SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Common Name:	Drug Coated Urethral Dilation Catheter
Device Trade Name:	Optilume® Urethral Drug Coated Balloon
Device Procode:	QRH
Applicant Name and Address:	Urotronic, Inc. 2495 Xenium Lane N Minneapolis, MN 55441
Date of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P210020
Date of FDA Notice of Approval:	December 3, 2021

II. INDICATIONS FOR USE

The Optilume® Urethral Drug Coated Balloon is used to treat patients with obstructive urinary symptoms associated with anterior urethral stricture. It is designed to be used in adult males for urethral stricture of ≤3 cm in length.

III. CONTRAINDICATIONS

The Optilume® Urethral Drug Coated Balloon is contraindicated for use in patients with known hypersensitivity to paclitaxel or structurally related compounds and in patients with urologic implants such as penile implants or artificial urinary sphincters.

IV. WARNING AND PRECAUTIONS

The warnings and precautions can be found in the Optilume® Urethral Drug Coated Balloon labeling.

V. DEVICE DESCRIPTION

The Optilume® Urethral Drug Coated Balloon (Optilume® DCB) is a 0.038" (0.97 mm) over-the-wire (OTW) guidewire compatible catheter with a dual lumen design and a tapered, atraumatic tip. The Optilume® DCB is used to exert radial force to dilate narrow urethral segments (strictures). The distal end of the catheter has a semi-compliant inflatable balloon that is coated with a proprietary coating containing the active pharmaceutical paclitaxel. The drug coating covers the working length of the balloon body and is evenly

distributed at a dose density of 3.5µg/mm^2. The device has two radiopaque marker bands that indicate the working length of the balloon where the drug coating is applied. The drug coated balloon is covered with a protective sheath that is discarded prior to use.

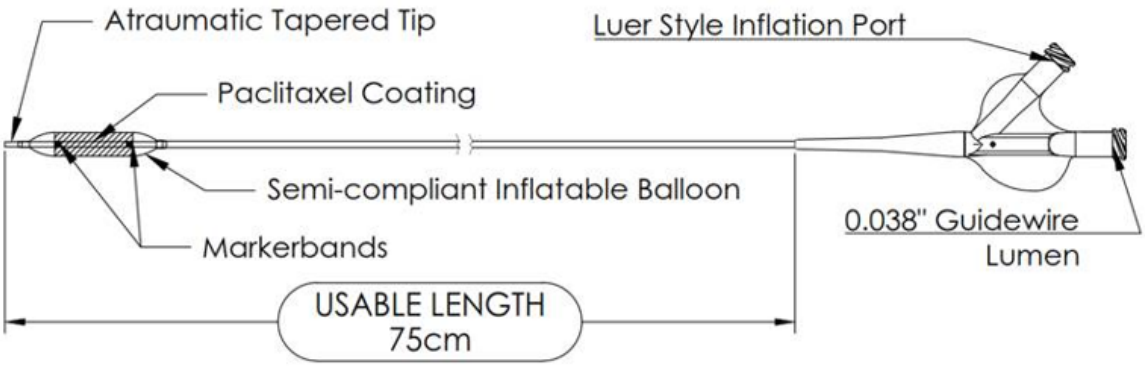

Figure 1. Device Schematic

The Optilume® DCB device sizes and catalogue numbers are provided in Table 1. The 18F to 30F (6-10 mm) diameter balloons are cystoscope compatible and can be placed through the working channel. The 36F (12mm) diameter balloons are not cystoscope compatible and need to be placed side-by-side with the cystoscope.

Table 1: Full Range of Balloon Sizes To be Marketed

Catalogue Number	Balloon Diameter	Balloon Length	Rated Burst Pressure	Nominal Paclitaxel Dose (µg)	Device Pre-Inflation Profile
1110-06030B	18F / 6mm	30 mm	12 atm	1,979	6.3F (0.083")
1110-06050B	18F / 6mm	50 mm	12 atm	3,299	6.3F (0.083")
1110-08030B	24F / 8mm	30 mm	12 atm	2,639	6.3F (0.083")
1110-08050B	24F / 8mm	50 mm	12 atm	4,398	6.3F (0.083")
1110-10030B	30F / 10mm	30 mm	10 atm	3,299	6.3F (0.083")
1110-10050B	30F / 10mm	50 mm	10 atm	5,498	6.3F (0.083")
1110-12030B[1]	36F / 12mm	30 mm	8 atm	3,958	9.0F (0.118")
1110-12050B[1]	36F / 12mm	50 mm	8 atm	6,597	9.0F (0.118")

[1] These DCB sizes are not compatible with flexible cystoscopes.

A. Active Pharmaceutical Ingredient

The active pharmaceutical ingredient (API) used in the Optilume® DCB coating is the small molecule drug paclitaxel. Paclitaxel is a lipophilic, anti-mitotic agent that inhibits cell mitosis. Several studies in animal models have also shown that paclitaxel applied locally inhibits smooth muscle cell and fibroblast proliferation and migration.

The CAS Registry number of paclitaxel is 33069-62-4. The chemical name is (2aR-(2aα,4β,4aβ,6β,9α(α R*,βS*),11α,12α,12bα))-β-(Benzoylamino) α-hydroxybenzenepropanoic acid 6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca(3,4)benz(1,2-b)oxet-9-yl ester and the chemical formula is $C_{47}H_{51}NO_{14}$. The chemical structure of paclitaxel is illustrated in Figure 2, below.

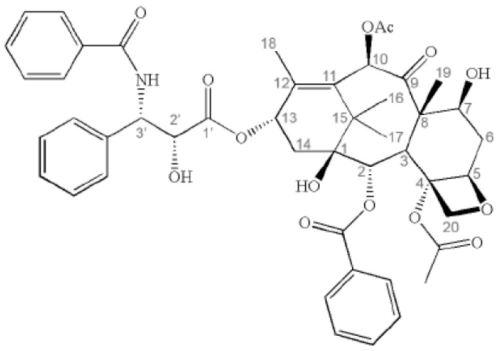

Figure 2. Chemical Structure of Paclitaxel

B. Principles of Operation

During treatment, the catheter is advanced over a guidewire to the portion of the urethra that has a stricture, the balloon is inflated to mechanically dilate the urethra and improve urine flow (primary mode of action). During the balloon inflation, paclitaxel is transferred from the balloon to the urethra wall to inhibit stricture recurrence (secondary mode of action).

The drug coating is evenly applied to the balloon body only, represented as the hatch marked area in Figure 1. The length of the balloon body is demarcated with two radiopaque marker bands. The majority of the drug substance is washed out of the body during voiding with sufficient drug retained on the surface to inhibit the cellular growth after dilation.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several alternatives for the treatment of urethral strictures including:

- Balloon dilation with an uncoated balloon
- Dilation with bougie urethral sounds
- Direct vision internal urethrotomy (DVIU)
- Surgical reconstruction of the urethra or urethroplasty

A patient should fully consider these alternatives and discuss with his physician(s) to select the best treatment that meets his expectation and lifestyle.

VII. MARKETING HISTORY

The Optilume® DCB was CE Marked in 2020 and is commercially available in the EU, Canada, Israel, Hong Kong, and New Zealand for treatment of anterior strictures. No products have been withdrawn from the market in any country for any reason.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

The potential adverse effects of the Optilume® DCB related to mechanical dilation are similar to urethral balloon dilation catheter and include but not limited to the following:

- Dissection of the urethra
- Perforation of the urethra
- Hematuria
- Inflammation
- Infection
- Recurrence of the stricture
- Detachment of a component of the catheter
- Bothersome urinary symptoms or painful urination
- Genital or pelvic pain

Although systemic effects from the paclitaxel coating are not anticipated, adverse effects observed during IV administration of paclitaxel for chemotherapy include but are not limited to the following:

- Allergic reaction
- Alopecia
- Anemia
- Gastrointestinal symptoms
- Hematological dyscrasia (including leucopenia, neutropenia, thrombocytopenia)
- Hepatic enzyme changes
- Myalgia/athralgia
- Myelosuppression
- Peripheral neuropathy

The Optilume® DCB contains paclitaxel, a known genotoxic aneugen. Because paclitaxel may be present in semen after treatment with the Optilume® DCB, men should abstain or wear a condom for 30 days after treatment to avoid exposure of their sexual partner to paclitaxel. Men with partners of child-bearing potential should use highly effective contraceptive and avoid fathering children until at least 6 months after treatment with the Optilume® DCB. Paclitaxel was detectable in semen in 60% (9/15), 39% (5/13) and 8.3% (1/12) of subjects at 1 month, 3 months, and 6 months post-treatment, respectively. The effect of treatment with the Optilume® DCB on sperm and spermatogenesis is unknown.

IX. SUMMARY OF PRECLINICAL STUDIES

This following non-clinical testing was conducted on the Optilume® DCB:

- Laboratory Studies
  - Biocompatibility Testing
  - Bench Testing
    - Mechanical Testing

        - Packaging Testing
        - Shelf-Life Testing
    - Analytical Testing
        - Drug Product Testing
        - Coating Characterization
    - Sterilization Validation
- Animal Testing
        - Pharmacokinetics
        - Safety
- Additional Studies
    - Stability and Shelf Life Studies

A. Laboratory Studies

1. BIOCOMPATIBILITY STUDIES

Biocompatibility testing was conducted per 21 CFR 58 Good Laboratory Practices (GLP) for Nonclinical Laboratory Studies in accordance with ISO 10993-1 and in compliance to FDA Guidance - Use of International Standard ISO 10993-1, Biological Evaluation of Medical Devices. Devices used for testing were manufactured utilizing Good Manufacturing Practices (GMP), sterilized and packaged in their final configuration.

Per ISO 10993-1, the device is categorized as follows:

- Device Category: Surface device contacting breached or compromised surface
- Contact Type: Mucosal membrane
- Contact Duration: Limited Exposure (≤ 24 hours)

Table 2. Biocompatibility Testing

Test	Test Description	Balloon w/excipient (no drug)	Balloon w/drug coating	Balloon Catheter w/excipient (no drug)	Balloon Catheter w/drug coating	Result (Standard)
Cytotoxicity	ISO MEM Elution Assay with L-929 Mouse Fibroblast Cells	x	x	x		Non-cytotoxic (10993-1: 2018)
Sensitization	ISO Guinea Pig Maximization	x		x	x	Non-sensitizing (10993-1: 2018)
Irritation	ISO Intracutaneous Reactivity	x		x	x	Non-irritating (10993-1:

Test	Test Description	Balloon w/excipient (no drug)	Balloon w/drug coating	Balloon Catheter w/excipient (no drug)	Balloon Catheter w/drug coating	Result (Standard)
						2018)
Acute Toxicity	ISO Systemic Toxicity	x			x	Non-acutely toxic (10993-1: 2018)

Material mediated pyrogenicity testing (USP Pyrogen Test Procedure – Section <151>, 14x50mm uncoated full catheter, per 10993-11) was also completed on the uncoated balloon catheter and the device was found to be non-pyrogenic. Additional toxicity testing (excipient qualification GLP study, elevated dose versus saline control), designed to characterize the general toxicity of the excipients when exposed to mucosal membrane, was completed on the excipients in the hamster buccal cavity. The toxicity test showed that the excipients are safe and non-toxic. The information provided demonstrates that the Optilume® DCB is biocompatible for its intended use.

2. BENCH TESTING

Functional engineering testing was conducted on the Optilume® DCB catheter to verify the design meets requirements for its intended use. A summary of the mechanical testing conducted on the Optilume® DCB can be found in Table 3.

Table 3. Mechanical Bench Testing

Product Specification Description	Acceptance Criteria	Result
Crossing Profile	≤ 10 mm balloon diameter: 0.083” >10 mm balloon diameter: 0.118”	Pass
Stricture Entry Profile	0.066” Max	Pass
Trackability	Tracked and delivered through anatomical model	Pass
Catheter Working Length	75 ± 2 cm	Pass
Balloon Lengths	± 7.5% of nominal	Pass
Balloon Diameter	≤10 mm: ± 0.5 mm of nominal	Pass
	>10 mm: ± 1 mm of nominal	
Balloon Burst Pressure	<10 mm (30F) balloon diameter: ≥12 atm	Pass
	10 mm (30F) balloon diameter: ≥10 atm	
	>10 mm (30F) balloon diameter: ≥8 atm	
Multicycle Fatigue	10 inflate/deflate cycles to Rated Burst Pressure w/o failure	Pass
Balloon Compliance	10% max	Pass
Inflation Time	≤10 mm (30F) balloon diameter: 60 sec max >10 mm (30F) balloon diameter: 120 sec max	Pass

Product Specification Description	Acceptance Criteria	Result
Deflate Time	≤10 mm (30F) balloon diameter: 60 sec max >10 mm (30F) balloon diameter: 120 sec max	Pass
Marker Band to Marker Band Distance	30mm length balloons: 30 ± 1.5 mm 50mm length balloons: 50 ± 2.5 mm	Pass
Distal Marker Band to Balloon Body Distance	0 ± 2 mm	Pass
Freedom from Leakage	No Leaks	Pass
Burst Mode	Radial Burst Mode: None allowed below RBP +3 atm 10% allowed between RBP +3 atm to +6 atm 30% allowed over RBP +6 atm	Pass
Proximal Balloon Bond Tensile	Min 6 lb_f	Pass
Distal Balloon Bond Tensile	Min 2.25 lb	Pass
Manifold to Shaft Bond Tensile	Min 6 lb_f	Pass
Kink Resistance	The balloon and catheter will not kink in a ¾" radius	Pass
Guidewire Compatibility	No guidewire lockup during tracking	Pass
Luer Compatibility	Luer Hub ISO 80369-7 Compatible	Pass
Cystoscope Compatibility (≤10mm balloon (30F) diameter)	Inserted w/o damage	Pass
Primary Tyvek Package Integrity	No leaks, continuous seal, with adequate peel strength	Pass
Secondary Foil Package Integrity	No leaks, continuous seal, with adequate peel strength	Pass

3. ANALYTICAL TESTING

Analytical testing was performed to determine the identity, safety, purity, and quality of the drug substance used in the Optilume® DCB.

Table 4. Analytical Drug Testing

Test	Testing Summary/Objective	Acceptance Criteria	Results
Identification	Test the drug substance for identity to ensure conformity to incoming specifications	Identity confirmed via two different tests	Pass
Coating Appearance	Visual inspection to verify the drug coating meets appearance specification	Must meet visual standard	Pass
Assay (potency)	Total paclitaxel content is quantified to ensure individual devices contain the labeled	Average within 90.0-110.0% of Label Claim	Pass

Test	Testing Summary/Objective	Acceptance Criteria	Results
	dosage		
Impurities and degradants	The type and amount of degradants and impurities are quantified to ensure they remain within acceptable levels	ICH Q3B(R2)	Pass
Drug Content Uniformity	The paclitaxel content uniformity from balloon to balloon is verified to ensure content uniformity meets specification	USP <905>	Pass
Coating Uniformity	The paclitaxel content on circumferential segments of an individual balloon is measured	Average of each segment must be within specified range	Pass
	The paclitaxel content on longitudinal segments of an individual balloon is measured	Average of each segment must be within specified range	
Dissolution	The *in vitro* release profile of paclitaxel from the finished device is verified to meet pre-specified criteria	USP <711>	Pass

4. STERILIZATION

The Optilume® DCB is sterilized with ethylene oxide (EO) to provide SAL of at least 10^{-6} and met ISO11135-1:2014 A1:2018 requirements. 100% EO sterilization process is used. The overkill sterilization method was used in the validation. Sterilization validation was performed by comparison to the 'worst case' devices. EO residual levels were within accepted limits (EO < 4 mg/device), per ISO 10993-7:2008.

B. Animal Studies

An *in vivo* animal study was conducted to evaluate the safety of the Optilume® DCB and the pharmacokinetics of paclitaxel distribution and elimination at the treatment site and in adjacent tissues. Large male canines were the animal models used for *in vivo* animal testing due to the similar anatomical size of the treated urethra. The animal study consists of 3 arms: a standard dose arm, a maximum dose arm and a control arm. Endpoints included acute device performance, clinical safety, and histological analysis, as well as the assessment of drug concentrations in target tissue and tissues in close proximity to the treatment site.

Canine urethras were treated with either a Control (uncoated balloon), a standard dose (single DBC at 2 treatment sites), or maximum dose (2x overlapping DCBs at 3 treatment sites) and followed for up to 70 days. An overview of the GLP study design is shown in Table 5.

Table 5. Number of Animals at Each Follow-up Timepoint

Study Arm	# Tx Sites per dog	# DCB per site	Total # DCB per dog	Total Paclitaxel per dog (mg)	Timepoints
Max Dose DCB N=12	3	2	6	15.8	28 Days (n=6) 70 Days (n=6)
Standard Dose DCB N=29	2	1	2	5.3	1 Hour (n=8) 7 Days (n=7) 28 Days (n=7) 70 Days (n=7)
Control (non-coated balloon) N=6	3	0	0	0	7 Days (n=3) 28 Days (n=3)

1. PHARMACOKINETICS

Paclitaxel concentration was measured over time in plasma, urethral tissue (target), and non-target urological tissues in close proximity to the treatment site. Plasma paclitaxel concentration was below the limit of quantification (BLQ) in 99% of samples taken (samples were taken at 1, 3, 7, 12 hours, 1,3 ,7, 14, 28, and 70 days), with only a single sample (1 of 143) registering above the limit of detection. Paclitaxel concentration in urethral tissue at the target site was maximal at 1-hour post-procedure and remained detectable at 28 and 70 days in the standard dose arm. Paclitaxel concentration in adjacent non-target urological tissues was also maximal at 1-hour post-procedure (<0.05 µg/g) and approached non-quantifiable levels after the 7-day timepoint.

2. SAFETY

Daily health assessments showed no adverse effects with normal healing. General cellular response to treatment included early denudation of the urothelium with stromal hypocellularity caused by balloon injury and subsequent drug effect at 7 days, followed by near complete healing by 28 days. No treatment-related changes were noted in adjacent tissues (bladder, prostate, vas deferens, ureters, epididymis, testes, kidneys, rectum, and sigmoid colon).

Histological analyses of the tissues were compared between test and control at all timepoints, with no abnormalities ascribable to the treatment. There was no evidence of abnormal cell division or detectable disruption in the urethral tissue (location of highest paclitaxel concentration).

C. Additional Studies

1. STABILITY AND SHELF LIFE STUDIES

Finished product stability studies were conducted according to USP and ICH guidelines to establish the shelf life for the Optilume® DCB finished product. Prior to accelerated aging, devices were subject to environmental conditioning per ISTA 2A (Partial Simulation Performance Test - Packaged-Products Weighing 150 lb (68 kg) or Less) and distribution

simulation per ASTM D4169-16 (Standard Practice for Performance Testing of Shipping Containers and Systems). After environmental conditioning and distribution simulation, all samples went through simulated aging per ASTM 1980-07 (Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices). The smallest/shortest (6x30) and the largest/longest (14x50) Optilume® DCB were tested as they represent appropriate worst-case sizes and bracket all device sizes. The expiration dating for the Optilume® DCB matrix is based on evaluation of test articles for each of the following category of tests:

- Catheter Mechanical Testing of aged samples to 2 years. Mechanical testing conducted for the 6x30 mm balloon catheters included Balloon Fatigue, Freedom from Leak, Balloon Compliance, Rated Burst Pressure, and Burst Mode. Mechanical testing conducted for the 14x50 mm balloon catheters included Catheter Working Length, Entry Profile OD, Balloon Fatigue, Freedom from Leak, Tensile (Proximal Bond, Distal Bond, Manifold), Balloon Treatment Length, Balloon Treatment Diameter, Balloon Compliance, Rated Burst Pressure, Burst Mode, Crossing Profile, Inflate/Deflate Time, and Kink Resistance.

- Packaging testing of aged samples to 2 years. Packaging testing included Seal Strength Tyvek (ASTM F88:2015), Bubble Leak Tyvek (ASTM F2096:2019), Seal Appearance (ASTM F1886:2016), Bubble Leak Foil (ASTM F2096:2019), and Seal Strength Foil (ASTM F88:2015).

- Drug stability testing of long term and accelerated aged samples to 1 year

Device samples are stored at room temperature for real time aging and tested to validate the accelerated aging studies as part of ongoing device monitoring. The testing includes an evaluation of potency, impurities, *in vitro* drug release, sterility, and drug content uniformity. Appropriate functional tests were also performed on aged product to ensure that the Optilume® DCB performed acceptably. The data generated from the mechanical, package integrity, and drug stability studies currently supports a 12-month shelf life for the product. The expiration date/shelf life of the finished product will be evaluated and extended as additional stability data becomes available.

X. SUMMARY OF PRIMARY CLINICAL STUDY

ROBUST III

Objective

The objective of the ROBUST III study was to evaluate the safety and effectiveness of the Optilume® DCB as compared to standard-of-care (SOC) endoscopic management of recurrent anterior urethral strictures.

A. Study Design

The ROBUST III study is a prospective, 2:1 randomized, multicenter, single blind trial

comparing the Optilume® DCB against SOC endoscopic management of recurrent anterior urethral strictures. Potential device or procedure related adverse events and all Serious Adverse Events were reviewed and adjudicated by an independent Clinical Events Committee. A Data Monitoring Committee oversaw the safety of the study. The study was designed as an adaptive study with a planned interim analysis after the first 60 subjects for sample size re-estimation. Subjects randomized to standard of care endoscopic management were allowed to cross over to receive the Optilume® DCB prior to the close of the 12-month follow-up window if stricture recurrence was confirmed by recurrent lower urinary tract symptoms (LUTS) and urethral diameter <12F measured by urethrogram.

A single arm of 15 subjects were enrolled and treated with the Optilume® DCB and pharmacokinetic data was gathered in this cohort.

1. CLINICAL INCLUSION AND EXCLUSION CRITERIA

Enrollment in the ROBUST III study was limited to subjects who met the eligibility criteria.

The full list of selection criteria is provided here:

Inclusion Criteria

1. Male subjects ≥ 18 years old
2. Visual confirmation of stricture via cystoscopy or urethrogram
3. Single, tandem or diffuse anterior urethral stricture(s), less than or equal to 3.0 cm total length measured by retrograde urethrogram. (Stricture length is defined as the distance between the most distal edge of the stricture to the most proximal edge of the stricture).
4. Two or more prior dilation treatments of the same stricture, including Direct Vision Internal Urethrotomy (DVIU). Note: Catheterization is not considered a dilation treatment.
5. Significant symptoms of stricture such as frequency of urination, dysuria, urgency hematuria, slow flow, feeling of incomplete emptying, recurrent urinary tract infections (UTI).
6. IPSS score of 11 or higher (assumed to be “35” if suprapubic catheter is present)
7. Lumen diameter ≤12F by urethrogram
8. Qmax <15 ml/sec (assumed to be “0” if suprapubic catheter is present)
9. Guidewire must be able to cross the lesion

Exclusion Criteria

1. Subjects with diffuse stricture length, greater than 3.0 cm in total length. (Stricture length is defined as the distance between the most distal edge of the stricture to the most proximal edge of the stricture).
2. Subjects with a history of hypersensitivity reactions to TAXOL®, on medication that may have negative interaction with paclitaxel, with solid tumors who have a baseline neutrophil counts of <1500 cells/mm3 or subjects with AIDS-related Kaposi’s sarcoma with baseline neutrophil counts of <1000 cells/mm3.
3. Subjects who had an indwelling suprapubic catheter longer than 3 months total prior to enrollment.

4. Previous urethroplasty within the anterior urethra
5. Stricture dilated or incised within the last six (6) weeks (urethral catheterization is not considered dilation)
6. Presence of local adverse factors, including abnormal prostate making catheterization difficult, urethral false passage or fistula.
7. Presence of signs of obstructive voiding symptoms not directly attributable to the stricture at the discretion of the physician
8. Diagnosis of untreated and unresolved Benign Prostatic Hyperplasia (BPH) or Bladder Neck Contracture (BNC)
9. Untreated stress urinary incontinence (SUI).
10. History of diagnosed radiation cystitis.
11. Diagnosis of carcinoma of the urethra, bladder or prostate within the last 2 years
12. Active kidney, bladder, urethral or ureteral stone passage in the last six (6) weeks or concern of stone passage in the next 6 weeks at the discretion of the investigator.
13. Diagnosis of chronic renal failure and treatment with hemodialysis
14. New diagnosis of overactive bladder (OAB) within the last 6 months
15. Use of alpha blockers, OAB medication, anticonvulsants (drugs that prevent or reduce the severity and frequency of seizures), and antispasmodics where the dose is not stable. (Stable dose is defined as having the same medication and dose in the last six months.)
16. Dependence on Botox (onabotulinumtoxinA) in urinary system
17. Presence of an artificial urinary sphincter, slings or stent(s) in the urethra or prostate
18. Known neurogenic bladder, sphincter abnormalities, or poor detrusor muscle function
19. Diagnosed with Lichen Sclerosus, or stricture due to balanitis xerotica obliterans (BXO)
20. Previous hypospadias repair
21. History of cancer in non-genitourinary system which is not considered in complete remission (except basal cell or squamous cell carcinoma of the skin). A potential participant is considered in complete remission if there has been no evidence of cancer within two years of enrollment
22. Any cognitive or psychiatric condition that interferes with or precludes direct and accurate communication with the study investigator regarding the study or affect the ability to complete the study quality of life questionnaires
23. Unwilling to use protected sex for 30 days' post treatment
24. Unwilling to abstain or use protected sex for 90 days' post treatment if sexual partner is of child-bearing potential.
25. Inability to provide Informed Consent Form (ICF) and/or comply with all the required follow-up requirements
26. Participation in other pre-market studies or treatment with an investigational drug or device. Long-term follow-up or post market study of an approved device is allowed.
27. Current active infection in the urinary system
28. Current uncontrolled diabetes (hemoglobin A1c > 8.0%) or evidence of poor wound healing due to diabetes
29. Diagnosed or suspected primary neurologic conditions such as multiple sclerosis or Parkinson's disease or other neurological diseases known to affect bladder function, sphincter function or poor detrusor muscle function.

30. Visible hematuria in subject's urine sample without known contributing factor
31. Invisible hematuria (or significant microscopic hematuria, i.e., hematuria of ≥ 3 RBC's/HPF) that may be caused by a clinically significant disease unless it is attributed to the urethral stricture disease or other causes which are benign and not requiring treatment.

2. FOLLOW-UP SCHEDULE

Follow-up visits were completed at the time of Foley removal (2-5 days), 30 days, 3 months, 6 months, and 12 months post-treatment. Subjects were blinded to treatment received through primary follow-up of 6 months. Long term follow-up is planned through 5 years for subjects receiving the Optilume® DCB.

Subjects crossing over to receive the Optilume® DCB will be followed according to the standard follow-up schedule yearly through 5 years, beginning on the date Optilume® DCB treatment was received.

Clinical assessments during follow up included:

- International Prostate Symptom Score (IPSS) questionnaire
- International Index of Erectile Function (IIEF) questionnaire
- Visual Analogue Scale (VAS) for Pain (Procedure through 30 days)
- Uroflowmetry, including peak urinary flow rate (Qmax) and post-void residual (PVR)
- Laboratory testing
- Physical exam

3. CLINICAL ENDPOINTS

Primary Efficacy Endpoint: The primary efficacy endpoint was defined as the proportion of subjects free from stricture recurrence at 6 months, which was defined as the ability to pass a 16F flexible cystoscope or 14F rubber catheter through the treated area.

The statistical hypothesis test for the primary efficacy endpoint was based on a two-sample continuity corrected Chi-square test at the two-sided 0.05 alpha level (equivalent to a one-sided 0.025 alpha level). For the trial to be successful, the statistical evaluation for the resolution of the stricture at 6 months of the Optilume arm will be statistically compared to the Control arm.

Ho: $P_t \leq P_c$

Ha: $P_t > P_c$

Where P_t is the stricture free rate at 6 months in the Optilume arm and P_C is the stricture free rate at 6 months in the Control arm.

Primary Safety Endpoint: The primary safety endpoint is defined as a composite of pre-defined device or procedure related serious complications through 3 months post-treatment. The proportion of subjects experiencing a serious device or procedure related event of the following types will be reported:

- Formation of rectal fistula
- Unresolved *de novo* stress urinary incontinence (requiring ≥ 1 pad per day)
- Urethral rupture or burst.

The primary safety endpoint was analyzed with descriptive statistics and nominal 95% confidence intervals.

Hypothesis tested secondary endpoints:

- Time to treatment failure through 6 months
- Change in Qmax at 6 months
- Responder Rate at 12 months (A responder is defined as subjects with an improvement of ≥50% from baseline in IPSS score.)

Ancillary endpoints:

- IPSS over time
- Percent responder over time
- Qmax, PVR over time
- Rate of acute urinary retention through 6 months
- Freedom from repeat intervention over time
- Change in erectile function

The primary analysis set was intention-to-treat (ITT). The ITT set was comprised of all subjects who were enrolled and randomized to receive either the Optilume® DCB or SOC endoscopic management. Primary and hypothesis tested secondary endpoints employed multiple imputation for handling missing data.

B. Accountability of PMA Cohort

A total of 141 subjects were enrolled at 22 investigational sites, 127 in the randomized cohort and 14 in the pharmacokinetics sub-study. Subject disposition and visit compliance through 1-year follow-up for each arm can be found in Table 6 and Figure 3.

Table 6. Visit Compliance for Randomized Cohort

Study Visit	Control Arm n/N (%)	Optilume Arm n/N (%)	All n/N (%)
Baseline	48/48 (100.0%)	79/79 (100.0%)	127/127 (100.0%)
Procedure	48/48 (100.0%)	79/79 (100.0%)	127/127 (100.0%)
Pre-Discharge	48/48 (100.0%)	79/79 (100.0%)	127/127 (100.0%)
Foley Removal	48/48 (100.0%)	78/79 (98.7%)	126/127 (99.2%)
30 Day	47/48 (97.9%)	78/79 (98.7%)	125/127 (98.4%)
3 Months	42/44 (95.5%)	75/78 (96.2%)	117/122 (95.9%)
6 Months	31/36 (86.1%)	69/75 (92.0%)	100/111 (90.1%)

Study Visit	Control Arm n/N (%)	Optilume Arm n/N (%)	All n/N (%)
1 Year	15/21 (71.4%)	60/68 (88.2%)	75/89 (84.3%)
Denominators are based on the number of subjects that are expected to have the visits by July 19th, 2021. Denominator excludes those that exited the study or crossed over prior to the opening of the stated visit window. Missing visits include subjects who missed the visit or were later identified as lost to follow-up.			

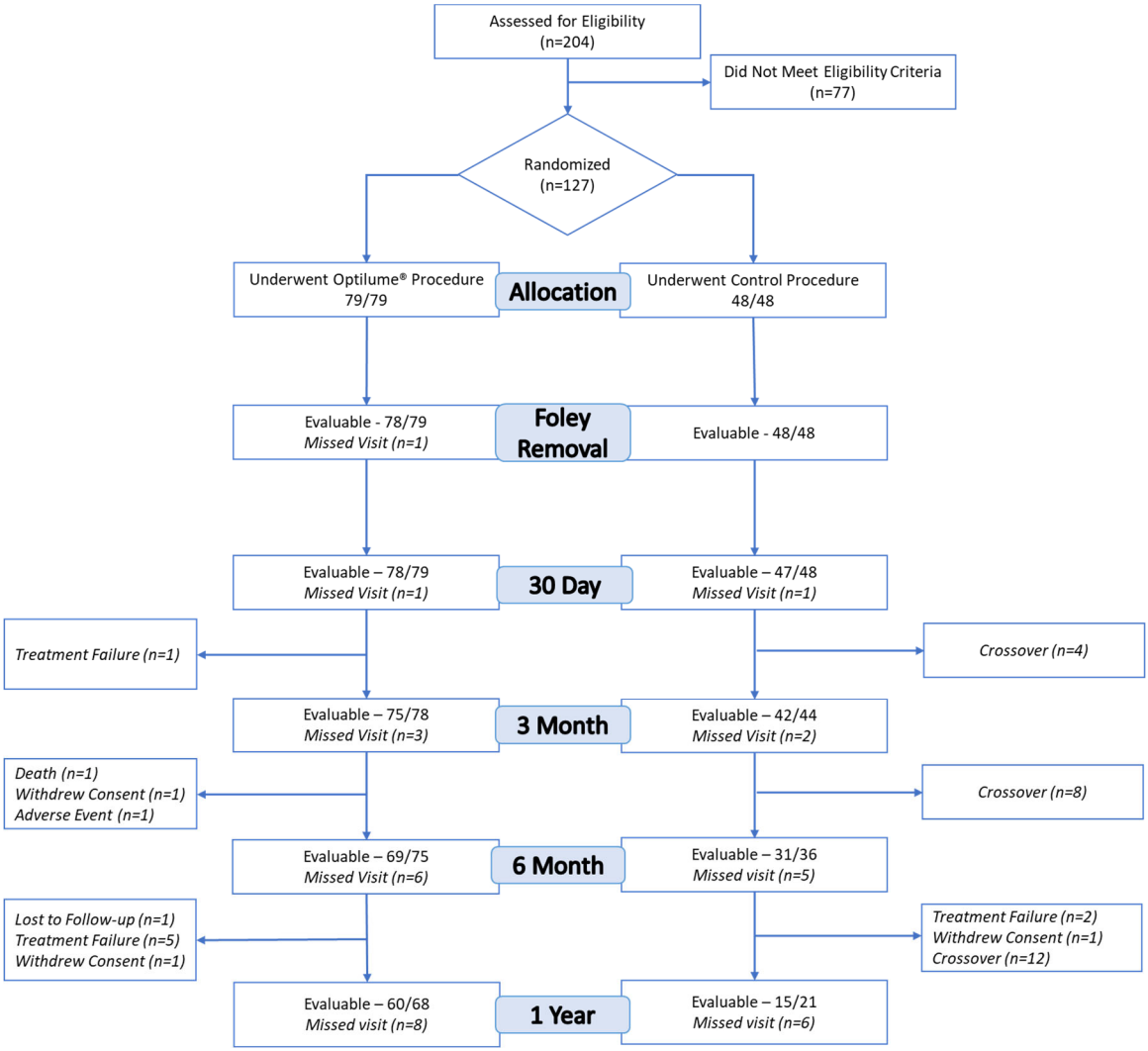

Figure 3. CONSORT Subject Accountability Diagram for Randomized Cohort

C. Subject Population Demographics and Baseline Parameters

Subject demographics and baseline characteristics were well matched between arms and are summarized in Table 7. The majority of subjects (82.5%) were Caucasian and were

considered overweight (average BMI 29.9). Approximately 30% of subjects had a history of BPH, with the rate being similar between arms. BPH was required to be considered resolved or well managed at the time of enrollment. Other common medical histories included UTI (34.6%), kidney stones (18.9%), and prostate cancer (10.2%). Approximately one in ten subjects had prior pelvic radiation therapy. The most common LUTS symptoms reported included poor stream, incomplete voiding, nocturia, frequency, and urgency.

Table 7. Baseline Demographics and Medical History

Characteristic	Control	Optilume® DCB	p-value
Demographics			
Age	60.6 ± 16.0 (48)	58.7 ± 15.5 (79)	0.500
Race			0.838
American Indian or Alaska Native	1/48 (2.1%)	0/78 (0.0%)	
Asian	2/48 (4.2%)	3/78 (3.8%)	
Black or African American	6/48 (12.5%)	9/78 (11.5%)	
Native Hawaiian or Pacific Islander	0/48 (0.0%)	1/78 (1.3%)	
White	39/48 (81.3%)	65/78 (83.3%)	
Ethnicity			0.673
Hispanic or Latino	3/48 (6.3%)	3/78 (3.8%)	
Not Hispanic or Latino	45/48 (93.8%)	75/78 (96.2%)	
BMI	28.9 ± 6.9 (48)	30.5 ± 6.7 (77)	0.206
Medical History / Risk Factors			
LUTS Presentation			>0.999
Dysuria	18/48 (37.5%)	36/79 (45.6%)	
Frequency	34/48 (70.8%)	63/79 (79.7%)	
Hematuria	12/48 (25.4%)	10/79 (12.7%)	
Hesitancy	29/48 (60.4%)	38/79 (48.1%)	
Incomplete Voiding	35/48 (72.9%)	57/79 (72.2%)	
Nocturia	41/48 (85.4%)	58/79 (73.4%)	
Pelvic Pain	3/48 (6.3%)	3/79 (3.8%)	
Poor Stream	43/48 (89.6%)	70/79 (88.6%)	
Retention	24/48 (50.0%)	27/79 (34.2%)	
Terminal dribbling	23/48 (47.9%)	33/79 (41.8%)	
Urgency	33/48 (68.8%)	54/79 (68.4%)	
Urinary Incontinence	4/48 (8.3%)	2/79 (2.5%)	0.198
Prior Pelvic Radiation	6/48 (12.5%)	9/79 (11.4%)	>0.999
Genitourinary History	33/47 (70.2%)	57/79 (72.2%)	0.837
Bacterial Prostatitis	3/48 (6.3%)	3/79 (3.8%)	
Benign Prostatic Hyperplasia	14/48 (29.2%)	25/79 (31.6%)	
Bladder Neck Contracture	1/48 (2.1%)	1/79 (1.3%)	
Bladder Stones	2/48 (4.2%)	4/79 (5.1%)	
Cystitis	1/48 (2.1%)	4/79 (5.1%)	

Characteristic	Control	Optilume® DCB	p-value
Fistula of Rectum	0/48 (0.0%)	1/79 (1.3%)	
Inflammatory Bowel Disease	0/48 (0.0%)	1/79 (1.3%)	
Kidney Stone	7/48 (14.6%)	15/79 (19.0%)	
Muscle Spasms	2/48 (4.2%)	0/79 (0.0%)	
Other	21/48 (43.8%)	31/79 (39.2%)	
Overactive Bladder	3/48 (6.3%)	8/79 (10.1%)	
Prostate Cancer	5/48 (10.4%)	8/79 (10.1%)	
Unusual Bladder Anatomy	0/48 (0.0%)	1/79 (1.3%)	
Urinary Tract Infection(s)	17/48 (35.4%)	27/79 (34.2%)	
p-values based on unpaired t-test for continuous variables and Fisher's exact test for categorical variables.			

The etiologies of urethral stricture were well matched between groups, with most being iatrogenic (29.6%) or idiopathic (51.2%) in nature (Table 8). Strictures were primarily located in the bulbar urethra (92.1%) and had an average length of 1.7 cm. The average diameter of the urethra at the stricture was 2.4 mm (approx. 7F), which was significantly reduced when compared to the reference normal urethra diameter distal to the stricture (9.3 mm, approx. 28F). Subjects had an average of 3.7 prior dilations at the time of treatment. The number of prior dilations was not significantly different between arms, however the average in the Control group was numerically higher primarily due to a single individual who had 53 prior dilations. The median number of prior dilations was similar between arms (3.0), as was the proportion of subjects with 5 or more prior dilations.

Table 8. Baseline Stricture Characteristics

Stricture Characteristics	Category	Control Arm n/N (%)	Optilume Arm n/N (%)	p-value
Urethral Stricture Etiology	Iatrogenic	16/47 (34.0%)	21/78 (26.9%)	0.566
	Idiopathic	22/47 (46.8%)	42/78 (53.8%)	
	Inflammatory	2/47 (4.3%)	1/78 (1.3%)	
	Traumatic	7/47 (14.9%)	14/78 (17.9%)	
Retention (luminal obliteration)	Obliterated / Near Obliterated	17/47 (36.2%)	26/79 (32.9%)	0.846
	Patent Urethra	30/47 (63.8%)	53/79 (67.1%)	
Anatomic Location	Bulbar	45/47 (95.7%)	71/79 (89.9%)	0.319
	Penile	2/47 (4.3%)	8/79 (10.1%)	
Stricture Length (cm)	n Mean ± SD	47 1.72 ± 0.73	78 1.63 ± 0.76	0.528
Diameter of Urethra at Stricture (mm)	n Mean ± SD	47 2.33 ± 0.88	78 2.46 ± 0.96	0.470

Stricture Characteristics	Category	Control Arm n/N (%)	Optilume Arm n/N (%)	p-value
Diameter of Heathy Urethra at Normal (mm)	n Mean ± SD	48 8.97 ± 2.19	78 9.52 ± 2.33	0.195
Number of Prior Dilations	n Mean ± SD Median Min, Max	48 4.3* ± 7.5 3.0 1, 53	79 3.2 ± 1.7 3.0 2, 10	0.321
	≥5 prior Dilations	10/48 (20.8%)	13/79 (16.5%)	0.636
*Data includes single subject with 53 prior dilations.				

D. Safety and Effectiveness Results

1. Device Sizes Used in the Study

A total of 129 devices were opened or used during 125 procedures., This includes 83 devices opened/used in the randomized cohort, 32 devices used during crossover procedures, and 14 devices used in the pharmacokinetic cohort. Four devices experienced device deficiencies (3 balloon burst and 1 balloon leak) and were replaced, and one was opened but not used (wrong size opened). The device deficiencies did not lead to adverse events.

Table 9. Device Sizes Used.

Balloon Diameter	**Balloon Length**	
	30 mm	**50 mm**
18F (6 mm)	0	0
24F (8 mm)	2	6
30F (10 mm)	33	83
36F (12 mm)	2	2

2. Safety Results

1. Primary Safety Endpoint

The primary safety endpoint was the proportion of subjects experiencing a composite of a serious device or procedure related fistula formation, unresolved de novo stress urinary incontinence, or urethral rupture or burst through 3 months post-procedure. No subjects experienced a primary safety endpoint event through 3 months post-treatment as adjudicated by the independent Clinical Events Committee (CEC).

Table 10. Primary Safety Endpoint Results

Endpoint	Control n/N (%)	Optilume® DCB n/N (%)
Serious device or procedure related complication through 3 months post-treatment	0/48 (0.0%)	0/79 (0.0%)
Formation of Fistula	0/48 (0.0%)	0/79 (0.0%)
Unresolved De Novo Stress Urinary Incontinence	0/48 (0.0%)	0/79 (0.0%)
Urethra Rupture or Burst	0/48 (0.0%)	0/79 (0.0%)

2. Adverse Events

A total of 240 adverse events have been reported in 92 subjects in the randomized cohort, a summary can be found in Table 11. The most common events adjudicated by the Clinical Events Committee as being 'Possibly', 'Probably', or 'Definitely' related to the Optilume® DCB and/or the procedure included post-operative hematuria (11.4%), dysuria (6.3%), and urinary tract infection (6.3%). Adverse event rates and types were generally well matched between arms, with the Optilume arm showing a trend toward higher rates of post-procedure hematuria and dysuria. These events were all mild in nature, and generally resolved within 30 days of onset.

Table 11. Adverse Events by Category for the Randomized Cohort.

Event Types	Control		Optilume® DCB	
	Events	Subjects	Events	Subjects
Any Adverse Events	89	39/48 (81.3%)	151	53/79 (67.1%)
Serious Adverse Events	*8*	*8/48 (16.7%)*	*10*	*9/79 (11.4%)*
Non-serious Adverse Event	*81*	*38/48 (79.2%)*	*141*	*53/79 (67.1%)*
Treatment Related Adverse Events	14	9/48 (18.8%)	47	31/79 (39.2%)
Device Related	*5*	*4/48 (8.3%)*	*35*	*28/79 (35.4%)*
Procedure Related	*9*	*5/48 (10.4%)*	*12*	*10/79 (12.7%)*

Events were coded using the Medical Dictionary for Regulatory Activities (MedDRA) and the renal and urinary events are reported in Table 11 according to System Organ Class (SOC) and Preferred Term (PT). Adverse event rates and types were generally well matched between arms, with the Optilume arm showing a trend toward higher rates of post-procedure hematuria and dysuria. These events were all mild in nature (Common Terminology Criteria for Adverse Events (CTCAE) Severity Grade 1), and generally resolved within 30 days of onset.

Table 12. Renal/Urinary Adverse Events by MedDRA SOC and PT for Randomized Cohort.

System Organ Class/ Preferred Term	Control Arm		Optilume Arm	
	Events	Subjects (N=48)	Events	Subjects (N=79)
Renal and Urinary Disorders	33	31/48 (64.6%)	47	31/79 (39.2%)
Urethral Stenosis	20	20/48 (41.7%)	9	9/79 (11.4%)
Dysuria	1	1/48 (2.1%)	7	7/79 (8.9%)
Urinary Retention	4	4/48 (8.3%)	7	6/79 (7.6%)
Bladder Spasm	2	1/48 (2.1%)	4	4/79 (5.1%)
Urine Flow Decreased	2	2/48 (4.2%)	4	3/79 (3.8%)
Hematuria	1	1/48 (2.1%)	3	3/79 (3.8%)
Lower Urinary Tract Symptoms	2	2/48 (4.2%)	1	1/79 (1.3%)
Terminal Dribbling	0	0/48 (0.0%)	3	3/79 (3.8%)
Urinary Incontinence	0	0/48 (0.0%)	2	2/79 (2.5%)
Bladder Neck Obstruction	0	0/48 (0.0%)	1	1/79 (1.3%)
Detrusor Sphincter Dyssynergia	0	0/48 (0.0%)	1	1/79 (1.3%)
Hypertonic Bladder	0	0/48 (0.0%)	1	1/79 (1.3%)
Pollakiuria	0	0/48 (0.0%)	1	1/79 (1.3%)
Urethral Cancer	0	0/48 (0.0%)	1	1/79 (1.3%)
Urethral Hemorrhage	0	0/48 (0.0%)	1	1/79 (1.3%)
Urethritis	0	0/48 (0.0%)	1	1/79 (1.3%)
Urge Incontinence	1	1/48 (2.1%)	0	0/79 (0.0%)

A summary of events adjudicated by the CEC as related to the device or procedure can be found in Table 13. No events were adjudicated as 'Definitely' related to the Optilume® DCB, while the previously noted trend toward higher rates of mild post-procedural hematuria and dysuria were generally deemed to be 'Possibly' or 'Probably' related to the device.

Table 13. Renal/Urinary Device/Procedure Related Adverse Events by MedDRA SOC and PT.

System Organ Class/ Preferred Term	Control Arm		Optilume Arm	
	Events	Subjects (N=48)	Events	Subjects (N=79)
Renal and Urinary Disorders	5	4/48 (8.3%)	19	16/79 (20.3%)
Dysuria	0	0/48 (0.0%)	5	5/79 (6.3%)
Bladder Spasm	2	1/48 (2.1%)	2	2/79 (2.5%)
Hematuria	0	0/48 (0.0%)	3	3/79 (3.8%)
Urethral Stenosis	1	1/48 (2.1%)	1	1/79 (1.3%)
Urinary Incontinence	0	0/48 (0.0%)	2	2/79 (2.5%)

System Organ Class/ Preferred Term	Control Arm		Optilume Arm	
	Events	Subjects (N=48)	Events	Subjects (N=79)
Urinary Retention	0	0/48 (0.0%)	2	2/79 (2.5%)
Urine Flow Decreased	1	1/48 (2.1%)	1	1/79 (1.3%)
Lower Urinary Tract Symptoms	1	1/48 (2.1%)	0	0/79 (0.0%)
Terminal Dribbling	0	0/48 (0.0%)	1	1/79 (1.3%)
Urethral Hemorrhage	0	0/48 (0.0%)	1	1/79 (1.3%)
Urethritis	0	0/48 (0.0%)	1	1/79 (1.3%)

3. Serious Adverse Events

A summary of all serious adverse events (SAE) categorized by MedDRA version 23.0 System Organ Class and Preferred Term (PT) is given in Table 13. An SAE was defined as any untoward medical occurrence that results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, requires medical/surgical intervention to prevent life-threatening illness or injury or to prevent permanent impairment of a body structure or function, or leads to a congenital anomaly or birth defect.

Serious adverse events were generally infrequent, with no single event type having a significantly higher rate in either arm. Each arm had two events adjudicated as 'Possibly', 'Probably', or 'Definitely' related to the device and/or procedure. These events included complications related to aspiration during anesthesia (one in each arm) and post-procedural urinary tract infection (UTI)/sepsis requiring hospitalization for IV antibiotics (one in each arm).

Table 14. Summary of Serious Adverse Events

System Organ Class/ Preferred Term	Control Arm		Optilume Arm	
	Events	Subjects (N=48)	Events	Subjects (N=79)
Cardiac Disorders	**1**	**1/48 (2.1%)**	**0**	**0/79 (0.0%)**
Bradycardia	*1*	*1/48 (2.1%)*	*0*	*0/79 (0.0%)*
Gastrointestinal Disorders	**0**	**0/48 (0.0%)**	**2**	**2/79 (2.6%)**
Intestinal Infarction	*0*	*0/48 (0.0%)*	*1*	*1/79 (1.3%)*
Abdominal Pain	*0*	*0/48 (0.0%)*	*1*	*1/79 (1.3%)*
General Disorders and Administration Site Conditions	**0**	**0/48 (0.0%)**	**1**	**1/79 (1.3%)**
Non-Cardiac Chest Pain	*0*	*0/48 (0.0%)*	*1*	*1/79 (1.3%)*
Infections and Infestations	**2**	**2/48 (4.2%)**	**2**	**2/79 (2.5%)**
COVID-19	*0*	*0/48 (0.0%)*	*1*	*1/79 (1.3%)*
COVID-19 Pneumonia	*1*	*1/48 (2.1%)*	*0*	*0/79 (0.0%)*
Sepsis	*1*	*1/48 (2.1%)*	*0*	*0/79 (0.0%)*

System Organ Class/ Preferred Term	Control Arm		Optilume Arm	
	Events	Subjects (N=48)	Events	Subjects (N=79)
Urinary Tract Infection	*0*	*0/48 (0.0%)*	*1*	*1/79 (1.3%)*
Injury, Poisoning and Procedural Complications	**1**	**1/48 (2.1%)**	**0**	**0/79 (0.0%)**
Anesthetic Complication Pulmonary	*1*	*1/48 (2.1%)*	*0*	*0/79 (0.0%)*
Nervous System Disorders	**2**	**2/48 (4.2%)**	**0**	**0/79 (0.0%)**
Intracranial Aneurysm	*1*	*1/48 (2.1%)*	*0*	*0/79 (0.0%)*
Thalamus Hemorrhage	*1*	*1/48 (2.1%)*	*0*	*0/79 (0.0%)*
Renal and Urinary Disorders	**2**	**2/48 (4.2%)**	**1**	**1/79 (1.3%)**
Urinary Retention	*2*	*2/48 (4.2%)*	*0*	*0/79 (0.0%)*
Urethral Cancer	*0*	*0/48 (0.0%)*	*1*	*1/79 (1.3%)*
Respiratory, Thoracic, Mediastinal Disorders	**0**	**0/48 (0.0%)**	**3**	**3/79 (3.8%)**
Pulmonary Embolism	*0*	*0/48 (0.0%)*	*1*	*1/79 (1.3%)*
Lung Adenocarcinoma	*0*	*0/48 (0.0%)*	*1*	*1/79 (1.3%)*
Pneumonia Aspiration	*0*	*0/48 (0.0%)*	*1*	*1/79 (1.3%)*
Surgical and Medical Procedures	**0**	**0/48 (0.0%)**	**1**	**1/79 (1.3%)**
Colectomy	*0*	*0/48 (0.0%)*	*1*	*1/79 (1.3%)*
Total	**8**	**8/48 (16.7%)**	**10**	**9/79 (11.4%)**

3. PRIMARY EFFICACY ENDPOINT

The primary efficacy endpoint was a comparison of the rate of subjects free from stricture recurrence through 6 months post-procedure. This endpoint was evaluated by the ability to pass a 16F flexible cystoscope or a 14F rubber catheter through the treated area at 6 months post-treatment. If a 16F scope was unable to pass, a 14F rubber catheter was attempted. If at least one of the stated instruments was able to pass through the treated area, the subject was considered a success for this endpoint. If neither instrument could pass through the treated area, the subject was considered a failure. Any subjects who have a second dilation procedure, pursue surgical intervention, or otherwise seek alternative treatment for the target stricture prior to the close of the 6-month visit window are considered treatment failures for the primary analysis.

Subjects crossing over from the Control arm to receive treatment Optilume® DCB or any subject in either arm receiving alternative therapy prior to 240 days (6-month window +30d) were considered a failure for this endpoint. The difference between arms was estimated using multiple imputation for missing values. The primary endpoint was met, with an estimated difference of 44.4% between groups at 6 months ($p<0.0001$).

Table 15: Primary Efficacy Endpoint – ITT, Multiple Imputation

Variable	Difference [95% CI]
Stricture free defined as the ability to pass a 16Fr flexible cystoscope or a 14Fr rubber catheter at 6 months post-treatment	44.4% [27.6% – 61.1%]
P-value	<0.0001
P-value is based on two-sample continuity corrected Chi-square test utilizing a weighted Z-score.	

A Complete Case assessment was conducted as a further sensitivity analysis, utilizing only observed values to calculate the difference between arms. (Complete Case analysis utilizes only the cases in a data set for which there are no missing values on any of the variables, i.e., observed data only with no imputation of missing outcomes.) The observed difference between arms was 47.8%, which is consistent with the estimated difference from the primary analysis. The primary efficacy endpoint was 74.6% in the Optilume® DCB arm and 26.8% in the standard-of-care Control arm. The Optilume® DCB showed statistical superiority to standard-of-care endoscopic management in maintaining freedom from stricture recurrence through 6 months post-treatment (p<0.001).

Table 16. Primary Efficacy Endpoint Results (Complete Case)

Endpoint	Control (n=48)	Optilume® DCB (n=79)	Difference [95% CI]	p-value
Proportion of Subjects Stricture Free	26.8% (11/41)	74.6% (50/67)	47.8% [28.6% – 66.9%]	<0.0001
p-value is based on two-sample continuity corrected Chi-square test. A total of 19 subjects are missing the primary endpoint assessment in the randomized cohort. The rate of missing primary endpoint data was balanced between arms, with 12 (15.2%) in the Treatment arm and 7 (14.6%) in the Control arm. Five (5) subjects missed their 6-month visit due to COVID concerns, 6 subjects had their 6-month visit done remotely due to site or government COVID policy, 4 subjects withdrew from the study prior to the 6-month visit, and 4 subjects missed their 6-month visit for reasons not known to be directly related to COVID.				

Hypothesis Tested Secondary Endpoints

i. Time to Treatment Failure

A hypothesis tested time-to-event analysis comparing time to treatment failure was

conducted. Treatment failure was defined as a subject receiving additional treatment of the study stricture or subject having been confirmed to have stricture recurrence (unable to pass 16F cystoscope or 14F catheter) through 240 days post-procedure. The Optilume® DCB was superior to standard-of-care in time to treatment failure (p<0.0001).

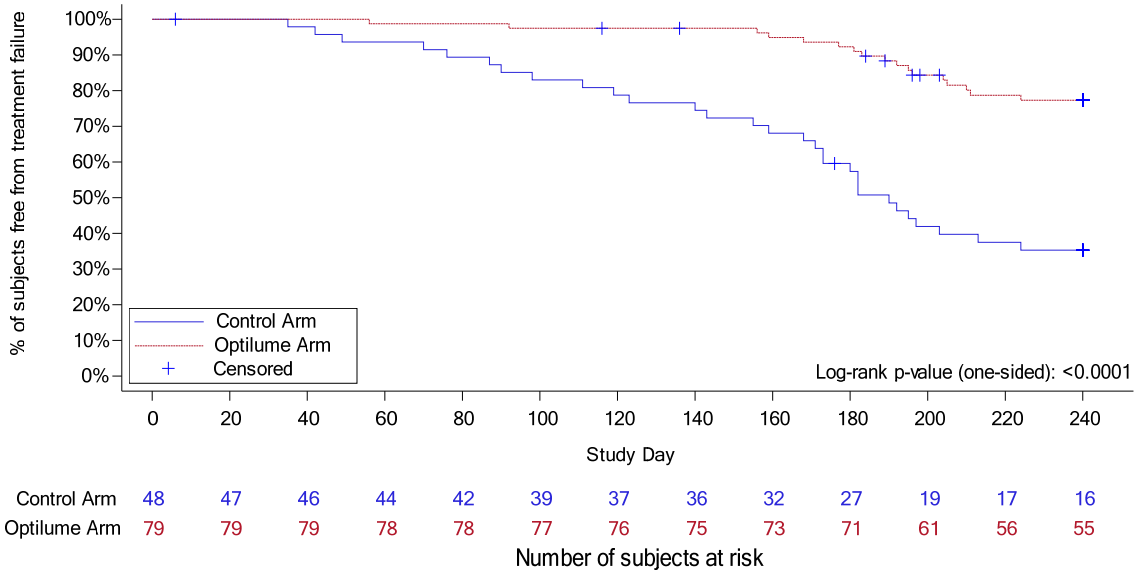

Figure 4. Kaplan-Meier Plot of Freedom from Treatment Failure Through 6 Months

ii. Change in Qmax at 6 Months

The change in Qmax at 6 months post-treatment was compared between arms. The Optilume® DCB showed a significantly higher increase in Qmax at 6 months compared to Control, with a point estimate for the difference between arms of +4.78 mL/sec favoring the Optilume arm (p=0.0031). Missing data was imputed via multiple imputation.

Table 17. Change in Qmax at 6 Months (ITT, Multiple Imputation)

Variable	Point Estimate of Difference [90% CI]
Change in Qmax	+4.78 [1.94, 7.61]
P-value (one-sided)	<0.0031
P-value is based on independent samples t-test.	

iii. Percent Responder at 12 Months (IPSS)

The rate of therapeutic responders, defined as subjects with an improvement of ≥50% from baseline in IPSS score, in the Optilume arm was compared against a performance goal of 50%. Subjects experiencing a treatment failure (Urethral Lumen Test, ULT failure or repeat treatment) were considered failures for this endpoint, while responder status for subjects missing IPSS scores at 1 year was imputed using multiple imputation with a linear regression model.

The point estimate of the responder rate at 12 months utilizing the multiple imputation approach was 59.6%, with the lower bound of the 90% confidence interval of 49.9% not meeting the pre-specified performance goal of 50% (p=0.051).

Table 18. Secondary Endpoint 3 – Responder Rate at 12 Months (ITT, Multiple Imputation)

Endpoint	Optilume Arm (N=79)
IPSS improvement of ≥ 50% from baseline at 1 Year	
% (90% CI)	59.6% (49.9%, 69.3%)
P-value	0.0514
A linear regression model was used to impute 1-year IPSS for those missing data. One-sided p-value for hypothesis test against a performance goal of 50%.	

Ancillary Endpoints

i. Change in IPSS Over Time

Table 19 provides the change in International Prostate Symptom Scores (IPSS) scores for both arms using a Failure Carried Forward analysis. Failure Carried Forward is a data analysis method which carries forward the worst value observed during follow-up for those who experienced treatment failure.

Table 19: IPSS Over Time (Failure Carried Forward)

Study Arm	Baseline	30-Day	3-Month	6-Month	1-Year
Control Arm					
n	47	47	45	43	42
Mean ± SD	22.8 ± 6.97	9.5 ± 7.40	12.4 ± 9.17	15.4 ± 9. 57	19.9 ± 7.46
Median	22.0	7.0	11.0	14.0	18.5
Min, Max	11, 35	1, 35	0, 35	1, 35	7, 35
Optilume Arm					
n	79	78	74	71	67
Mean ± SD	22.0 ± 6.78	7.6 ± 5.70	7.4 ± 5.76	8.3 ± 6.15	9.0 ± 7.12
Median	22.0	6.0	6.0	8.0	8.0
Min, Max	11, 35	0, 26	0, 24	0, 26	0, 26

ii. Percent Responder Over Time

Table 20 provides the percent responder over time using the failure carried forward analysis. An International Prostate Symptom Scores (IPSS) responder is defined as a subject with a ≥50% improvement in IPSS.

Table 20. IPSS Responder (≥50% Improvement) Over Time (Failure Carried Forward)

Study Arm	30-Day	3-Month	6-Month	1-Year
Control				
n/N (%)	28/47 (59.6%)	21/45 (46.7%)	12/43 (27.9%)	1/42 (2.4%)
90% CI	46.5%, 71.7%	33.8%, 59.9%	17.0%, 41.3%	0.1%, 10.8%
Optilume® DCB				
n/N (%)	57/78 (73.1%)	56/74 (75.7%)	50/71 (70.4%)	39/67 (58.2%)
90% CI	63.6%, 81.2%	66.1%, 83.6%	60.3%, 79.2%	47.4%, 68.4%
Confidence intervals (CI) are estimated using the Clopper-Pearson (exact) approach. Improvement from baseline is calculated by subtracting post-baseline values from baseline values.				

iii. Peak Flow Rate (Qmax) Over Time

Table 21 provides the peak flow rate (Qmax) values for both groups using the failure carried forward analysis.

Table 21. Peak Flow Rate Over Time (Failure Carried Forward)

Study Arm	Baseline	30-Day	3-Month	6-Month	1-Year
Control Arm					
n	47	44	39	44	41
Mean ± SD	7.4 ± 3.5	15.8 ± 8.5	13.3 ± 9.3	11.1 ± 7.6	7.6 ± 4.0
Median	7.9	14.8	11.4	9.9	7.5
Min, Max	0.0, 14.5	1.3, 38.5	0.0, 41.9	0.0, 31.2	0.0, 14.8
Optilume Arm					
n	78	75	71	67	65
Mean ± SD	7.6 ± 3.4	18.3 ± 9.1	18.6 ± 10.9	16.6 ± 8.9	15.5 ± 9.0
Median	7.2	17.4	15.1	15.0	13.5
Min, Max	0.0, 14.9	1.6, 44.4	1.6, 54.0	1.6, 48.5	1.6, 48.8

iv. Post Void Residual (PVR) Urine Volume

Table 22 provides the PVR for both treatment arms using the failure carried forward analysis.

Table 22. Post Void Residual Volume Over Time (Failure Carried Forward)

Study Arm	Baseline	30-Day	3-Month	6-Month	1-Year
Control Arm (N=48)					
n	46	45	41	44	42
Mean ± SD	133.8 ± 155.1	79.1 ± 87.3	113.4 ± 124.2	141.4 ± 194.1	181.5 ± 201.7
Median	76.0	43.0	59.0	90.5	128.0
Min, Max	0, 703	0, 402	0, 467	0, 999	0, 999
Optilume Arm (N=79)					
n	77	75	70	67	66
Mean ± SD	109.8 ± 116.9	75.6 ± 86.2	103.4 ± 134.4	73.1 ± 117.7	94.6 ± 121.79
Median	60.0	39.0	54.0	30.0	50.5
Min, Max	0, 557	0, 378	0, 650	0, 634	0, 546

v. Rate of Acute Urinary Retention Through 6 Months

The rate of acute urinary retention (AUR) events requiring catheterization that occurred prior to the close of the 6-month window was evaluated using the ITT analysis population.

Table 23. Rate of Acute Urinary Retention Requiring Catheterization Through 6 Months (ITT)

Endpoint	Control Arm (N=48)	Optilume Arm (N=79)	Difference (95% CI)
Rate of acute urinary retention requiring catheterization by 6 months	3/48 (6.3%)	1/79 (1.3%)	-5.0% (-22.7%, 12.9%)
Confidence Intervals (CI) for the difference are estimated using the exact approach.			

vi. Freedom from Repeat Intervention Over Time

Repeat intervention in this study included repeated dilation of the study stricture with sounds, balloon dilation (including crossover treatment with Optilume® DCB), Direct Visual Internal Urethrotomy (DVIU), and urethroplasty. Kaplan-Meier estimates of freedom from repeat intervention was 83.2% in the Optilume arm compared to 21.7% in the Control arm. In this analysis, completed using the ITT population, subjects were censored at the time of their last visit or at 395 days, whichever is earliest. Censoring these subjects at the date of the snapshot or 395 days results in point estimates of 86.3% for Optilume and 23.1% for Control.

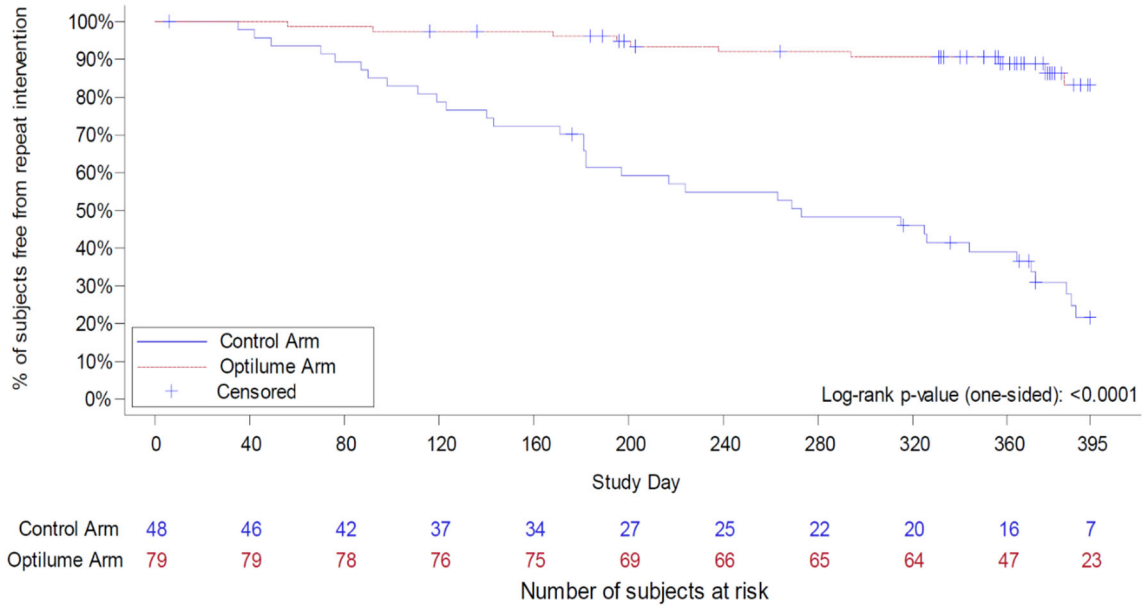

Figure 5. Kaplan Meier Curve for Freedom from Repeat Intervention (ITT)

vii. Change in Erectile Function

The impact of study treatment of erectile function was assessed utilizing the International Index for Erectile Function (IIEF) questionnaire. The IIEF is a validated 5-part, 15 item questionnaire that evaluates erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction. The 'Overall Satisfaction' (OS) score ranges from 2-10, with higher scores indicating higher satisfaction. Using the Complete Case analysis, there was no change in the OS score from baseline to 1 year follow-up for either arm, indicating there is no impact on patient reported sexual function by either the Optilume® DCB or standard of care endoscopic treatments.

4. SUBGROUP ANALYSIS

a. Crossover Population

Baseline characteristics for the Crossover cohort were generally similar to the randomized cohort with the notable exception being that subjects had an average number of prior treatments of 5.9 compared to 3.2 in the randomized Optilume arm. Excluding the single subject with 60 prior dilations the average falls to 4 prior dilations in the Crossover cohort, which as expected is 1 more than the average in the randomized cohort (i.e. addition of index Control procedure).

Procedure characteristics for the Crossover cohort are similar to the Randomized cohort, with most subjects (87%, 28/32) receiving pre-dilation with an uncoated balloon. Similar to the randomized cohort most subjects (91%, 29/32) received a 30F diameter DCB.

b. Primary Efficacy Endpoint – Stricture Free Rate at 6 Months

The ability to pass a 16F flexible cystoscope or 14F rubber catheter was evaluated at 6 months post crossover to treatment with the Optilume® DCB. The proportion of subjects with anatomical success in the Crossover cohort was comparable to that in the Randomized cohort (59.3% (16/27) vs 74.6% (50/67)).

c. Secondary Efficacy Endpoint 1 – Time to Treatment Failure

The time to treatment failure (ULT failure, repeat treatment) was compared for crossover subjects after their randomized therapy (Control) to the time to treatment failure after receiving the Optilume® DCB. Overall, stricture recurrence occurred more quickly after Control therapy as compared to after Optilume® DCB therapy within individual subjects receiving both.

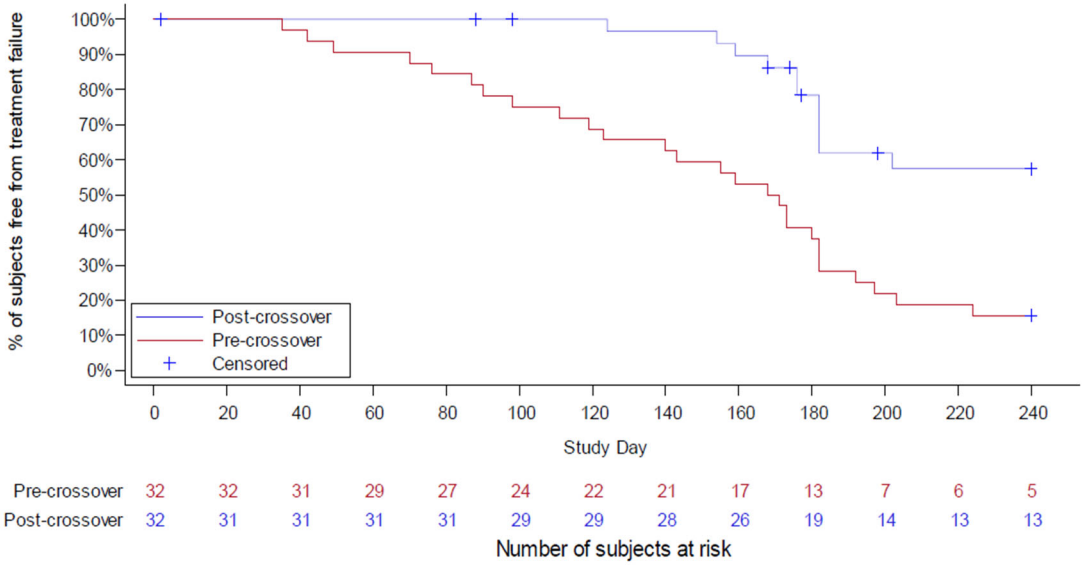

Figure 6. Time to Treatment Failure for Crossover Subjects Receiving Initial (Control) Therapy and Optilume® DCB

The change in Q_{max} at 6 months and responder rate at 12 months were not measured for the crossover cohort.

d. Ancillary Efficacy Endpoints

Ancillary results for the crossover cohort were consistent with the pivotal study cohort.

5. PHARMACOKINETIC SUB-STUDY

A sub-study including 15 non-randomized subjects was conducted to determine the pharmacokinetic profile of paclitaxel in blood (plasma), urine, and semen after treatment

with the Optilume® DCB. Determination of plasma paclitaxel concentration was evaluated immediately after completion of the procedure, at 1, 3, and 5 hours, and at Foley removal, 30 days, 3 months, and 6 months post-procedure. Urine paclitaxel concentration was evaluated immediately post-procedure, at Foley removal, and at 30 days, 3 months, and 6 months. Semen paclitaxel concentration was evaluated at 30 days, 3 months, and 6 months post-procedure. Clinical follow-up without additional pharmacokinetic sampling will continue through 5 years post-procedure.

A summary of pharmacokinetic parameters, including maximum concentration (C_{max}) and time to maximum concentration (T_{max}) for plasma is in Table 17. Paclitaxel concentration over time in urine and semen can be found in Table 18 and Table 19, respectively. On average, paclitaxel concentration in plasma fell below the limit of quantitation of the method (0.10 ng/mL or 0.1 part per billion) by 5 hours post-procedure, while average paclitaxel concentration in urine fell below the limit of quantitation by 30 days. The average paclitaxel concentration in semen was near the limit of quantitation (0.12 ng/mL) by 6 months.

Table 17. Summary of Plasma Pharmacokinetic Parameters

Parameter	**Plasma**
C_{max} (ng/mL) n Mean Min, Max	 15 0.12 ± 0.15 <0.10, 0.52
T_{max} (hr) n Median Min, Max	 15 0.25 ± 0.96 0.25, 3

Table 18. Paclitaxel concentration over time in urine

Measure	**Urine Concentration (ng/mL)**					
	Baseline	**0hr**	**Foley Removal**	**30 Days**	**3 Months**	**6 Months**
Mean ± St Dev	<0.1 ± 0.0	414.4 ± 484.8	13.8 ± 14.6	<0.1 ± 0.0	<0.1 ± 0.0	<0.1 ± 0.0
Median	<0.1	231.0	11.1	<0.1	<0.1	<0.1
Max, Min	<0.1	1940, 46.4	54.4, 0.9	0.18, <0.1	<0.1	<0.1
Subjects with Measurable Amt	0/15 (0.0%)	15/15 (100.0%)	15/15 (100.0%)	4/15 (26.7%)	0/15 (0.0%)	0/14 (0.0%)

Table 19. Paclitaxel concentration over time in semen

Measure	Semen Concentration (ng/mL)			
	Baseline	30 Days	3 Months	6 Months
Mean ± St Dev	<0.10 ± 0.00	2.99 ± 4.88	0.48 ± 0.98	0.12 ± 0.23
Median	<0.10	0.27	<0.10	<0.10
Max, Min	<0.10	17.60, <0.10	3.45, <0.10	0.85, <0.10
Subjects with Measurable Amt	0/14 (0.0%)	9/15 (60.0%)	5/13 (38.5%)	1/12 (8.3%)

6. PEDIATRIC EXTRAPOLATION

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

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 81 investigators of which none were full-time or part-time employees of the sponsor, and two had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described in Table 20.

Table 20: Disclosable Financial Interest/Arrangements

Compensation to the investigator where the value could be influenced by the outcome of the study	None of the Investigators
Significant payment of other sorts	Two Investigators
Proprietary interest in the product tested held by the Investigator	None of the Investigators
Significant equity interest held by the Investigator in sponsor of covered study	None of the Investigators

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. The information provided does not raise any questions about the reliability of the data.

XI. SUMMARY OF ANCILLARY CLINICAL STUDIES

A. ROBUST I Study

ROBUST I was a prospective, multicenter, single arm study evaluating the safety and efficacy of the Optilume® DCB in recurrent anterior urethral strictures. A total of 53 subjects were enrolled at 4 investigational centers in Panama and the Dominican Republic. Key eligibility criteria included anterior urethral strictures ≤2 cm in length with 1-3 prior dilations. Subjects with prior urethroplasty, Lichen Sclerosis, penile implants or artificial urinary sphincters, and prior pelvic radiation were excluded. Follow up is planned through 5 years post-treatment.

Study strictures were an average of 0.9 cm in length, with an average of 1.7 prior dilations. Subject follow-up is complete through 3 years. Subjects experienced immediate and sustained functional and symptomatic improvement as measured by the IPSS questionnaire, Patient Reported Outcome Measure (PROM) questionnaire, and Qmax. Freedom from stricture recurrence was measured by the ability to pass a 16F flexible cystoscope and was 75% (36/48) at 6 months and 77% (36/47) at 12 months. Freedom from repeat intervention was 77% (33/43) at 3 years.

Table 21: ROBUST I Efficacy Results

Measure	Baseline	3 Months	6 Months	1 Year	2 Years	3 Years
IPSS Mean ± SD n	25.2 ± 4.5 (53)	6.1 ± 7.6 (51)	4.6 ± 5.2 (45)	4.5 ± 3.9 (40)	6.9 ± 7.7 (38)	5.5 ± 6.9 (33)
IPSS QoL Mean ± SD n	4.9 ± 0.9 (53)	0.8 ± 1.3 (51)	0.7 ± 0.9 (45)	0.7 ± 0.9 (40)	0.9 ± 1.5 (38)	0.7 ± 1.2 (33)
Qmax (mL/sec) Mean ± SD n	5.0 ± 2.6 (46)	22.2 ± 12.5 (51)	19.8 ± 10.8 (45)	20.1 ± 10.0 (39)	17.5 ± 10.4 (38)	15.1 ± 8.3 (33)
PVR (mL) Mean ± SD n	141.4 ± 105.1 (43)	36.5 ± 37.7 (51)	30.0 ± 42.8 (45)	24.6 ± 32.1 (39)	45.5 ± 49.5 (38)	50.2 ± 62.5 (33)

The primary safety endpoint was a composite of device and procedure-related serious complications at 3 months including formation of urethral fistula, de novo severe urinary retention lasting >14 days, unresolved de novo stress urinary incontinence, and urethra rupture or burst. None of the subjects experienced such an event (0/53, 0.0%). Treatment related complications were mild and consisted of common events experienced after urological procedures such as post-procedural hematuria, urinary tract infection, and dysuria.

B. ROBUST II Study

ROBUST II is a prospective, multi-center, single arm study evaluating the safety and early feasibility of the Optilume® DCB. Subject follow-up is complete through 2 years. A total of

16 subjects were enrolled at 5 investigational centers. Key eligibility criteria were similar to ROBUST I with the exception of allowing stricture length up to 3cm and requiring a minimum of 2 prior endoscopic treatments of the stricture.

Study strictures were an average of 2.1cm in length and had an average of 4.1 prior dilations. Freedom from stricture recurrence at 6 months was 73% (11/15), as measured by the ability to pass a 16F flexible cystoscope through the treated area.

Table 22: ROBUST II Efficacy Results

Measure	Baseline	3 Months	6 Months	1 Year	2 Years
IPSS Mean ± SD n	18.4 ± 4.9 (16)	7.5 ± 6.4 (16)	7.0 ± 6.7 (14)	6.0 ± 6.1 (9)	4.2 ± 4.1 (9)
IPSS QoL Mean ± SD n	4.4 ± 1.3 (16)	1.8 ± 1.8 (16)	1.6 ± 1.5 (14)	1.4 ± 1.5 (9)	1.2 ± 1.2 (9)
Qmax (mL/sec) Mean ± SD n	6.9 ± 3.7 (16)	18.9 ± 16.4 (15)	17.5 ± 9.4 (13)	20.8 ± 9.1 (9)	25.4 ± 26.1 (8)
PVR (mL) Mean ± SD n	187.1 ± 227.1 (16)	79.3 ± 80.3 (15)	64.1 ± 40.2 (14)	66.4 ± 57.5 (9)	65.5 ± 79.3 (8)

No subject met the primary safety composite endpoint of formation of urethral fistula, new strictures requiring intervention, unresolved de novo stress urinary incontinence, and urethra rupture or burst at 3 months.

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

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Gastroenterology-Urology Devices 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 PRE-CLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The ROBUST III trial met its primary effectiveness endpoint for freedom from stricture recurrence, demonstrating superiority of the Optilume® DCB against SOC endoscopic management. Secondary effectiveness endpoints showed superiority of the Optilume® DCB against SOC endoscopic management in time to treatment failure and superiority in the increase in peak urinary flow rate through 6 months post-procedure. Evidence from the ROBUST I and ROBUST II studies indicate the treatment effect of the Optilume® DCB remains durable through 3 years post-treatment.

B. Safety Conclusions

The safety of the device was evaluated utilizing non-clinical bench testing, preclinical animal studies, as well as in three clinical studies as described above. Bench and preclinical testing showed a reasonable assurance that the device is safe and will perform as intended. The Optilume® DCB device met its primary safety endpoint in the ROBUST III trial, with no subjects meeting the pre-specified composite safety endpoint. Review of safety data from the entire ROBUST clinical program did not detect a significant safety signal with respect to rare or long-term adverse device or drug effects. These results support the safety of the Optilume® DCB for the treatment of anterior urethral strictures.

C. Benefit-Risk Conclusions

The probable benefits of the device are based on data collected in a clinical study conducted to support PMA approval as described above. The probable benefit of maintaining urethral patency outweighs the probable risks of the mild adverse events such as hematuria, UTI and urinary retention of short duration and the risk of persistent paclitaxel in the semen associated with the use of the device.

The rate of subjects free from stricture recurrence at 6 months for the Optilume® DCB catheter is superior to the standard of care endoscopic methods, with a difference of 44.4% (P-value <0.0001, ITT, Multiple Imputation, [95% CI, 27.6%, 61.1%]). Analysis of the ITT population via a Complete Case assessment resulted in a difference of 47.8% (P-value <0.0001, [95% CI, 28.7%, 66.9%]) between the two arms (Control Arm = 26.8% vs. Optilume Arm = 74.6%). (No subjects experienced a primary safety endpoint event, defined as freedom from device/procedure related composite serious complications at 3 months, including formation of fistula, unresolved de novo stress urinary incontinence, or urethra rupture or burst.)

Patient Perspectives:

This submission did not include specific information on patient perspectives for this device.

In conclusion, given the available information above, the data support that for device indication (stated above) the probable benefits outweigh the probable risks.

D. Overall Conclusion

The data in this PMA application support with reasonable assurance the safety and effectiveness of the Optilume® DCB when used in accordance with the instructions for use.

XIV. CDRH DECISION

CDRH issued an approval order on December 3, 2021. The final clinical conditions of approval cited in the approval order are described below.

The applicant must conduct the following post-approval studies:

1. The ROBUST-LT post-approval study (PR1277-001rA, received in a November 8, 2021

email) is a continuation of the ROBUST clinical program and is designed to verify the continued safety and effectiveness for the Optilume® Urethral Drug-Coated Balloon (DCB). It is intended to assess durability of outcomes after 6-months follow-up of the 194 patients currently enrolled in the ROBUST clinical program. Each patient's follow-up will be continued out to 5 years post-treatment. Each of the studies in the ROBUST clinical program defined various endpoints within the study protocol and statistical analysis plan for each study. Individual study reports will continue to be generated and written in accordance with the endpoint definitions specified in their respective protocols and statistical analysis plans. In addition, the analysis plan will harmonize endpoint definitions and data handling rules that will be utilized in program wide analyses and reported in a separate summary report. The harmonized primary effectiveness endpoint is defined as a patient experiencing a ≥30% improvement in International Prostate Symptom Score (IPSS) from baseline without the need for additional intervention. Additional harmonized endpoints include freedom from repeat intervention, uroflowmetry, IPSS, adverse event summary, and International Index of Erectile Function (IIEF). The primary safety endpoint is mortality rate that will be calculated for each study and reported as the number of deaths per 100 patient years. All adverse event (AE) data will be collected. Progress reports will be submitted to the FDA annually after PMA approval.

2. The "Post-market Study Evaluating the Safety and Efficacy of the Optilume® Urethral Drug Coated Balloon in a Real-World Setting" study (PR1276, v 0.2, received in a November 8, 2021 email) is a prospective, single arm, multi-center, post market clinical trial evaluating the continued safety and effectiveness for Optilume® Urethral DCB in a real-world clinical use. The study will enroll 150 patients at up to 15 sites in the European Union. The study will be open to men 18 years of age or older who meet the selection criteria. Clinical follow-up will be conducted at 3-, 6- and 12-months post-procedure, and annually thereafter through 5 years. The primary effectiveness endpoint is the responder rate, defined as the proportion of subjects experiencing a ≥30% improvement in symptom scores without repeat intervention, at 12 months. The responder rate will be compared against a performance goal of 60% at 1 year. Ancillary endpoints include freedom from repeat intervention, improvement in IPSS over time, and improvement in urethral stricture surgery patient-reported outcome measure (USS-PROM) over time. The primary safety endpoint is freedom from treatment-related serious adverse events (SAE) through 3 months post-treatment. The ancillary safety endpoints include frequency and severity of device/procedure-related adverse events (AE).

3. The "Evaluation of the Impact of the Optilume® Urethral Drug Coated Balloon on Semen Characteristics Post-Treatment" study (PR1275 v0.1, received in a November 8, 2021 email) is a single-arm, prospective study assessing semen quality after treatment with the Optilume® Urethral DCB in men younger than 55 years of age. The objective of the study is to determine if treatment with the Optilume® Urethral DCB negatively impacts semen characteristics in men with normal baseline semen characteristics. The study will enroll 34 patients at up to 5 sites in the United States and will be open to male subjects between 22 and 55 years of age who meet the selection criteria. Semen quality parameters will be

assessed at baseline, 3 months, and 6 months post-treatment. Parameters will include ejaculate volume (mL), sperm concentration (million/mL), total sperm per ejaculate (million), motility (% of sperm that is motile), progressive motility (%), and morphology (% normal). Values at each timepoint will be the average of two samples collected within 1-2 weeks of each other. Clinical follow-up will be conducted at 30 days, 3 months, 6 months, and 12 months post-treatment evaluating Lower Urinary Tract Symptoms (LUTS), sexual function, and voiding function. There is no hypothesis tested effectiveness endpoint. Ancillary effectiveness endpoints include improvement in International Prostate Symptom Score (IPSS) over time, and improvement in maximal flow rate (Qmax) and post-void residual volume (PVR) over time. The primary safety endpoint is the average change in sperm concentration from baseline. Secondary safety endpoints include proportion of subjects experiencing ≥50% decrease in sperm concentration from baseline, change in semen characteristics from baseline, change in erectile function and overall satisfaction IIEF sub-scores, and device/-procedure--related adverse events.

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.