**Date of Visit: \_\_\_\_/\_\_\_\_/\_\_\_\_\_**

## SCREENING VISIT

##### Informed Consent

|  |  |  |  |
| --- | --- | --- | --- |
|  | Yes | No | N/A |
| Did the subject sign and date the informed consent form prior to any study procedures being done? | [ ]  | [ ]  |  |
| Did the subject consent to the optional PK study? (if applicable to your site) | [ ]  | [ ]  | [ ]  |
| Did the subject consent to the optional RHC study? (if applicable to your site) | [ ]  | [ ]  | [ ]  |

Between 3 days up to 120 days prior to the scheduled Baseline visit complete the following activities, after obtaining voluntary informed consent:

[ ]  Evaluate Inclusion/Exclusion Criteria

[ ]  Record Demographic Information

[ ]  Record PAH History

[ ]  Record Medical History

[ ]  Perform a Physical Examination

[ ]  Record WHO Functional Class

[ ]  Record Vital Signs after five minutes of seated rest

[ ]  Time subject took second or third dose of inhaled treprostinil (*please circle the dose and update Tyvaso Dosing Log*)

 Dose time \_\_\_:\_\_\_ 24-clock (00:00-23:59) Dose \_\_\_\_\_\_ breaths

[ ]  12-Lead ECG following at least a 5-minute rest in a semi-recumbent position (**1-2 hrs (± 15 minutes)** **after** second or third inhaled treprostinil dose, or approximately 4-6 hours after waking)

 QTc Calculation Method: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

 Sinus Rhythm (circle one): Abnormal / Normal

[ ]  Conduct an unencouraged 6-Minute Walk Test (**1-2 hrs (± 15 minutes) after** second or third inhaled treprostinil dose, or approximately 4-6 hours (± 15 minutes) after waking)

[ ]  Record Borg Dyspnea Score

[ ]  Obtain blood and urine samples for Clinical Laboratory Parameters (serum chemistry, hematology, coagulation, urinalysis and NT-pro-BNP) – Central Lab

[ ]  Obtain a **Serum** pregnancy test (for women of childbearing potential) – Central Lab [ ] N/A

[ ]  Record current medications

[ ]  Record adverse events

[ ]  Schedule Baseline Visit

[ ]  For Tyvaso naïve subjects, complete Accredo “Notice of Enrollment of New Tyvaso Patient” form

**Completed by: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date: \_\_\_\_/\_\_\_\_/\_\_\_\_\_**

**BASELINE VISIT – DAY 1**

**Baseline Day 1 Date of Visit: \_\_\_\_/\_\_\_\_/\_\_\_\_\_**

***Prior to randomization***

□ **Optional RHC assessment may be performed within 0-21 days prior to, or on, Day 1 of the scheduled**

**Baseline Visit.**

**Date RHC assessment completed: \_\_\_\_/\_\_\_\_/\_\_\_\_\_**

For subjects who consent to participate, RHC should be performed within 1-2 hours (± 15 minutes) after the second or third dose of inhaled treprostinil. Please record second or third daily dose (circle one) of inhaled treprostinil and update the Tyvaso Dosing log.

Dose time \_\_\_:\_\_\_ 24-clock (00:00-23:59) Dose \_\_\_\_\_\_ breaths

□ **N/A**

[ ]  Update Medical History, as necessary

[ ]  Perform a Physical Examination

[ ]  Record WHO Functional Class

[ ]  Record Vital Signs after five minutes of seated rest

[ ]  Obtain blood and urine samples for Clinical Laboratory Parameters

(serum chemistry, hematology, coagulation, urinalysis and NT-pro-BNP) – Central Lab

[ ]  Perform a **urine** pregnancy test (for women of childbearing potential) [ ] N/A

 Results: [ ]  Positive (do not enroll) [ ]  Negative

[ ]  Update concomitant medications, as necessary

[ ]  Confirm Inclusion/Exclusion Criteria. Please have the investigator sign off on the Inclusion/Exclusion Criteria worksheet and eCRF to confirm eligibility.

***Randomization and following***

[ ]  Randomize subject in IRT

[ ]  Conduct an unencouraged 6-Minute Walk Test (within 1 hour (± 15 minutes) before the second or third dose of inhaled treprostinil)

[ ]  Record Borg Dyspnea Score

[ ]  Administer second or third dose of inhaled treprostinil (*please circle the dose and update Tyvaso Dosing Log*)

 Dose time \_\_\_:\_\_\_ 24-clock (00:00-23:59) Dose \_\_\_\_\_\_ breaths per dose

[ ]  Record a 12-Lead ECG following a 5-minute rest in a semi-recumbent position (between **1-2 hrs (± 15 minutes)** **after** second or third inhaled treprostinil dose)

 QTc Calculation Method: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Sinus Rhythm (circle one): Abnormal / Normal

[ ]  Record concomitant medications

[ ]  Record adverse events

[ ]  For Tyvaso experienced subjects, complete Accredo “Notice of Clinical Study Randomization for Current

Tyvaso Patient” form

**Completed by: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date: \_\_\_\_/\_\_\_\_/\_\_\_\_\_**

**BASELINE VISIT – DAY 2**

**Baseline Day 2 Date of Visit: \_\_\_\_/\_\_\_\_/\_\_\_\_\_**

[ ]  Provide Tyvaso starter kits for experienced Tyvaso users, and document any training

 Nebulizer 1 Serial number: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Lot Number: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

 Nebulizer 2 Serial number: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

[ ]  Record the Tyvaso starter kit information for inexperienced Tyvaso users, after they receive their kit from the Acreedo nurse

Nebulizer 1 Serial number: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Lot Number: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

 Nebulizer 2 Serial number: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

[ ]  If subject’s specialty pharmacy is other than Acreedo, site staff should call specialty pharmacy to discontinue Tyvaso supply.

[ ]  Supply study drug starter kit supply

[ ]  Provide training/instructions for subject participation in the study: study drug (packaging, storage, accountability, etc), daily QID dosing for study drug and inhaled treprostinil, regular telephone calls, date of next study visit, and importance of attending all study visits, etc.

[ ]  Conduct an unencouraged 6-Minute Walk Test (within 1 hour (± 15 minutes) prior to the second or third dose of inhaled treprostinil and study drug)

[ ]  Record Borg Dyspnea Score

[ ]  Observe and record the co-administration of the second or third daily dose of inhaled treprostinil and initial dose of study drug. *(please circle the dose and update appropriate logs)*

***The subject must be followed for a 2-3 hour observation period following this dose.***

Study Drug Dose Time:\_\_\_\_\_\_\_\_24-clock (00:00-23:59) Dose:\_\_\_\_1\_\_\_\_tab QID

 Inhaled Treprostinil Dose Time:\_\_\_\_\_\_\_\_24-clock (00:00-23:59) Dose:\_\_\_\_\_\_\_\_breaths per dose

[ ]  Assess subject’s tolerability to BPS-314*d*-MR dose

[ ]  Record concomitant medications

[ ]  Record adverse events

[ ]  For subjects electing to participate in the optional plasma concentration assessment, provide Week 4 and Week 12 (first quarterly visit) drug dosing record.

[ ]  Subject was reminded to call study site coordinator or investigator at any time to discuss any issues.

[ ]  Subject was reminded they will be called 5-7 days into each weekly dose. Assess best day/time to contact subject.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  |  |  |  |
| **Best Day to Contact Subject** |  | **Best Time to Contact Subject** |  | **Phone Number** |

**Completed by: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date: \_\_\_\_/\_\_\_\_/\_\_\_\_\_**

**Date of Telephone Call: \_\_\_\_/\_\_\_\_/\_\_\_\_\_**

**PHONE CALL**

***Calls will occur at least weekly during the first 12 weeks of the study.*** *Call subject 5-7 days into each weekly dose during the Treatment Phase to assess AEs, concomitant medications, and whether subject has reached an intolerable dose of study drug.* ***Thereafter, telephone call will occur at least monthly****. No call is required during the week/month in which the subject has a study visit.*

Was Subject Contacted? Yes [ ]  No [ ]

If no, specify reason: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Was the contact scheduled or unscheduled? [ ]  Scheduled [ ]  Unscheduled

Did subject experience any new or changes to existing adverse events?

[ ]  No [ ]  Yes *(If yes, update Adverse Event log)*

Did subject take any new or changes to existing concomitant medications?

[ ]  No [ ]  Yes *(If yes, update Conmed log)*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Were any changes made to study drug dosing? Yes [ ]  No [ ]   *(If yes, update Study Drug Dosing Log)*Comments: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_  |  |  |  |  |

Did subject have any Clinical Worsening events (as defined by the protocol)? [ ]  No [ ]  Yes

Did the subject have any study drug and inhaled trepostinil doses that were not administered

Concurrently (within 15 minutes)? [ ]  No [ ]  Yes (*If yes, enter information on dose logs)*

If using specialty pharmacy other than Acreedo, did site staff call their specialty pharmacy to discontinue Tyvaso supply? Yes [ ]  No [ ]  NA [ ]

Remind to call the study site coordinator or investigator at any time to discuss any issues.

**Optional Plasma Concentration Evaluation:** Weeks 3 and 11, remind the subject to abstain from caffeine or alcohol containing beverages on the day of their next scheduled visit (Weeks 4 and 12). Also remind the subject to record all study drug and Tyvaso doses taken in the 7 days prior to the Plasma Concentration sampling day on the “Week 4 and 12 Dose Time Record Sheet”.

**Additional Notes:**

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Completed by: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date: \_\_\_\_/\_\_\_\_/\_\_\_\_\_**

**Date of Visit:** \_\_\_\_/\_\_\_\_/\_\_\_\_\_

**WEEK 4 VISIT**

Subjects will return to the clinical site at Week 4 (± 3 days) for the following procedures:

□**OPTIONAL Plasma Concentration Evaluation:** Obtain two 10 mL trough blood samples (15 minutes prior to the second daily dose of study drug) for subjects who are participating in the optional Plasma Concentration Evaluation.

*\*Subjects should be contacted one week (7 days) prior to the visit and reminded to record the timing of study drug and inhaled treprostinil dosing for the week leading up to the study visit*

□Confirm no alcohol or caffeine was consumed by the subject on the day of this visit

□Record first daily dose of study drug and inhaled treprostinil *(please update appropriate logs)*

 Study Drug Dose Time:\_\_\_\_\_\_\_\_24-clock (00:00-23:59) Dose:\_\_\_\_\_\_\_\_tab/s QID

 Inhaled Treprostinil Dose Time:\_\_\_\_\_\_\_\_24-clock (00:00-23:59) Dose:\_\_\_\_\_\_\_\_breaths per dose

□**N/A**

[ ]  Record second or third daily dose of study drug and inhaled treprostinil

*(please circle the dose and update appropriate logs)*

 Study Drug Dose Time:\_\_\_\_\_\_\_\_24-clock (00:00-23:59) Dose:\_\_\_\_\_\_\_\_tab/s QID

 Inhaled Treprostinil Dose Time:\_\_\_\_\_\_\_\_24-clock (00:00-23:59) Dose:\_\_\_\_\_\_\_\_breaths per dose

[ ]  Perform a Physical Examination

[ ]  Record WHO Functional Class

[ ]  12-Lead ECG following a 5-minute rest in a semi-recumbent position (**1-2 hrs (± 15 minutes) after** second or third daily dose of study drug and inhaled treprostinil).

QTc Calculation Method: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Sinus Rhythm (circle one): Abnormal / Normal

[ ]  Record Vital Signs after five minutes of seated rest

[ ]  Conduct an unencouraged 6-Minute Walk Test (**1-2 hrs (± 15 minutes)** **after** second or third daily dose of

study drug and inhaled treprostinil)

[ ]  Record Borg Dyspnea Score

[ ]  Assess Clinical Worsening

[ ]  Obtain blood and urine samples for Clinical Laboratory Parameters (serum chemistry, hematology, coagulation,

urinalysis and NT-pro-BNP) – Central Lab

[ ]  Obtain a **Serum** pregnancy test (for women of childbearing potential) – Central Lab [ ]  N/A

[ ]  Record adverse events

[ ]  Record concomitant medications

[ ]  Record Drug Accountability and assess compliance

[ ]  Record study drug and inhaled treprostinil changes, as applicable

[ ]  Supply subject with a 1 month supply of study drug

[ ]  Collect from the subject “Week 4 Dose Time Record Sheet” if participating in Optional Plasma Concentration Evaluation

[ ]  Subject was reminded to call the study site coordinator or investigator at any time to discuss any issues.

**Completed by: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date: \_\_\_\_/\_\_\_\_/\_\_\_\_\_**

**Date of Visit**: \_\_\_\_/\_\_\_\_/\_\_\_\_\_

### WEEK 8 VISIT

Subjects will return to the clinical site at Week 8 (± 4 days) for the following procedures:

[ ]  Record second or third daily dose of study drug and inhaled treprostinil *(please circle the dose and update appropriate logs)*

Study Drug Dose Time:\_\_\_\_\_\_\_\_24-clock (00:00-23:59) Dose:\_\_\_\_\_\_\_\_tab/s QID

 Inhaled Treprostinil Dose Time:\_\_\_\_\_\_\_\_24-clock (00:00-23:59) Dose:\_\_\_\_\_\_\_\_breaths per dose

[ ]  Perform a Physical Examination

[ ]  Record WHO Functional Class

□ **OPTIONAL:** 12-Lead ECG following a 5-minute rest in a semi-recumbent position (**1-2 hrs (± 15 minutes)** **after** second or third daily dose of study drug and inhaled treprostinil)

 QTc Calculation Method: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Sinus Rhythm (circle one): Abnormal / Normal

□**N/A**

[ ]  Record Vital Signs after five minutes of seated rest

[ ]  Conduct an unencouraged 6-Minute Walk Test (**1-2 hrs (± 15 minutes)** **after** second or third daily dose of

study drug and inhaled treprostinil)

[ ]  Record Borg Dyspnea Score

[ ]  Assess Clinical Worsening

[ ]  Obtain blood and urine samples for Clinical Laboratory Parameters (serum chemistry, hematology,

coagulation, urinalysis and NT-pro-BNP) – Central Lab

[ ]  Obtain a **Serum** pregnancy test (for women of childbearing potential) – Central Lab [ ] N/A

[ ]  Record adverse events

[ ]  Record concomitant medications

[ ]  Record Drug Accountability and assess compliance

[ ]  Record study drug and inhaled treprostinil changes, as applicable

[ ]  Supply subject with a 4 week supply of study drug

[ ]  Subject was reminded to call the study site coordinator or investigator at any time to discuss any issues.

**Completed by: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date: \_\_\_\_/\_\_\_\_/\_\_\_\_\_**

**Date of Visit: \_\_\_\_/\_\_\_\_/\_\_\_\_\_**

### WEEK 12 VISIT

Subjects will return to the clinical site at Week 12 (± 10 days) for the following procedures:

□ **OPTIONAL Plasma Concentration Evaluation:** Obtain four sets of two 10 ml blood samples around the second daily dose (15 min prior, 15 min, 1 hour and 2.5 post-dose; ±5 minutes)

*\*Subjects should be contacted one week (7 days) prior to the visit and reminded to record the timing of study drug and inhaled treprostinil dosing for the week leading up to the study visit*

□Confirm no alcohol or caffeine was consumed by the subject on the day of this visit

□Record first daily dose of study drug and inhaled treprostinil *(please update appropriate logs)*

 Study Drug Dose Time:\_\_\_\_\_\_\_\_24-clock (00:00-23:59) Dose:\_\_\_\_\_\_\_\_tab/s QID

 Inhaled Treprostinil Dose Time:\_\_\_\_\_\_\_\_24-clock (00:00-23:59) Dose:\_\_\_\_\_\_\_\_breaths per dose

□**N/A**

[ ]  Record second or third daily dose of study drug and inhaled treprostinil

*(please circle the dose and update appropriate logs)*

 Study Drug Dose Time:\_\_\_\_\_\_\_\_24-clock (00:00-23:59) Dose:\_\_\_\_\_\_\_\_tab/s QID

Inhaled Treprostinil Dose Time:\_\_\_\_\_\_\_\_24-clock (00:00-23:59) Dose:\_\_\_\_\_\_\_\_breaths per dose

[ ]  Perform a Physical Examination

[ ]  Record WHO Functional Class

[ ]  12-Lead ECG following a 5-minute rest in a semi-recumbent position (**1-2 hrs (± 15 minutes)** **after** second or third daily dose of study drug and inhaled treprostinil)

 QTc Calculation Method: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

 Sinus Rhythm (circle one): Abnormal / Normal

[ ]  Record Vital Signs after five minutes of seated rest

[ ]  Conduct an unencouraged 6-Minute Walk Test (**1-2 hrs (± 15 minutes)** **after** second or third daily dose of

study drug and inhaled treprostinil)

[ ]  Record Borg Dyspnea Score

[ ]  Assess Clinical Worsening

[ ]  Obtain blood and urine samples for Clinical Laboratory Parameters (serum chemistry, hematology, coagulation,

urinalysis and NT-pro-BNP) – Central Lab

[ ]  Obtain a **Serum** pregnancy test (for women of childbearing potential) – Central Lab [ ] N/A

[ ]  Record adverse events

[ ]  Record concomitant medications

[ ]  Record Drug Accountability and assess compliance

[ ]  Record study drug and inhaled treprostinil changes, as applicable

[ ]  Supply subject with a 3 month supply of study drug

[ ]  Collect from the subject “Week 12 Dose Time Record Sheet” if participating in Optional PC Evaluation.

[ ]  Subject was reminded to call the study site coordinator or investigator at any time to discuss any issues. **Completed by: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date: \_\_\_\_/\_\_\_\_/\_\_\_\_\_**

**Date of Visit: \_\_\_\_/\_\_\_\_/\_\_\_\_\_**

### QUARTERLY VISIT

Subjects will return to clinical site every quarter (± 10 days) starting from Week 12 Visit for the following procedures:

[ ]  Record second or third daily dose of study drug and inhaled treprostinil

*(please circle the dose and update appropriate logs)*

 Study Drug Dose Time:\_\_\_\_\_\_\_\_24-clock (00:00-23:59) Dose:\_\_\_\_\_\_\_\_tab/s QID

 Inhaled Treprostinil Dose Time:\_\_\_\_\_\_\_\_24-clock (00:00-23:59) Dose:\_\_\_\_\_\_\_\_breaths per dose

□ **OPTIONAL Hemodynamic Sub-study:** Right Heart Catheterization (RHC):

□Perform RHC for subjects who are participating in the optional hemodynamic sub-study

□RHC will be performed approximately 1-2 hours after the second dose of study drug

***Note:*** *Subjects participating in the hemodynamic sub-study may have RHC procedures performed at any time within ±7 days of the scheduled* ***Month 6 visit*** *only.*

□**N/A**

[ ]  Perform a Physical Examination

[ ]  Record WHO Functional Class

[ ]  12-Lead ECG following a 5-minute rest in a semi-recumbent position (**1-2 hrs (± 15 minutes)** **after** second or third daily dose of study drug and inhaled treprostinil)

 QTc Calculation Method: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Sinus Rhythm (circle one): Abnormal / Normal

[ ]  Record Vital Signs after five minutes of seated rest

[ ]  Conduct an unencouraged 6-Minute Walk Test (**1-2 hrs (± 15 minutes)** **after** second or third daily dose of

study drug and inhaled treprostinil)

[ ]  Record Borg Dyspnea Score

[ ]  Assess Clinical Worsening

[ ]  Obtain blood and urine samples for Clinical Laboratory Parameters (serum chemistry, hematology, coagulation,

urinalysis and NT-pro-BNP) – Central Lab

[ ]  Obtain a **Serum** pregnancy test (for women of childbearing potential) – Central Lab [ ] N/A

[ ]  Record adverse events

[ ]  Record concomitant medications

[ ]  Record Drug Accountability and assess compliance

[ ]  Record study drug and inhaled treprostinil changes, as applicable

[ ]  Supply subject with a 3 month supply of study drug

[ ]  Subject was reminded to call the study site coordinator or investigator at any time to discuss any issues. **Completed by: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date: \_\_\_\_/\_\_\_\_/\_\_\_\_\_**

**Date of Visit: \_\_\_\_/\_\_\_\_/\_\_\_\_\_**

## End of STUDY (EARLY TERMINATION) Visit

Subjects who do not enroll in the Open Label Extension or who terminate early from the study

will be down-titrated off of BPS-314*d*-MR at the discretion of the Investigator. The maximum

decrement should not exceed one tablet QID per day and the minimum decrement should be one

tablet QID per week. Prior to the End of Study Visit, subjects should be contacted to determine

whether they will enroll in the Open Label Extension Study. Following down-titration and

permanent discontinuation of study drug, the subject should return to the study site for an End of

Study Visit for the procedures outlined below:

[ ]  Perform a Physical Examination

[ ]  Record WHO Functional Class

[ ]  12-Lead ECG following a 5-minute rest in a semi-recumbent position (**1-2 hrs (± 15 minutes)** **after** second or third daily dose of inhaled treprostinil, or, if enrolling in the open label extension study, conduct after second or third dose of inhaled treprostinil and study drug.)

 QTc Calculation Method: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Sinus Rhythm (circle one): Abnormal / Normal

[ ]  Record Vital Signs after five minutes of seated rest

[ ]  Conduct an unencouraged 6-Minute Walk Test (**1-2 hrs (± 15 minutes) after** second or third daily dose of inhaled treprostinil, or, if enrolling in the open label extension study, conduct after second or third dose of inhaled treprostinil and study drug.)

[ ]  Record Borg Dyspnea Score

[ ]  Assess Clinical Worsening

[ ]  Obtain blood and urine samples for Clinical Laboratory Parameters (serum chemistry, hematology,

coagulation, urinalysis and NT-pro-BNP) – Central Lab

[ ]  Obtain a **Serum** pregnancy test (for women of childbearing potential) – Central Lab [ ] N/A

[ ]  Record adverse events

[ ]  Record concomitant medications

[ ]  Record Drug Accountability and assess compliance (and collect remaining unused study drug and packaging

for uses/partially used study drug)

[ ]  Complete Study Termination CRF

[ ]  Complete Accredo “Notice of Patient Discontinuation from Clinical Trial” form

[ ]  Will the subject enter the open-label study?  Yes  No\*

\*If No, remind the subject that the subject will be contacted in 3 months by phone to assess overall status.

**Completed by: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date: \_\_\_\_/\_\_\_\_/\_\_\_\_\_**

**Date of Visit: \_\_\_\_/\_\_\_\_/\_\_\_\_\_**

**UNSCHEDULED VISIT**

Subjects may visit the study site at the investigator’s discretion. Unscheduled visits may involve the following procedures:

[ ]  Perform a Physical Examination

[ ]  Record WHO Functional Class

[ ]  12-Lead ECG following a 5-minute rest in a semi-recumbent position (**1-2 hrs (± 15 minutes)** **after** second or third daily dose of study drug and inhaled treprostinil)

 QTc Calculation Method: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Sinus Rhythm (circle one): Abnormal / Normal

[ ]  Record Vital Signs after five minutes of seated rest

[ ]  Conduct an unencouraged 6-Minute Walk Test (**1-2 hrs (± 15 minutes) after** second or third daily dose of

study drug and inhaled treprostinil)

[ ]  Record Borg Dyspnea Score

[ ]  Assess Clinical Worsening

[ ]  Obtain blood and urine samples for Clinical Laboratory Parameters (serum chemistry, hematology,

coagulation, urinalysis and NT-pro-BNP) – Central Lab

[ ]  Plasma concentration sample, if feasible, for drug related SAEs (obtain two 10mL tubes)

[ ]  Obtain a **Serum** pregnancy test (for women of childbearing potential) – Central Lab [ ] N/A

[ ]  Record adverse events

[ ]  Record concomitant medications

[ ]  Record Drug Accountability and assess compliance

[ ]  Record study drug and inhaled treprostinil changes, as applicable

[ ]  Supply subject with study drug as applicable

[ ]  Subject was reminded to call the study site coordinator or investigator at any time to discuss any issues.

**Completed by: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date: \_\_\_\_/\_\_\_\_/\_\_\_\_\_**

**STUDY TERMINATION**

Date that Subject Completed or Discontinued the study:\_\_\_\_\_\_/\_\_\_\_\_\_/\_\_\_\_\_\_

Time of Completion/Discontinuation: \_\_\_\_\_:\_\_\_\_\_ 24-hr clock

Check completed or primary reason for Discontinuation

 COMPLETED Study

 Adverse Event

 Lack of Efficacy

 Lost to Follow-up

 Physician Decision

 Clinical Worsening/Progression of Disease

 Voluntary Withdraw of the Subject

 Study Termination by the Sponsor

 Screen Failure

 Other, specify: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Was treatment unblinded by the PI? □ No □ Yes

 If yes, date blind broken:\_\_\_\_\_\_/\_\_\_\_\_\_/\_\_\_\_\_\_ and time blind broken: \_\_\_\_\_:\_\_\_\_\_ 24-hr clock

Did the subject enter the open-label extension study? □ Yes □ No

Did the subject down-titrate off study drug? □ Yes □ No

Was the subject alive at the time the sponsor concluded the study?

□ Yes Date of confirmation: \_\_\_\_\_\_/\_\_\_\_\_\_/\_\_\_\_\_\_

□ No Date of death: \_\_\_\_\_\_/\_\_\_\_\_\_/\_\_\_\_\_\_

**THREE-MONTH FOLLOW-UP**

*\*Please include the information recorded below in the “Study Termination” eCRF.*

Date that the three-month follow-up was conducted: \_\_\_\_\_\_/\_\_\_\_\_\_/\_\_\_\_\_\_

Was the subject alive at the time the follow-up was conducted?

□ Yes Date of confirmation: \_\_\_\_\_\_/\_\_\_\_\_\_/\_\_\_\_\_\_

□ No Date of death: \_\_\_\_\_\_/\_\_\_\_\_\_/\_\_\_\_\_\_

**Completed by: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date: \_\_\_\_/\_\_\_\_/\_\_\_\_\_**