SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name	Stent, Urethral, Prostatic, Permanent Or Semi-Permanent
Device Trade Name	Zenflow Spring® Implant and Delivery System
Device Product Code	MER
Company Name and Address	Zenflow, Inc. 395 Oyster Point Blvd., Suite 501 South San Francisco, CA 94080
Date of Panel Recommendation	None
PMA Number	P250007
Date of FDA Notice of Approval	December 11, 2025

II. INDICATIONS FOR USE

The Zenflow Spring Implant and Delivery System is indicated for the treatment of obstructive lower urinary tract symptoms secondary to benign prostatic hyperplasia (BPH) in men with prostatic urethral lengths between 25 and 45 mm and prostate volumes between 25 and 80 cc.

III. CONTRAINDICATIONS

- Patients with a previous laser prostatectomy, hyperthermia, brachytherapy, or invasive treatment to the prostate or pelvis area
- Patients with acute urethral stricture disease, meatal stenosis, or bladder neck stricture – either current or recurrent
- Patients with active urolithiasis
- Prostate cancer or previous external or internal gamma radiation therapy for prostate or proximal urethral cancer
- Known allergy to nickel, titanium, or stainless steel
- Patients with urinary tract infections (UTIs)
- Patients with acute infection (acute urethritis, acute prostatitis, acute epididymitis)
- Patients with hematuria with an undiagnosed cause
- Patients with an existing prostatic foreign body
- Urinary incontinence due to an incompetent external sphincter

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Zenflow Spring® Implant and Delivery System labeling.

V. DEVICE DESCRIPTION

The Zenflow Spring® System consists of the Spring Implant and Delivery System, Spring Scope, Camera Control Unit (CCU), and Implant Retrieval Device (IRD). The Spring Implant and Delivery System, Spring Scope, and Implant Retrieval Device, are packaged separately, supplied sterile, and indicated for single use only. The CCU is intended to be used outside the sterile field, supplied non-sterile, and can be reused for multiple procedures. Only the Spring Implant and Delivery System are the subject devices of this PMA. The Spring Scope and Camera Control Unit were cleared under K251140.

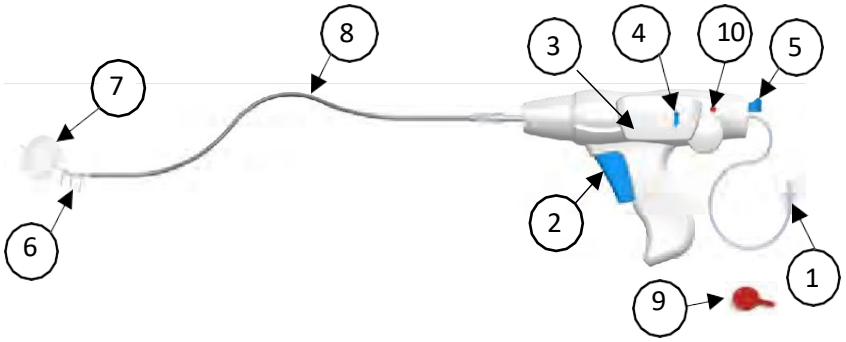
Spring Implant

The Spring Implant is an electropolished and passivated nickel titanium alloy (nitinol) implant. The implant is constructed from a single wire strand formed into ring elements connected by spine sections. Implant sizes range between 15 mm – 21 mm in length (as shown in Figure 1) to accommodate prostate lengths between 25 mm – 45 mm. The ends of the implant have rounded balls to assist in grasping the device. The device is designed to be removable and retrieved at any time after deployment.

Figure 1. Zenflow Spring Implant Sizes (left to right 15/18/21 mm, not to scale)

Delivery System

As shown in Figure 2, the Zenflow Delivery System consists of a handle and a catheter shaft. The Spring Implant is designed to be straightened and to reside within a lumen of the 11.5 Fr Delivery System catheter for insertion. When inflated, a compliant balloon at the distal end of the catheter is designed to anchor and position the Delivery System during Implant delivery.



No.	Part	Function
1	Balloon Inflation Port	Allows user to inflate balloon anchor.
2	Trigger	Allows the user to deploy or retract the Implant.
3	Handle	Allows user to grip and control the device.
4	Directional Switch	Chooses whether Implant is deployed or retracted with each trigger pull.
5	Unlock Knob	Allows the Implant to be released.
6	Spring Implant (pre-attached but not loaded)	Implantable device
7	Balloon (shown inflated)	Provides anchor on bladder neck during Implant delivery.
8	Delivery System Shaft	Houses Implant during delivery and connects to handle.
9	Abort Key	Pushes the recessed Abort Button.
10	Abort Button (recessed)	Used if Delivery System is unable to advance or retract, leaving the implant partially deployed.

Figure 2. Labeled Zenflow Delivery System with Spring Implant

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the treatment of lower urinary tract symptoms (LUTS) attributed to BPH. According to the American Urological Association's (AUA) guidelines [(1)], these alternatives include:

Medical Therapy

Medical therapy is typically the first treatment approach for BPH. Drug classes used to treat BPH include alpha blockers, 5-alpha reductase inhibitors, or a combination thereof, and phosphodiesterase-5 inhibitors.

Surgical Therapy

Surgical interventions for BPH include transurethral resection of the prostate (TURP), prostatectomy, transurethral incision of the prostate (TUIP), transurethral vaporization of the prostate (TUVP), photoselective vaporization of the prostate (PVP), prostatic urethral lift (PUL), water vapor thermal therapy (WVTT), laser enucleation, robotic waterjet

treatment (RWT), prostate artery embolization (PAE), and temporary and permanently implanted prostatic devices (TIPD).

Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with their physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The Zenflow Spring® Implant and Delivery System has not been marketed in the United States or any foreign 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 Zenflow Spring Implant:

- Dysuria
- Hematuria
- Urgency
- Incontinence
- Retention
- Constipation
- Nocturia
- Bladder spasms
- Back pain
- Infection
- Lower urinary tract system pain
- Ejaculatory/sexual dysfunction or pain
- Urethral stricture
- Obstruction secondary to tissue in-growth

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

IX. SUMMARY OF NON-CLINICAL STUDIES

A. Laboratory Studies

Biocompatibility

The applicant completed a biological risk assessment for the Zenflow Spring® Implant and Delivery System per ISO 10993-1:2018 *Biological Evaluation of Medical Devices – Part 1: Biological Evaluation and Testing Within a Risk Management Process,* the FDA guidance document "Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process" issued in September 2023, and ISO 14971:2019 *Medical Devices - Application of Risk Management to Medical Devices*.

The Spring Implant is categorized as an implant device with long-term duration tissue contact, and the Delivery System is categorized as an external communicating device for a limited contact duration. Table 1 lists the biocompatibility testing completed on the Spring Implant and the Delivery System.

Test Name	Spring Implant	Delivery System
Cytotoxicity (MEM Elution) ISO 10993-5 2009	X	X
Sensitization (Magnusson-Kligman) ISO 10993-10 2021	X	X
Irritation or Intracutaneous Reactivity ISO 10993-10 2021	X	X
Acute Systemic Toxicity ISO 10993-11 2017	X	X
Material Mediated Pyrogenicity USP-NF M98900_01_01 2021 <151>	X	X
Subchronic Toxicity ISO 10993-11 2017	X	n/a
Genotoxicity ISO 10993-3 2014	X	n/a
Implantation ISO 10993-6 2016	X	n/a
Chronic Toxicity ISO 10993-11 2017	Rationale based on TRA	n/a
Carcinogenicity ISO 10993-3 2014	Rationale based on TRA	n/a

Table 1. Biocompatibility Testing for the Zenflow Spring® Implant and Delivery System

Nickel elution was evaluated in accordance with the FDA guidance document, Technical Considerations for Non-Clinical Assessment of Medical Devices Containing Nitinol, issued in July 2021. The amount detected did not exceed 35 µg/day (0.5 µg/kg/day for a 70 kg adult), the recommended tolerable intake (TI) limit cited in the guidance.

The chemical characterization study was performed based on the requirements of ISO 10993-18:2005 and an updated toxicological risk assessment (TRA) was conducted in conformance with ISO 10993-17 2023.

The results of biocompatibility testing demonstrated that all patient-contacting components of the Zenflow Spring® Implant and Delivery System are biocompatible.

Zenflow Spring Implant - Magnetic Resonance (MR) Compatibility

The Spring Implant was subjected to a series of tests to characterize its behavior while encountering potential hazards in the MR environment, including RF-induced heating at 1.5T and 3T, magnetically induced force, torque, and image distortion (FTID). Analyses and testing demonstrated that the Spring Implant conforms with the FDA guidance document, Testing and Labeling Medical Devices for Safety in the Magnetic Resonance (MR) Environment issued on October 10, 2023 as well as standards ASTM F2182-19, ASTM F2119-24, ASTM F2052-21.

Zenflow Spring Implant Mechanical Testing

As described in Table 2, design verification testing was conducted to demonstrate that the system met all design inputs. The results of design verification testing demonstrated that all design input requirements for the Zenflow Spring® Implant and Delivery System were met.

Test	Method	Acceptance Criteria	Results
Implant Mechanical Testing			
Spring Implant mechanical testing – fatigue	ISO 25539-2 (2017), ISO 25539-2 (2012) and ASTM F2477 (2013)	The implant must withstand radial fatigue associated with a 30-year lifecycle, or 1 million fatigue cycles and 1560 ejaculation cycles. Assessed via visual inspection of ring, spine, or tail fractures, lumen collapse, and wall apposition throughout test.	Pass
Spring Implant Corrosion	ASTM F2129-17b (2017) and ASTM F2129-19a (2019)	The breakdown potential (Eb) must be larger than or equal to 300 mV. (Eb ≥ 300 mV).	Pass
Spring Delivery System Design Verification Testing			
Unlock Knob Actuation Force	Applicant internal method	Force required to unlock delivery system prior to deployment shall not exceed 9.3 lbf.	Pass

Test	Method	Acceptance Criteria	Results
Instant Release Actuation Force [Unlock Knob Connection]	Applicant internal method	The Instant Release Mechanism shall require no more than 5.91lbf to actuate.	Pass
Unlock Knob connection to the Record Player housing during actuation of the Unlock Knob	Applicant internal method	The Unlock Knob shall remain connected to the Record Player Housing during actuation of the Unlock Knob.	Pass
Push Wire to Reel Tensile Strength	Applicant internal method	The Push Wire to Reel connection withstands a tensile load of at least 4.45lbf without failure.	Pass
Balloon to Tether Shaft Bond	Applicant internal method	The distal end of the Tether Shaft resists a load of at least 5.10 lbf without failure.	Pass
Trigger Deployment Force	Applicant internal method	Force applied to the trigger during deployment of the Implant shall not exceed 15.0 lbf.	Pass
Delivery System Insertion	Simulated procedure	The Delivery System must pass through the Scope working channel	Pass
Implant Deployment/ Unsheathing	Simulated procedure	System must enable 3 deployments of the implant in an untangled, axial configuration before release.	Pass
Average Trigger Retraction Force	Applicant internal method	Average force applied to the trigger during any full deployment or retraction of the Implant shall not exceed 4.67 lbf.	Pass
Balloon Seal	Simulated procedure	When inflated to 40cc of air, the balloon remains inflated throughout the procedure.	Pass
Balloon Deflation	Simulated procedure	When inflated with 40cc of air, the balloon must deflate in less than 15 seconds when pulling full vacuum on a 60cc syringe.	Pass

Test	Method	Acceptance Criteria	Results
Balloon Diameter	Simulated procedure	When inflated with 40cc, the balloon must measure at least 3 cm in diameter.	Pass
Balloon Burst Volume	Simulated procedure	The balloon must be able to withstand inflation with 44cc of air (equal to 1.1x an inflation volume of 40cc).	Pass
Tether Hold	Simulated procedure	The Tether must retain the proximal Implant tail until it is manually released by the user.	Pass
Implant Release	Simulated procedure	The system must release the Implant when manually actuated by the user, without significantly affecting Implant position.	Pass
Delivery System / Scope Rotation Detent	Simulated procedure	The Scope groove with the Delivery System plunger must ensure that the scope handle does not passively (inadvertently) rotate during implant delivery. In addition, the scope should be able to be rotatable (actively) from the delivery system if or when desired by the user.	Pass
Inflation Tube to Inflation Manifold Tensile Strength	EN1618 (1997).	The Inflation Tube to Inflation Manifold joint resists a load of at least 9.83 lbf without failure.	Pass
Tether Balloon Subassembly to Inflation Tube Tensile Strength	EN1618(1997)	The distal end of the Tether Shaft resists a load of at least 9.83 lbf without failure.	Pass
Actuation Sheath Subassembly Tensile Strength	EN1618(1997)	The Square Tether Cover to Actuation Sheath weld resists a load of at least 4.42 lbf without failure.	Pass
Actuation Sheath to Tether Collar Tensile Strength	EN1618 (1997)	The Actuation Sheath to Tether Collar joint resists a tensile load of at least 4.42 lbf without fail.	Pass

Test	Method	Acceptance Criteria	Results
Tygon Tube to Inflation Manifold Tensile Strength	EN1618 (1997)	The Inflation Manifold to Tygon Tube bond joint resists a tensile load of at least 2.88 lbf without failure.	Pass
Square Tether Body to Inflation Tube Weld Tensile Strength	EN1618 (1997)	The Square Tether Body to Inflation Tube weld resists a load of at least 2.84 lbf without failure.	Pass
Implant and Pocket Coupling	EN1618 (1997)	Implant and pocket coupling must be able to withstand a tensile load of at least 4.45 lbf without failure.	Pass
Inner Shaft Subassembly Tensile Strength	EN1618 (1997)	The Inner Shaft (from the tip of the shaft to the square tube) must withstand a tensile force of at least 4.45 lbf.	Pass
Lock Force	Applicant internal method	In the locked condition, the delivery device drivetrain should withstand a grip force of at least 44.6 lbf applied to the trigger of the device without moving past the lock position.	Pass
Pocket Body to Push Wire Tensile Test	Applicant internal method	The Pocket Body to Pocket Wire connection withstands a tensile load of at least 4.45 lbf.	Pass
Inner Shaft Nut Subassembly Tensile Test	Applicant internal method	The Inner Shaft Nut Subassembly (which includes the bond to the Square Tube) must withstand a tensile force of at least 4.45 lbf.	Pass
Simulated Use Testing			
Design Validation	Simulated use	Performance rating ≥ 2 (minimally suitable for clinical use) for any requirement.	Pass

Table 2. Bench testing conducted to support the performance of the Zenflow Spring Implant and Delivery System

Sterilization

The Zenflow Spring® Implant and Delivery System is provided sterile and intended for single use. Sterilization information according to the FDA guidance document,

Submission and Review of Sterility Information in Premarket Notification (510(k)) Submissions for Devices Labeled as Sterile (2024) is provided in Table 3.

Sterilization Method	Ethylene Oxide
Sterilization Site	Steris Applied Sterilization Technologies 43425 Business Park Drive Temecula, California 92590
Sterilization Validation Standards	ISO 11135:2014, Sterilization of health-care products - Ethylene oxide - Requirements for the development, validation and routine control of a sterilization process for medical devices. ISO 10993-7:2008, Biological evaluation of medical devices - Part 7: Ethylene oxide sterilization residuals. ISO 11138-1:2017, Sterilization of Healthcare Products - Biological Indicators - Part I: General Requirements. ISO 11138-2:2017, Sterilization of Healthcare Products - Biological Indicators - Part 2: Biological Indicators for Ethylene Oxide Sterilization Processes. ISO 11737-1:2018, Sterilization of medical devices - Microbiological methods - Part I: Determination of population of microorganisms on products. ISO 11737-2:2019, Sterilization of medical devices - Microbiological methods - Part 2: Tests of sterility in the definition. validation and maintenance of a sterilization process. ISO 11139:2018,Sterilization of health care products - Vocabulary - Terms used in sterilization and related equipment and process standards. AAMI TIRl4:2016, Contract sterilization using ethylene oxide. AAMI TIR15:2016/(R)2024, Physical aspects of ethylene oxide sterilization. AAMI TIRl6:2023, Microbiological aspects of ethylene oxide sterilization. AAMI TIR28:2016/(R)2024, Product adoption and process equivalence for ethylene oxide sterilization.
Sterility Assurance Level (SAL)	10^{-6}
Sterile Packaging	The device is packaged in a thermoformed tray, which is placed in a Tyvek/Mylar pouch. Packaging validation demonstrated that the sterile barrier is not compromised under simulated transit conditions.
Bacterial Endotoxin	Pyrogen testing is performed on a lot-by-lot basis.
Shelf-Life	Shelf-life testing, including testing the sterile barrier after preconditioning and transit simulation (visual inspection, bubble leak, and seal strength tests) and functional testing as described in Table 2, was performed with results supporting a 30-month shelf life.

Table 3. Sterilization Information for the Zenflow Spring® Implant and Delivery System

B. Animal Studies

Preclinical animal studies included three pilot studies and one additional study conducted over a 1.5-year period and including 13 dogs (2 beagles and 11 hounds) with duration of implantation ranging from 7 to 269 days. The purpose of animal studies for the Zenflow Spring System was to demonstrate the overall *in vivo* safety of the device for the

following acceptance criteria: ability to deploy the device in the urethra; absence of migration when sized and placed appropriately; absence of encrustation or other adverse biologic response; absence of excessive "ingrowth" of urethral tissue; overall systemic biologic tolerance; presence of device integration into the urethral mucosa; ability of a living subject to void when the Spring Implant is in place; and visibility of the Spring Implant under fluoroscopy.

The results and conclusions, particularly of the final animal study, supported the safety and effectiveness of the Zenflow Spring Implant. Due to the limitations of the animal model, the Zenflow Delivery System was not used; and therefore, delivery accuracy was a noted limitation of the model. Proper sizing and placement were attained in the final four animals, and no migration was observed. Implants in place for greater than 240 days showed minimal to no mucosal hyperplasia, and gross necropsy was unremarkable. The long-term histopathological images did not raise concern for significant edema or permanent tissue trauma.

X. SUMMARY OF PRIMARY CLINICAL STUDIES

The applicant conducted one First-In-Man (FIM) and three pilot studies, treating a total of 85 patients in the pilot studies, prior to initiating the BREEZE pivotal study. These initial studies supported the conceptual design, initial safety and effectiveness of the Spring Implant, and its viability as a treatment method for men with LUTS due to BPH. The pilot studies were used as evidence to support the initiation of the BREEZE pivotal study .

ZEST First-In-Man (FIM) Study
This FIH study evaluated the Zenflow Spring® Implant and Delivery System for treating LUTS due to BPH in men up to 50 years of age. The study was conducted at four sites with 13 participants enrolled and was extended from 12 months to three years of follow-up.

Deployment Success:

- 85% successful deployment rate (11 of 13 subjects received implants under fluoroscopic guidance).
- 69% device success rate (defined as proper placement without serious/unanticipated adverse events for study duration).

Long-term Outcomes:

- 7 of 11 originally implanted subjects retained their implants at 3-year follow-up.
- 4 subjects required implant removal due to various complications, including migration, inadequate symptom relief, and possible displacement during non-urological surgery.

All explanted patients were successfully treated with alternative BPH surgeries (TURP, laser) without complications. Three serious adverse events (SAEs) occurred within the first year, including device migration requiring removal/replacement, infection with hematuria and retention, and urinary retention requiring suprapubic catheter and device

removal. All SAEs were transient and resolved quickly. No unanticipated device-related serious adverse events were reported. The primary effectiveness endpoint was met, with greater than or equal to 3-point IPSS improvement maintained at all follow-up visits. The FIH study identified key areas for improvement in future trials, particularly the need for enhanced Zenflow Spring Implant placement under direct visualization and refined patient selection criteria.

ZEST 1 Pilot Study

The ZEST 1 Pilot Study was a multi-center, prospective, single-arm clinical trial evaluating the Zenflow Spring® Implant and Delivery System for treating symptomatic LUTS associated with BPH conducted at four sites (Mexico-3, Australia-1). It involved men 45 years and older with symptomatic LUTS/BPH, prostate volume 25-80g, prostatic urethral length 25-45 mm, and baseline IPSS score ≥13. Thirty seven subjects consented, with 8 Roll-In subjects, and 22 Intent-to-Treat (ITT) subjects. Follow-up was originally planned for 24 months, extended to 60 months with assessments at 2 weeks, 1, 3, 6, 12, 24, 36, 48, and 60 months.

- There was a 95.5% success rate (21/22 ITT subjects) for procedural success.
- Improvements in IPSS Total Score at all timepoints through 36 months.
- Improvements in IPSS-QoL scores maintained through 36 months.
- Peak flow rate (Qmax) improved from 9.9 mL/s at baseline to 14.8 mL/s at 48 months, with improvements through 24 months.
- 66.7% of subjects (20/30) reported at least one adverse event, with 42 total events recorded.
- 16 device-related AEs in 8 subjects (26.7%), with urinary retention being the most common (n=11).
- 8 SAEs in 4 subjects, with 3 related to device/procedure (1 procedure-related acute urinary retention, 2 device-related testicular abscesses in same subject).
- No deterioration in erectile or ejaculatory function as measured by Sexual Health Inventory for Men (SHIM) and Male Sexual Health Questionnaire – Ejaculatory Domain (MSHQ-EjD) questionnaires.
- 7 removals occurred (primarily due to patient choice/lack of effectiveness), all performed without adverse events

The results informed design modifications for the subsequent ZEST 2 study to enhance visualization, delivery precision, and overall usability.

ZEST 2 Pilot Study

The ZEST 2 Pilot Study was a multi-center, prospective, single-arm safety, performance and effectiveness trial conducted across 7 sites in New Zealand and Australia, evaluating the Zenflow Spring® Implant and Delivery System for treating LUTS secondary to BPH with ongoing long-term follow-up through 5 years in 47 men aged 45 years and older with symptomatic LUTS associated with BPH who had failed, were intolerant to, or chose not to take medication.

- There was a 97.9% (46 of 47) procedural success rate.

- IPSS Total Score showed improvements at all timepoints through 36 months, above the validated minimum clinically important difference.
- IPSS-QoL scores showed improvements through 60 months of follow-up.
- Peak flow rates (Qmax) improved from 9.0 mL/s at baseline to 21.3 mL/s at 60 months.
- No device-related deaths or unanticipated adverse device effects.
- One procedure-related SAE (acute urinary retention, resolved).
- No deterioration in erectile or ejaculatory function.
- 17 device removals performed without adverse events.

The results supported progression to pivotal IDE studies for regulatory approval.

ZEST 3 Pilot Study

The ZEST 3 Pilot Study was a multi-center, prospective, single-arm safety, performance, and effectiveness trial **c**linical trial evaluating the Zenflow Spring® Implant and Delivery System for treating LUTS secondary to BPH at 3 investigational sites in Canada in men ≥45 years with symptomatic LUTS associated with BPH. Fifty-eight subjects were consented, with 9 in Intent-to-Treat (ITT) subjects and 8 in Per Protocol (PP) subjects. Those treated were followed 2 weeks through 5 years. Safety endpoints including catheterization rates and serious adverse events; performance endpoints including procedural success and IPSS improvement.

- There was a procedural success rate of 91% (10 of 11 subjects).
- Improvement in IPSS Total Scores at all timepoints through 36 months.
- Improvements in QoL scores and urinary flow metrics.
- No device or procedure-related deaths or serious adverse events.
- No extended post-operative catheterization incidents.
- Three SAEs reported in 2 subjects, all unrelated to device/procedure.
- Sexual health maintained throughout follow-up.
- One device removal due to lack of effectiveness (no adverse events).

BREEZE Pivotal Clinical Trial

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of the Zenflow Spring® Implant and Delivery System in the treatment of symptoms due to urinary outflow obstruction secondary to BPH in the US and Canada under IDE G210096. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

Patients were treated between September 2021 and March 2023. The database for this PMA reflected data collected through October 2024 and included 231 patients. There were 28 investigational sites.

The study was a prospective, multi-center, multinational, 2:1 randomized treatment:sham), single-blinded, controlled clinical study.

The trial execution and safety results were reviewed by both a Clinical Events Committee (CEC) and Data Safety Monitoring Board (DSMB).

The control group included patients randomized to the sham arm following cystoscopic visualization. A catheter was inserted into the urethra of the sham arm patients, a balloon was deployed and inflated and tugged slightly to simulate a procedure, and no implant was deployed.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the BREEZE study was limited to patients who met the following inclusion criteria:

1. Subject is able and willing to comply with all the assessments of the study
2. Subject or subject's legal representative has been informed of the nature of the study, agrees to participate and has signed the informed consent form,
3. ≥ 45 years of age,
4. Baseline IPSS score ≥ 13; ≥ 1 in the IPSS voiding to storage sub-score ratio (IPSS-V/S) Sub Score ratio is (Q1+Q3+Q5+Q6)/(Q2+Q4+Q7)
5. Prostate volume 25 - 80 cc by transrectal ultrasound (TRUS)
6. Prostatic urethral length between 25 and 45 mm, as measured by cystoscopic pull-back and evaluation from the bladder neck to the verumontanum using the Spring Scope,
7. Failed, intolerant, or subject choice to not take a medication regimen for the treatment of LUTS.

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

1. Subjects who met any of the following exclusion criteria were not eligible for the study: Obstructive intravesical median prostatic lobe as determined by ultrasound (i.e., more than 10 mm intravesical prostatic protrusion on sagittal mid-prostate plane via ultrasound),
2. High bladder neck with the absence of lateral lobe encroachment indicating a high likelihood of primary bladder neck obstruction as determined by the Investigator,
3. Urethral stricture, meatal stenosis, or bladder neck stricture - either current or recurrent,
4. Anatomical anomalies that will not accommodate the Implant, as determined by cystoscopy (e.g., prostatic urethral length to height geometry),
5. Requires indwelling catheter or intermittent catheterization to void,
6. Baseline prostate serum antigen (PSA) > 10 ng/mL or confirmed or suspected prostate cancer (Subjects with a PSA level above 2.5 ng/mL, or age specific, or local reference ranges should have prostate cancer excluded to the Investigator's satisfaction),

7. One of the following baseline test results, taken from a single uroflowmetry reading:
    a. Urinary volume void < 125mL (pre-bladder urinary volume of ≥ 150 mL required),
    b. Peak urinary flow rate (Qmax) of < 5 mL/second and > 15 mL/second,
    c. Post-void residual volume (PVR) > 250 mL
8. History of other diseases causing voiding dysfunction including urinary retention (e.g., uncontrolled diabetes, diagnosis of neurogenic bladder, Parkinson's disease, multiple sclerosis, etc.),
9. Subjects with overactive bladder in the absence of benign prostatic obstruction,
10. Acute urinary tract infection (UTI) or finding of asymptomatic bacteriuria (Note: subject can be enrolled if the UTI is treated and followed with a negative urine test result), or subjects with history of recurrent UTIs (defined as > 3 UTIs in the past 12 months),
11. Concomitant bladder stones,
12. Previous pelvic irradiation or radical pelvic surgery,
13. Previous prostate surgery, including: enucleation, resection, vaporization, thermotherapy, ablation, stenting or prostatic urethral lift,
14. Chronic prostatitis, recurrent prostatitis, chronic pelvic pain syndrome (CPPS), or painful bladder syndrome within the past 12 months,
15. Known allergy to nickel,
16. Life expectancy less than 60 months,
17. Inability to stop taking anticoagulants and/or antiplatelets for at least 3 days prior to the procedure or coumadin for at least 5 days prior to the procedure (Note: low dose aspirin therapy (81 mg) is permitted),
18. Use of Type II 5-alpha reductase inhibitor such as finasteride (Proscar, Propecia) within 3 months of baseline assessment,
19. Use of Type I 5-alpha reductase inhibitor such as dutasteride (Avodart) within 6 months of baseline assessment,
20. Taking one of the following within 2 weeks of baseline evaluation:
    a. alpha-blockers,
    b. tricyclic anti-depressants (e.g., imipramine),
    c. anticholinergics,
    d. cholinergic gonadotropin releasing hormonal analogues,
    e. Phosphodiesterase-5 Enzyme Inhibitors (Tadalafil) in doses for BPH,
    f. Beta-3 adrenergic receptor agonist (Mirabegron),
21. Taking androgens, unless eugonadal state for at least 3 months or greater as documented by the Investigator,
22. Taking one of the following within 24 hours of pre-treatment (baseline) evaluation: a. phenylephrine, or, b. pseudoephedrine,
23. Future fertility concerns, or,
24. In the Investigator's opinion, the subject has a physical, psychological, or medical impairment that might prevent study completion or would confound study results (including subject questionnaires).

2. Follow-up Schedule

All patients were scheduled to return for follow-up examinations at 2 weeks, 1 month, 3 months, 6 months, and 12 months.

Preoperatively, the following assessments were performed:

- Uroflowmetry
- PVR
- IPSS
- QoL Questionnaire
- MSHQ + EjD Questionnaire
- SHIM Questionnaire
- concomitant medications

Postoperatively, the objective parameters measured during the study included the following:

- Uroflowmetry
- PVR
- IPSS
- QoL Questionnaire
- MSHQ + EjD Questionnaire
- SHIM Questionnaire
- concomitant medications

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

With regards to safety, the co-primary safety outcomes were the rate of extended post-operative urinary catheterization (> 7 days from treatment) for inability to void among subjects treated with the Zenflow Spring System and the rate of device or procedure related serious adverse events, at discharge through the 12-month follow-up visit.

The secondary safety endpoints were:

- Rate of device or procedure related adverse events at all time points,
- Comparison of pain at discharge to 2-week, 1- and, 3-month follow-up visits per Visual Analogue Scale (VAS) questionnaire,
- Change in sexual health characterized by change in SHIM and MSHQ-EjD at 3-, 6-, 12-, and 24- month post treatment,
- Assessment of adverse events outcomes related to a Spring Implant removal procedure, and
- Proportion of subjects with adverse events classified as Clavien-Dindo Grade IIIb or higher or any event resulting in persistent disability evidenced through 3-month follow-up visit.

With regards to effectiveness, the co-primary efficacy outcomes were:

- the percent of subjects who experience at least a 30 percent improvement in IPSS from their baseline pre-treatment score at the 3-month follow-up visit and
- the mean percent change in IPSS for the Spring Treatment Arm being at least 30% improved over baseline at 12 months.

The secondary effectiveness endpoints were:

- the mean change from baseline in IPSS at all timepoints through 12 Months,
- the percent of subjects in the Spring Implant arm who experience at least a 30% improvement in IPSS from their baseline pre-treatment score at 6-, and 12-month follow-up visits,
- the mean percent change in the IPSS Total Score in the treatment arm compared to baseline at all timepoints other than the primary endpoints,
- the mean change from baseline in uroflowmetry measures of peak flow rate (Qmax) at follow-up visits,
- the post-procedure incidence of secondary reintervention using an alternate surgical procedure for LUTS therapy, and
- the post-procedure incidence of secondary reintervention using standard pharmacological agents for LUTS therapy.

With regard to success/failure criteria, the study is considered a success when the following conditions are met:

- The percentage of subjects who experience at least a 30 percent improvement in IPSS from their baseline pre-treatment score at the 3-month follow-up visit is greater in the treatment arm than in the sham arm.
- At 12 months, the mean percent improvement in IPSS for the Spring Implant group is at least 30%. Since a decrease in IPSS is consistent with improvement, this equates to showing that the mean percent change from baseline in IPSS for the Spring Implant group is less than -30%.
- The device demonstrates an acceptable safety profile.

B. Accountability of PMA Cohort

At the time of database lock, of 231 patients enrolled in the PMA study and who received an index procedure, 163 subjects received an implant (roll-in cohort, n=26, treatment arm, n=137). There were 68 subjects in the control arm who were not implanted. One hundred and forty-nine implanted subjects (149/163, 91.4%) were available for analysis at the 12-month post-operative visit. Patients were considered enrolled after signing the informed consent form. Subject disposition flowcharts are provided in Figures 3 and 4.

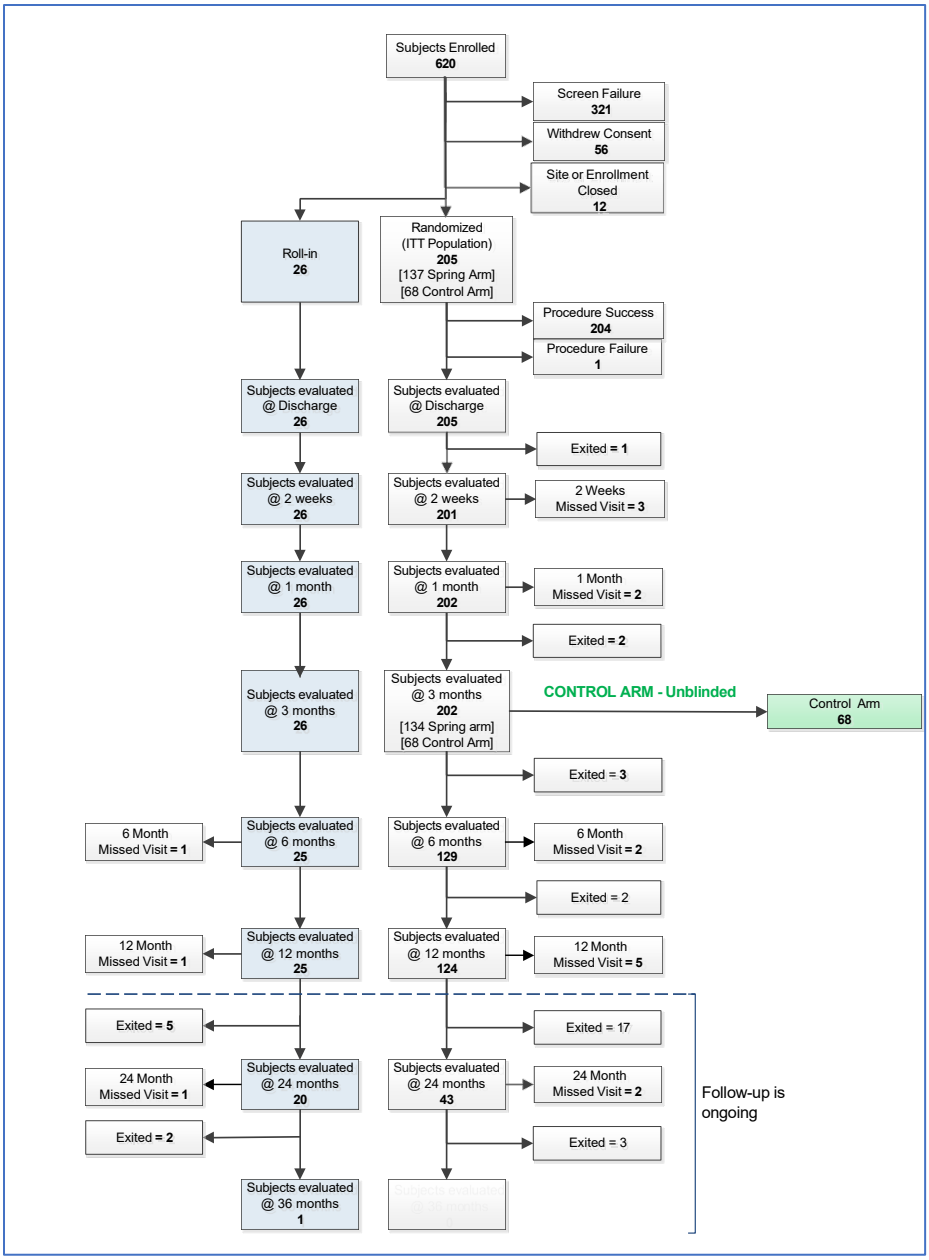


Figure 3. Subject Disposition Flowchart (ITT Population)

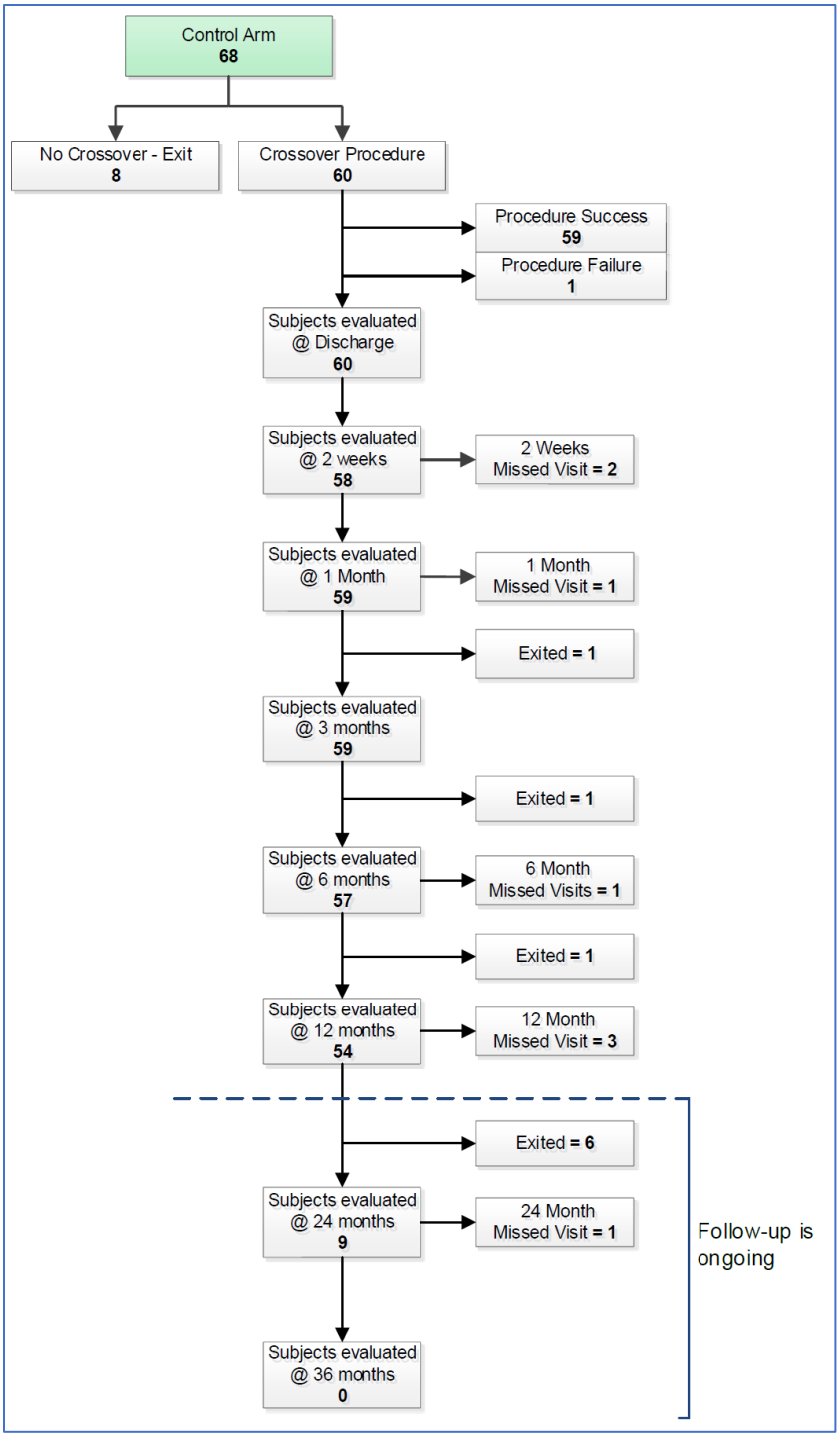


Figure 4. Subject Disposition Flowchart (Crossover Population)

Analysis Population

Intent-to-Treat (ITT) and Safety

The ITT/Safety cohort includes all subjects who were randomized and started the treatment procedure (insertion of the Zenflow Delivery System into the Spring Scope) or sham procedure (catheter insertion and balloon inflation). Where there is an attempt to treat, the subject was considered enrolled in the ITT/Safety cohort, regardless of the procedural outcome.

The ITT/Safety cohort was used to analyze all primary and secondary efficacy endpoints and all safety endpoints. For efficacy endpoints, outcomes were evaluated according to the subjects' randomized treatment assignment. For safety endpoints, outcomes were evaluated according to the actual treatment subjects received.

Crossover

The crossover cohort includes the sham arm subjects who elected after the 3-month follow-up visit to undergo the Spring Implant procedure. Data from the crossover cohort were descriptively summarized, separately from the subjects who are randomized to the Spring Implant arm. They were not included with randomized subjects in the endpoint evaluations of the study.

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a BPH study performed in the US.

Demographic and baseline characteristics responses were summarized with descriptive statistics by treatment group and for all subjects for the ITT population. Demographics of study subjects and study subject baseline IPSS are summarized in Table 4 and Table 5. Treatment and control arms were similar at baseline.

	Spring System (N=137)	Sham Device (N=68)
Age (years)		
n	137	68
Mean (SD)	66.5 (8.17)	66.9 (7.17)
Median	67.0	67.0
Min, Max	45, 85	52, 83
Ethnicity - n/N (%)		
Hispanic or Latino	14/137 (10.2%)	6/68 (8.8%)
Not Hispanic or Latino	122/137 (89.1%)	62/68 (91.2%)
Not Reported	1/137 (0.7%)	0/68 (0.0%)
Race - n/N (%)		
White	126/137 (92.0%)	63/68 (92.6%)
Asian	2/137 (1.5%)	4/68 (5.9%)
Middle Eastern	1/137 (0.7%)	1/68 (1.5%)
Black	4/137 (2.9%)	0/68 (0.0%)
Other	4/137 (2.9%)	0/68 (0.0%)
Height (cm)		
n	137	68
Mean (SD)	176.3 (8.42)	175.7 (7.52)
Median	175.3	177.7
Min, Max	155, 201	155, 191
Weight (kg)		
n	135	68
Mean (SD)	91.0 (17.86)	91.4 (16.64)
Median	89.8	88.2
Min, Max	58, 184	67, 154
BMI (kg/m^2)		
n	135	68
Mean (SD)	29.35 (5.945)	29.67 (5.428)
Median	28.12	28.25
Min, Max	20.5, 62.3	21.1, 45.8
History of smoking - n/N (%)		
Non-smoker	78/137 (56.9%)	39/68 (57.4%)
Current/recently quit	14/137 (10.2%)	2/68 (2.9%)
Former smoker	45/137 (32.8%)	27/68 (39.7%)

Table 4. Summary of Demographic and Baseline Characteristics by Treatment Arm (ITT Population)

	Spring System (N=137)	Sham Device (N=68)
IPSS		
Total Score		
n	137	68
Mean (SD)	23.7 (5.35)	22.7 (4.56)
Median	24.0	22.5
Min, Max	13, 34	14, 31
95% CI of Mean	22.8, 24.6	21.6, 23.8
QoL Score		
n	137	68
Mean (SD)	4.5 (1.12)	4.6 (1.01)
Median	5.0	5.0
Min, Max	2, 6	2, 6
95% CI of Mean	4.3, 4.7	4.3, 4.8

Table 5. Summary of Baseline IPSS by Treatment Arm (ITT Population)

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the ITT/safety cohort of 205 patients (Spring Implant, n=137; sham, n=68) available for the 12-month evaluation. The key safety outcomes for this study are presented below in Tables 6 to 9. Adverse effects are reported in Tables 10 to 13.

Primary Safety Endpoints

There were no reports of any extended post-operative urinary catheterization and there were no device or procedure related serious adverse events reported in the Spring Implant arm subjects through 12 months of follow-up.

Secondary Safety Endpoints

The first secondary safety endpoint was the rate of device or procedure related adverse events at all time points (Table 6). Because the sham arm subjects were only followed for 3 months before crossover, events are reported for procedure through the 3-month timepoint only for those subjects. Within the 3-month follow-up period, there were 4 device related AEs reported for the Spring Implant arm subjects (2.9%) and none for the sham arm. After 3 months, two additional subjects had device-related AEs reported in the Spring Implant arm through 12 months of follow-up. The cumulative by subject rate of all device-related adverse events reported from procedure through 12 months of follow-up was 4.4% (6/137). The rate of procedure-related events in the 3-month period was 9.5% (n=13) in the Spring Implant arm and 4.4% (n=3) in the sham arm. Two additional procedure-related events were reported in the Spring Implant arm subjects between 3 and 12 months of follow-up.

	Spring System (N=137)	Sham Device (N=68)	Difference (Treatment - Control, 95% CI)
Rate of Device Related Adverse Events - n/N (%)			
Within 3 Months	4/137 (2.9%) (1.1%, 7.3%)	0/68 (0.0%) (0.0%, 5.3%)	2.9% (-2.7%, 7.3%)
Within 12 Months*	6/137 (4.4%) (2.0%, 9.2%)		
Rate of Procedure Related Adverse Events - n/N (%)			
Within 3 Months	13/137 (9.5%) (5.6%, 15.6%)	3/68 (4.4%) (1.5%, 12.2%)	5.1% (-3.6%, 11.8%)
Within 12 Months	15/137 (10.9%) (6.7%, 17.3%)		

*Cumulative – includes all events reported from procedure through 12 months
The 95% CIs are derived using the score-based method (Wilson approach for individual proportions and Newcombe approach for proportion difference).

Table 6. Secondary Safety Endpoint: Rate of Device or Procedure Related Adverse Events (ITT Population)

The second secondary safety endpoint was the comparison of pain at discharge to 2- week, 1- and, 3-month follow-up visits per a Visual Analogue Scale (VAS) questionnaire (Table 7). The mean improvement in VAS from discharge was summarized by treatment group and descriptive statistics for the ITT population. The analysis of the mean change from discharge to 2-weeks, 1 and 3-months in VAS in the Spring Implant arm found that the mean scores decreased with time, such that by one month after the procedure VAS scores were comparable to those observed in the sham control arm. At discharge, the mean VAS score in the Spring Implant subjects was 2.4 (on a scale of 0-10).

	Baseline	Discharge	2 Weeks	1 Month	3 Months
Zenflow Spring System (N=137)					
VAS (cm)					
n	136	137	134	135	133
Mean (SD)	0.6 (1.11)	2.4 (2.39)	1.1 (1.96)	0.7 (1.38)	0.4 (0.75)
Median	0.0	1.6	0.1	0.1	0.0
Min, Max	0, 5	0, 9	0, 9	0, 7	0, 5
95% CI of Mean	0.4, 0.8	2.0, 2.8	0.8, 1.4	0.5, 1.0	0.3, 0.5
VAS Change from Discharge					
n			134	135	133
Mean (SD)			-1.3 (2.60)	-1.6 (2.38)	-2.0 (2.36)
Median			-0.7	-1.0	-1.4
Min, Max			-8, 8	-8, 5	-9, 2
95% CI of Mean			-1.7, -0.8	-2.0, -1.2	-2.4, -1.6
Sham Device (N=68)					
VAS (cm)					
n	68	68	66	66	68
Mean (SD)	0.8 (1.64)	0.8 (1.38)	0.4 (0.94)	0.4 (1.01)	0.5 (1.25)
Median	0.0	0.2	0.0	0.0	0.0
Min, Max	0, 8	0, 7	0, 4	0, 4	0, 8
95% CI of Mean	0.4, 1.2	0.5, 1.2	0.1, 0.6	0.2, 0.7	0.2, 0.8
VAS Change from Discharge					
n			66	66	68
Mean (SD)			-0.5 (1.61)	-0.4 (1.32)	-0.4 (1.55)
Median			-0.1	0.0	0.0
Min, Max			-7, 4	-7, 4	-7, 7
95% CI of Mean			-0.9, -0.1	-0.8, -0.1	-0.8, -0.0

The 95% CIs are constructed based on t-distribution.
Reported data only with no imputation for missing data.

Table 7. Secondary Safety Analysis: Summary of Visual Analogue Scale (VAS) (ITT Population)

The third secondary safety endpoint was the change in sexual health characterized by change in Sexual Health Inventory for Men (SHIM) and Male Sexual Health Questionnaire – Ejaculatory Domain (MSHQ-EjD) at 3, 6, and 12 months post treatment (Tables 8 and 9). The results from the Sexual Health Inventory in Men (SHIM) reported during the study indicated that the subjects experienced no deterioration in erectile function following treatment with the Zenflow Spring System through 12 months of follow-up. The results from the MSHQ-EjD

questionnaire found that subjects experienced no deterioration in ejaculatory function following treatment with the Zenflow Spring System through 12 months of follow-up.

	Baseline	3 Months	6 Months	12 Months
Zenflow Spring System (N=137)				
Not Sexually Active - n/N (%)	28/137 (20.4%)	19/134 (14.2%)	26/129 (20.2%)	33/124 (26.6%)
SHIM Total Score				
n	109	115	103	91
Mean (SD)	16.2 (6.69)	16.5 (7.21)	17.4 (6.51)	17.5 (6.45)
Median	17.0	18.0	19.0	19.0
Min, Max	1, 25	1, 25	1, 25	1, 25
95% CI of Mean	14.9, 17.5	15.1, 17.8	16.1, 18.7	16.1, 18.8
SHIM Change from Baseline				
n		101	94	85
Mean (SD)		0.5 (5.47)	1.1 (4.47)	1.1 (4.07)
Median		1.0	1.0	1.0
Min, Max		-20, 19	-13, 14	-13, 14
95% CI of Mean		-0.5, 1.6	0.2, 2.0	0.2, 1.9
Sham Device (N=68)				
Not Sexually Active - n/N (%)	13/68 (19.1%)	11/68 (16.2%)		
SHIM Total Score				
n	55	57		
Mean (SD)	14.5 (6.18)	14.3 (7.55)		
Median	15.0	15.0		
Min, Max	2, 25	1, 25		
95% CI of Mean	12.8, 16.1	12.3, 16.3		
SHIM Change from Baseline				
n		51		
Mean (SD)		0.7 (5.74)		
Median		0.0		
Min, Max		-11, 14		
95% CI of Mean		-0.9, 2.4		

The 95% CIs are constructed based on t-distribution.
Reported data only with no imputation for missing data.

Table 8. Secondary Safety Analysis: Sexual Health Inventory for Men (SHIM) Score by Visit (ITT Population)

	Baseline	3 Months	6 Months	12 Months
Zenflow Spring System (N=137)				
Not Sexually Active - n/N (%)	36/137 (26.3%)	29/134 (21.6%)	26/129 (20.2%)	31/124 (25.0%)
MSHQ-EjD Ejaculatory Function Score				
n	101	105	103	93
Mean (SD)	9.0 (2.72)	10.7 (3.09)	10.9 (2.87)	10.2 (2.82)
Median	9.0	11.0	11.0	11.0
Min, Max	3, 15	1, 15	1, 15	3, 15
95% CI of Mean	8.5, 9.6	10.1, 11.3	10.3, 11.5	9.6, 10.8
MSHQ-EjD Change from Baseline				
n		91	91	86
Mean (SD)		1.7 (3.24)	2.1 (3.10)	1.3 (2.87)
Median		2.0	2.0	1.0
Min, Max		-9, 8	-6, 9	-8, 7
95% CI of Mean		1.1, 2.4	1.5, 2.8	0.7, 1.9
Sham Device (N=68)				
Not Sexually Active - n/N (%)	20/68 (29.4%)	20/68 (29.4%)		
MSHQ-EjD Ejaculatory Function Score				
n	48	48		
Mean (SD)	8.5 (2.83)	10.2 (3.13)		
Median	9.0	11.0		
Min, Max	1, 13	4, 15		
95% CI of Mean	7.7, 9.3	9.3, 11.1		
MSHQ-EjD Change from Baseline				
n		43		
Mean (SD)		1.5 (2.85)		
Median		1.0		
Min, Max		-4, 12		
95% CI of Mean		0.6, 2.4		

The 95% CIs are constructed based on t-distribution.
Reported data only with no imputation for missing data.

Table 9. Secondary Safety Analysis: MSHQ-EjD Ejaculatory Function Score by Visit (ITT Population)

The fourth secondary safety endpoint was an assessment of adverse events outcomes related to a Spring Implant removal procedure. None of the subjects who

had an implant removed reported an AE associated with the implant removal procedure. Two subjects (1 ITT and 1 crossover) had a prophylactic catheter placed following the removal procedure at the Investigator's discretion.

The fifth secondary safety endpoint was the proportion of subjects with adverse events classified as Clavien-Dindo Grade IIIb or higher or any event resulting in persistent disability evidenced through 3-month follow-up visit. There were no reported adverse events classified as Clavien-Dindo Grade IIIb or higher for any of the ITT population subjects from procedure through 12 months of follow-up.

Adverse effects (AE) that occurred in the PMA clinical study:

There were 152 reported AEs and, of these, 24 (15.8%) were reported as related to the Spring Implant or sham procedure (Table 10). Thirty (21.9%) of the Spring Implant subjects and 11 (16.2%) of the sham subjects reported adverse events. There were 8 device-related AEs (5.3%). The remaining 120 AEs (78.9%) were reported as having no relationship to the device or procedure.

	Zenflow Spring System (N=137)		Sham Device (N=68)	
	Events	Subjects n/N (%)	Events	Subjects n/N (%)
Any treatment emergent adverse events	51	30/137 (21.9%)	15	11/68 (16.2%)
Serious adverse events	3	3/137 (2.2%)	1	1/68 (1.5%)
Severe adverse events	2	2/137 (1.5%)	1	1/68 (1.5%)
Fatal adverse events	1	1/137 (0.7%)	0	0/68 (0.0%)
Not related adverse events	30	19/137 (13.9%)	10	9/68 (13.2%)
Device- or procedure-related adverse events	21	16/137 (11.7%)	5	3/68 (4.4%)
Device-related adverse events	4	4/137 (2.9%)	0	0/68 (0.0%)
Procedure-related adverse events	17	13/137 (9.5%)	5	3/68 (4.4%)
Adverse events with Clavien-Dindo Grade IIIb or higher	0	0/137 (0.0%)	0	0/68 (0.0%)
Serious adverse events	0	0/137 (0.0%)	1	1/68 (1.5%)
Severe adverse events	0	0/137 (0.0%)	1	1/68 (1.5%)
Fatal adverse events	0	0/137 (0.0%)	0	0/68 (0.0%)

Table 10. Summary of Adverse Event Characteristics through 3 Months (ITT Population)

During the first three months of follow-up, 66 events were reported in 41 subjects (Table 11). There were 21 device- or procedure-related adverse events in the Spring Implant group and 5 in the sham group. Of those in the Spring Implant group, 4 were noted as device-related and 15 were noted as procedure-related. Of those in the sham group, none were noted as device-related and 3 were noted as procedure-related. Four AEs were not adjudicated as device- or procedure-related but were instead adjudicated for severity.

System Organ Class Lowest Level Term	Relationship	Zenflow Spring System (N=137) Events	Subjects n/N (%)	Sham Device (N=68) Events	Subjects n/N (%)
Subjects reporting any device- or procedure-related treatment emergent adverse events		21	16/137 (11.7%)	5	3/68 (4.4%)
Reproductive system and breast disorders		11	8/137 (5.8%)	2	2/68 (2.9%)
Painful ejaculation	Unrelated	0	0/137 (0.0%)	0	0/68 (0.0%)
	Procedure Related	6	6/137 (4.4%)	0	0/68 (0.0%)
	Device Related	1	1/137 (0.7%)	0	0/68 (0.0%)
Penile pain	Unrelated	0	0/137 (0.0%)	0	0/68 (0.0%)
	Procedure Related	0	0/137 (0.0%)	1	1/68 (1.5%)
	Device Related	1	1/137 (0.7%)	0	0/68 (0.0%)
Painful external genitals	Unrelated	0	0/137 (0.0%)	0	0/68 (0.0%)
	Procedure Related	1	1/137 (0.7%)	0	0/68 (0.0%)
	Device Related	0	0/137 (0.0%)	0	0/68 (0.0%)
Perineal pain	Unrelated	0	0/137 (0.0%)	0	0/68 (0.0%)
	Procedure Related	1	1/137 (0.7%)	0	0/68 (0.0%)
	Device Related	0	0/137 (0.0%)	0	0/68 (0.0%)
Retrograde ejaculation	Unrelated	0	0/137 (0.0%)	0	0/68 (0.0%)
	Procedure Related	1	1/137 (0.7%)	0	0/68 (0.0%)
	Device Related	0	0/137 (0.0%)	0	0/68 (0.0%)
Perineal discomfort	Unrelated	0	0/137 (0.0%)	0	0/68 (0.0%)
	Procedure Related	0	0/137 (0.0%)	1	1/68 (1.5%)
	Device Related	0	0/137 (0.0%)	0	0/68 (0.0%)
Renal and urinary disorders		7	7/137 (5.1%)	1	1/68 (1.5%)
Dysuria	Unrelated	0	0/137 (0.0%)	0	0/68 (0.0%)
	Procedure Related	5	5/137 (3.6%)	1	1/68 (1.5%)
	Device Related	2	2/137 (1.5%)	0	0/68 (0.0%)
Musculoskeletal and connective tissue disorders		2	2/137 (1.5%)	0	0/68 (0.0%)
Back pain	Unrelated	0	0/137 (0.0%)	0	0/68 (0.0%)
	Procedure Related	1	1/137 (0.7%)	0	0/68 (0.0%)
	Device Related	0	0/137 (0.0%)	0	0/68 (0.0%)
Groin pain	Mild	1	1/137 (0.7%)	0	0/68 (0.0%)
	Moderate	0	0/137 (0.0%)	0	0/68 (0.0%)
	Severe	0	0/137 (0.0%)	0	0/68 (0.0%)
Gastrointestinal disorders		1	1/137 (0.7%)	0	0/68 (0.0%)
Rectal pain	Mild	1	1/137 (0.7%)	0	0/68 (0.0%)
	Moderate	0	0/137 (0.0%)	0	0/68 (0.0%)
	Severe	0	0/137 (0.0%)	0	0/68 (0.0%)
General disorders & administration site conditions		0	0/137 (0.0%)	1	1/68 (1.5%)
Fever	Mild	0	0/137 (0.0%)	1	1/68 (1.5%)
	Moderate	0	0/137 (0.0%)	0	0/68 (0.0%)
	Severe	0	0/137 (0.0%)	0	0/68 (0.0%)
Infections and infestations		0	0/137 (0.0%)	1	1/68 (1.5%)
Urinary tract infection	Mild	0	0/137 (0.0%)	0	0/68 (0.0%)
	Moderate	0	0/137 (0.0%)	0	0/68 (0.0%)
	Severe	0	0/137 (0.0%)	1	1/68 (1.5%)

Table 11. Procedure and Device Related Adverse Events Between Procedure and 3 Months (ITT Population)

Between 3 and 12 months, a total of 52 events in the Spring Implant arm were reported in 34 subjects. Four of these events (in 2 subjects) were device related, and 2 events (in 2 subjects) were procedure related. The remaining 46 events were not related to the device or procedure. These are summarized in Table 12 and 13.

	Zenflow Spring System (N=137)	
	Events	Subjects n/N (%)
Any treatment emergent adverse events	52	34/134 (25.4%)
Serious adverse events	8	8/134 (6.0%)
Severe adverse events	5	5/134 (3.7%)
Fatal adverse events	2	2/134 (1.5%)
Not related adverse events	46	32/134 (23.9%)
Device- or procedure-related adverse events	6	3/134 (2.2%)
Device-related adverse events	4	2/134 (1.5%)
Procedure-related adverse events	2	2/134 (1.5%)
Adverse events with Clavien-Dindo Grade IIIb or higher	0	0/134 (0.0%)
Serious adverse events	0	0/134 (0.0%)
Severe adverse events	0	0/134 (0.0%)
Fatal adverse events	0	0/134 (0.0%)

Table 12. Summary of Adverse Event Characteristics between 3 and 12 Months (ITT Population, Spring Implant Arm)

System Organ Class Lowest Level Term	Relationship	Zenflow Spring System (N=137) Events	 Subjects n/N (%)
Subjects reporting any device- or procedure-related treatment emergent adverse events		6	3/134 (2.2%)
Renal and urinary disorders		3	3/134 (2.2%)
Dysuria	Unrelated	0	0/134 (0.0%)
	Procedure Related	0	0/134 (0.0%)
	Device Related	2	2/134 (1.5%)
Urethral stricture	Unrelated	0	0/134 (0.0%)
	Procedure Related	1	1/134 (0.7%)
	Device Related	0	0/134 (0.0%)
Reproductive system and breast disorders		3	2/134 (1.5%)
Painful ejaculation	Unrelated	0	0/134 (0.0%)
	Procedure Related	1	1/134 (0.7%)
	Device Related	1	1/134 (0.7%)
Perineal pain	Unrelated	0	0/134 (0.0%)
	Procedure Related	0	0/134 (0.0%)
	Device Related	1	1/134 (0.7%)

Table 13. Procedure and Device Related Adverse Events Between 3 and 12 Months by (ITT Population, Spring Implant Arm)

There were no device related patient deaths or other device related SAEs, and there were no unanticipated adverse device effects. A total of 16 SAEs were reported in 14 patients. One SAE that occurred in a sham subject was possibly related to the index procedure (urinary tract infection). The remaining 15 SAEs were not related to either the procedure or device. Three of those 15 SAEs were subject deaths, none of which were related to participation in the study.

Zenflow Spring Implant Removals

Eighteen patients (13.1%) had the device removed through 24 months. There were no reported removal procedure-related adverse events. The number of Spring Implants removed during the 1-year and 2-year follow-up periods and the reasons for removal are provided below:

- 12 Months (n=3; 2.2%)
  - Painful urination/migration (n=1)
  - Patient choice (n=2)
- 24 Months (n=15, 10.9%)
  - Medically indicated for non BPH reason (n=2)
  - Observed BPH disease progression (n=5)
  - Patient choice (n=8)

2. Effectiveness Results

The analyses of effectiveness were based on the 205 evaluable patients at the 12-month time point. Key effectiveness outcomes are presented in Tables 14 to 26.

Co-Primary Efficacy Endpoint #1 - ITT Population

An analysis of the proportion of subjects achieving ≥30% improvement from baseline to 3 months in IPSS in the ITT population found that 51.8% (71/137) of subjects met this threshold in the Spring Implant arm and 39.7% (27/68) of subjects met this threshold in the sham arm (Table 14). The results of the hypothesis test found that the between-group difference did not achieve statistical significance in the ITT population (p=0.102).

	Zenflow Spring System (N=137)	Sham Device (N=68)
Proportion of Subjects Achieving ≥30% Improvement from Baseline in IPSS Score at 3 Months - n/N (%) (95% CI)	71/137 (51.8%) (43.5%, 60.0%)	27/68 (39.7%) (28.9%, 51.6%)
Difference (Treatment - Control, 95% CI)	12.1% (-2.4%, 25.7%)	
P-value	0.102	

The 95% CIs are derived using the score-based method (Wilson approach for individual proportions and Newcombe approach for proportion difference).
The p-value is computed using Pearson's Chi-squared test.
The Conditional Value Carried Forward approach is used for subjects missing their 3-Month IPSS (Spring arm BPH med use n=1, Early discontinuation not due to removal, n=3).

Table 14. Co-Primary Efficacy Endpoint #1: Proportion of Subjects Achieving ≥30% Improvement from Baseline in IPSS Score at 3 Months (ITT Population)

Co-Primary Efficacy Endpoint #2 - ITT Population

The mean percent change in IPSS total score for the Spring Implant arm from baseline to 12 months was 32.1% (Table 15). Compared to a clinical success threshold of 30%, the Spring Implant arm did not achieve statistical significance for the ITT population (p=0.231).

	Zenflow Spring System (N=137)
IPSS Score Percent Change from Baseline to 12 Months	
n	137
Mean (SD)	-32.1 (32.58)
Median	-31.3
Min, Max	-100, 42
95% CI of Mean	-37.6, -26.6
P-value	0.231

The 95% CI is constructed based on t-distribution.
The p-value is computed using one-sided single-sample t-test, comparing against a performance goal of -30%.
The Conditional Value Carried Forward approach is used for subjects missing their 12-Month IPSS. (Spring arm BPH med use n=6, Early discontinuation or missed visits not due to removal, n=8, Device removal n=3).

Table 15. Co-Primary Efficacy Endpoint #2: Percent Change from Baseline in IPSS Score at 12 Months (ITT Population)

The device met neither of the pre-specified co-primary effectiveness endpoints using the ITT analysis set. The ITT population includes 38 subjects (27 Spring Implant and 11 sham control subjects) who were erroneously enrolled in the ITT population and should have been excluded due to the presence of intravesical prostatic protrusion >10 mm and/or obstructive median prostatic lobe protrusion. These subjects were identified during a retrospective review of baseline imaging and confirmed via an independent retrospective review and analysis of all randomized subject screening imaging. As a result, the applicant completed an analysis of the effectiveness endpoints using the modified Intent-To-Treat/Intended Use (mITT/IU) population which excludes the subjects who did not meet these eligibility criteria.

Table 16 and Table 17 provided the analysis of the co-primary effectiveness endpoints for the mITT/IU population.

	Zenflow Spring System (N=109)	Sham Device (N=57)
Proportion of Subjects Achieving ≥30% Improvement from Baseline in IPSS Score at 3 Months - n/N (%) (95% CI)	65/109 (59.6%) (50.2%, 68.4%)	19/57 (33.3%) (22.5%, 46.3%)
Difference (Treatment - Control, 95% CI)	26.3% (10.3%, 40.2%)	

The 95% CIs are derived using the score-based method (Wilson approach for individual proportions and Newcombe approach for proportion difference).
The Conditional Value Carried Forward approach is used for subjects missing their 3-Month IPSS.

Table 16. Co-Primary Efficacy Endpoint #1: Proportion of Subjects Achieving ≥30% Improvement from Baseline in IPSS Score at 3 Months (mITT/IU Population)

	Zenflow Spring System (N=109)
IPSS Score Percent Change from Baseline to 12 Months	
n	109
Mean (SD)	-37.2 (32.68)
Median	-39.1
Min, Max	-100, 39
95% CI of Mean	-43.4, -31.0

The 95% CI is constructed based on t-distribution.
The Conditional Value Carried Forward approach is used for subjects missing their 12-Month IPSS.

Table 17. Co-Primary Efficacy Endpoint #2: Percent Change from Baseline in IPSS Score at 12 Months (mITT/IU Population)

Secondary Efficacy Endpoints

The Spring Implant arm saw improvements in IPSS from baseline at all follow-up timepoints through 12 months (Table 18). The sham arm also saw improvements through 3 months.

	Baseline	2 Weeks	1 Month	3 Months	6 Months	12 Months
Zenflow Spring System (N=137)						
IPSS Total Score						
n	137	135	135	134	131	129
Mean (SD)	23.7 (5.35)	18.5 (7.19)	15.5 (7.06)	15.6 (7.99)	14.8 (6.99)	15.7 (7.78)
Median	24.0	20.0	14.0	15.0	15.0	16.0
Min, Max	13, 34	1, 31	1, 33	2, 33	2, 34	0, 35
95% CI of Mean	22.8, 24.6	17.2, 19.7	14.3, 16.7	14.2, 16.9	13.6, 16.0	14.3, 17.0
IPSS Total Score Change from Baseline						
n		135	135	134	131	129
Mean (SD)		-5.2 (7.94)	-8.1 (7.60)	-8.0 (8.03)	-8.8 (7.36)	-7.9 (7.77)
Median		-4.0	-8.0	-8.0	-8.0	-7.0
Min, Max		-31, 16	-30, 12	-32, 9	-29, 13	-27, 8
95% CI of Mean		-6.5, -3.8	-9.4, -6.8	-9.4, -6.7	-10.1, -7.6	-9.2, -6.5
Sham Device (N=68)						
IPSS Total Score						
n	68	66	66	68		
Mean (SD)	22.7 (4.56)	17.1 (7.29)	16.1 (7.84)	16.9 (8.25)		
Median	22.5	17.5	16.5	19.0		
Min, Max	14, 31	2, 30	1, 32	1, 31		
95% CI of Mean	21.6, 23.8.	15.3, 18.9.	14.2, 18.0.	14.9, 18.9		
IPSS Total Score Change from Baseline						
n		66	66	68		
Mean (SD)		-5.5 (7.64)	-6.5 (8.02)	-5.8 (8.52)		
Median		-4.0	-5.0	-5.0		
Min, Max		-24, 14	-27, 17	-29, 15		
95% CI of Mean		-7.4, -3.6	-8.5, -4.5	-7.8, -3.7		

The 95% CIs are constructed based on t-distribution.
For subjects treated with BPH medications or those who undergo removal of the Spring device (not related to a device-related AE) from post-procedure through the 12-month study period, IPSS values recorded prior to the use of BPH medications or Spring device removal are carried forward to all subsequent visits through the 12-month visit. For subjects who undergo removal of the Spring device due to a device-related AE, the Baseline Value Carried Forward approach is applied. No imputation is performed for other missing IPSS scores.

Table 18. Secondary Analysis: IPSS Total Score by Visit (ITT Population)

Responder rates (>30% improvement) were consistent through 12 months for the Spring Implant group (Table 19).

	Zenflow Spring System (N=137)
6 Months	
n	131
Responder Rate - n/N (%)	78/131 (59.5%)
95% CI of Responder Rate	51.0%, 67.6%
12 Months	
n	129
Responder Rate - n/N (%)	69/129 (53.5%)
95% CI of Responder Rate	44.9%, 61.9%

A responder is a subject whose IPSS score improves at least 30% from baseline.
The 95% CIs are constructed based on t-distribution for continuous data, and score-based methods Wilson approach for categorical data.
For subjects treated with BPH medications or those who undergo removal of the Spring device (not related to a device-related AE) at any time from post-procedure through the 12-month study period, IPSS values recorded prior to the use of BPH medications or Spring device removal are carried forward to all subsequent visits through the 12-month visit. For subjects who undergo removal of the Spring device due to a device-related AE, the Baseline Value Carried Forward approach is applied. No imputation is performed for other missing IPSS scores.

Table 19. Secondary Analysis: Proportion of Subjects Achieving ≥ 30% Improvement from Baseline in IPSS Score at 6 and 12 Months (ITT Population)

The mean percent change from baseline in IPSS score in the Spring Implant arm showed was higher than the sham arm at 3 months (Table 20).

	2 Weeks	1 Month	3 Months	6 Months	12 Months
Zenflow Spring System (N=137)					
IPSS Total Score Percent Change from Baseline					
n	135	135	134	131	129
Mean (SD)	-19.1 (35.20)	-32.8 (32.34)	-33.1 (33.38)	-36.4 (29.79)	-32.7 (32.70)
Median	-16.7	-36.8	-34.8	-36.8	-31.8
Min, Max	-96, 123	-94, 75	-94, 60	-91, 68	-100, 42
95% CI of Mean	-25.1, -13.1	-38.3, -27.3	-38.8, -27.4	-41.5, -31.2	-38.3, -27.0
Sham Device (N=68)					
IPSS Total Score Percent Change from Baseline					
n	66	66	68		
Mean (SD)	-22.6 (33.91)	-27.5 (35.31)	-23.8 (38.27)		
Median	-17.0	-24.6	-21.1		
Min, Max	-92, 93	-96, 113	-96, 100		
95% CI of Mean	-30.9, -14.2	-36.2, -18.9	-33.0, -14.5		
Difference in Mean (95% CI)	3.5 (-6.8, 13.8)	-5.2 (-15.1, 4.7)	-9.3 (-19.7, 1.0)		

A responder is a subject whose IPSS score improves at least 30% from baseline.
The 95% CIs are constructed based on t-distribution for continuous data, and score-based methods (Wilson approach for individual proportions and Newcombe approach for proportion difference) for categorical data.
For subjects treated with BPH medications or undergo implant removal (not related to a device-related AE) post-procedure through 12-months, IPSS values prior to use of BPH medications or implant removal are carried forward to all visits through the 12-month visit. For subjects who undergo implant removal due to a device-related AE, the Baseline Value Carried Forward approach is applied. No imputation is performed for other missing IPSS scores.

Table 20. Secondary Analysis: Percent Change from Baseline in IPSS Total Score by Visit (ITT Population)

Peak flow rate (Qmax) improved from baseline through 12 months in the Spring Implant group (Table 21).

	Baseline	2 Weeks	1 Month	3 Months	6 Months	12 Months
Zenflow Spring System (N=137)						
Qmax (mL/2s)						
n	134	108	119	114	114	106
Mean (SD)	9.43 (2.714)	12.16 (3.961)	12.78 (5.069)	12.05 (4.953)	11.72 (5.245)	11.21 (4.570)
Median	9.20	12.00	11.50	11.00	10.95	10.00
Min, Max	5.0, 15.0	5.0, 26.0	3.0, 30.0	4.0, 31.0	4.0, 33.0	4.0, 26.5
95% CI of Mean	8.97, 9.90	11.40, 12.91	11.86, 13.70	11.13, 12.97	10.75, 12.70	10.33, 12.09
Qmax Change from Baseline						
n		107	117	113	113	105
Mean (SD)		2.70 (3.868)	3.55 (4.662)	2.54 (5.185)	2.27 (5.616)	1.82 (4.659)
Median		2.50	3.00	2.00	1.40	1.10
Min, Max		-9.5, 12.0	-6.4, 20.0	-7.5, 21.6	-7.5, 23.6	-8.9, 16.0
95% CI of Mean		1.96, 3.44	2.70, 4.41	1.57, 3.50	1.22, 3.32	0.92, 2.72
Qmax Percent Change from Baseline						
n		107	117	113	113	105
Mean (SD)		34.9 (46.00)	42.9 (54.85)	33.2 (63.85)	32.5 (70.56)	24.8 (54.38)
Median		28.0	35.8	22.6	20.0	13.9
Min, Max		-66, 183	-56, 250	-53, 300	-55, 358	-67, 267
95% CI of Mean		26.1, 43.7	32.9, 53.0	21.3, 45.1	19.4, 45.7	14.3, 35.3
Sham Device (N=68)						
Qmax (mL/2s)						
n	66	58	61	66		
Mean (SD)	9.15 (2.595)	10.92 (6.044)	11.80 (4.724)	11.13 (3.887)		
Median	9.20	10.00	11.00	10.85		
Min, Max	5.0, 14.0	4.0, 48.0	6.0, 35.0	4.0, 22.0		
95% CI of Mean	8.51, 9.79	9.33, 12.51	10.59, 13.01	10.17, 12.08		
Qmax Change from Baseline						
n		56	59	64		
Mean (SD)		1.79 (5.553)	2.54 (4.794)	1.90 (3.553)		
Median		1.00	2.50	1.35		
Min, Max		-4.2, 36.5	-5.9, 23.5	-4.0, 13.9		
95% CI of Mean		0.31, 3.28	1.29, 3.79	1.01, 2.78		

Table 21. Secondary Analysis: Peak Flow Rate (Qmax) by Visit (ITT Population)

The results of the secondary efficacy endpoints for the mITT/IU population are presented in Tables 22 to 25.

	Baseline	2 Weeks	1 Month	3 Months	6 Months	12 Months
Zenflow Spring System (N=109)						
IPSS Total Score						
n	109	107	107	106	105	104
Mean (SD)	23.3 (5.11)	18.0 (6.85)	14.5 (6.75)	14.1 (7.52)	13.4 (6.21)	14.4 (7.52)
Median	23.0	19.0	14.0	14.0	14.0	14.0
Min, Max	13, 34	1, 31	1, 33	2, 33	2, 30	0, 31
95% CI of Mean	22.3, 24.2	16.7, 19.3	13.2, 15.8	12.6, 15.5	12.2, 14.6	12.9, 15.8
IPSS Total Score Change from Baseline						
n		107	107	106	105	104
Mean (SD)		-5.2 (7.47)	-8.7 (7.32)	-9.1 (8.01)	-9.8 (6.87)	-8.8 (7.84)
Median		-4.0	-8.0	-9.5	-10.0	-8.0
Min, Max		-31, 11	-30, 12	-32, 9	-29, 7	-27, 7
95% CI of Mean		-6.6, -3.7	-10.1, -7.3	-10.6, -7.5	-11.1, -8.5	-10.3, -7.3
Sham Device (N=57)						
IPSS Total Score						
n	57	56	56	57		
Mean (SD)	22.7 (4.60)	17.4 (7.27)	16.2 (7.52)	18.0 (7.87)		
Median	23.0	19.0	17.0	20.0		
Min, Max	14, 31	2, 30	1, 32	1, 31		
95% CI of Mean	21.5, 23.9	15.5, 19.4	14.2, 18.2	15.9, 20.1		
IPSS Total Score Change from Baseline						
n		56	56	57		
Mean (SD)		-5.3 (7.94)	-6.4 (8.23)	-4.7 (8.61)		
Median		-3.5	-5.0	-4.0		
Min, Max		-24, 14	-27, 17	-29, 15		
95% CI of Mean		-7.4, -3.1	-8.6, -4.2	-7.0, -2.4		

The 95% CIs are constructed based on t-distribution.
For subjects treated with BPH medications or those who undergo removal of the Spring device (not related to a device-related AE) at any time from post-procedure through the 12-month study period, IPSS values recorded prior to the use of BPH medications or Spring device removal are carried forward to all subsequent visits through the 12-month visit. For subjects who undergo removal of the Spring device due to a device-related AE, the Baseline Value Carried Forward approach is applied. No imputation is performed for other missing IPSS scores.

Table 22. Secondary Analysis: IPSS Total Score by Visit (mITT/IU Population)

	Zenflow Spring System (N=109)
	Zenflow Spring System (N=109)
6 Months	
n	105
Responder Rate - n/N (%)	69/105 (65.7%)
95% CI of Responder Rate	56.2%, 74.1%
12 Months	
n	104
Responder Rate - n/N (%)	64/104 (61.5%)
95% CI of Responder Rate	51.9%, 70.3%

A responder is a subject whose IPSS score improves at least 30% from baseline.
The 95% CIs are constructed based on the Wilson score method.
For subjects treated with BPH medications or those who undergo removal of the Spring device (not related to a device-related AE) at any time from post-procedure through the 12-month study period, IPSS values recorded prior to the use of BPH medications or Spring device removal are carried forward to all subsequent visits through the 12-month visit. For subjects who undergo removal of the Spring device due to a device-related AE, the Baseline Value Carried Forward approach is applied. No imputation is performed for other missing IPSS scores.

Table 23. Secondary Analysis: Proportion of Subjects Achieving ≥ 30% Improvement From Baseline in IPSS Score at 6 and 12 Months (mITT/IU Population)

	2 Weeks	1 Month	3 Months	6 Months	12 Months
Zenflow Spring System (N=109)					
IPSS Total Score Percent Change from Baseline					
n	107	107	106	105	104
Mean (SD)	-20.0 (32.59)	-36.1 (30.65)	-38.2 (32.53)	-41.4 (26.06)	-37.3 (32.83)
Median	-16.7	-38.7	-45.3	-41.9	-38.5
Min, Max	-96, 73	-94, 75	-94, 39	-91, 30	-100, 39
95% CI of Mean	-26.3, -13.8	-41.9, -30.2	-44.5, -32.0	-46.5, -36.4	-43.7, -30.9
Sham Device (N=57)					
IPSS Total Score Percent Change from Baseline					
n	56	56	57		
Mean (SD)	-21.0 (34.92)	-26.3 (35.93)	-18.3 (37.63)		
Median	-16.7	-23.4	-17.4		
Min, Max	-92, 93	-96, 113	-96, 100		
95% CI of Mean	-30.4, -11.7	-35.9, -16.7	-28.3, -8.3		
Difference in Mean (95% CI)	1.0 (-9.9, 11.9)	-9.7 (-20.3, 0.9)	-19.9 (-31.1, -8.7)		

Table 24. Secondary Analysis: Percent Change from Baseline in IPSS Total Score by Visit (mITT/IU Population)

	Baseline	2 Weeks	1 Month	3 Months	6 Months	12 Months
Zenflow Spring System (N=109)						
Qmax (mL/2s)						
n	108	88	96	92	96	87
Mean (SD)	9.49 (2.717)	12.58 (3.986)	13.00 (5.269)	12.53 (5.178)	12.00 (5.455)	11.57 (4.805)
Median	9.20	12.00	12.00	11.85	11.00	10.00
Min, Max	5.0, 15.0	5.0, 26.0	3.0, 30.0	4.0, 31.0	4.0, 33.0	4.3, 26.5
95% CI of Mean	8.97, 10.00	11.73, 13.42	11.93, 14.07	11.46, 13.60	10.89, 13.11	10.55, 12.60
Qmax Change from Baseline						
n		87	96	92	95	87
Mean (SD)		3.02 (3.859)	3.60 (4.940)	3.01 (5.391)	2.52 (5.747)	2.05 (4.848)
Median		2.70	3.00	2.20	1.90	1.20
Min, Max		-5.3, 12.0	-6.4, 20.0	-7.0, 21.6	-7.5, 23.6	-8.9, 16.0
95% CI of Mean		2.19, 3.84	2.60, 4.60	1.89, 4.13	1.35, 3.69	1.02, 3.08
Sham Device (N=57)						
Qmax (mL/2s)						
n	55	51	51	55		
Mean (SD)	9.36 (2.423)	11.08 (6.299)	11.53 (4.643)	11.31 (3.905)		
Median	9.30	10.00	10.50	11.00		
Min, Max	5.0, 14.0	4.5, 48.0	6.0, 35.0	4.0, 22.0		
95% CI of Mean	8.71, 10.01	9.31, 12.85	10.23, 12.84	10.25, 12.36		
Qmax Change from Baseline						
n		49	49	53		
Mean (SD)		1.67 (5.844)	1.91 (4.360)	1.85 (3.240)		
Median		0.60	2.40	1.50		
Min, Max		-4.2, 36.5	-5.9, 23.5	-4.0, 10.0		
95% CI of Mean		-0.01, 3.35	0.66, 3.16	0.96, 2.74		

The 95% CIs are constructed based on t-distribution.
Reported data only with no imputation for missing data.

Table 25. Secondary Analysis: Peak Flow Rate (Qmax) by Visit (mITT/IU Population)

The results of the IPSS Total score and responder rates by visit for the Crossover population are presented in Table 26.

	Baseline*	2 Weeks	1 Month	3 Months	6 Months	12 Months
IPSS Total Score						
n	60	58	58	59	58	57
Mean (SD)	22.6 (4.47)	16.6 (8.21)	13.7 (7.42)	14.0 (6.91)	13.5 (7.14)	13.8 (7.48)
Median	22.0	14.5	13.0	14.0	14.0	13.0
Min, Max	14, 31	3, 34	2, 31	1, 27	2, 31	1, 29
95% CI of Mean	21.4, 23.7	14.4, 18.7	11.8, 15.7	12.2, 15.8	11.6, 15.3	11.9, 15.8
Change from Baseline						
n		58	58	59	58	57
Mean (SD)		-6.1 (8.47)	-8.9 (7.45)	-8.7 (6.61)	-9.2 (6.93)	-8.9 (6.91)
Median		-7.0	-9.5	-9.0	-10.0	-9.0
Min, Max		-18, 11	-25, 9	-23, 7	-22, 8	-24, 7
95% CI of Mean		-8.3, -3.9	-10.9, -7.0	-10.4, -7.0	-11.0, -7.4	-10.7, -7.0
Percent Change from Baseline						
n		58	58	59	58	57
Mean (SD)		-25.4 (38.43)	-38.9 (32.67)	-38.1 (29.67)	-40.4 (31.76)	-39.4 (30.79)
Median		-32.2	-39.7	-38.5	-44.1	-42.9
Min, Max		-83, 73	-91, 45	-95, 44	-91, 50	-94, 35
95% CI of Mean		-35.5, -15.3	-47.5, -30.3	-45.8, -30.3	-48.7, -32.0	-47.6, -31.2
Responder Rate - n/N (%)		30/58 (51.7%)	38/58 (65.5%)	33/59 (55.9%)	34/58 (58.6%)	35/57 (61.4%)
95% CI of Responder Rate		39.2%, 64.1%	52.7%, 76.4%	43.3%, 67.8%	45.8%, 70.4%	48.4%, 72.9%

* Baseline values are those reported by subject at study entry.
A responder is a subject whose IPSS score improves at least 30% from baseline.
The 95% CIs are constructed based on t-distribution for continuous data, and score-based methods (Wilson approach) for categorical data.
For subjects treated with BPH medications or those who undergo removal of the Spring device (not related to a device-related AE) at any time from post-procedure through the 12-month study period, IPSS values recorded prior to the use of BPH medications or Spring device removal are carried forward to all subsequent visits through the 12-month visit. No imputation is performed for other missing IPSS scores.

Table 26: IPSS Total Score and Responder Rates by Visit (Crossover Population)

There were no surgical secondary interventions reported in the first year for the ITT population. Use of pharmacological agents within the first year was 4.4% following Spring Implant placement in the ITT population.

3. Subgroup Analyses

The following baseline characteristics were evaluated for potential association with safety and effectiveness outcomes: baseline IPSS (<20 versus ≥20) and age (<65, ≥65 years). There was no strong evidence for differential treatment effects between subgroups.

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

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 29 investigators of which 0 were full-time or part-time employees of the sponsor and 3 had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: 0
- Significant payment of other sorts: 2
- Proprietary interest in the product tested held by the investigator: 0
- Significant equity interest held by investigator in sponsor of covered study: 1

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

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-Urology review panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

Although the ITT population did not demonstrate statistical significance for the primary effectiveness endpoints, the mITT population had a rate of success in the treatment arm greater than 25% compared to the control arm at 3 months. Also, in the mITT population, the mean percent change in IPSS total score at 12 months in the Spring Implant arm exceeded the pre-specified clinical success threshold of 30%. Results of the secondary endpoint analyses including the mean improvement in IPSS from baseline, the responder rates (>30% improvement), and the mean percent change from baseline in IPSS score, showed greater improvement in the Spring Implant arm than in the sham arm. The mean improvement in peak urinary flow in the Spring

Implant subjects exceeded the minimal clinically important difference (MCID) of 2.0 mL/s at all follow-up timepoints through 12 months. Additionally, the post-procedure rates of secondary intervention for LUTS therapy using either 1) alternative surgical procedures, or 2) standard pharmacological agents were low and comparable to those observed for similar non-ablative BPH treatments.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory data and animal studies as well as data collected in the clinical studies conducted to support PMA approval and described above.

In the pivotal study, there were no device or procedure related serious adverse events reported in the Spring Implant arm subjects through 12 months of follow-up. There were 152 reported adverse events, and of these, 24 (15.8%) were reported as being related to the index (Spring Implant or sham) procedure. There were 8 device related adverse events (5.3%). The remaining 120 adverse events (78.9%) were reported as having no relationship to the device or procedure. During the first three months of follow-up, 66 events were reported in 41 subjects. Thirty (21.9%) of the Spring Implant subjects and 11 (16.2%) of the sham subjects reported adverse events. The rates of procedure and device related events were comparable between study arms. Between 3 and 12 months, a total of 52 events in the Treatment Arm were reported in 34 subjects. Four of these events (in 2 subjects) were device related, and 2 events (in 2 subjects) were procedure related. The remaining 46 events were not related to the device or procedure. There were no device-related patient deaths or other device-related serious adverse events (SAE), and there were no unanticipated adverse device effects (UADE). A total of sixteen SAEs were reported in fourteen patients. One SAE that occurred in a sham subject was related to the index procedure (urinary tract infection)m; the remaining 15 SAEs were not related to either the procedure or device. Three of those 15 SAEs were subject deaths, none of which were related to participation in the study. The most common procedure- and device-related adverse events included painful ejaculation and dysuria.

C. Benefit-Risk Determination

The probable benefits of the device are also based on data collected in clinical studies conducted to support PMA approval as described above. The results from the pivotal clinical study show that the Zenflow Spring Implant and Delivery System provides a clinically meaningful improvement in symptomatic improvement of LUTS secondary to BPH. In this study, patients implanted with the Zenflow Spring Implant and forming the mITT population experienced a clinically meaningful improvement in mean IPSS from baseline, and a higher proportion of subjects in the Zenflow Spring Implant arm achieved >30% improvement in IPSS total score at 3 months than in the sham arm.

The mITT population is a modified ITT population excluding subjects with major eligibility deviations that should not have received the Spring Implant and accordingly

did not experience benefit. As such, the mITT population more accurately reflects the intended use population.

An analysis of the mean change from baseline in IPSS at 3 months is the preferred co-primary endpoint assessment at 3 months for studies evaluating improvement in LUTS secondary to BPH. This assessment allows for a comparison between the treatment arm and the sham arm using the MCID for IPSS. For the BREEZE study, a co-primary effectiveness endpoint using the difference in responder rate between the device and sham control groups is acceptable given the observed responder rate in the device arm and the observed difference in responder rates between the device and sham groups.

The probable risks of the device are also based on data collected in clinical studies conducted to support PMA approval as described above. The safety profile of the Zenflow Spring Implant and Delivery System has been characterized though 12 months post-procedure. There were no device- or procedure-related SAEs. Device and procedure-related AEs were mild, transient and commonly associated with urological procedures.

Additional factors to be considered in determining probable risks and benefits for the Zenflow Spring Implant and Delivery System device included the number of implants that were removed during the BREEZE pivotal study out to 2 years post-implantation. Devices were removed for various reasons, including at the patient's request. There were no AEs related to device removal. Published patient preference information[(2)(3)] demonstrate that patients, in considering minimally invasive surgical therapies (MIST) therapies, prioritize easy reversal of complications over device benefit and that inability to later seek other treatments for BPH and long-term complications are important considerations to patients.

Given that the prior device of this type was removed from the market by its manufacturer due to long-term safety concerns and need to better characterize device removals, a post-approval study following the pivotal study to 5 years post implant is required to obtain additional information about long-term safety and effectiveness.

1. Patient Perspective

   The sponsor used patient-reported outcomes (PROs) including the International Prostate Symptom Score (IPSS), Sexual Health Inventory for Men (SHIM), Male Sexual Health Questionnaire – Ejaculatory Domain (MSHQ-EjD), and Visual Analog Scale (VAS) for pain in the BREEZE clinical trial. Results from these PROs indicate that subjects experienced a decrease in urinary symptoms, no deterioration in erectile function or ejaculatory function or increased bother or dissatisfaction with ejaculatory function through 12 months of follow-up, and that the procedure was well tolerated with low pain scores.

In conclusion, given the available information above, the data support that for the treatment of symptoms due to urinary outflow obstruction secondary to benign prostatic

hyperplasia (BPH) in men with prostatic urethral lengths between 25 and 45 mm and prostate volumes between 25 and 80 cc, the probable benefits outweigh the probable risks.

D. Overall Conclusions

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

The results of the BREEZE pivotal clinical trial demonstrate that the Zenflow Spring System is safe and effective for the treatment of LUTS due to BPH and that the patient population for whom the device is intended can be expected to achieve clinically significant results. This conclusion is based on the greater improvement observed in the treatment arm relative to the sham arm at 3 months and improvement in the treatment arm across all study timepoints for primary and secondary efficacy endpoints. The device and procedure related AE rates are acceptable and similar to other urological procedures of this type. Even though there were incidences of device removal, there were no AEs associated with device removals. Considering all safety and effectiveness results, the benefits outweigh the risks.

XIV. CDRH DECISION

CDRH issued an approval order on December 11, 2025. The final clinical conditions of approval cited in the approval order are described below.

The BREEZE Study - PMCF (CLIN-0130-1, Rev H, December 10, 2025, email)

This study was initiated prior to device approval and is a prospective, multi-center, double-blind, 2:1 randomized, sham controlled clinical study. It was conducted at 22 sites and enrolled 231 subjects. One hundred thirty six (136) patients were implanted with the Spring Implant in the treatment arm and 68 were exposed to the sham control. An additional 59 subjects were implanted with the Spring Implant following crossover from the sham control arm, and 26 subjects were implanted with the Spring Implant as part of a roll-in training cohort. A total of 221 subjects were implanted with the Spring Implant. The 12-month outcomes from this study were used to support PMA approval. The 60-month follow-up data from this study will be used to evaluate the continued safety and effectiveness of the Zenflow Spring Implant and Delivery System.

No greater than 20% of the patients enrolled in the study (i.e., patients enrolled in the treatment arm and patients crossed over from the sham to treatment arm) will be lost to follow up through 60-months.

You must collect and report the following clinical outcomes annually through 60-months:

Effectiveness

- Percent of subjects who experience at least a 30 percent improvement in IPSS from their baseline pre-treatment score.
    - Mean change from baseline in International Prostate Symptom Score (IPSS)
- Mean change from baseline in uroflowmetry measures of peak flow rate (Qmax)
- Mean improvement from baseline in post void residual (PVR) volume
- Mean change in International Consultation on Incontinence Questionnaire – Urinary Incontinence Short Form (ICIQ-SF)
- Mean change in BPH Impact Index (BII) Questionnaire
- Post-procedure device removal rate and summary of the reasons for removal (including the number and rate for each reason)
- Post-procedure incidence of secondary reintervention using an alternate surgical lower urinary tract symptoms (LUTS) therapy
- Post-procedure incidence of secondary reintervention using standard pharmacological agents for LUTS therapy

Safety

- Rate of device or procedure related adverse events
- Change in sexual health characterized by change in Sexual Health Inventory for Men (SHIM) and Male Sexual Health Questionnaire – Ejaculatory Domain (MSHQ-EjD)
- Assessment of adverse events outcomes related to a Spring Implant removal procedure
- Post implant removal assessment at 6 months for inability to subsequently safely undergo alternative treatments for LUTS associated with BPH (if no alternative treatments for BPH were performed by 6 months post removal the assessment will be repeated as 12 months)
- Proportion of subjects with adverse events classified as Clavien-Dindo Grade IIIb or higher or any event resulting in persistent disability.

Data must be summarized descriptively, without statistical testing. Patient and physician labeling must be updated annually via a PMA supplement to include the effectiveness and safety outcomes listed above after the patients enrolled in this study complete each annual year of follow up.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) 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

(1) Sandhu JS, Bixler BR, Dahm P, et al. Management of lower urinary tract symptoms attributed to benign prostatic hyperplasia (BPH): AUA Guideline amendment 2023. J Urol. 2023;10.1097/JU.0000000000003698. https://doi.org/10.1097/JU.0000000000003698

(2) Huffman PJ, et al. Evaluating Patient Preferences in Benign Prostatic Hyperplasia Treatment Using Conjoint Analysis. Urology. 2022 Jun;164:211-217.

(3) Winograd J, et al. Quality of life and surgical treatment regret in patients with benign prostatic hypertrophy: a multicenter study. Can J Urol. 2025 Jun 27;32(3):219-227.