	Missing (%)
Age (years)	26	-	53.0	-	76	51.5	11.8	50 (100)	0 (0)
Height (cm)	148	-	170.0	-	200	170.8	11.3	50 (100)	0 (0)
Weight (kg)	53	66.0	80.0	88.0	118	78.2	14.7	50 (100)	0 (0)
BMI (kg/m²)	18.7	23.4	26.55	29.7	35.8	26.81	4.41	50 (100)	0 (0)
Sex, male	-	-	-	-	-	-	-	28 (56)	0 (0)
Sex, female	-	-	-	-	-	-	-	22 (44)	0 (0)
Hiatal hernia	1	-	2.5	-	3.2	2.51	0.58	37 (74)	0 (0)
GERD-HRQL (0-50)	9	24	29.5	33	49	28.8	7.3	50 (100)	0 (0)
Esophageal pH <4 (%)	4.3	6.6	10.55	19.3	94.8	16.35	16.6	50 (100)	0 (0)
Esophagitis Grade A	-	-	-	-	-	-	-	13 (26)	0 (0)
Grade B								9 (18)	0 (0)
Grade C or D								-	-
Dissatisfied	-	-	-	-	-	-	-	45 (90)	0 (0)
Neutral	-	-	-	-	-	-	-	4 (8)	0 (0)
Satisfied	-	-	-	-	-	-	-	1 (2)	0 (0)

Table 5. RXI001 Demographics Before Surgery, Safety Analysis Set (n=50)

Variable	Min	Q25	Median	Q75	Max	Mean	SD	N (%)	Missing (%)
Gastric emptying test	No severe delayed gastric emptying observed							50 (100)	0 (0)

Definitions: "Min" = Minimum; "Q25" = First Quartile; "Q75" = Third Quartile; "Max" = Maximum; "SD" Standard Deviation; "CI" = Confidence Interval

The age distribution in the study sample, with a median age of 53 years and a range of 26 to 76 years, aligns well with the known prevalence of GERD across different age groups. The study's sex distribution includes 56% male and 44% female participants. The study sample has a mean BMI of 26.81 kg/m², with a range from 18.7 to 35.8, indicating that a mix of normal-weight and overweight individuals were included.

The severity of GERD in the study sample is evident from the high prevalence of hiatal hernia (74%) and the presence of esophagitis in 26% of patients. GERD severity was reflected in a mean GERD-HRQL score of 28.8, indicating significant symptoms. This suggests that the study primarily included patients with moderate to severe GERD rather than those with mild or occasional reflux symptoms.

D. Safety and Effectiveness Results

1. Safety Results

Primary Safety Endpoint Results

The primary safety endpoint of the pivotal clinical study was: The incidence of SADEs and procedure-related SAEs at 6 months. All SAEs are outlined in **Table 6**. below. The results for the primary endpoint and throughout the entire 5-year study are summarized as follows:

- At 6 months and throughout the entire study period, no device related serious or non-serious adverse events (SADEs or ADEs) were reported.
- Two (2) procedure-related severe SAEs were observed: one (1) case of infection with an abscess and three diagnoses; and one (1) case of hematoma drainage due to spontaneously stopped bleeding from short gastric vessels. Both subjects recovered fully well treated from their acid reflux following appropriate treatment.
- One (1) elective re-operation occurred (Moderate SAE) during the entire study period due to a loose fundoplication suture that was in an elective procedure re-sutured with the device remaining intact in its pouch. Too much fat in the suture line had hindered the fibrotic healing/adherence of fundus to esophagus. The suturing was performed in the same way as the original

procedure.

- Not severe SAEs included: one (1) broken needle which was removed subcutaneously, and one (1) self-healing pleuritis.

Thus, in total, five (5) subjects had SAEs assessed as related to the study procedure, whereof one (1) patient with one (1) infection was provided three diagnoses. All procedure-related SAEs occurred prior to the Year 1 visit (all but one in the first 30 days following surgery), had a duration between 1-52 days, and all were resolved and patients well treated for their acid reflux.

Table 6. RXI001 Procedure-Related Serious Adverse Events for Entire 5-year Study, Safety Analysis Set (n=50)

				Total (N=50)					
				Mild		Moderate		Severe	
System Organ Class/Preferred Term	Outcome	Time to Onset	Duration	n (%)	m	n (%)	m	n (%)	m
Any adverse event				**1 (2.0%)**	**1**	**2 (4.0%)**	**2**	**2 (4.0%)**	**4**
Injury, poisoning and procedural complications				**1 (2.0%)**	**1**	**1 (2.0%)**	**1**	**0**	**0**
Foreign body subcutaneously broken needle	RECOVERED/ RESOLVED	0 to ≤30 days	1 days	1 (2.0%)	1	0	0	0	0
Suture rupture fundoplication	RECOVERED/ RESOLVED	>4.5 to ≤9 months	1 days	0	0	1 (2.0%)	1	0	0
Infections and infestations				**0**	**0**	**0**	**0**	**1 (2.0%)**	**3**
Abdominal & Mediastinal abscess, and Empyema	RECOVERED/ RESOLVED	0 to ≤30 days	52 days	0	0	0	0	1 (2.0%)	3
Gastrointestinal disorders				**0**	**0**	**0**	**0**	**1 (2.0%)**	**1**
Intra-abdominal hemorrhage drainage of hematoma	RECOVERED/ RESOLVED	0 to ≤30 days	1 days	0	0	0	0	1 (2.0%)	1

Table 6. RXI001 Procedure-Related Serious Adverse Events for Entire 5-year Study, Safety Analysis Set (n=50)

				Total (N=50)					
				Mild		Moderate		Severe	
System Organ Class/Preferred Term	Outcome	Time to Onset	Duration	n (%)	m	n (%)	m	n (%)	m
Respiratory, thoracic and mediastinal disorders				**0**	**0**	**1 (2.0%)**	**1**	**0**	**0**
Pleurisy	RECOVERED/ RESOLVED	0 to ≤30 days	11 days	0	0	1 (2.0%)	1	0	0

n = number of subjects, m = number of events.
Percentages are based on the total number of subjects.

There were no SADEs during the entire study period, as shown in **Table 7** below.

Table 7. RXI001 Device-Related Serious & Non-Serious Adverse Events for Entire 5-year Study, Safety Analysis Set (n=50)

				Total (N=50)					
				Mild		Moderate		Severe	
System Organ Class/Preferred Term	Outcome	Time to Onset	Duration	n (%)	m	n (%)	m	n (%)	m
Any device related adverse event				**0**	**0**	**0**	**0**	**0**	**0**

n = number of subjects, m = number of events.
Percentages are based on the total number of subjects.

Secondary Safety Endpoint Results

Notably, 97.9% of subjects (46/47) did not report any dysphagia between Years 1-5, a symptom often seen in standard-of-care anti-reflux surgery with frequencies between 30-70%. This finding emphasizes the device's advantage in minimizing

dysphagia, a common complication associated with traditional anti-reflux procedures, further demonstrating its favorable safety and tolerability profile.

Table 8. RXI001 Procedure-Related Non-Serious Adverse Events for Entire 5-year Study, Safety Analysis Set (n=50)

				Total (N=50)					
				Mild		Moderate		Severe	
System Organ Class/Preferred Term	**Outcome**	**Time to Onset**	**Duration**	**n (%)**	**m**	**n (%)**	**m**	**n (%)**	**m**
Any adverse event*				**5 (10.0%)**	**6**	**2 (4.0%)**	**3**	**0**	**0**
Abdominal pain due to incisional hernia, see below**	UNKNOWN	>4.5 to ≤9 months		0	0	1 (2.0%)	1	0	0
Dyspepsia	NOT RECOVERED / NOT RESOLVED	>1.5 to ≤2.5 years		0	0	1 (2.0%)	1	0	0
Dysphagia	RECOVERED / RESOLVED	>2.5 to ≤3.5 years	3 years 101 days	1 (2.0%)	1	0	0	0	0
Temporary intestinal paresis postoperative (gastroparesis postop)	RECOVERED / RESOLVED	0 to ≤30 days	4 days	1 (2.0%)	1	0	0	0	0
Incisional hernia**	UNKNOWN	>4.5 to ≤9 months		0	0	1 (2.0%)	1	0	0
Procedural pneumothorax	RECOVERED / RESOLVED	0 to ≤30 days	1 days	1 (2.0%)	1	0	0	0	0

** In addition, 3 Mild incidents/adverse events in two subjects occurred and were resolved during surgery: hepatic lesion and adhesiolysis with hemorrhage*
*** Incisional hernia with pain in the same patient, no action taken*
An = number of subjects, m = number of events.
Percentages are based on the total number of subjects.

The most frequently observed AEs were gastritis (14%), upper abdominal pain (10%) (which also is a symptom of gastritis), and coronavirus infection (10%).

Table 9. RXI001 Dysphagia Adverse Events, Full Analysis Set (FAS, n=50)

Dysphagia (FAS)	As per GERD-HRQL daily symptoms at baseline* (n=50)		Reported AEs 0-1 year (n=50) †		Recovered /Resolved	Reported AEs 1-5 years (n=50) †		Recovered /Resolved
None	39	78%	49	98%	-	49	98%	-
Mild	6	22%	1‡	2%	Yes	1¥	2%	Yes
Moderate	3		0		-	0		-
Severe	2		0		-	0		-

**Baseline figures represent GERD-HRQL-relevant individual question score >2 (symptoms everyday).*

† *Three (3) subjects terminated the study: two (2) at 6 months and one (1) at 3 months; data at the time of that visit have been carried forward to use in the FAS.*

‡ *One (1) subject had early onset symptoms of dysphagia immediately following surgery, lasting ~2 weeks.*

¥ *One (1) subject had severe dysphagia before surgery with a GERD-HRQL question dysphagia score of 5.0 with subsequent decrease to 2.0 at 3-year follow-up, indicating treatment success as opposed to AE.*

Overall Safety Result Discussion

The study results were achieved with minimal dysphagia and gas bloating, symptoms commonly associated with the current standard of care with incidence rates between 30-50% at 5 years as per a recently published literature review[v], and only minimal incidence of other AEs. This has further been confirmed by the 5-year follow-up with contrast swallow x-ray imaging presenting no device migration, device dislocation, or re-herniation at Year 5.

2. Effectiveness Results

Primary Effectiveness Results

The analysis of effectiveness was based on the 47 evaluable subjects at the 6-month time point, the outcomes of which are presented in **Table 10** below. The primary effectiveness results are also presented in **Table 11**, when including data at 1 year for two (2) of the subjects and at 3 months for one (1) subject.

The study met the primary effectiveness endpoint, defined as 60% of the subjects reaching at least 50% improvement in the GERD-HRQL total score from baseline figures. At 6 months, 95.7% of subjects had mean reduction of 89.1% in GERD-HRQL score from baseline. The 95% CI was (83.8-94.3%), and thus, the primary endpoint was fulfilled with a large margin.

Table 10. RXI001 Primary Effectiveness Endpoint, Full Analysis Set

Time (months)	Group	Mean Reduction (%)	95% Confidence Interval	Study Subject Success - ≥50% GERD-HRQL reduction since baseline	Number of subjects (n)
6.0	FAS	89.1	(-83.8, -94.3)	**95.7 %** **Study group success yes**(≥60%)	**n = 47**

Table 11. RXI001 Primary Effectiveness Endpoint with supplemental data, Full Analysis Set

Time (months)	Group	Mean Reduction (%)	95% Confidence Interval	Study Subject Success - ≥50% GERD-HRQL reduction since baseline	Number of subjects (n)
6.0 months (47) 12 months (2) 3 months (1)	FAS	88.7	(-82.0, -95.3)	**96.0%** **Study group success yes** (≥60%)	**n = 50**[*] including data from subjects at 1year (2) and 3 month (1)

** Two subjects did not perform the questionnaire at 6 months follow-up, however, both joined the 1-year follow-up, which data have been used in this reporting; One subject terminated the study after the 3 months visit well-treated and the 3 months data has been used in this reporting.*

The follow-up data for up to 5 years indicates sustained effectiveness. The primary endpoint conditions applied to the 5-year results also show total study success with a considerable margin.

Table 12. RXI001 Effectiveness results at Year 5, Full Analysis Set

Time (months)	Group	GERD-HRQL median score at baseline (50)	GERD-HRQL median score at follow-up	Improvement of GERD median scores	Number of subjects at follow-up (n)
60.0	FAS	29.5	3.0	90%	**5 years follow-up n=44**
60.0	FAS	29.5	3.0	90%	**End of Study† n=47** Including 5yr (n=44) 4yr (n=2) & 3yr (n=1)
Study success when including subjects with <50% improvement of GERD-HRQL score as successfully treated subjects, when 24-h pH monitoring is normal (%) (eliminating subjects with gastritis and SIBO affecting GERD-HRQL scores for reasons other than GERD)					
60.0	FAS	**97.9%‡ TOTAL STUDY SUCCESS at Year 5**			**End of study† n=47** (Including subjects lost to COVID at 4yr n=2 & 3yr n=1)

† *The end of study results include imputation carried-forward for the three affected by COVID-19, totaling 47 subjects, of which two include results from year 4 and one subject from year 3.*

‡ *When including subjects with <50% improvement in GERD-HRQL score from baseline with normal 24-hour pH monitoring results as successful subjects, study success reaches 97.9%.*

Based on overall RefluxStop® effectiveness outcomes, it is evident that the treatment provides substantial improvement in GERD-HRQL score, indicating effective treatment of reflux symptoms in patients with severe GERD. This was achieved with a very low number of complications and side effects. Specifically, the primary endpoint at 6 months was reached with a large margin and was 39% higher than the stipulated 60% (i.e., at 6 months, 60% of the individuals in the study should be below the lower end of the 95% CI of the percentage of subjects with ≥50% improvement of the GERD-HRQL score from baseline).

The lower end of the CI 85.5% at 6 months in the FAS was, as mentioned, higher than the stipulated 60%. The median total GERD-HRQL score was reduced from 29.5 before surgery to 3.0 at 5-year follow-up, a reduction of 90%. The End of study analysis on GERD-HRQL were performed as ad hoc analysis.

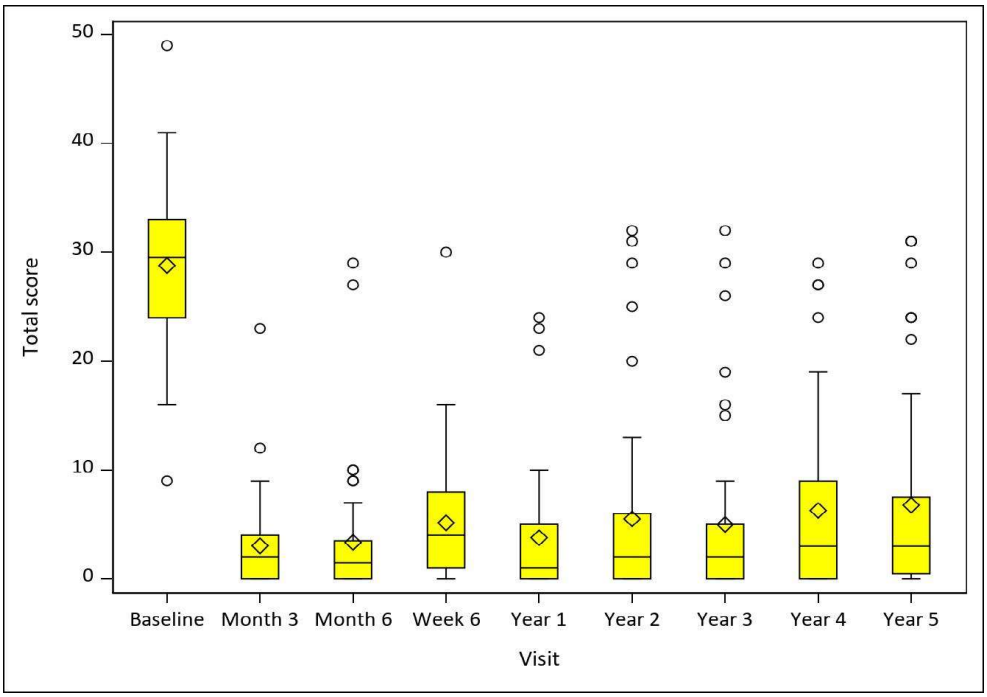

Figure 5. GERD-HRQL Questionnaire Scores Over Time

NOTE: The central line within each box indicates the median score, while the diamond symbol represents the mean score. The boundaries of each box correspond to the 25th (bottom) and 75th (top) percentiles, and the whiskers extend to the range of non-outlier values. Circles beyond the whiskers denote outlier values. Outlier values are dominated by patients with gastritis, the most common adverse event in this study, with 12 patients having gastritis. Refer to Table 17.

Secondary Effectiveness Endpoint Results

24-hour pH monitoring

The total lower esophageal acid exposure time across all FAS subjects at baseline, 6 months, and 5 years post-treatment is presented in **Figure 6** below. A reduction in duration was observed at 6 months and 5 years compared to baseline. Specifically, mean duration decreased from 16.35% (± 16.60%) at baseline to 0.80% (± 1.56%) at 6 months and 1.57% (± 2.10%) at 5 years post-treatment. This

represents an absolute reduction of 15.79% and 15.10% at 6 months and 5 years, respectively. Furthermore, the mean duration of 1.57% at 5 years is substantially lower than the pathologic threshold value for acid reflux (>4.5%), underscoring the sustained therapeutic effectiveness of the device.

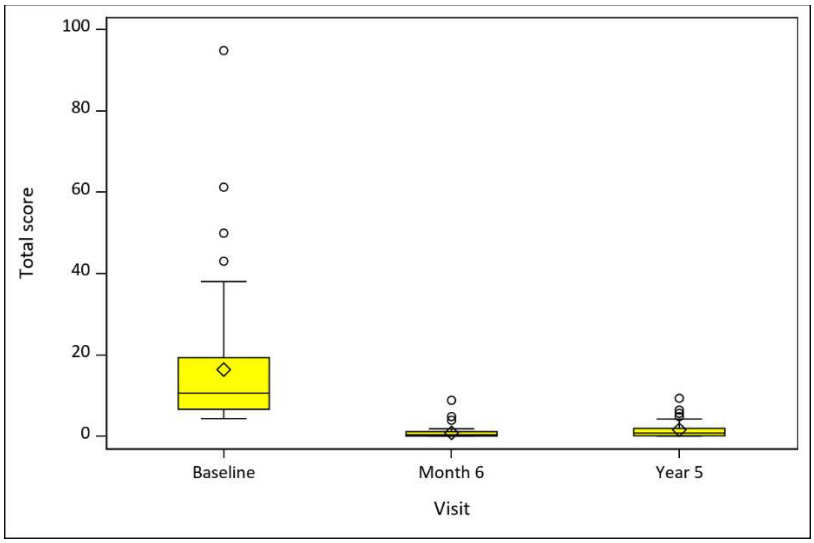

Figure 6. 24-hour pH Monitoring Comparing Baseline, 6-month, and 5-year Values

NOTE: The central line within the box indicates the median score, while the diamond symbol represents the mean score. The boundaries of the box correspond to the 25th (bottom) and 75th (top) percentiles, and the whiskers extend to the range of non-outlier values. Circles beyond the whiskers denote outlier values

Figure 7 below highlights the total lower esophageal acid (pH <4) exposure time, represented as the percentage of time over a 24-hour pH monitoring period, for each subject in the FAS, measured at baseline and 5 years post-treatment. Most subjects demonstrated a reduction in acid exposure time by Year 5 compared to baseline, as reflected by the downward trend lines. These results indicate a sustained therapeutic effect of the device, with most subjects experiencing a marked decrease in the duration of acid reflux throughout the post-treatment period.

Using the definition of pH normalization or ≥50% pH reduction from baseline, as used in other acid reflux treatment studies' FDA Memorandum[vi], no subject failed the 24-hour pH monitoring at Year 5 and one subject failed at Month 6. In **Figure 7** below, each patient's pH improvement is disclosed as a separate line, allowing for visualization of individual patient success graphically. Only one subject had the combination of total time pH <4 of >4.5% and being dissatisfied with the procedure.

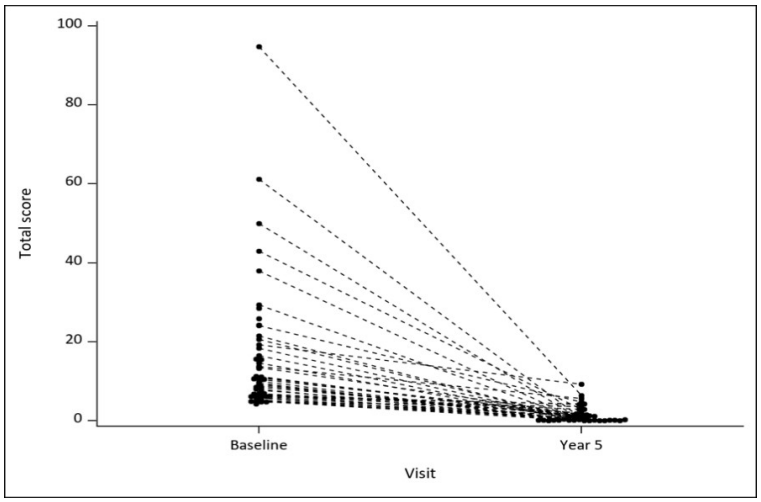

Figure 7. 24-hour pH Monitoring Comparing Individual's Acid Exposure at Baseline and 5-year Values

NOTE: Each dashed line represents an individual subject's acid exposure at baseline and Year 5.

Table 13 summarizes the percentage of overall time of lower esophageal acid exposure among FAS subjects at baseline, 6 months, and 5 years post-treatment. From baseline to the first follow-up assessment at 6 months, the mean duration dropped from 16.35% to 0.80%, reflecting a mean change of 15.79 percentage points and notable reduction in the proportion of time spent at a pH <4. Results remained consistent up to 5 years post-treatment at which point the proportion of time spent at pH <4 was 1.57%. On average, a 90.4% reduction of 24-hour monitoring results based on total time pH <4 was appreciated.

Table 13. RXI001 24-hour pH Monitoring (pH < 4), Full Analysis Set

% Overall time pH < 4	**Total (N=50)**
Baseline	
n/nmiss	50/0
Mean (SD)	16.35 (16.60)
Median	10.55
Q1, Q3	6.60, 19.30
Min, Max	4.3, 94.8
Month 6	

Table 13. RXI001 24-hour pH Monitoring (pH < 4), Full Analysis Set

% Overall time pH < 4	Total (N=50)
n/nmiss	45/5
Mean (SD)	0.80 (1.56)
Median	0.30
Q1, Q3	0.00, 1.10
Min, Max	0.0, 8.8
Year 5	
n/nmiss	40/10
Mean (SD)	1.57 (2.10)
Median	0.75
Q1, Q3	0.10, 1.90
Min, Max	0.0, 9.3

n/nmiss = number of subjects with evaluable/missing data, SD = standard deviation.

A total of 47 subjects underwent pH testing at minimum one time point.

PPI Usage

Table 14 outlines the daily intake of PPIs at various timepoints throughout the study period. At the 5-year follow-up visit, 97.7% of subjects (43/44) were not taking daily PPIs. When including the three (n=3) COVID-affected subjects (deaths (2) & bedbound with long-COVID (1)) before falling ill with COVID-19, with available 3-year (n=2) and 4-year (n=1) data, 97.9% of subjects (46/47) were not using any PPIs. These results suggest that the device offers therapeutic benefit in preventing acid reflux, as all but one (1) subject no longer required daily PPI use by the 5-year mark.

Table 14. RXI001 PPI Usage, Full Analysis Set

	Months / n(%)						
Daily, regular PPI intake	**0**	**6**	**12**	**24**	**36**	**48**	**60**
No	**0 (0)**	**47 (97.9)**	**43 (93.5)**	**44 (93.6)**	**47 (100)**	**44 (95.7)**	**43 (97.7)**
Yes, due to GERD with pathologic 24-h pH	**49 (98)**	**0 (0)**	**0 (0)**	**1 (2.1)**	**0 (0)**	**0 (0)**	**0 (0)**

Table 14. RXI001 PPI Usage, Full Analysis Set

	Months / n(%)						
Daily, regular PPI intake	**0**	**6**	**12**	**24**	**36**	**48**	**60**
Yes, not due to acid reflux – normal 24-h pH	1 (2)*	1 (2)	2(4.3)	2 (4.2)	0 (0)	2(4.3)	0 (0)
Yes, 24-h pH is missing	0	0	1 (2.2) †	0	0	0	1 (2.3)
(Total, n)	50	48	46	47	47	46	44

** 24-h pH total time 4.3% and esophagitis grade B*

† Normal pH at 5 years

NOTE: These results were achieved with minimal dysphagia and gas bloating, symptoms that are very common with the current standard of care with incidence rates between 30-50% at 5 years, and only minimal incidence of other AEs per literature review. This has further been confirmed by the 5-year contrast swallow x-ray images presenting no device migration, device dislocation, or re-herniation. Inability to belch and/or vomit after standard-of-care (i.e., LNF) surgery occurs in about 40% of subjects at 5 years, as shown in a large systematic literature review on randomized studies of Nissen fundoplication, and no inability to belch and vomit was present in this pivotal study[v].

Satisfaction

At 5-year follow-up, a total of 43/44 subjects reported status satisfied or neutral or were dissatisfied with normal pH monitoring, meaning their dissatisfaction is for reasons other than GERD.

Gas Bloating

An improvement in gas bloating was observed based on the change in gas bloating symptomatology from baseline to the 5-year follow-up visit based on question 9 of the GERD-HRQL questionnaire, with the average score decreasing from 3.5 at baseline to 1.5 at the 5-year follow-up. Moreover, 95.5% of subjects (42/44) reported either no gas bloating, an improvement, or equal to baseline in their scores at the 5-year mark, whereof 6.8% were unchanged compared to before surgery.

Table 15. RXI001 GERD-HRQL Questionnaire (Gas Bloating), Full Analysis Set

Do you have bloating or gassy feeling (n=50)	**Base-line**	**3 months**	**6 m**	**1 year**	**2 years**	**3 years**	**4 years**	**5 years**
Change of symptoms at Follow-up compared to Baseline								
n	50	49	47	42	47	47	46	44
Mean (SD)	**3.5 (1.5)**	**1.2 (1.5)**	**1.3 (1.5)**	**1.1 (1.3)**	**1.4 (1.6)**	**1.4 (1.6)**	**1.5 (1.5)**	**1.5 (1.4)**
Median	**4.0**	**1.0**	**1.0**	**1.0**	**1.0**	**1.0**	**1.0**	**1.0**
No symptoms at Baseline and at current visit		**2 (4.1%)**	**2 (4.3%)**	**3 (7.1%)**	**4 (8.5%)**	**4 (8.5%)**	**3 (6.5%)**	**2 (4.5%)**
Equal symptoms		5 (10.2%)	4 (8.5%)	2 (4.8%)	7 (14.9%)	3 (6.4%)	2 (4.3%)	3 (6.8%)
Improved		**39 (79.6%)**	**38 (80.9%)**	**36 (85.7%)**	**36 (76.6%)**	**38 (80.9%)**	**40 (87.0%)**	**37 (84.1%)**
Worsening		3 (6.1%)	3 (6.4%)	1 (2.4%)	0	2 (4.3%)	1 (2.2%)	2 (4.5%)

Regurgitation

Figure 8 illustrates the changes in reported regurgitation throughout the study period, as assessed by the Foregut questionnaire. Including the three COVID-affected subjects with available data at year 3 (n=1) and year 4 (n=2), 93.6% of subjects (44/47) reported no or minimal regurgitation at the 5-year follow-up visit. In total, 95.5% (42/44) of subjects had improved or no regurgitation compared to baseline.

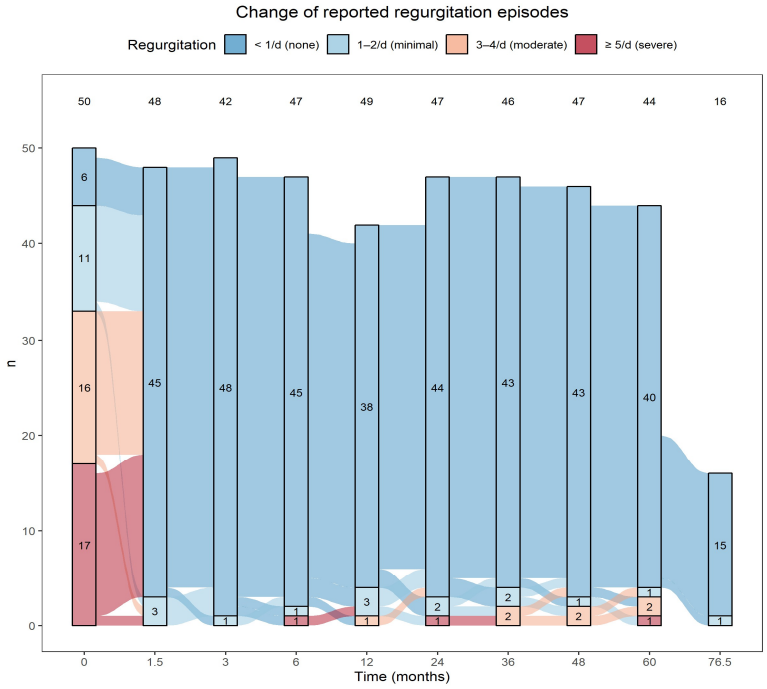

Figure 8. Change in Regurgitation Over Time

Inability to Belch/Vomit

RefluxStop® did not induce inability to belch and/or vomit in any patient in this study, a side effect very common in standard-of-care surgery (i.e., 52.7% at year 5 in a systematic literature review on Nissen fundoplication)[v].

Table 16. RXI001 Ability to Belch/Vomit, Full Analysis Set

Are you able to belch and vomit	Total (n=50)
Year 5	
No	0
Yes	41 (100.0%)
Missing	9

As a supplement to the GERD-HRQL Questionnaire, Implantica conducted a review of subjects that experienced any adverse events which may be related to an inability to belch/vomit. Including the four subjects that had AE epigastric pain (the main symptom of gastritis) there were a total of 12 subjects with gastritis (24%), which corresponds to the known incidence in the Western world of 25-35% having gastritis[vii,viii,ix,x,xi,xii]. Thus, it is not unusual to have gastritis following treatment, since RefluxStop® only treats GERD. These subjects represent most of the GERD-HRQL high scores and are the reason why pH measurement is necessary.

Table 17. RXI001 Subjects with Gastritis, Full Analysis Set

Subjects with gastritis out of the total (N=50)	n (%)	m
Any Gastritis diagnosis plus subjects with gastritis symptom AE epigastric pain	**12 (24.0%)**	**13**
Any Gastritis diagnosis three-quarter based on Endoscopy	8 (16.0%)	9
Any Gastritis by severity		
Mild	5 (10.0%)	6
Moderate	3 (6.0%)	3
Severe	0	0
Additional subjects with main symptom of gastritis – AE epigastric pain	4 (8%)	4

Esophagitis

The secondary endpoint esophagitis at 6 months showed that 46 out 48 (95.8%) subjects had no esophagitis compared to 22 out of 50 subjects (44%) had grade A or B esophagitis at baseline.

Re-herniation or Device Dislocation/Migration

Five-year post-implantation re-herniation and device location were evaluated through contrast swallow x-ray imaging, the results of which are presented in **Table 18** below. At the 5-year follow-up visit, no FAS subjects had experienced re-herniation, device dislocation, or device migration.

Table 18. RXI001 Results of 5-Year Contrast Swallow X-Ray, Full Analysis Set

Contrast swallow x-ray (n=40)	Year 5
Re-herniation	0 (0)
Device dislocation	0 (0)
Device migration	0 (0)

3. Subgroup Analyses

The following preoperative characteristics were evaluated for potential association with outcomes for the primary effectiveness endpoint: gender, age, BMI.

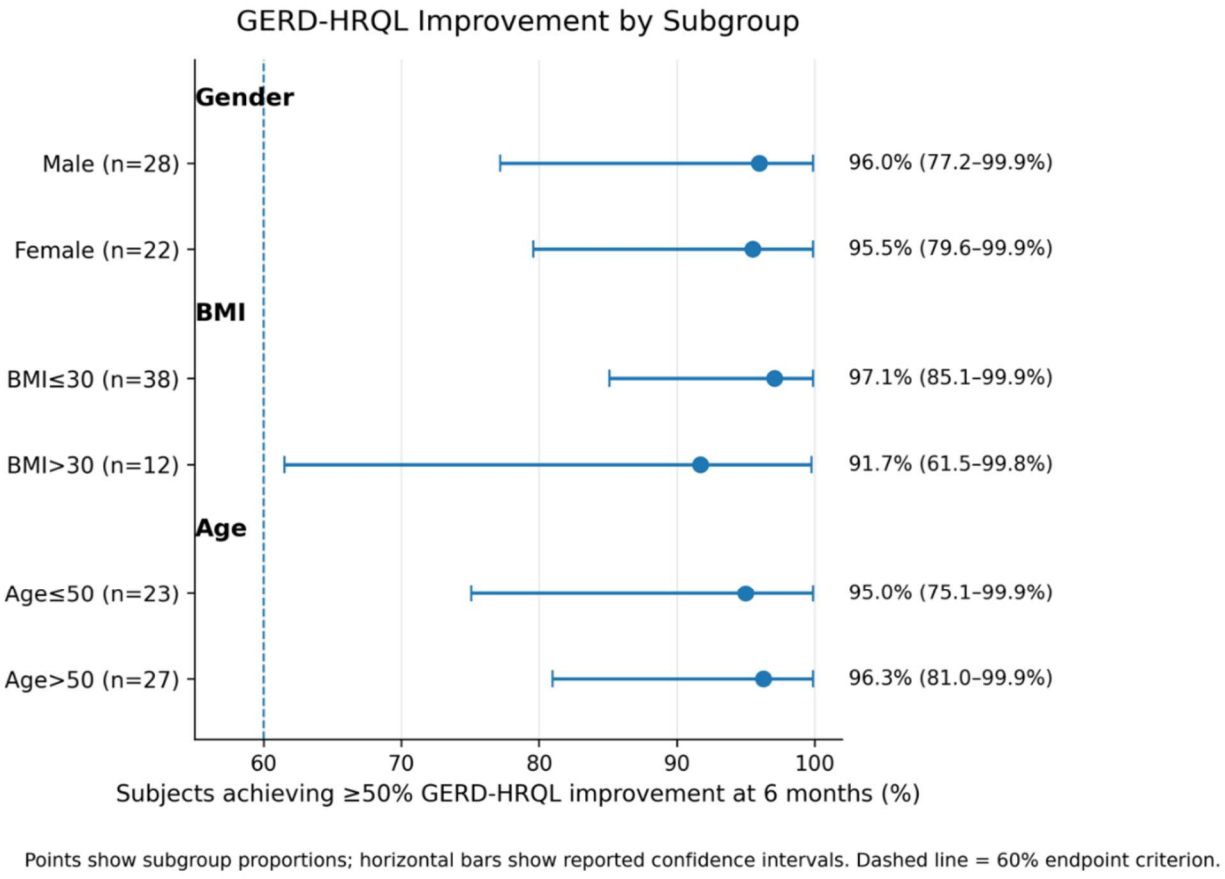

Figure 9. GERD-HRQL Improvement by Subgroup

All the subgroups examined met the primary effectiveness endpoint.

4. Pediatric Extrapolation

In this premarket application, existing clinical data was leveraged to support the *reasonable assurance of safety and effectiveness* of the proposed device in *the pediatric sub-population of adolescents 18 and older. The pivotal clinical study included subjects 18-75 years.*

XI. 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 26 investigators. None of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

XII. 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 Gastroenterology and Urology Devices Panel, an FDA advisory committee, for review and recommendation.

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The pivotal clinical study supports the effectiveness of the RefluxStop® System in treating GERD:

- The primary endpoint with 60% of study subjects reaching the individual target of 50% improvement in total GERD-HRQL score was fulfilled with 85.5% as the lower CI value compared to the 60% stipulated target:
  - At 6 months, the mean change of GERD-HRQL score from baseline was 89.1% (95% CI: 83.8-94.3%). At least 50% improvement from baseline occurred in 95.7% (85.5, 99.5%).
- At 3-, 4-, and 5-year follow-ups, the median GERD-HRQL score remained very consistently at 3.0 or below and tracked closely to the mean scores at respective time points.
- Median GERD-HRQL score was reduced from 29.5 before surgery to 3.0 at follow-up, a reduction of 90% at 5-year follow-up.
- pH monitoring resulted in a 1.57% mean total time with pH <4, substantially lower than the threshold of a pathologic value of >4.5%, at 5-year follow-up.
  - Defining normal 24-hour pH monitoring as all subjects also with >50% improvement of total time pH <4, all subjects in this pivotal study had normal 24-hour pH monitoring outcome.

- According to the Lyon Consensus definition of normal esophageal acid exposure (total time pH <4 <6%), 95% of subjects that performed pH measurement at year 5 had normal values. The remaining two subjects (5%) were also clinically well treated, with no regurgitation, no PPI use, satisfied, and very low GERD-HRQL scores.

- 46 out of 47 subjects (97.9%) did not report any dysphagia AEs between years 1 and 5, a symptom often seen in standard-of-care anti-reflux surgery with frequencies between 30-70%.
- 46 out of 47 subjects did not experience dissatisfaction due to GERD (based on objective pathologic 24-hour pH monitoring) at year 5 when including the three COVID subjects (before their severe COVID at year 3-4, i.e., two COVID deaths and one long COVID bedbound).
- 44 out of 47 subjects reported None or Minimal Regurgitation (this 5-year result includes carried-forward imputation for the three COVID subjects using the last value before the onset of severe COVID at years 3-4). In total, 95.5% (42/44) of
- subjects had improved or no regurgitation compared to baseline.
- Gas bloating dramatically improved, with the average score of symptom question 9 on the GERD-HRQL questionnaire reduced from 3.5 at baseline to 1.5 at 5 years. At 5-year follow-up, 39 of 44 subjects had either no gas bloating or had improved scores from baseline (2 subjects worsened). In total, 95.5% (42/44) of subjects had
- non-worsening gas bloating compared to baseline.

B. Safety Conclusions

The device's safety profile is supported by preclinical bench testing and clinical data from the pivotal study, which demonstrated no device-related serious or non-serious adverse events (i.e., SADEs or ADEs) over the entire 5-year study period.

- No device deficiencies
- No device migrations
- No esophageal dilatations
- No device explants

5-year contrast swallow confirmed

- No device dislocations
- No re-herniations
- No migration/erosion

For the primary endpoint, in addition to no SADEs at 6 months and throughout the entire study period, five (5) subjects reported SAEs assessed as related to the procedure (one subject had three diagnoses from the same infection), and all were satisfactorily resolved. Only two (2) SAEs were severe and included the mentioned infection and a drainage of hematoma from a bleeding of the short gastric vessels, adverse events occurring in all

standard-of-care anti-reflux surgeries. The most common AEs overall were gastritis, upper abdominal pain (i.e. a typical symptom of gastritis) and Corona virus infection. Only two subjects reported a procedure-related AE between Year 1 and 5: one mild dysphagia and one moderate dyspepsia.

The study results were achieved with minimal dysphagia and gas bloating, symptoms commonly associated with the current standard of care with incidence rates between 30-50% at 5 years as per a recently published literature review[v], and only minimal incidence of other AEs.

Moreover, when reviewing the literature regarding the standard of care, RefluxStop® results indicate a substantial improvement.

A recently published systematic literature review of RCTs pertaining to standard-of-care Nissen fundoplication[v] has shown high complication rates, exemplified by that 39.8% of subjects could not belch and vomit, a gas bloating rate of 52.7% and dysphagia rate of 28.9% at 5 years after surgery (based on AEs). Thus, this naïve indirect comparison shows a substantial difference in outcomes compared to RefluxStop® pivotal study, which had no inability to belch and vomit at year 5, only one AE dysphagia reported between year 1-5 which was resolved at 5 years, and 95.5% of subjects (42/44) reported either no gas bloating, an improvement, or equal to baseline in their scores at the 5-year mark with average GERD-HRQL-specific bloating question score reduced from 3.5 at baseline to 1.5 at 5-year follow-up.

More than 1,500 patients have undergone the RefluxStop® procedure thus far, as presented after the pivotal study results, and >50 centers in Europe are regularly performing RefluxStop® surgery. The clinical literature is supportive of and consistent with the RefluxStop® pivotal clinical study results.

A summary of safety data from 22 RefluxStop® centers on 602 patients presented at SAGES, has been published in Nature Scientific Reports[xiii], presented serious events with reoperation in 1.99% of the 602 cases. Only two types of serious events occurred in a frequency >1/602 patients (0.17%) and these were:

Firstly, re-herniation occurred in 1.33% whereof about slightly more than one-third in large hernia cases similar to the frequency of large hernia operated. In all cases patients were reoperated with a straightforward reposition of fundus with the device intact in its pouch and in 1/8 case the device was explanted and extended fundoplication performed. A new hiatal repair was performed often using mesh.

Secondly, early penetration of the device into the stomach cavity was seen in 0.66% of cases as part of the learning curve for 4/22 surgeons and in 4/602 cases. This was related to a too tight invagination of the pouch (including the device) in the stomach wall, one case per each surgeon occurred in the early learning curve and has not happened since new improved procedures have been implemented. Since the device hangs like a teardrop into the stomach cavity sutured in a row on top, it will erode into the stomach cavity and due to its design disintegrate in its 5 pieces and move out through the digestive tract naturally. This event happened asymptomatically, and no further action was needed (no reoperation).

C. Benefit-Risk Determination

The benefits of the device are based on data collected in a clinical study conducted to support PMA approval as described above, which has been supported by real-world evidence in >1500 cases. Many different centers have published their results, which all are aligned with the excellent results from the pivotal study (today 33 articles have been published and more in the process of being published). In a large study focusing on safety from 602 patients and 22 centers in Europe, which includes the learning curve of a new procedure, serious events with re-operation only occurred in 1.9% of patients. Two-thirds of these reoperations were due to re-herniation, which was possible to restore with a straightforward reposition of fundus, with the device intact in its pouch.

In the pivotal study, the RefluxStop® Device demonstrated clinical benefits in reducing GERD symptoms, normalizing gastric acid exposure with 90.4% improvement in acid exposure at year 5, and decreasing usage of PPIs with only one subject taking PPI at the 5-year follow-up. The median GERD-HRQL score decreased from 29.5 at baseline to 3.0 at the 5-year follow-up, representing a 90% improvement. At 6 months, GERD-HRQL mean scores demonstrated an 89.1% ±17.9% (95% CI: 83.8%, 94.3%) reduction from baseline fulfilling the Primary endpoint, with scores remaining consistent through the 3-, 4-, and 5-year follow-ups.

Thus, the clinical study demonstrated that the RefluxStop® Device effectively improved GERD symptoms and quality of life for most patients, with consistent positive results maintained over a five-year period. Gastric acid exposure was reduced, and the majority of patients experienced a substantial reduction in typical GERD symptoms, including regurgitation and gas bloating. Patient satisfaction was high, and the device showed a low rate of adverse events, indicating a favorable safety profile compared to traditional anti-reflux surgical interventions.

The risks associated with the RefluxStop® Device are primarily related to the surgical implantation procedure, including risks such as bleeding, infection, and anesthesia-related complications. Overall, the RefluxStop® Device exhibited a strong safety profile, with minimal AEs and low incidence of SAEs, with no device-related adverse events during the entire study. The absence of severe device-related complications such as migration, explantation, or major re-operation further supports the conclusion that the RefluxStop® Device is a safe option for the treatment of GERD. Additionally, the favorable comparison to other anti-reflux treatments, both in terms of lower AE rates and reduced severity of complications, underscores the potential benefits of this innovative approach for patients seeking long-term relief from GERD symptoms. Since RefluxStop® does not encircle the food passageway, it provides favorable outcomes compared to standard anti-reflux surgeries in terms of encircling-related events such as dysphagia, odynophagia, inability to belch and vomit, and gas bloating that often occur in high numbers in standard of care procedures. The primary severe event recorded in the study was COVID-19 in three (3) subjects, which was unrelated to the device or procedure.

The benefit-risk profile of the RefluxStop® Device is favorable. The benefits, including an 89.1% reduction in GERD symptoms and a reduction in gastric acid exposure as measured by 24-hour pH monitoring and a low incidence of adverse events, outweigh the manageable risks associated with the device and its implantation. Compared to traditional anti-reflux surgeries, the RefluxStop® Device demonstrated favorable safety and effectiveness outcomes in an indirect comparison, including lower rates of dysphagia, gas bloating, re-operation, and failure in acid reflux control. The RefluxStop® Device offers a compelling alternative, providing effective symptom relief without the anatomical alterations and higher complication rates typically associated with such procedures. By avoiding encircling and putting pressure on the food passageway, the functionality of which is often damaged over time by repeated acid exposure, a normal sphincter function is restored and results in a reduction of side-effects typically seen in standard of care anti-reflux procedures. Overall, the clinical evidence supports the RefluxStop® Device as a safe and effective treatment for patients with GERD, offering sustained improvements in quality of life and symptom management, and the probable benefits from RefluxStop® treatment outweigh its associated risks.

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 the RefluxStop® System the probable benefits outweigh the probable risks when used in accordance with the indications for use - an implantable sterile medical device intended to treat acid and non-acid reflux in patients diagnosed with gastroesophageal reflux disease (GERD). The device ensures maintenance of a normal physiological situation for the gastroesophageal junction (GEJ) in a defined intra-abdominal position, allowing a natural physiological function of the lower esophageal sphincter (LES), thereby reducing or eliminating acid and non-acid reflux. The RefluxStop® Deployment Tool is indicated for patients diagnosed with Gastroesophageal Reflux Disease (GERD), defined by abnormal impedance pH and/or pH testing, and indicated for RefluxStop® implantation.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of the RefluxStop® System when used in accordance with the indications for use.

The device has demonstrated substantial clinical benefits in treating gastroesophageal reflux disease (GERD), as evidenced by long-term improvements in GERD-related health metrics. The clinical study has shown that the benefits of using the device outweigh the risks, with a significant portion of the patient population achieving clinically meaningful improvements.

The primary safety endpoint was met, as no serious adverse device effects (SADEs) were reported at month six or at any time during the investigation and the five (5) subjects with procedure-related SAEs were satisfactorily resolved.

The primary effectiveness endpoint was successfully met, with implantation of the RefluxStop® Device resulting in a significant reduction in GERD-HRQL scores at six months post-surgery. The mean percent (SD) change from baseline was -89.1% (17.9), with a 95% confidence interval of -94.3 to -83.8. Notably, 95.7% of evaluable subjects achieved at least a 50% improvement in GERD symptoms at six months, demonstrating robust efficacy across the study population

In conclusion, the RefluxStop® System represents an advancement in GERD treatment, offering durable symptom relief, improved esophageal acid exposure, and a reduced reliance on PPIs. The pivotal study supported by substantial equally favorable real-world data support that a significant portion of the patient population will achieve clinically meaningful results, with minimal risks. The long-term safety and effectiveness profile of the device justifies its clinical use, making it a compelling alternative to current GERD management options.

XIV. CDRH DECISION

CDRH issued an approval order on August 20, 2026. The final clinical conditions of approval cited in the approval order are described below.

REVEAL: A post-market study to assess safety and effectiveness of RefluxStop® in the treatment of Gastroesophageal Reflux Disease (GERD) in general hospital practice New Enrollment PAS (Study Number RXI009, Version 7.0, dated July 30, 2026):

This is a prospective, single-arm, multi-center study designed to evaluate the short- and long-term safety and effectiveness of RefluxStop® in the treatment of GERD. The PAS will enroll a total of 200 patients with hiatal hernia size ≤ 3 cm, who will be implanted with RefluxStop® and followed for 5 years. Study participants will be enrolled at up to 10 clinical sites (minimum of 4 sites), with at least 50% of sites located in the United States and at least half of all procedures conducted at U.S. sites.

The primary safety endpoint is the incidence of procedure- and device-related serious adverse device effects (SADEs), serious adverse events (SAEs) and device deficiencies (DDs) at 1 year. The rate of this composite endpoint will be compared to a performance goal (PG) of 16.2%. The primary effectiveness endpoint is pathologic acid in the lower esophagus measured by 24-hour pH monitoring (total percentage of time pH <4) at 1 year

Secondary study endpoints are as follows. Secondary safety endpoints include: incidence of procedure- and device-related SADEs, SAEs and DDs at all time points excluding at year 1, comprising month 6 as well as years 2 to 5; and incidence of procedure- or device-related Adverse Events (ADEs or AEs) at 6 months and annually thereafter up to 5 years. Secondary effectiveness endpoints include: subjects with <50% improvement of GERD-HRQL since

baseline due to GERD; reduction in GERD-HRQL group score, measured at 6 months and years 1 to 5 compared to baseline; regular daily PPI usage due to GERD/acid reflux at 6 months and years 1 to 5; total percentage of time pH <4 measured by 24-hour pH monitoring at year 1; pathologic 24-hour pH monitoring and on-label device position at years 2 to 5; and incidence of inability to belch at 6 months and at years 1 to 5.

The main 1-year safety and effectiveness endpoints will be analyzed as follows:

- The incidence of procedure- and device-related SADEs, SAEs and DDs at year 1 (primary safety endpoint) will be compared to a performance goal of <16.2%.
- Proportion of patients having pathologic 24-hour pH monitoring at year 1 (primary effectiveness endpoint) will be compared to a performance goal of 40%.
- Proportion of patients having <50% improvement of GERD-HRQL score at year 1 compared to baseline (secondary effectiveness endpoint) will be compared to a performance goal of <40%.

For each of the three evaluations of 1-year endpoints, a descriptive summary will be provided on the observed rates compared to the defined performance goals.

In addition, a long-term evaluation of device performance will be conducted by comparing 5-year endpoints in the PAS to long-term results following Nissen fundoplication based on literature.

Descriptive analysis will be conducted on all other clinical endpoints.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality Management System (QMSR) regulation (21 CFR 820).

XV. 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.

XVI. REFERENCES

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