STUDY TITLE	**The ALPFA Medical BPH Pivotal Study** A Prospective Randomized Pivotal Trial of the ALPFA Medical Prostate Ablation System Compared with Cystoscopy in Men with Symptomatic Benign Prostatic Hyperplasia
SPONSOR	ALPFA MEDICAL, INC. 1880 EMBARCARDERO ROAD PALO ALTO, CA 94303 USA PHONE: 669.257.3263
OBJECTIVE	The primary objective of this study is to establish the safety and effectiveness of the ALPFA BPH PFA System for treating symptomatic BPH.
STUDY DESIGN	• Prospective, double-blind, 2:1 randomized, sham-control (flexible cystoscopy), 3-month crossover. • ~250 subjects at ~30 qualified sites in the US, Canada, and Europe. • Follow-up at Discharge, Day 14, 30, 90, 180, 360 days, then 2, 3, 4, 5 years post-procedure
PRIMARY ENDPOINTS	There are two (2) co-primary effectiveness endpoints for this study as follows, both of which must pass in order for the trial to be considered successful: 1. IPSS responder rate at 3 months in the Treatment group compared to the Control. A responder is defined as a subject who has an IPSS improvement of ≥30% at 3-months post-treatment compared to baseline. 2. Demonstrate durability of treatment effect with the ALPFA BPH PFA System at 12 months, defined as Treatment subject mean change in IPSS from baseline to 12 months.
OTHER OUTCOMES	1. Evaluate the change in BPH symptoms measured by IPSS changes between Treatment and Control groups at 3-month post-procedure. a. Test of difference b. Test of superiority by a 25% relative margin (“super-superiority”) Change in Qmax from Baseline to 3 months between Treatment and Control.

INCLUSION CRITERIA	Study subjects are required to meet all the following inclusion criteria to participate in this study as determined by the Investigator: 1. ≥ 40 years of age on the day of enrollment. 2. Symptomatic BPH meeting all the following criteria determined within 30 days preceding enrollment and after fulfilling the concomitant medication washout period(s): a. Symptom Score: Baseline IPSS score ≥13, with an IPSS voiding/storage ratio >1 b. Flow Rate: Single uroflow test with a minimum voided volume ≥ 125 mL and a Qmax ≥ 5 mL/sec and ≤ 12 mL/s c. Residual: ultrasound-determined PVR of ≤ 250 mL 3. Prostate size 25-120 g, measured by transrectal ultrasound. Willing and able to provide consent and comply with study requirements.
EXCLUSION CRITERIA	Subjects will be excluded from the study if they meet any one of the following exclusion criteria, as determined by the Investigator: 1. Medical conditions that would prevent participation in the study, interfere with assessment or therapy, significantly raise the risk of study participation, or confound data or its interpretation, including but not limited to: a. Cardiovascular: i. History of clinically significant heart failure (NYHA III/IV) ii. Uncontrolled arrhythmia. iii. Stroke, TIA, myocardial infarction, unstable angina, percutaneous coronary intervention, or any cardiac surgery within 180 days of enrollment. iv. Uncontrolled hypertension b. Renal: Serum creatinine > 2.0 mg/dL or any history of renal dialysis or renal transplant. c. Metabolic: Clinically uncontrolled diabetes mellitus or a baseline HbA1c ≥ 8.0%, or clinically significant liver disease. d. Non-urologic cancer: Active malignancy, or within 3 years of enrollment, a history of treated malignancy

	now in full remission, except basal cell or squamous cell carcinoma of the skin. e. Respiratory: Severe lung disease or respiratory illness requiring hospitalization. f. Immunosuppression: Known immunosuppression, including but not limited to AIDS, immunosuppressive medication, or current chemotherapy. g. Transplant: Solid organ or hematologic transplant or currently being evaluated for an organ transplant. h. Substance abuse: Active alcoholism or drug addiction. 2. Urologic conditions that would prevent participation in the study, interfere with assessment or therapy, significantly raise the risk of study participation, or confound data or its interpretation, including but not limited to: a. Operative: Previous prostate surgery or interventional procedure, including but not limited to BPH surgery, radiation, laser, prostate arterial embolism, balloon dilatation, or hyperthermic treatment. b. Infection: Active urinary tract infection at the time of the Index Procedure (may be treated and enrolled upon negative urine culture). c. Incontinence: History of urinary incontinence. d. Retention: Requires indwelling catheter or intermittent catheterization to void or had an episode of spontaneous urinary retention within 30 days of enrollment. e. Prostatitis: History of prostatitis within 2 years of enrollment. f. Cystolithiasis: Active bladder stones g. Neurogenic bladder: Neurogenic or atonic bladder or sphincter, including etiologies of uncontrolled diabetes, Parkinson's disease, multiple sclerosis, cerebrovascular accident, or polyneuropathy. h. Anatomic abnormality: Prior or current urethral stricture, meatal stenosis, bladder neck contracture or other urologic anatomic abnormalities that would interfere with planned treatment or confound subsequent assessment.

	i. Implants: Any urinary tract implants including stents, sutures, penile implants, or artificial sphincters. 3. Bladder cancer: Actively being treated or suspected cancer of the bladder. 4. Prostate cancer: a. Confirmed or history of prostate cancer b. A PSA value > 10 ng/mL within 30 days of enrollment c. If PSA is between 4.5 ng/mL and 10 ng/mL, prostate cancer must be ruled out via an MRI study (≤ PIRADS-3), unless negative prostate biopsy prior to enrollment or negative MRI (≤ PIRADS-3) within the past 12 months 5. Prior pelvic or rectal interventions: a. Previous pelvic irradiation or radical pelvic surgery b. Previous rectal surgery (other than hemorrhoidectomy) or a history of rectal disease that may be impacted by Index Procedure. 6. Peri-procedural anticoagulation: Unable to stop anti-platelet or anticoagulation treatment for the Index Procedure per site standard of care. 7. Subjects who cannot or will not comply with the following washout medication requirements within the time period specified prior to enrollment: a. 24-Hours: i. Taking phenylephrine or pseudoephedrine within 24 hours of the Baseline evaluation and Index Procedure. b. 1 Week: i. Antihistamine, anticonvulsant, or antispasmodics medications within 1 week of enrollment unless documented on a stable (unchanged) for 180 days prior to enrollment. c. 2 Weeks: i. Use of alpha blockers or daily dosage of PDE5 inhibitors (tadalafil [Cialis]) for BPH within 2 weeks prior to enrollment. ii. Use of anticholinergics or beta-3 adrenergic receptor agonists (e.g., mirabegron, vibegron) within 2 weeks prior to enrollment, unless documented on a stable dose for 30 days prior to enrollment.

	d. <u>3 Months</u>: i. Taking estrogen, drugs producing androgen suppression, or androgens within 90 days prior to enrollment, unless documented on a stable dosage for at least 90 days prior to enrollment. ii. Use of Type II 5-alpha reductase inhibitor medication (e.g., finasteride [Proscar, Propecia]) within 90 days of enrollment OR anticipated use within the first 12 months of follow-up. e. <u>6 Months:</u> i. Use of any Type I 5-alpha reductase inhibitor medication (e.g., dutasteride [Avodart]) within 180 days prior to enrollment OR anticipate use within the first 12 months of follow-up. ii. Taking tricyclic antidepressants that are not on a stable dose for the 180 days prior to enrollment OR anticipate stopping or changing treatment in the first 12 months of follow-up. 8. Subjects who wish to maintain their fertility. Current or anticipated enrollment in any other randomized or interventional clinical study (registry or retrospective studies permitted).

SCHEDULE OF EVENTS

Assessment	Baseline	Index Procedure	Discharge ***	2-Week (14±3 days)	4-Week (30± 7 days)	3-Month (90± 14 days)	6-Month (180± 30 days)	12-Month (365± 30 days)	Annually to 5 Years (± 60 days)	Unscheduled BPH Visit
Informed consent	X									
Demographics, medical history, physical exam	X									
CBC, HbA1c, BUN, Creatinine, Urinalysis	X									
PSA test	X						X	X	x	
Digital Rectal Exam (DRE)	X									
Uroflowmetry + PVR Scan	X			X	X	X	X	X	x	x
Transrectal ultrasound	X							X		
MRI of the prostate (only if PSA 4.5-10ng/mL at baseline)	X						X			
Flexible Cystoscopy (Recorded)*	X							X		
Questionnaires: BPH-II, ICIQ-UI-SF, IPSS, MSHQ-EjD, SHIM	X				X	X	X	X	x	x
Pain Assessment (VAS)	X		X	X	X	X				If ≤90 days
Blinding Assessment			X			X				
Ablation/Sham procedure + data		X				X**				
Urinary catheter status			X - TOV	X	X					
Patient Satisfaction Assessment								X		
Concomitant medications	X	X	X	X	X	X	X	X	x	x
Adverse events	X	X	X	X	X	X	X	X	x	x