Official Title: Multicenter, Randomized, Double-blind Placebo-controlled, Crossover Study to Investigate Effects of V117957 in Female Subjects with Overactive Bladder Syndrome

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Protocol Number:	OAG1030
Protocol Title:	Multicenter, Randomized, Double-blind Placebo-controlled, Crossover Study to Investigate Effects of V117957 in Female Subjects with Overactive Bladder Syndrome
Brief Title:	Study of V117957 in Overactive Bladder Syndrome
Compound:	V117957 Tosylate
Phase:	Phase 1b
Sponsor:	Purdue Pharma L.P. One Stamford Forum Stamford, CT 06901-3431 USA
Protocol Approval Date:	11-Oct-2021
Amendment Number	**2**
GCP Statement:	This study is to be performed in compliance with International Conference on Harmonisation (ICH) and applicable Good Clinical Practices (GCPs) and federal and local regulations.
Confidentiality:	This document is confidential. It contains proprietary information of Purdue Pharma. Any viewing or disclosure of such information that is not authorized in writing by the Sponsor (or designee) is strictly prohibited. Such information may be used solely for the purpose of reviewing or performing this study.

[redacted]

Overall Design:

Phase 1b, multicenter, randomized, double-blind, placebo-controlled, crossover study

Brief Summary:

The purpose of this study is to investigate the effects of oral administration of 1 mg/day V117957 each evening in female subjects with overactive bladder syndrome as compared to placebo. The study will consist of a Screening/ Washout Period (up to 4 weeks), Single-blind Placebo Run-in Period (2 weeks), Double-blind Treatment Period (8 weeks), Single-blind Placebo Washout Period (1 week), and Follow-up Period (up to 1 week).

Number of Participants:

It is estimated that up to 150 subjects will be screened to yield approximately 75 subjects that will enter Single-blind Run-in Period to yield approximately 44 subjects that will enter the Double-blind Treatment Period. A sample size of 38 completers will have 81% power to detect a treatment difference in means of numbers of micturition per 24 hours of 0.5, assuming a standard deviation of differences of 1.4, using a paired t-test with a 10% one-sided significance level. Assuming a 15% dropout rate, a sample size of 44 would be needed.

Treatment Groups and Duration:

V117957 (6-weeks) and Placebo (5-weeks).

Schema:

Phase	**Pre-randomization**			**Post-randomization**									
Period	Screening / washout	Single-blind Run-in		Double-blind Treatment								Single-blind washout	Follow-up
Day	-42 to -16	-15	-1[A]	1	14	15	28	35	42	49	56	63	70
Clinic Visit	V1	V2	V3[A]		V4		V5		V6		V7	V8	V9
Phone call [B]				P1		P2		P3		P4			
Tx Sequence A		Placebo		Placebo		V117957						Placebo	
Tx Sequence B		Placebo		V117957						Placebo		Placebo	

[A] Visit 3, Day -1, is end of Single-blind Run-in Period and start of the Double-blind Treatment Period. At visit 3, a subject that has met all inclusion/exclusion criteria, has met all randomization eligibility criteria, and has completed all study procedures, will be dispensed double-blind study-drug with instruction to ingest first dose that evening 30 minutes before bedtime.
[B] Phone contact between clinic visits to assess tolerability and review diary/dosing instructions.

1.2. Schedule of Assessments

Table 1. Schedule of Assessments: Pre-randomization Phase

Period	Screening/ washout	Single-blind Run-in	
Day	-42 to -16	-15	-1
Clinic Visit [A]	V1	V2 [B]	V3
Assessment			
Informed consent	X		
Medical history	X		
Demographics	X		
Inclusion/exclusion	X	X	X
Physical exam, full	X		
Physical exam, brief		X	X
Vital signs	X	X	X
Clinical labs (chem/heme/urine)	X	X	X
Urine culture test	X	X	X
Urine drug screen	X		X
Serum pregnancy test	X		
Urine pregnancy test		X	X
12-lead ECG	X	X	X
C-SSRS	X	X	X
Concomitant medications	X	X	X
Adverse events	X	X	X
BPIC-SS [C], MESA-IQ [C]	X	X	X
PPBC		X	X
OAB-q LF		X	X
SGRA		X	X
ESS		X	X
SISQ (diary)		Once daily, in morning	
Void Diary assessment (includes PPIUS)		During the week prior to clinic visit (V3), subject will record micturition time, type, and urgency for each episode for a minimum of 3 and up to 7-days; and will *also record* urine volume during 2-day weekend (or other 2-day timeframe convenient to subject work/life schedule).	
Study drug dosing (diary)		Once daily, in evening	
Diary/dosing instruction		X	X
Dispensing study drug		X	X
Drug accountability			X
OAB Symptoms characterized		X[D]	
Randomization criteria checklist			X
Randomization			X

BPIC-SS= Bladder Pain/ Interstitial Cystitis Symptom Score; CSSRS= Columbia-Suicide Severity Rating Scale; ECG= Electrocardiogram; ESS= Epworth Sleepiness Scale; MESA-IQ= Medical, Epidemiologic and Social Aspects of Aging incontinence questionnaire, OAB-q LF= Overactive Bladder Questionnaire long form; PPBC= Patient Perception of Bladder Condition; PPIUS= Patient Perception of Intensity of Urgency Scale; SGRA= Subject Global Response Assessment; SISQ= Symptom Impact on Sleep Questionnaire; V= Visit.

[A] Visit window is ±1 day. [B] Visit 2, Day -15, is end of Screening/Washout Period and start of the Single-blind Run-in Period. At visit 2, a subject that has met all inclusion/exclusion criteria, has stopped their current medication treatment for OAB, and has completed all study procedures, will be dispensed single-blind study-drug with instruction to ingest first dose that evening 30 minutes before bedtime. [C] Exclusion criteria. [D] See Section 8.1.2.8; this must be completed at the clinic visit on the same day that study drug is dispensed to subject; the subject will ingest first dose of study drug that evening.

Table 2. Schedule of Assessments: Post-randomization Phase

Period	Double-blind Treatment									Single-blind washout	Follow-up
Day	-1	1	14	15	28	35	42	49	56	63	70
Clinic Visit [A]	V3 [B]		V4		V5		V6		V7	V8/ EOT/ET	V9/ EOS [C]
Phone call [D]		P1		P2		P3		P4			
Assessment											
Physical exam, brief	See Table 1, V3 Day -1		X		X		X		X	X	
Vital signs			X		X		X		X	X	
Clinical labs (chem/hem/urine)			X		X		X		X	X	
Urine culture test			X		X		X		X	X	
Urine drug screen										X	
Serum pregnancy test										X	
Urine pregnancy test			X		X		X		X		
12-lead ECG			X		X		X		X	X	
C-SSRS			X		X		X		X	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
[redacted]											
[redacted]											
[redacted]											
[redacted]											
[redacted]	[redacted]										
Void Diary assessment (includes PPIUS)	During the week prior to each clinic visit (V4, V5, V6, V7, and V8), subject will record micturition time, type, and urgency for each episode for a minimum of 3 and up to 7-days; and will *also record* urine volume during 2-day weekend (or other timeframe convenient to subject work/life schedule).										
Study drug dosing (diary)	Once daily, in evening.										
Diary/dosing instruction	See Table 1, V3 Day-1	X	X	X	X	X	X	X	X		
Dispensing Study Drug			X		X		X		X		
Drug accountability			X		X		X		X	X	

C-SSRS=Columbia-Suicide Severity Rating Scale; ECG=Electrocardiogram; ESS= Epworth Sleepiness Scale; EOS= End of Study; EOT= End of Treatment; ET= Early Termination; OAB-q LF= Overactive Bladder Questionnaire long form; P=Phone; PPBC= Patient Perception of Bladder Condition; PPIUS= Patient Perception of Intensity of Urgency Scale; SGRA=Subject Global Response Assessment; SISQ= Symptom Impact on Sleep Questionnaire; V=Visit.

[A] Visit window is ±1 day.

[B] Visit 3, Day -1, is end of Single-blind Run-in Period and start of the Double-blind Treatment Period. At visit 3, a subject that has met all inclusion/exclusion criteria, has met all randomization eligibility criteria, and has completed all study procedures, will be dispensed double-blind study-drug with instruction to ingest first dose that evening 30 minutes before bedtime.

[C] May be phone call instead of clinic visit if no safety issue identified.

[D] Phone contact between clinic visits to assess tolerability and review diary/dosing instructions.

1.3. Study Population

Enrolled population: The group of subjects who sign informed consent.

Randomized safety population: The group of subjects who are randomized and receive at least 1 dose of the study drug and have at least 1 safety assessment.

Full analysis population: The group of subjects who are randomized, receive study drug, and have at least 1 valid efficacy measurement.

Per protocol population: The group of subjects who are included in the full analysis population but excluding those with major protocol deviations and those who do not receive the actual treatment they were randomized to receive.

Subjects and profiles/metrics excluded from the analysis set will be documented in the statistical analysis plan.

1.4. Efficacy Analysis

Listings, tables, and figures of efficacy variables will be based on the full analysis population.

1.4.1. Primary Efficacy Analyses

The baseline, post-baseline and change from baseline for number of micturition episodes in 24 hours, number of incontinence episodes in 24 hours as well as volume voided will be summarized by treatment group using descriptive statistics and presented graphically at each scheduled time point. The differences between treatment effects within sequence can be assessed by means of a paired t-test for samples using the intra-individual differences between the outcomes in both periods as the raw data. Comparison of the active treatment to placebo will be tested at the one-sided significance level 0.10 by means of the corresponding contrast. Plots of the mean change from baseline, 90% confidence Intervals (CIs) will be produced by treatment group.

[redacted]

1.4.3. Safety Analyses

All safety data (adverse events [AEs], clinical laboratory results, vital signs, physical examinations, electrocardiograms [ECGs], and Columbia-Suicide Severity Rating Scale [C-SSRS] and Epworth Sleepiness Scale [ESS]) will be listed for subjects in the enrolled and randomized safety populations.

AEs will be categorized into Preferred Term (PT) and associated System Organ Class (SOC) using the Medical Dictionary for Regulatory Activities (MedDRA). Treatment-emergent adverse events (TEAEs) will be defined as AEs that start after or increase in intensity after the first dose of study drug. TEAEs will be summarized by presenting the incidence of AEs for each treatment group by the MedDRA PT, nested within SOC for the safety population. Medical history will be coded to MedDRA terms. Coded medical history terms will be summarized for all subjects in the randomized safety population.

Laboratory evaluations and vital signs will be summarized by treatment and time point for the randomized safety population. Concomitant and prior medications will be coded using the latest version of the World Health Organization Drug Dictionary (WHO-DD) and presented in tables and listings.