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**TABLO**  
**(The EvAluation of TaBlo In-CLInic and In-HOme)**  
**Study # 2014-01**

**A Prospective Multicenter, Open Label, Non-Randomized, Cross-Over Study Evaluating the Use of the Tablo™ Hemodialysis System In-Center and In-Home by Subjects with End Stage Renal Disease (ESRD) who are on Stable Dialysis Regimens.**

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## 1 PROTOCOL SYNOPSIS

<b>Title</b>	A Prospective, Multicenter, Open Label, Non-randomized, Cross-Over Study Evaluating the Use of the Tablo™ Hemodialysis System In-Center and In-Home by Subjects with End Stage Renal Disease (ESRD) who are on stable dialysis regimens.
<b>Study Device</b>	The Tablo™ Hemodialysis System (The Tablo™ System)
<b>Study Design</b>	<p>This is a prospective, multicenter, open label, non-randomized, cross-over study. Subjects will be enrolled in the trial for approximately 21 weeks and will use the Tablo™ Hemodialysis System for their dialysis treatments for all study phases, according to the schedule outlined in four periods as follows:</p> <ul style="list-style-type: none"> <li>• <b>Run-in</b>— Subjects undergo study staff administered dialysis treatment 4 times/week for 1 week In-Center.</li> <li>• <b>Treatment Period 1, In-Center</b> – Subjects undergo study staff administered dialysis treatment 4 times/week for 32 treatments (approximately 8 weeks) In-Center. Subjects are expected to undergo no more than 4 complete treatments per week during this treatment period.</li> <li>• <b>In-Home Transition</b>— Subjects undergo device training for the study, perform self-care dialysis 4 times/week for approximately 4 weeks, and are assessed for stability in the new care environment.</li> <li>• <b>Treatment Period 2, In-Home</b> – Subjects undergo self-care dialysis treatment 4 times/week for 32 treatments (approximately 8 weeks) In-Home. Subjects are expected to undergo no more than 4 complete treatments per week during this treatment period.</li> <li>• <b>Follow-Up</b>---Subjects treatment modality will be followed for up to 5 years post study completion.</li> </ul>
<b>Study Objective</b>	To evaluate the Tablo™ Hemodialysis System when used In-Center by trained individuals and In-Home by trained Subjects.
<b>Enrollment</b>	This study will enroll up to 50 Subjects to result in 30 evaluable Subjects at 10-20 sites in the U.S.
<b>Primary Efficacy Endpoint</b>	Delivery of a standardized weekly Kt/V of greater than or equal to 2.1.

<p><b>Primary Safety Endpoint</b></p>	<p>The primary safety endpoint will be calculated using the mean number of adverse events from the pre-specified list observed during a dialysis interval:</p> <ol style="list-style-type: none"> <li>1. <b>Serious Adverse Event:</b> any serious adverse event that:             <ul style="list-style-type: none"> <li>○ Results in death,</li> <li>○ Is life-threatening,</li> <li>○ Requires hospitalization or prolongs existing hospitalization,</li> <li>○ Requires intervention to prevent permanent impairment or damage, or</li> <li>○ Results in persistent or significant disability/incapacity.</li> </ul> </li> <li>2. <b>Allergic Reaction:</b> Type A, anaphylactoid or Type B dialyzer reactions to dialyzer, blood tubing or chemical disinfectant.</li> <li>3. <b>Blood Loss:</b> blood loss resulting in hemodynamic compromise that leads to death, transfusion or fluid resuscitation with greater than 1 liter of crystalloid IV fluids.</li> <li>4. <b>Hemolytic Reaction:</b> hemolytic reactions due to disinfectant exposure, dialysate temperature, mechanical failure or other device related causes.</li> <li>5. <b>Infection:</b> any infection related to catheter, its tunnel or exit site, AV fistula, or AV graft.</li> <li>6. <b>Intra-Dialysis Event:</b> a significant clinical event such as loss of consciousness, cardiac arrest, or seizure caused by device failure.</li> <li>7. <b>Vascular Access Complication:</b> defined as AVF or AVG clotting during the dialysis procedure, bleeding for more than 30 minutes post-dialysis for 3 consecutive sessions, difficulty with vascular access resulting in inability to initiate or complete dialysis treatments or complications related to hemodialysis catheters (not including reduced blood flow in catheter or TPA or catheter exchange).</li> <li>8. <b>Pyrogenic Reaction:</b> onset of objective chills (visible rigors) and fever (oral temperature greater than or equal to 37.5 degrees Celsius) in a Subject who was afebrile and who had no recorded signs or symptoms of infection before treatment.</li> </ol>
<p><b>Secondary Outcome Measure</b></p>	<p>The ultrafiltration (fluid removal) value as reported by the device will be within 10% of the expected fluid removal based on the UF prescription and the Tablo Console fluid removal algorithm.</p>

<p><b>Inclusion Criteria</b></p>	<ol style="list-style-type: none"> <li>1. Subject has provided informed consent and has signed a Health Insurance Portability and Accountability Act of 1996 (HIPAA) compliant authorization statement.</li> <li>2. Subject is at least 18 years and less than 75 years of age.</li> <li>3. Subject has end stage renal disease (ESRD) adequately treated by maintenance dialysis achieving a Kt/V <math>\geq</math> 1.2 and has been deemed stable for at least three months by his/her treating nephrologist.</li> <li>4. Subject has a well-functioning and stable vascular access that allows a blood flow of at least 300 ml/min.</li> <li>5. Subject understands the nature of the procedures and the requirements of the study protocol, including home-based dialysis.</li> <li>6. Subject is willing and able to comply with the protocol requirements and return to the treatment center for all required treatments and clinical evaluations.</li> <li>7. Subject has identified an individual to be trained and available as needed. The identified individual must be considered competent in the use of the device by the prescribing physician.</li> <li>8. Subject has a documented psychosocial evaluation by a qualified social worker, treating physician or home hemodialysis nurse.</li> <li>9. Subject has no childbearing potential or has a negative pregnancy test within 7 days prior to the start of the first study treatment and will be utilizing medically acceptable means of contraception during the study period.</li> </ol>
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<p><b>Exclusion Criteria</b></p>	<ol style="list-style-type: none"> <li>1. Subject is unable to read English or Spanish.</li> <li>2. Subject has dementia or lacks capacity for self-care.</li> <li>3. Life expectancy less than 12 months from first study procedure.</li> <li>4. Subject unable to understand or cooperate with hemodialysis nurse and dialysis care team.</li> <li>5. Subject has a documented history of non-adherence to dialysis therapy that would prevent successful completion of the study.</li> <li>6. Subject has had a recent major cardiovascular adverse event within the last 3 months.</li> <li>7. Subject has New York Class III or IV Congestive Heart Failure, or ejection fraction less than 30%.</li> <li>8. Subject has a persistent pre-dialysis sitting systolic blood pressure less than 100 mmHg despite medical therapy.</li> <li>9. Subject has symptomatic intra-dialytic hypotension requiring medical intervention in two of their last three treatments.</li> <li>10. Subject has an active infection requiring antibiotics within last 7 days.</li> <li>11. Subject with fluid overload due to intractable ascites secondary to liver cirrhosis.</li> <li>12. Subject has uncontrolled blood pressure (e.g. sustained/persistent pre-dialysis systolic blood pressure greater than 180 mmHg despite maximal medical therapy in two of the last three treatments).</li> <li>13. Subject is intolerant to heparin.</li> <li>14. Subject is seroreactive for Hepatitis B Surface Antigen.</li> <li>15. Subject has an active, life-threatening, rheumatologic disease.</li> <li>16. Subject has a history of adverse reactions to dialyzer membrane material.</li> <li>17. Subject is participating in another investigative drug or device clinical study related to Home Hemodialysis which conflicts with the execution of this study.</li> <li>18. Subject is expected to receive an organ transplant during the course of the study.</li> <li>19. Subject has a life-threatening malignancy actively receiving treatment that would prevent successful completion of the study protocol.</li> <li>20. Any other documented condition that the Investigator feels would prevent the Subject from successful inclusion in the study.</li> </ol>
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## 2 BACKGROUND

End-Stage Renal Disease (ESRD) has become a major public health problem and is associated with considerable co-morbidity and mortality. Currently, routine hemodialysis is the most prevalent treatment for ESRD and it is typically conducted in a dialysis outpatient facility.<sup>1</sup> These patients must typically travel three times a week to the outpatient clinic and sit for hours while being dialyzed. The realities of outpatient dialysis facilities render more frequent dialysis less practical for most patients, providers and caregivers.

In recent years a significant body of evidence has emerged establishing the clinical, social and economic benefits of more frequent dialysis.<sup>2,3,4,5,6</sup> Frequent dialysis is challenging in a clinic-based delivery model due to a variety of reasons (e.g. travel three times/week), which has led to a growing interest within the dialysis community to shift hemodialysis therapy to persons' homes. In-Home treatment allows for more frequent dialysis sessions, which more closely mimics the natural function of the kidneys.

Additionally, home hemodialysis (HHD) also offers numerous medical advantages over conventional In-Center hemodialysis. Studies have demonstrated improved blood pressure control, reductions in use of hypertension medication<sup>7</sup> and improvements in left ventricular function.<sup>8</sup> Improved control of hyperphosphatemia,<sup>9</sup> improvements in quality of sleep including patient reported quality of rest, decrease in episodes of apneic episodes, and decrease in restless leg syndrome severity have also been reported.<sup>10</sup> Most importantly, improvements in overall patient survival rates have been shown with more frequent but shorter dialysis times,<sup>11</sup> which are best met by HHD.

A continuum of renal replacement therapies ranging from wearable artificial kidneys to better home hemodialysis technologies are in development, but many of the technologies are unproven or will take many years to mature. The Outset philosophy has been to couple the proven mechanisms of today's In-Center hemodialysis with targeted technology innovation that will bring the benefits of frequent hemodialysis to more patients.

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### 3 STUDY OBJECTIVE

To evaluate the Tablo™ Hemodialysis System when used In-Center by trained individuals and In-Home by trained Subjects.

#### 3.1 Device and Study Rationale

The Tablo™ Hemodialysis System (System) makes hemodialysis more accessible to ESRD Subjects through meaningful improvements in usability.

### 4 DEVICE DESCRIPTION

The Tablo™ Hemodialysis System is a self-contained hemodialysis system (Hemodialysis System or System), intended for acute and chronic dialysis therapy with or without ultrafiltration, in an acute or chronic care facility. The System is modular in design and contains two components: 1) the Tablo™ Console (Console), a single module consisting of multiple fluidic systems that perform the activities of a Water Purification System (WPS) and a conventional Dialysis Delivery System (DDS), and 2) the Tablo™ Cartridge (Cartridge), consisting of a single-use blood tubing set attached to an Organizer. A disposable Cartridge is inserted onto the front panel of the Console for each dialysis treatment.

#### 4.1 Tablo™ Hemodialysis System Overview

Incoming water is pretreated in the Sediment and Carbon Filtration subsystem. This pre-treated water then passes through the Reverse Osmosis (RO) system where polyamide thin-film composite membranes purify the incoming water. This process reduces the levels of chemical and microbial contaminants, producing water for dialysis meeting AAMI/ANSI/ISO 13959 limits. After cycling through the WPS, the purified water enters the Dialysis Delivery System.

The Dialysis Delivery System de-aerates the treated water, then proportions and mixes in acid and bicarbonate concentrates. The resulting dialysate fluid passes through an ultrafilter to assure the dialysate meets the AAMI/ANSI/ISO 11663 limits for microbial contaminants. During routine use, both heat and chemical disinfections are utilized throughout both the Water Purification System and the Dialysis Delivery System to maintain water quality. Heat disinfection and chemical disinfection are performed at defined intervals to reduce the microbial burden that may occur in the fluid path and components.

The Cartridge, consisting of a single-use disposable blood tubing set attached to an Organizer, draws blood from the Subject through interaction with a peristaltic pump, and passes the blood through a dialyzer before returning the treated blood to the Subject. The disposable Cartridge is provided sterile. Therefore, neither the blood tubing set nor Organizer is treated with heat or chemical disinfectant.

#### 4.2 Principle of Operation

During treatment, the water purification system produces dialysis-quality water, which is delivered to the Dialysis Delivery System where the water is mixed with the proportioned concentrates. The resulting dialysate passes through the ultrafilter and enters the dialyzer.

Within 24 hours following treatment the Tablo Console performs a heat disinfection cycle, during which the fluid path components of both the water purification system and the Dialysis Delivery System are heated. After the heat disinfection cycle is completed, the Console shuts down and any residual hot water in the Console cools. The Console performs a pre-treatment cycle before the next treatment begins during which the entire fluid path is flushed with freshly purified water.

In addition to post-treatment heat disinfection, a chemical disinfection cycle is performed periodically. During this cycle, a peracetic acid type of disinfectant (e.g. Peracidin) disinfects the fluid path. After the chemical disinfection, the fluid path is rinsed until no detectable residual peracetic acid is present (as

determined by conductivity measurements). After rinsing the chemical disinfectant, another heat disinfection cycle is performed as previously described. The complete disinfection cycle concludes when the Console shuts down and any remaining water cools. Prior to the next treatment, the user is prompted by the user interface to perform a water test to ensure no residual disinfectant remains.

### 4.3 Proposed Indications For Use

The Tablo™ System is indicated for use in patients with acute and/or chronic renal failure, with or without ultrafiltration, in an acute or chronic care facility. Treatments must be administered under physician's prescription, with a trained individual available as needed who is considered competent in the use of the device by the prescribing physician. The Tablo™ System is also indicated for use in the home.

### 4.4 Device Instructions

A comprehensive User Manual for the Tablo Console and Instructions for Use for the Tablo Cartridge, including warnings and precautions, has been created. Please refer to the most current version for complete details on preparation and procedural use of the device.

#### 4.4.1 Medical Informatics

USB flash drives connected directly to the Tablo™ Hemodialysis Console will capture individual treatment details. Treatment data captured will include, but is not limited to, prescription details, blood pressure readings, heparin infusion data (from the heparin pump), changes to treatment parameters, total fluid removed during treatment, and alarms and errors. This data may also be collected via wireless capabilities.

**Note:** If a heparin bolus is prescribed for the Subject to be administered prior to the initiation of treatment, the dosage amount will not be saved to the USB drive and will need to be manually recorded in the Subject's medical record and transcribed to the case report form.

#### 4.4.2 Device Set-up

##### 4.4.2.1 Initial Device Set-up

The Tablo Console must be connected to an incoming water source, an outgoing drain line, and an electrical outlet. Additional instructions on the Console set-up can be found in the User Manual.

##### 4.4.2.2 Supplies for Dialysis Therapy

Prior to beginning set-up for each dialysis treatment, the clinical site personnel (In-Center) and/or the Subject (In-Home), should collect the following supplies:

Supplies provided by Outset

- 1 Container of Acid Concentrate (red label)
- 1 Container of Bicarbonate Concentrate (blue label)
- 1 Tablo Cartridge (blood tubing set)
- 1 Commercially Available Dialyzer
- 1 USB flash drive for prescription upload and treatment data capture

General Supplies provided by the Dialysis Center

- 1-2 Saline Bags (Subject dependent)
  - Heparin (per Subject’s prescription)
  - Dialysis Needles
  - Syringes for heparin pump and initial heparin dose
- Note:** the syringe for use with the heparin pump should be one of the following types: Beckton Dickinson 10ml, Terumo 10ml, or Kendall Monoject 12ml
- Cleaner for vascular access site
  - Gauze pads and tape for vascular access
  - Gloves, mask and safety glasses
  - Biohazard box and bag
  - Chlorine Test Kit

**4.4.2.3 Prescription for Dialysis Therapy**

Subject prescription details will be uploaded to the Tablo™ Console using a Subject specific USB flash drive. Before treatment can begin, the user must validate the prescription details via a user interface confirmation screen (**Table 1**). The user interface will allow treatment to begin **only** after the prescription is verified. Tablo’s prescription screen includes two “on/off” options, including use of the heparin pump and the ability to capture standing blood pressure readings in addition to the required sitting blood pressure readings.

Table 1: Prescription Details				
Subject Settings	Treatment Settings	Dialysate Settings	Blood Pressure Settings	Heparin Settings
<ul style="list-style-type: none"> <li>• Estimated Dry Weight</li> <li>• Access Type</li> <li>• Blood Clot Time (defaulted to 3 min.)</li> <li>• Saline Bolus Volume (defaulted to 100 ml)</li> </ul>	<ul style="list-style-type: none"> <li>• Blood Flow Rate</li> <li>• Length of Treatment</li> </ul>	<ul style="list-style-type: none"> <li>• Concentrate Type</li> <li>• Sodium Setting</li> <li>• Bicarbonate Setting</li> <li>• Potassium Setting</li> <li>• Dialysate Temperature</li> <li>• Dialyzer Type</li> </ul>	<ul style="list-style-type: none"> <li>• Standing Blood Pressure (on/off)</li> <li>• Blood Pressure Frequency</li> </ul>	<ul style="list-style-type: none"> <li>• Heparin Pump (on/off)</li> <li>• Heparin Flow Rate</li> <li>• Heparin Stop Time</li> <li>• Heparin Concentrate</li> <li>• Heparin Syringe Type</li> </ul>

**4.4.2.4 Heparin Dosing for Dialysis Therapy**

If an initial heparin bolus is prescribed for treatment with the Tablo™ Hemodialysis System, then a heparin dose will be manually delivered to the Subject with a syringe prior to commencement of treatment. Heparin dosing during dialysis treatment may be delivered manually or automatically using the heparin pump. Heparin therapy during dialysis treatment will be prescribed according to institutional practices and at the discretion of the Investigator. To optimize therapy, it is suggested that Subjects receive a heparin bolus of 30 units/kg at the start of treatment, followed by 15 units/kg hourly. For arterial, venous, fistula or graft Subjects heparin administration should be discontinued 30 minutes before the end of treatment.

#### 4.4.2.5 System Interfaces

The user will interact with multiple system interfaces when using the Tablo™ Console. All interfaces described are through the Tablo touchscreen. A summary of each interface is described below:

- 1. Pre-Treatment Mode (Set-Up)** - The user interface employs a checklist approach to guide users through the sequence of steps in “pre-treatment mode”, including (1) connection of the concentrate containers, Tablo™ Cartridge, dialyzer, saline, and heparin, (2) verification of the Subject prescription settings, (3) Subject pre-treatment vitals, (4) system priming, (5) water chlorine test, and (6) Subject vascular access. Preparation for treatment via this mode can be accessed in the user interface via the Home Screen “Get Started” button.
- 2. Treatment Mode (During Dialysis)** - Treatment mode covers the dialysis therapy process from initial blood flow from the Subject to the extracorporeal circuit through to final blood return to the Subject after treatment completion. The user interface employs a single main treatment progress screen which monitors blood pressure and pulse measurements, saline bolus delivery, fluid removal (ultrafiltration) and blood pump cessation, and changes to treatment settings. Additionally, the main treatment screen tracks treatment time. A secondary user interface screen monitors additional treatment information like arterial and venous pressure readings and a log of blood pressure and pulse readings. The treatment mode user interface also includes confirmation screens for delivering a saline bolus, stopping fluid removal, and stopping the blood pump. Additionally, the user interface guides the user to save changes to treatment settings and to replace a saline bag.
- 3. Post-Treatment Mode** - The user interface also employs a checklist approach to guide users through the sequence of steps in “post-treatment mode”, including (1) disconnection of the Subject blood lines, (2) access site closure, (3) Subject post-treatment vitals, and (4) disconnection and disposal of the concentrate containers, Tablo Cartridge, dialyzer, saline, and heparin from the Tablo™ Console. The Tablo™ Console can be programmed to automatically begin a heat disinfection cycle.
- 4. Maintenance Mode** - The user interface employs a checklist approach to guide users through the sequence of steps for periodic maintenance activities, including (1) heat disinfection, (2) chemical disinfection with a water test, (3) carbon filter replacement, (4) sediment filter replacement, and (5) ultrafilter replacement. The user interface is designed to automatically remind users when a maintenance activity is required. Additionally, the maintenance functions can be accessed in the user interface via the Home Screen “Maintenance” button.

## 5 STUDY ENDPOINTS

### 5.1 Evaluation of Efficacy

The primary effectiveness endpoint is the delivery of a standardized weekly Kt/V of greater than or equal to 2.1. The standardized weekly Kt/V value will be computed by the Sponsor and included in the study database from laboratory data provided/recorded by the site via the Case Report Forms (CRFs).

This analysis will be based on the Intent-to-Treat (ITT) population (section 11.1.1) with a supportive analysis for the Per-Protocol (PP) population (section 11.1.2).

## 5.2 Evaluation of Safety

The primary safety endpoint will be calculated using the mean number of adverse events from the pre-specified list observed during a dialysis interval as follows:

1. **Serious Adverse Event:** any serious adverse event that:
  - Results in death,
  - Is life-threatening,
  - Requires hospitalization or prolongs existing hospitalization,
  - Requires intervention to prevent permanent impairment or damage, or
  - Results in persistent or significant disability/incapacity.
2. **Allergic Reaction:** Type A, anaphylactoid or Type B dialyzer reactions to dialyzer, blood tubing or chemical disinfectant.
3. **Blood Loss:** blood loss resulting in hemodynamic compromise that leads to death, transfusion or fluid resuscitation with greater than 1 liter of crystalloid IV fluids.
4. **Hemolytic Reaction:** hemolytic reactions due to disinfectant exposure, dialysate temperature, mechanical failure or other device related causes.
5. **Infection:** any infection related to catheter, its tunnel or exit site, AV fistula, or AV graft.
6. **Intra-Dialysis Event:** a significant clinical event such as loss of consciousness, cardiac arrest, or seizure caused by device failure.
7. **Vascular Access Complication:** defined as AVF or AVG clotting during the dialysis procedure, bleeding for more than 30 minutes post-dialysis for 3 consecutive sessions, difficulty with vascular access resulting in inability to initiate or complete dialysis treatments or complications related to hemodialysis catheters (not including reduced blood flow in catheter or TPA or catheter exchange).
8. **Pyrogenic Reaction:** onset of objective chills (visible rigors) and fever (oral temperature greater than or equal to 37.5 degrees Celsius) in a Subject who was afebrile and who had no recorded signs or symptoms of infection before treatment.

A dialysis interval is defined as the start of one dialysis treatment until the start of the next dialysis treatment. The primary safety analysis will be performed on the Intent-to-Treat (ITT) population.

## 5.3 Secondary Outcome Measure

The ultrafiltration (fluid removal) value as reported by the device will be within 10% of the expected fluid removal based on the UF prescription and the Tablo Console fluid removal algorithm.

## 5.4 Other Data and Analyses

Baseline and demographic characteristics will be summarized for all Subjects. Continuous variables will be displayed via summary statistics (mean, median, sample size, standard deviation, minimum, and maximum). Categorical variables will be summarized via counts and percentages. In addition, summary statistics will be computed on the number of pre-specified adverse events per dialysis interval for each treatment period. The same summary statistics will be calculated by treatment period for the rate of pre-specified adverse events per 100 dialysis treatments. Concomitant medications that may affect the study endpoints will also be collected and analyzed. These include, but are not limited to, blood thinners, diuretics, hypertensives and iron supplements.

## 6 STUDY DESIGN

### 6.1 Overview

This is a prospective, multicenter, open label, non-randomized, cross-over study. Subjects will be enrolled in the trial for approximately 21 weeks during which time Subjects will use the Tablo™ Hemodialysis

System for dialysis treatments in all study phases. There are four periods during which the Tablo System will be utilized; run-in, treatment period 1, training/transition and treatment period 2.

- **Run-in** – Subjects will undergo dialysis treatment 4 times/week for 1 week In-Center. Treatments will be administered by study staff.

Confirmation of study eligibility will be assessed after the Subject completes this one-week run-in period.

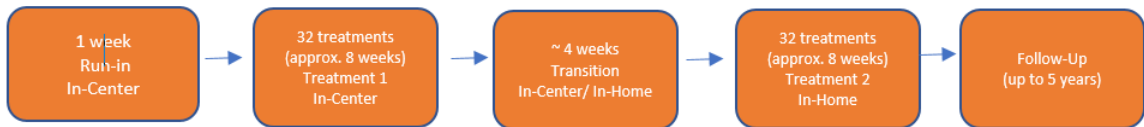
- **Treatment Period 1, In-Center** – Subjects will undergo dialysis treatment 4 times/week for 32 treatments (approximately 8 weeks) In-Center. Treatments will be administered by study staff. Subjects are expected to undergo no more than 4 complete treatments per week during this treatment period.

Subjects are considered enrolled in the study if they meet all inclusion and exclusion criteria and have started the first study treatment during the first treatment period.

- **In-Home Transition**– Subjects will undergo device training for the study, then perform self-care dialysis 4 times/week for approximately 4 weeks. Treatments performed during the first portion will be completed In-Center under supervision. Treatments performed during the second portion will be completed In-Home. This second portion will assess subject stability in a new care environment. Supervision will be at the discretion of the Investigator.

- **Treatment Period 2, In-Home** – Subjects will undergo self-care dialysis treatment 4 times/week for 32 treatments (approximately 8 weeks) In-Home. Subjects are expected to undergo no more than 4 complete treatments per week during this treatment period.

- **Follow-Up**---Subjects treatment modality will be followed for up to 5 years post study completion.



**Figure 1: Study Design**

Data collected during Treatment Period 1 and Treatment Period 2 will be used to assess the primary endpoints.

In the event a subject undergoes more than 4 complete treatments per week, during Treatment Period 1 and Treatment Period 2, the additional treatment(s) will be reported as a protocol deviation per Section 13.3.2.

**6.2 Efforts to Minimize Bias**

To maintain a balanced population in the study, no single Investigational Site will be permitted to enroll more than 30% of the entire study population.

**6.3 Blinding and Randomization**

This study is a prospective, multicenter, open label, non-randomized, cross-over study comparing In-Center and In-Home hemodialysis performance using the Tablo™ Hemodialysis System. Both Subjects and

attending clinicians will know the System delivering dialysis treatments, therefore, blinding is not required.

Each Subject will serve as his or her own control in terms of treatment period comparisons (In-Center versus In-Home), and as such, randomization procedures are not required.

#### 6.4 Clinical Events Committee

In order to minimize bias, an independent Clinical Events Committee (CEC) will assess clinical events to determine the following:

- Confirm whether or not the event should be included as one of the 8 pre-specified adverse events (defined in Section 9.1.5) that will be analyzed as the Primary Safety Endpoint for the study.
- Event was related to the device as defined in Section 9.2.3.
- Event was related to the dialysis procedure and is considered an additional treatment observation (ATO) as defined in Section 9.1.3. These adverse events are generally associated with dialysis and are a consistent with the Subject's established history on dialysis.
- Event was related to a pre-existing condition.

### 7 SUBJECT SELECTION

#### 7.1 Study Population

Subjects with a diagnosis of end stage renal disease (ESRD) who meet the inclusion and exclusion criteria will be eligible for participation in this study. The eligibility criteria for the TABLO study are designed to capture diverse Subjects, such as those patients who are currently undergoing In-Center, In-homehemodialysis, or peritoneal dialysis. In addition, Subjects with all vascular access types are eligible for the study and may include catheters, grafts, and fistulas. Potential study candidates should be screened for eligibility according to the study inclusion and exclusion criteria.

To be considered enrolled in the study, the Subject must meet all inclusion and exclusion criteria and have started the first study treatment during the first treatment period.

#### 7.2 Informed Consent

**IMPORTANT: The Code of Federal Regulations requires that the consent form signed by the Subject must be dated at the time consent is given. Also, medical records must contain documentation that informed consent was obtained prior to participation in a study. (21 CFR Parts 50 and 812)**

The Investigator may determine whether potential Subjects are interested in participating in an investigation, but shall not request the written informed consent of any Subject to participate, and shall not allow any Subject to participate before obtaining Institutional Review Board (IRB) and FDA approval. The consent process shall begin before care is altered beyond the scope of a routine comprehensive examination for the purpose of participating in this study.

All Subjects in this research study should be completely informed about the purpose, duration, and pertinent details of the study. The informed consent process must be documented using a written form that has been approved by the IRB and includes all *Basic Elements of Informed Consent* and pertinent *Additional Elements* (21 CFR Part 50.25).

The Investigator must keep the original signed copies of all consent forms in the Subject's medical records and provide a copy to each Subject.



**Appendix A** outlines the screening and enrollment process and illustrates the point where informed consent should be obtained.

### 7.3 Subject Privacy

In accordance with the Health Insurance Portability and Accountability Act of 1996 (HIPAA), all Subjects should be informed of potential uses and disclosures of their medical information for research purposes, and their rights to access information about them by covered entities. Each Investigator will follow the procedures for securing HIPAA compliance as directed by their respective IRB or Privacy Board, and to obtain written authorization to use and disclose Subject information for all clinical research and research involving questioning of the Subject's or Subjects' physician(s). Per individual site procedures, this authorization may be included as part of the Subject informed consent form.

### 7.4 Inclusion Criteria

Subjects must meet **ALL** of the inclusion criteria to be enrolled in the study.

1. Subject has provided informed consent and has signed a Health Insurance Portability and Accountability Act of 1996 (HIPAA) compliant authorization statement.
2. Subject is at least 18 years and less than 75 years of age.
3. Subject has end stage renal disease (ESRD) adequately treated by maintenance dialysis achieving a Kt/V  $\geq$  1.2 and has been deemed stable for at least three months by his/her treating nephrologist.
4. Subject has a well-functioning and stable vascular access that allows a blood flow of at least 300 ml/min.
5. Subject understands the nature of the procedures and the requirements of the study protocol, including home-based dialysis.
6. Subject is willing and able to comply with the protocol requirements and return to the treatment center for all required treatments and clinical evaluations.
7. Subject has identified an individual to be trained and available as needed. The identified individual must be considered competent in the use of the device by the prescribing physician.
8. Subject has a documented psychosocial evaluation by a qualified social worker, treating physician or home hemodialysis nurse.
9. Subject has no childbearing potential or has a negative pregnancy test within 7 days prior to the start of the first study treatment and will be utilizing medically acceptable means of contraception during the study period.

### 7.5 Exclusion Criteria

If **ANY** of the exclusion criteria are met, the Subject is excluded from the study.

1. Subject is unable to read English or Spanish.
2. Subject has dementia or lacks capacity for self-care.
3. Life expectancy less than 12 months from first study procedure.
4. Subject unable to understand or cooperate with hemodialysis nurse and dialysis care team.
5. Subject has a documented history of non-adherence to dialysis therapy that would prevent successful completion of the study.

6. Subject has had a recent major cardiovascular adverse event within the last 3 months.
7. Subject has New York Class III or IV Congestive Heart Failure, or ejection fraction less than 30%.
8. Subject has a persistent pre-dialysis sitting systolic blood pressure less than 100 mmHg despite medical therapy.
9. Subject has symptomatic intra-dialytic hypotension requiring medical intervention in two of their last three treatments.
10. Subject has an active infection requiring antibiotics within last 7 days.
11. Subject with fluid overload due to intractable ascites secondary to liver cirrhosis.
12. Subject has uncontrolled blood pressure (e.g. sustained/persistent pre-dialysis systolic blood pressure greater than 180 mmHg despite maximal medical therapy in two of the last three treatments).
13. Subject is intolerant to heparin.
14. Subject is seroreactive for Hepatitis B Surface Antigen.
15. Subject has an active, life-threatening, rheumatologic disease.
16. Subject has a history of adverse reactions to dialyzer membrane material.
17. Subject is participating in another investigative drug or device clinical study related to Home Hemodialysis which conflicts with the execution of this study.
18. Subject is expected to receive an organ transplant during the course of the investigation.
19. Subject has a life-threatening malignancy actively receiving treatment that would prevent successful completion of the study protocol.
20. Any other documented condition that the Investigator feels would prevent the Subject from successful inclusion in the study.

## 7.6 Subject Discontinuation and Replacement

Every Subject should remain in the study until completion of the required follow-up period. Subjects may voluntarily withdraw from the study at any time with or without reason and it will not have any negative impact on subsequent treatment. Conceivable reasons for Subject discontinuation may include, but are not limited to, the following:

- **Subject Withdrawal:** Subject participation in this clinical study is voluntary. The Subject may choose to discontinue participation (refuse all subsequent testing) at any time without loss of benefits or penalty.
- **Discontinuation:** Subject participation may be discontinued by the Subject or Investigator because of a treatment modality change, organ transplant, transfer, death or prolonged hospitalization.
- **Investigator Termination:** The Investigator may terminate the Subject's participation without regard to the Subject's consent if the Investigator believes it is medically necessary.
- **Exclusion Criterion Discovered After Enrollment:** A small number of Subjects may be enrolled despite meeting an exclusion criteria due to timing of study required clinical procedures. This will be documented by the study personnel on the Case Report Form (CRF), and will be considered a protocol deviation.

- **Lost-to-Follow-up:** If the Subject fails to complete **eight** consecutive treatments, regardless of whether or not they fall into a single treatment period or a total of up to eight missed treatments, consecutive or not, per period, but has not formally withdrawn from the study, he or she will be considered lost-to-follow-up. The data from this Subject is still eligible for the intent to treat dataset. Site personnel should make all reasonable efforts to locate and communicate with the Subject, at each contact time point, including:
  - A minimum of two telephone calls to contact the Subject should be attempted. Each attempt should be recorded in the Subject's medical record, including date, time, and initials of site personnel attempting the contact.
  - If telephone calls are unsuccessful, a certified letter should be sent to the Subject.

If the above-mentioned attempts at communicating with the Subject are unsuccessful, the Subject will be considered lost-to-follow-up.

**NOTE: If the Subject can be contacted, study treatments will resume at the point when the last treatment was conducted.**

In all cases, the reason(s) for withdrawal, if given, must be recorded on the appropriate CRF and in the Subject's medical record. If more than one reason is cited for withdrawal, study personnel must identify the most significant reason and record this reason on the CRF. Investigators must also report all Subject withdrawals to their IRB as defined by their institutions' procedures. Subjects who withdraw or are withdrawn from the study, or are lost to follow-up may be replaced.

## 8 STUDY PROCEDURES

### 8.1 Baseline Evaluation

The baseline evaluation will include, but is not limited to, the following testing and assessments, and will be conducted prior to initiating the Run-In period per Appendix B:

- Documentation of consent
- Demographics (Sex, Age, Ethnicity, Race)
- Physical Examination
- Medical History (including history of vascular access)
- Hemodialysis prescription (e.g., equipment, number of times dialyzed per week, and whether in-home or in-clinic settings)
- Laboratory Values
  - Documentation of Laboratory values for 3 months prior to Run-In.
  - Laboratory Testing (hematology and chemistry) as needed\*
- Assessment of kinetics
- Routine signs and symptoms
- Concomitant medications

\* If the subject has had lab work within two weeks of the run-in period that contains all of the protocol specified tests, a repeat lab draw at baseline is not necessary.

If, after completion and review of the above data, the Subject appears to be a good candidate for study enrollment and is assessed as being able to perform self-care, the Investigator will proceed with the run-in period using the Tablo Hemodialysis System.

## 8.2 1-week Run-in

The 1-week run-in period will include, but is not limited to, the following testing, procedures, and assessment per Appendix B:

- Subject's Dialysis Prescription Settings
- Pre-dialysis vitals, including body weight, temperature, blood pressure, and heart rate (pulse)
- Number of dialysis sessions completed
- Post-Dialysis body weight
- Assessment of Kinetics
- Concomitant Medications
- Assessment of dialysis interval adverse events (if any)
- Final assessment of Subject eligibility

All treatments will be performed using the Tablo™ Hemodialysis System. Dialysis personnel, trained on the use of the device, will input the dialysis prescription as detailed below:

The dialysis prescription will include:

- Access blood flow (set between 300 and 400 ml/min.)
- Dialysate temperature (between 36 and 39 degrees Celsius adjustable by 0.5 degrees increments)
- Composition of dialysate: potassium (limited to 2 mEq/dL versus 3 mEq/dL), bicarbonate (30 to 40 mEq/L adjustable in 1 mEq/L intervals), sodium concentrations (135-145 mEq/L in 1mEq/liter increments)
- Treatment length in minutes between 160 minutes and 240 minutes
- Blood pressure parameters for ultrafiltration
- Heparin dose and anticoagulation parameters

Using established center protocols, and after adequate patient training for performing their own first cannulation, dialysis personnel will observe or perform: 1) the Subjects' dialysis access (i.e., catheter, fistula or graft) preparation using In-Center aseptic technique, and 2) cannulation of the fistula or graft, or connection to a catheter. Dialysis will then be initiated and ongoing monitoring of the Subject will be done per center protocol. During treatment, vital signs, including blood pressure measurements and heart rate (pulse), will be collected every 30 minutes for the first hour, then hourly until the completion of the treatment.

Post-treatment vitals, including body weight, temperature, blood pressure and heart rate (pulse), will also be collected.

Each Subject will be prescribed dialysis therapy using the Tablo™ Hemodialysis System for four times per week with no inter-dialytic (end of treatment period to start of next treatment) period greater than 2 days. No isolated ultrafiltration will be available on the device during the study.

During the Run-In period, Investigators or their designee, may use other clinical assessment indicators to determine the Subject's ability to perform self-care (including but not limited to, self-cannulation and assessment of the home environment). Any issues which would prevent dialysis from being performed, or that would require a change in dialysis procedure will be communicated to Outset.

If, after completion of the baseline evaluation and Run-In period, the Investigator determines the Subject meets all inclusion and exclusion criteria, the Subject will begin Treatment Period 1, In-Center dialysis using the Tablo Hemodialysis System.

### **8.3 Treatment Period 1 (In-Center)**

Investigators or their designee will perform routine pre-dialysis assessment of adverse events, infections, medication changes, and subject's vitals including body weight, blood pressure, temperature, and heart rate (pulse). Any issues which would prevent normal dialysis from being performed or that would require a change in dialysis procedure will be communicated with the study Sponsor.

Dialysis personnel, trained on the use of the device, will perform device set-up, input the dialysis prescription and administer dialysis therapy In-Center during Treatment Period 1 according to the Investigator's instruction.

Prior to treatment, pre-dialysis vitals, including body weight, temperature, blood pressure, and heart rate (pulse), will be collected. Using established center protocols, dialysis personnel will observe or perform: 1) the Subjects' dialysis access (i.e., catheter, fistula or graft) preparation using In-Center aseptic technique, and 2) cannulation of the fistula or graft, or connection to a catheter. Dialysis will then be initiated and ongoing monitoring of the Subject will be done per center protocol. During treatment, vital signs, including blood pressure measurements and heart rate (pulse), will be collected every 30 minutes for the first hour, then hourly until the completion of the treatment.

Post-treatment vitals, including body weight, temperature, blood pressure and heart rate (pulse), will also be collected.

**NOTE: Subjects are considered enrolled in the Study if they have met all inclusion and exclusion criteria and the first treatment during Treatment Period 1 has been started.**

Each Subject will be prescribed dialysis therapy for four times per week with no inter-dialytic (end of treatment period to start of next treatment) period greater than 2 days. No isolated ultrafiltration will be available on the device during the study.

During therapy, each Subject is encouraged to limit food and water intake. Subjects will document any alarms that occurred which required intervention (such as medication or saline administration or a change in treatment parameters), under what conditions they occurred, and final resolution. A summary of alarm occurrence will be tabulated from data transmitted to Outset Medical. Subjects will also document any signs or symptoms that they experienced during treatment.

### **8.4 Transition Period (In-Center/In-Home dialysis treatment)**

Over the four-week transition period, Investigational site personnel will confirm the Subject is stable in the new care environment, has been appropriately trained on the set up and use of the Tablo Hemodialysis System and has satisfactorily completed the items of the patient skills assessment. The Subject will be responsible for device set up and initiating therapy under the supervision of study personnel In-Center during the first portion. The second portion of the transition period In-Home will be supervised at the discretion of the investigator.

Prior to treatment, pre-dialysis vitals, including body weight, temperature, blood pressure, and heart rate (pulse), will be collected. Using established center protocols, the subject or identified trained individual

will: 1) prep Subject's dialysis access (i.e., catheter, fistula or graft) using trained aseptic technique, and 2) perform cannulation of the fistula or graft, or connection to a catheter.

Once all pre-treatment steps are complete, the Subject will initiate dialysis and monitor their treatment according to the center protocol. During treatment, vital signs, including blood pressure measurements and heart rate (pulse), will be collected every 30 minutes for the first hour, then hourly until the completion of the treatment.

Post-treatment vitals, including body weight, temperature, blood pressure and heart rate (pulse), will also be collected.

During therapy, each Subject is encouraged to limit food and water intake. Subjects will document any alarms that occurred which required intervention (such as medication or saline administration or a change in treatment parameters), under what conditions they occurred, and final resolution. A summary of alarm occurrence will be tabulated from data transmitted to Outset Medical. Subjects will also document any signs or symptoms that they experienced during treatment.

Each Subject will be prescribed dialysis therapy for four times per week with no inter-dialytic (end of treatment period to start of next treatment period) period greater than 2 days. No isolated ultrafiltration will be available on the device during the study.

### **8.5 Treatment Period 2 (In-Home dialysis treatment)**

Subject will administer dialysis therapy at home during Treatment Period 2 according to the Investigator's instruction. After device setup, the Subject will take his/her pre-dialysis vitals, including body weight, temperature, blood pressure, and heart rate (pulse), and confirm the dialysis prescription.

Using established center protocols, the subject or identified trained individual will: 1) prep Subject's dialysis access (i.e., catheter, fistula or graft) using trained aseptic technique, and 2) perform cannulation of the fistula or graft, or connection to a catheter.

Once all pre-treatment steps are complete, the Subject will initiate dialysis and monitor their treatment according to the center protocol. During treatment, vital signs, including blood pressure measurements and heart rate (pulse), will be collected every 30 minutes for the first hour, then hourly until the completion of the treatment.

Post-treatment vitals, including body weight, temperature, blood pressure and heart rate (pulse), will also be collected.

During therapy, each Subject is encouraged to limit food and water intake. Subjects will document any alarms that occurred which required intervention (such as medication or saline administration or a change in treatment parameters), under what conditions the alarms occurred, and final resolution. A summary of alarm occurrence will be tabulated from data transmitted to Outset Medical. Subjects will also document any signs or symptoms that they experienced during treatment. .

Each Subject will be prescribed dialysis therapy for four times per week with no inter-dialytic (end of treatment period to start of next treatment period) period greater than 2 days. No isolated ultrafiltration will be available on the device during the study.

### **8.6 Weekly Visits during the In-Center and In-Home Treatment Periods**

Weekly visits for each Subject will be conducted by a study staff member during Treatment Periods 1 (In-Center) and 2 (In-Home). During this weekly visit, signs and symptoms experienced by the Subject both since the last dialysis treatment as well as those experienced during dialysis treatments will be reviewed, as well as compliance to treatment time. The study staff member will also review the definitions of adverse and serious adverse events and re-educate the Subject where necessary.

## 8.7 Laboratory Assessments

Each Subject will be required to provide approximately 120ml or 8 tablespoons of total blood for the duration of the trial to monitor the Subject's blood chemistry. Samples will be collected as outlined in Appendix B.

For weekly draws to calculate the Urea Reduction Ratio (URR) and thereby quantify dialysis treatment adequacy, collect approximately 54-57ml into **Yellow top or serum separator tubes** in increments of 3ml or 0.6 teaspoons for pre and post dialysis treatment BUN.

For pre BUN, prior to connecting to Tablo or administering heparin bolus, fill appropriate tubes according to the standard of care.

For post BUN, pull the sample at the conclusion of therapy by reducing the blood pump speed to 100 ml per minute. Allow one minute to elapse at that blood flow rate, then collect the sample according to the standard of care.

Additionally, at least twice during each treatment period (Treatment Period 1, In-Center and Treatment Period 2, In-Home), collect both chemistry and hematology, and iron indices as specified (see Appendix B for tests and timing).

For chemistry, collect approximately 54-57ml into **Tiger top** or serum separator tubes in increments of 3ml or 0.6 teaspoons, according to the standard of care.

For hematology, collect approximately 12ml in **Lavender top** tubes in increments of 3ml or 0.6 teaspoons according to the standard of care.

During visits when both Chemistry and CBC labs will be drawn, the recommended draw order is **Tiger top** or serum separator **followed** by **Yellow top** or serum separator. All samples will be processed according to reference laboratory requirements. No blood samples will be stored or used for permanent or immortal cell lines.

## 8.8 Follow Up

Subjects' treatment modalities will be followed for up to 5 years post study completion.

## 8.9 Device Malfunction

Device malfunctions are instances where the device does not perform as intended. During device set-up, treatment administration and post-treatment, site personnel and/or the Subject will be requested to inspect and identify any defective parts. The study Investigator (or designee) will notify the Sponsor and comply with Sponsor procedures for returned goods.

## 8.10 Subject Assessment

Each Subject will be asked to complete questions weekly regarding whether or not the device was easy to use, whether assistance was needed, and the length of recovery time required post treatment. In addition, the Subject will be asked to complete a questionnaire regarding signs and symptoms experienced during each treatment (see section 9.2 Recording Adverse Events).

## 8.11 Device Water and Dialysate Testing

During device installation in-center and in-home and monthly thereafter, water and dialysate samples will be collected and tested. Samples above the limits ( $\geq 100$  CFU/ml or  $\geq 0.50$  EU/ml for dialysate and  $\geq 100$  CFU/ml or  $> 0.25$  EU/ml for water) may be considered device failures. If results are above the action limit

( $\geq 50$  CFU/ml or  $\geq 0.50$  EU/ml for dialysate and  $\geq 50$  CFU/ml or  $>0.25$  EU/ml for water) a chemical disinfection cycle will be run, a new sample will be drawn and new test results obtained. In addition, Sponsor will review the culture and disinfection logs and determine if the system should be removed from patient use. If above the action limit upon retesting the device will be removed from use.

## 9 ADVERSE EVENT REPORTING

### 9.1 Adverse Event Definitions

#### 9.1.1 Adverse Event (AE):

An adverse event (AE) is any undesirable medical occurrence in a clinical study Subject, whether it is considered to be related to the device or not, that includes a clinical sign, symptom or condition.

#### 9.1.2 Serious Adverse Events (SAEs)

An AE is considered to be serious if it:

- results in death;
- is life-threatening;
- requires Subject hospitalization or prolongation of existing hospitalization;
- requires intervention to prevent permanent impairment or damage;
- results in persistent or significant disability/incapacity

#### 9.1.3 Additional Treatment Observations (ATOs)

Additional Treatment Observations (ATOs) are observations of interest that are not considered adverse events. These observations will be recorded as measured. These include, but are not limited to:

- Blood pressure measurements
- Phosphorous and potassium levels
- Alarms that end treatment
- Subjects feeling cold during treatment
- Study Subject drop out
- clinically significant alarms during treatment as reported by the Tablo Console
  - air in venous bloodline,
  - low systolic blood pressure,
  - high/low venous pressure, and
  - blood leak in dialyzer

#### 9.1.4 Unanticipated Adverse Device Effects (UADEs)

An unanticipated Adverse Device Effect means any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of Subjects.





### 9.1.5 Primary Safety Endpoint

This category includes the 8 pre-specified adverse events that will be analyzed as the Primary Safety Endpoint for the study:

1. **Serious Adverse Event:** any serious adverse event that:
  - Results in death,
  - Is life-threatening,
  - Requires hospitalization or prolongs existing hospitalization,
  - Requires intervention to prevent permanent impairment or damage, or
  - Results in persistent or significant disability/incapacity.
2. **Allergic Reaction:** Type A, anaphylactoid or Type B dialyzer reactions to dialyzer, blood tubing or chemical disinfectant.
3. **Blood Loss:** blood loss resulting in hemodynamic compromise that leads to death, transfusion or fluid resuscitation with greater than 1 liter of crystalloid IV fluids.
4. **Hemolytic Reaction:** hemolytic reactions due to disinfectant exposure, dialysate temperature, mechanical failure or other device related causes.
5. **Infection:** any infection related to catheter, its tunnel or exit site, AV fistula, or AV graft.
6. **Intra-Dialysis Event:** a significant clinical event such as loss of consciousness, cardiac arrest, or seizure caused by device failure.
7. **Vascular Access Complication:** defined as AVF or AVG clotting during the dialysis procedure, bleeding for more than 30 minutes post-dialysis for 3 consecutive sessions, difficulty with vascular access resulting in inability to initiate or complete dialysis treatments or complications related to hemodialysis catheters (not including reduced blood flow in catheter or TPA or catheter exchange).
8. **Pyrogenic Reaction:** onset of objective chills (visible rigors) and fever (oral temperature greater than or equal to 37.5 degrees Celsius) in a Subject who was afebrile and who had no recorded signs or symptoms of infection before treatment.

## 9.2 Recording Adverse Events

### 9.2.1 Adverse Event Categorization

Reported Adverse Events will be categorized into one of the following two categories:

1. **Primary Safety Endpoint:** This category includes the 8 pre-specified adverse events that will be analyzed as the Primary Safety Endpoint for the study.
2. **Other Adverse Events:** This category includes all reported adverse events that meet the definition in Section 9.

The proposed categorization will serve to focus reporting, adjudicating, and analysis efforts to those categories most relevant for demonstrating the investigational device's relevant safety profile.

It is the intention of the Sponsor that AE's be collected in a uniform manner over the course of the study (independent of study arm) through the use of a Subject questionnaire. The Subject will be asked to complete a questionnaire regarding signs and symptoms experienced during each treatment. During regularly scheduled clinical follow-up visits during the trial, study staff will review the signs and symptoms noted by the Subject and provide education, as needed, on how they are documented. The study staff will determine whether subject reported signs and symptoms meet the definition of an AE as specified in Section 9. This approach attempts to eliminate any potential observed differences in AE rates between the study arms that are solely due to reporting sources or techniques.

Prior to analysis, all adverse events (AEs) will be coded using the Medical Dictionary for Regulatory Activities (MedDRA). Based on these coded terms, treatment emergent AEs will be summarized by treatment period, by severity, relation to procedure and relation to device.

### 9.2.2 Other Adverse Events

The Investigator will monitor the occurrence of adverse events for each Subject during the course of the study. All AEs will be listed on the adverse event case report forms. All pre-existing medical conditions and baseline dialysis stability signs and symptoms will be recorded on baseline case report forms for medical history and signs and symptoms.

Starting with the first treatment during Treatment period 1 with the Tablo™ Hemodialysis System, any new event/experience that was not present at baseline, or worsening of an event present at baseline, is considered an adverse event. Recorded Adverse Events will include, but are not limited to:

- infections (other than those defined in the Primary Safety Endpoint),
- hypotension,

**Note:** Unchanged, chronic conditions are **not** adverse events and should not be recorded on the adverse event page of the CRF.

**Note:** Laboratory values that are abnormal will **not** be considered as adverse events unless medical intervention is required. Clinical laboratory data will be monitored and values that are outside of the normal ranges will be separately summarized by time point for each treatment period (In-Center and In-Home). During the In-Center treatment period, summary statistics (mean, standard deviation, median, range, n) on laboratory values collected will be computed on the raw data. During the In-Home treatment period, summary statistics (mean, standard deviation, median, range, n) on laboratory values collected will be computed on the raw data. Individual tables will be created for each laboratory panel and quantitative parameter combination. In addition, a summary table will be created for each laboratory panel (hematology and chemistry) to display the number and percentage of subjects who have results that fall out of the normal ranges for each laboratory parameter by time point for each of Treatment Period 1 and 2.

Adverse events will be monitored until they are adequately resolved or explained. Should an adverse event be ongoing at the end of the Subject's last study treatment the medical care plan for the Subject will be described and documented.

### 9.2.3 Determination of the Relationship

Determination of whether there is a reasonable possibility that the investigational device caused or contributed to an AE is to be determined by the Investigator and recorded on the CRFs as **not related, related or unknown**. Determination should be based on assessment of temporal relationships, biologic plausibility, association (or lack of association) with underlying disease, and presence (or absence) of a more-likely cause.

Definitions for determination of the relationship include:

**Not Related:** Exposure to the investigational device has not occurred, or the occurrence of the adverse event is not reasonably related in time, or the adverse event is considered unlikely to be related to the use of the investigational device (biologically implausible).

**Related:** Exposure to the investigational device and the adverse event are reasonably related in time and the investigational device is more likely than other causes to be responsible for the adverse event, or is the most likely cause of the adverse event.

**Unknown:** Exposure to the device and the occurrence of adverse event cannot be reasonably determined to be unrelated to the device. If the relationship is identified as unknown it will be treated as related to the investigational device.

If any adverse event is considered related to the use of the investigational device, that event will be followed until resolution or until the Investigator determines the event to be chronic or stable.

#### 9.2.4 Determination of Adverse Events (Clinical Events Committee, CEC)

In order to ensure that events reported as AEs meet clinically recognized and accepted standards and are reported in a uniform manner across sites, AEs that have been assessed by the site Principal Investigator to be device related, severe in nature, and/or meets the definition of one the primary safety endpoint events, will be reviewed and adjudicated by a CEC. Adjudication of reported adverse events will be performed by a multi-physician panel. Adjudication will be done against the standard of whether a reasonable attending nephrologist would attribute the AE to one of the causes listed as part of the Primary Safety Endpoint above. In the case of disagreement by the adjudication panel, determination will be made by majority vote. The CEC also will confirm those reported events indicated as such, do indeed meet the Safety Endpoint criteria. In addition, the CEC will periodically review all AEs, including those that are not included as a primary endpoint, to assess overall study safety.

#### 9.3 Reporting Requirements of SAEs or UADEs

The Investigator must report all SAEs or UADEs immediately upon awareness to Outset. The site should contact the following person by telephone to provide the initial notification:

Chad Hoskins  
Vice President, Commercial and Corporate Strategy  
1830 Bering Drive  
San Jose, CA 95112  
[choskins@outsetmedical.com](mailto:choskins@outsetmedical.com)  
415.254.3094 (cell)

The Investigator must follow up the initial telephone notification by providing a written report by facsimile or mail describing the SAE or UADE to Outset. This report may be accomplished by completing the AE CRF. Any missing or additional relevant information concerning the SAE or UADE should be provided in the form of a written follow-up report.

The Investigator is required to comply with applicable regulations regarding the notification of SAE/UADE to the reviewing IRB consistent with any IRB conditions of approval.

## 10 RISKS AND BENEFITS

### 10.1 Potential Risks

The potential risks and benefits of participation in this study are identified in the Subject Informed Consent Form (ICF) and are to be explained to the Subject and/or their legal representative prior to participating in the study. It is not anticipated that there will be any additional risks to the Subject with use of the Tablo™ System that are different than those expected during routine dialysis procedures.

#### 10.1.1 Procedure Risks

Potential adverse events that may be associated with a hemodialysis procedure include, but are not limited to, the following:

- Abdominal pain
- Adynamic bone disease
- Air embolism
- Epigastric fullness
- Fatigue
- Fever
- Occult hemorrhage
- Pain
- Pericardial tamponade

- Allergic reaction
- Allergic skin reactions
- Aluminum toxicity
- Anaphylaxis
- Anemia
- Angioedema
- Anuria
- Anxiety
- Arrhythmia
- Ascites
- Atlanto-cervical spondylopathy
- Back pain
- Bleeding complications from the use of blood thinners
- Bleeding from access
- Cerebrovascular disease
- Chest pain
- Chills/Rigors
- Chronic dementia
- Circumoral paresthesia
- Cold extremities
- Colitis
- Complement activation
- Confusion
- Congestive heart failure
- Constipation
- Cough
- Cramps
- Depression
- Dialysis-associated neutropenia
- Dialyzer reaction
- Diarrhea
- Difficulty swallowing
- Digestion or absorption disorders
- Disequilibrium syndrome
- Dizziness
- Edema
- Electrolyte Imbalance
- Fluid overload
- Hallucinations
- Headaches
- Heart palpitations
- Hematoma
- Hemolysis
- Hemothorax
- Hepatitis B
- Hepatitis C
- Urticaria
- Hyperparathyroid bone disease
- Hyperparathyroidism
- Hypertension
- Hypoglycemia
- Hypotension
- Hypovolemia
- Hypoxemia
- Ileus
- Infection
- Inflammation
- Insomnia
- Intracranial bleeding
- Iron deficiency
- Ketoacidosis
- Lactic acidosis
- Left ventricular hypertrophy
- Lipid abnormalities
- Liver function abnormalities
- Loss of consciousness
- Malnourished
- Metabolic acidosis/alkalosis
- Metabolic disorders
- Mononeuropathies
- Myocardial infarction
- Nasal congestion
- Nausea
- Neutropenia
- Perspiration
- Pneumothorax
- Pruritus
- Pulmonary edema
- Restless leg syndrome
- Seizures
- Septicemia
- Sexual dysfunction
- Shortness of Breath
- Sleep apnea
- Slurred speech
- Syncope
- Tetany
- Thrombocytopenia
- Thrombosis
- Tremors
- Uremia
- Uremic encephalopathy
- Uremic neuropathy
- Vascular access complications
- Vascular calcification
- Vomiting
- Weakness
- Weight gain
- Weight loss
- Wheezing

There may be other potential risks that are unforeseen at this time.

**10.2 Risk Management Procedures**

Eligibility criteria have been selected that exclude Subjects who are at a higher risk for experiencing an anticipated adverse event in order to reduce the risks to Subjects who participate in this study. In addition, Subjects enrolled in this study will receive their hemodialysis treatments by qualified dialysis center staff when undergoing treatments In-Center and will perform their own hemodialysis treatments after having completed device study training when performing treatments In-Home.

Monitoring will take place throughout the course of treatment and adverse events will be recorded in the Subject’s charts and on Case Report Forms developed for the study.

In addition, engineering testing has been performed on the Tablo™ System to help mitigate any risks to the Subjects due to product failure.

Investigational device training will be conducted at each initiated study center and appropriate training records will be maintained.

### 10.3 Potential Benefits

There are no guaranteed additional benefits from participation in this study; however, dialysis with the Tablo™ System is expected to provide the Subject with the required urea clearance. Information gained from the conduct of this study may be of no benefit to others with the same medical condition.

## 11 STATISTICAL METHODS AND CONSIDERATIONS

The Statistical Analysis Plan (SAP) for the study will describe the data sets to be analyzed, the methods of analysis, and the specific analyses to be conducted in support of the study's primary endpoints. Those key elements are outlined below.

### 11.1 Data Sets Analyzed

All Subjects who meet all of the Inclusion and Exclusion Criteria and who start the **first study treatment** during the **first treatment period** will be considered enrolled and will be included in the Intent-to-Treat Population (ITT). The primary effectiveness endpoint analysis will be based on the ITT population with a supportive analysis for the Per-Protocol population (PP).

#### 11.1.1 Intent to Treat Population (ITT)

The ITT population will consist of all Subjects who are enrolled in the study. The primary analysis set will be the ITT analysis set with no missing value imputation with a sensitivity analysis performed on the ITT with missing value imputation population.

#### 11.1.2 Per Protocol Population (PP)

The PP population will consist of all Subjects who are enrolled in the study, have successfully completed at least 75% of their dialysis treatments, have at least one valid value of the primary effectiveness variable and have no major protocol deviations while enrolled in the study. A successfully completed dialysis treatment is defined as one completed as prescribed by the physician. A major protocol deviation is defined as any protocol deviation that affects the soundness of the data or a Subject's rights. Subjects to be excluded from the PP analysis set, and the reasons for their exclusion, will be determined and documented prior to statistical analysis. These decisions will not be outcome-data driven.

The analysis of the primary efficacy endpoint will be conducted on ITT and PP populations.

### 11.2 Safety Population

The safety population will consist of all Subjects who are enrolled in the study. All safety analyses will be conducted on the safety population.

### 11.3 Analysis of Primary Endpoint

The study is based on the primary endpoints for effectiveness and interval estimates of the safety of the device. The study will be considered a success from a statistical standpoint if:

1. Both primary analysis variables pass their respective hypotheses, i.e.,  $H_{a0}$  and  $H_{b0}$  below are rejected in favor of  $H_{a1}$  and  $H_{b1}$ , respectively,
2. The rate of pre-specified adverse events per dialysis interval is estimated to be within the specified error of estimation for each treatment period.

#### 11.4 Analysis of Weekly Standardized Kt/V

The following hypotheses will be tested at a one-sided  $\alpha=0.025$  level of significance:

$$H_{a0}: \mu_{IC} \leq 2.1 \text{ vs. } H_{a1}: \mu_{IC} > 2.1$$

and

$$H_{b0}: \mu_{IH} \leq 2.1 \text{ vs. } H_{b1}: \mu_{IH} > 2.1$$

where  $\mu_{IC}$  is the treatment period mean weekly standardized Kt/V value for the In-Center arm and  $\mu_{IH}$  is the treatment period mean weekly standardized Kt/V value for the In-Home arm. This hypothesis will be tested using the Least Square Mean for the respective treatment period from a repeated measures analysis of variance (RMANOVA) containing terms for Subject, arm and time points (weeks) and using an AR(1) covariance structure.

The weekly standardized Kt/V value will be calculated using the Leypoldt (Seminar in Dialysis, 17(2); March-April 2004) formula of:

$$\text{Standard Kt/V (stdKt/V)} = 168 * (1 - \exp(-Kt/V)) / t / ((1 - \exp(-t/V)) / (Kt/V) + 168 / (N * t) - 1)$$

Where: N=number of treatments / week; t= treatment time in hours

Summary statistics (mean, sample size, standard deviation, minimum, maximum, and median) will be computed on the weekly standardized Kt/V values for each treatment period.

#### 11.5 Analysis of Secondary Endpoint

The analysis of the secondary endpoint of ultrafiltration rate (UFR) will be conducted on ITT and PP populations. The UFR will be calculated using the following method:

$$\text{UF Rate} = (\text{Fluid Removal Goal} + \text{Rinse Back Volume}) / \text{Treatment Duration}$$

Where,

$$\text{Fluid Removal Goal} = \text{Today's Weight} - \text{Prescribed Estimated Dry Weight}$$

And,

Rinse Back Volume = The volume of saline, 300mL, returned to the patient at the end of treatment.

#### 11.6 Analysis of Adverse Events

All study-emergent AEs occurring during the study sessions will be recorded and classified on the basis of MedDRA terminology for the ITT population. Study-emergent AEs are those AEs with an onset on or after the date of first study treatment. All study-emergent AEs will be categorized by study period (In-Center or In-Home), the number of Subjects reporting study-emergent AEs, severity, device relationship, and seriousness. Serious adverse events (SAEs) will be listed by Subject. SAEs will be categorized by study period, severity, and device relationship. Each Subject will be counted only once within a category using the event with the greatest device relationship and greatest severity.

For each treatment period, a 95% confidence interval will be computed on the pre-specified adverse event rate per dialysis interval. This confidence interval will be computed using the Least Square Mean for the respective treatment period from a generalized linear model containing terms for Subject, arm and time points (i.e., a repeated measures analysis using GEE) using a Poisson link function and AR(1) covariance structure .

Summary statistics (mean, sample size, standard deviation, minimum, maximum, median) will be computed on the number of pre-specified adverse events per dialysis interval for each treatment period. The same summary statistics will be calculated by treatment period for the rate of pre-specified adverse events per 100 dialysis treatments.

### 11.7 Interim Analysis

No formal statistical interim analyses will be conducted during this study.

### 11.8 Sample Size Analysis

The estimated sample size for the trial was based on the safety endpoint and yields an estimate of the rate of pre-specified adverse events per 100 dialysis treatments in each treatment period (In-Center and In-Home use), to a margin of error of less than 1 event per 100 treatments. With a two-sided  $\alpha=0.05$ , in order to construct a 95% confidence interval on the rate of pre-specified adverse events per 100 dialysis treatments with half-width less than 1 event per 100 treatments, the sample size required would be  $n=30$  Subjects with 4 dialysis intervals per week for a minimum of 8 weeks (i.e., 30 subjects with a minimum of 32 treatments). The sample size calculation was based on an asymptotic normal theory one sample test using variance estimates that included covariance terms for repeated measurements (4 dialysis intervals per week for 8 weeks) on each Subject with a block diagonal first order autoregressive (AR(1)) covariance structure. This sample size calculation assumed a standard deviation of 0.8 AEs per dialysis interval and a within Subject correlation of pre-specified AE counts of  $\rho=.50$ .

## 12 STUDY RECORD MANAGEMENT

For the study duration, the Investigator will maintain complete and accurate documentation, including but not limited to, medical records, study progress records, laboratory reports, CRFs, signed and dated informed consent forms, all correspondence with the IRB, Sponsor personnel/representatives, and other regulatory agencies, the protocol, and documentation for each deviation from the protocol, records of receipt, use, or disposition of each device, record of the exposure to the investigational device, adverse event records, information regarding Subject discontinuation or completion of the study, any other supporting data, and any other records that FDA requires to be maintained by regulation or by specific requirement.

### 12.1 Source Documentation

Regulations require that an Investigator maintain information in the Subject's medical records which can corroborate data collected on study CRFs. In order to comply with these regulatory requirements, at a minimum, the following information should be recorded in the Subject's medical record:

- Medical history and physical condition of the Subject prior to participation in the study sufficient to verify inclusion/exclusion criteria.
- Dated and signed study progress or clinic notes on the day of entry into the study referencing the Tablo™ protocol number, site, Subject ID number assigned, and a statement that informed consent was obtained.
- Dated and signed notes from each Subject's weekly visit.



- All collected AE/SAEs and their resolution, including supporting documents such as discharge summaries and diagnostic test results.
- Subject medical condition upon completion of or withdrawal from the study.

Data recorded in the Subject's medical records will be reviewed for verification of agreement with critical data on the CRFs as specified in the monitoring plan. The Investigator/Study personnel will allow the Sponsor (or designee) and appropriate regulatory authorities access to these records. If a non-study physician, at a non-study institution, sees a study Subject, a copy of the medical record for this unscheduled visit will be copied and placed in the Subject's medical record and made available for review.

### **12.2 Data Collection and Case Report Form Completion**

All study data will be collected and recorded by authorized study personnel on the required Case Report Forms (CRFs). Identifiable Subject information will not be recorded in the CRFs. Subjects will be assigned unique study ID numbers. Only study site personnel directly involved with study and Sponsor monitors or designee(s) will have access to the documentation that links the study ID numbers to identifying Subject information.

The CRFs will capture information relevant to the Subjects' clinical presentation, medical history, laboratory values, and results of clinical and/or dialysis testing. Follow-up clinical data will include laboratory assessments, current medications, physician office visits, hospitalizations, and/or adverse events that have occurred since study enrollment or from the prior visit.

The site Principal Investigators will be required to sign and date the completed CRFs on the appropriate page(s) to verify that he/she has reviewed the recorded data, and assures its accuracy and completeness.

### **12.3 Case Report Forms (CRF) and Device Data Storage**

Prescription details, blood pressure readings, heparin infusion data, changes to treatment parameters, and total fluid removed during treatment will be captured on a Subject specific USB flash drive. Additional study information will be collected on standardized CRFs. Site numbers, Subject numbers and Subject initials will be used to track Subject information throughout the study.

### **12.4 Device Accountability**

The Investigator shall maintain adequate records of the receipt, use, and disposition of the Investigational Device.

### **12.5 Missing Data**

All missing values within the treatment period will be imputed using a multiple imputation procedure (Markov Chain Monte Carlo (MCMC) method). Parameter estimates and inferences for each treatment period will be based on the multiple imputations as described in Little and Rubin (2002). For subjects who did not finish the study but have accumulated partial data for the primary effectiveness endpoint, missing data for Kt/V will be imputed by taking the average of the subject's non-missing Kt/V responses.

For all other endpoints, missing value imputation will be described in the Statistical Analysis Plan (SAP).

### **12.6 Data Processing**

Overall data management will be the responsibility of the study Sponsor. All data will be managed in a 21 CFR Part 11-compliant database. Data edit checks will be performed and the study sites will be queried as needed to ensure completeness and consistency of study data.

All above-mentioned tasks will be performed according to the Data Management Plan and Sponsor SOPs. Audits may be performed for quality assurance of procedures and data handling.

## **13 TRAINING**

### **13.1 Site Training**

The study Sponsor or its designee will conduct site training to develop a common understanding of the study objectives, clinical protocol, CRFs, study procedures and informed consent process. Site initiation may include Investigator(s), nurses and technicians, site research coordinator(s) and Sponsor representatives and/or designee(s). Training activities will include, but are not limited to, review of the clinical protocol including the study procedures, data collection procedures, adverse event reporting procedures, monitoring guidelines, and applicable regulatory requirements. All trained personnel will be required to sign a Training Log.

Teleconferences and/or web-meetings may also be used throughout the study to train Investigators and other study personnel.

Investigators and study site personnel will not be allowed to participate in the study until they have completed appropriate study training.

### **13.2 Monitoring**

#### **13.2.1 Site Monitoring Procedures**

All study monitoring activities will be managed and performed by the study Sponsor or designee. CRFs will be source-document verified according to the monitoring plan. These tasks will be performed according to relevant Sponsor SOPs.

The number of monitoring visits and their duration will be conducted according to the monitoring plan. By verifying compliance, these activities will ensure:

- The study is conducted in accordance with the study protocol, relevant Good Clinical Practice (GCP), and International Conference on Harmonization (ICH) guidelines, as well as in conjunction with 21 CFR Part 812, 50, 54, 56 and other applicable government regulations.
- Adequate protection of the rights and safety of the informed Subjects involved in the study by thoroughly providing accurate and complete data.
- Quality and integrity of the data.

The frequency and scope of periodic site visits will be determined according to the monitoring plan, but at a minimum, shall occur at least once per year. Monitoring activities may include: review of informed consent and research authorization confirmation, regulatory document review, overall investigational plan adherence, GCP/ICH compliance, facility assessment, study staff assessment and additional study related functions that contribute to the safety of study Subjects and the integrity of study data.

Investigators must provide adequate time and resources to the study protocol and will be available to the study monitor and/or designee via telephone, and in person during site visits. The Investigator will also provide the study monitor with a suitable working environment for review of study-related documents.

### **13.3 Compliance**

#### **13.3.1 Site Compliance**

The study at the investigational site may be subject to an audit by the Sponsor or its designees for quality assurance purposes, as well as inspection by appropriate regulatory authorities.

In the event that an Investigator is contacted by a Regulatory Agency in relation to this study, the Investigator shall notify the study Sponsor immediately. The Investigator shall permit authorized representatives from appropriate regulatory authorities, at reasonable times and in a reasonable manner, to:

- Enter and inspect any establishment where the device is held or records relating to the investigational device are kept, inspect and copy records relating to the investigational device use.
- Inspect and copy records that identify Subjects upon notice that the Regulatory Agency has reason to suspect that adequate informed consent was not obtained, or that reports required to be submitted by the Investigator to the Sponsor or IRB have not been submitted or are incomplete, inaccurate, false, or misleading.

The Investigator must provide the Sponsor with copies of all correspondence that may affect the review of the current trial (e.g. Form FDA 483, Inspectional Observations, and Warning Letters). The study Sponsor may provide any needed assistance in responding to regulatory audits.

### **13.3.2 Protocol Deviations**

A deviation is defined as any departure from clinical study requirements, including those cited within International Conference Harmonization (ICH)/Good Clinical Practice (GCP) guidelines. Protocol deviations that affect the rights, safety, or welfare of human Subjects must be reported to the study Sponsor as soon as possible from the occurrence of the deviation. Major protocol deviations are defined as any protocol deviation that affects the soundness of the data or a Subject's rights.

Protocol deviations include, but are not limited to:

- Appropriate informed consent was not obtained prior to performing any study-specific procedures (requires Sponsor notification within 24 hours)
- Enrollment of a Subject who does not meet the study inclusion/exclusion criteria
- Any deviation from the protocol
- Failure to perform study procedures or performing clinical procedures outside of protocol requirements
- Subjects receiving more than 4 complete treatments per week during Treatment Period 1 and Treatment Period 2.

Protocol deviations must be reported to the IRB per the institutional review board's reporting requirements. The occurrence of protocol deviations will be monitored by the study Sponsor for evaluation of Investigator compliance to the study protocol, ICH/GCP guidelines, and regulatory requirements. Protocol deviations will be reviewed and evaluated by the study Sponsor on an ongoing basis.

## **14 QUALITY CONTROL AND ASSURANCE**

### **14.1 Selection of Sites and Investigators**

The Sponsor will select Investigators who are qualified by training and experience to perform the procedures as required per protocol and to participate in the investigation of TABLO. A site selection process will be followed, including a qualification visit to each institution as necessary. Study sites will be selected based upon review of a recent site assessment, the qualifications of the Investigator, research infrastructure including personnel support and standard operating procedures, and the availability of

required equipment and supplies. In order to participate in the clinical study, the Investigator must provide a current Curriculum Vitae to validate his/her experience.

#### **14.2 Financial Disclosure**

All Investigators must provide the Sponsor with documentation of financial interest related to Outset. Investigator's must complete and provide Financial Disclosure in compliance with 21CFR 812.43 (c) (5) to the Sponsor during the approval process of the site.

#### **14.3 Institutional Review Board Protocol and Informed Consent Approvals**

A sample Informed Consent form (ICF) will be provided for the study Investigator(s) to prepare for use at his/her site prior to participation in the study. The written Informed Consent documents should be prepared in the language(s) of the potential Subject population. The ICFs that are used should be in accordance with the current guidelines as outlined by the 21CFR Part 50, Good Clinical Practices (GCP) guidelines and the International Conference on Harmonization (ICH).

The study Sponsor and reviewing IRB must first approve the language and the content within the Informed Consent form that is to be used by each study site. A copy of the proposed Informed Consent form, other written Subject information and any proposed advertising material must be submitted to the IRB for written approval. A copy of the written IRB approval of the protocol and Informed Consent form must be received by the study Sponsor before recruitment and enrollment of Subjects into the study. The written approval must identify the study, protocol version, and the date of approval. The Investigational site must submit to and, where necessary, obtain approval from, the IRB for all subsequent protocol amendments and changes to the Informed Consent Form prior to implementation.

The Investigator will be responsible for obtaining annual IRB approval and renewal throughout the duration of the study. The Investigator and site personnel must forward copies to the Sponsor of all required correspondence with the IRB, including the annual and continuing review reports and IRB continuance of approval. Copies of such correspondence should be filed in the Investigational site study files. Additionally, the Investigator will provide an IRB membership list or assurance number to the Sponsor annually.

#### **14.4 Protocol Amendments**

This protocol will only be altered by written amendments from the study Sponsor. All significant protocol changes must receive written approval from appropriate Sponsor personnel and from the IRB prior to implementation at the study site. Upon IRB approval, the protocol amendment(s) will be distributed to all site study personnel and training will be performed as appropriate.

#### **14.5 Confidentiality**

All information and data sent to Outset, and its authorized representatives, concerning Subjects or their participation in this study will be considered confidential. All data used in the analysis and reporting of this evaluation will be used in a manner without identifiable reference to the Subject.

The Investigator will ensure that this study is conducted in full conformity with the current revision of the regulations and guidelines of FDA (21 CFR Part 812, 50, 54 and 56, and the relevant parts of the ICH Guidelines for Good Clinical Practice).

#### **14.6 Study Administration**

##### **14.6.1 Pre-Study Documentation Requirements**

Prior to Subject enrollment at any clinical site, the following documents must be provided to the Sponsor:

- A signed and dated Investigator Agreement
- A copy of the IRB approval letter of the protocol and Informed Consent
- A copy of the IRB approved Informed Consent Form
- A copy of the signed and dated Curriculum Vitae of the Investigator
- A signed and dated Financial Disclosure Form
- A copy of the medical license of the Principal Investigator

#### **14.6.2 General Investigator Responsibilities**

In order to ensure that the protocol is conducted in compliance to applicable regulations, each site Investigator must:

- Conduct the study in accordance with the study protocol, the signed Clinical Study Agreement, the International Conference on Harmonization (ICH) Guidelines for Good Clinical Practices and Title 21 of the U.S. Code of Federal Regulations (CFR) Parts 812, 50, 54, and 56.
- Assure that the study is not commenced until IRB/EC approval has been obtained.
- Complete all study related documents promptly.
- Agree to participate in an appropriate training program prior to first Subject enrolled and as required by the Sponsor throughout the conduct of the study.
- Sign and adhere to the Investigator Agreement / Financial Disclosure Form.
- Assure that informed consent is obtained from each Subject prior to enrollment, using the IRB-approved Subject Informed Consent Form. Informed Consent must be obtained before conducting any study-specific tests or procedures (including activities to determine Subject eligibility for the study) and without any coercion of or undue influence of Subjects to participate.
- Ensure adverse events are reported within the guidelines provided in this protocol.
- Provide all required data and agree to source document verification of study data with Subject's medical records. Allow study Sponsor staff and its authorized representatives to inspect and copy any documents pertaining to this clinical study.
- Adhere to any institutional clinical care guidelines or protocols.
- Comply with all required elements of this protocol (e.g., perform testing and follow-up as specified, especially during personnel transitions).

#### **14.6.3 Record Retention**

The Investigator agrees to maintain all essential study documents and source documentation, in original format, that support the data collected on the study Subjects in compliance with the ICH/GCP guidelines (the Investigator's File, including signed Informed Consent forms and Subject-related materials) in a location that is secure and to which access can be gained if required.

Documents must be retained for at least two years after (1) study completion, or (2) the study has been terminated by the Sponsor. These documents will be retained for a longer period of time by agreement with the Sponsor or in compliance with other regulatory requirements. When these documents no longer need to be maintained, it is the study Sponsor's responsibility to inform the Investigator. The Investigator will take measures to ensure that these essential documents are not accidentally damaged or destroyed. If, for any reason, the Investigator withdraws responsibility for maintaining these essential documents,

custody must be transferred to an individual who will assume responsibility. The Sponsor must receive written notification of this custodial change.

#### **14.6.4 Criteria for Suspending/Terminating a Study Center**

The study Sponsor reserves the right to terminate the enrollment of Subjects at a study center at any time after the study initiation visit if no Subjects have been enrolled, if the site has multiple or severe protocol deviations without justification, or fails to follow remedial actions. Possible reasons for suspending/terminating a study center include:

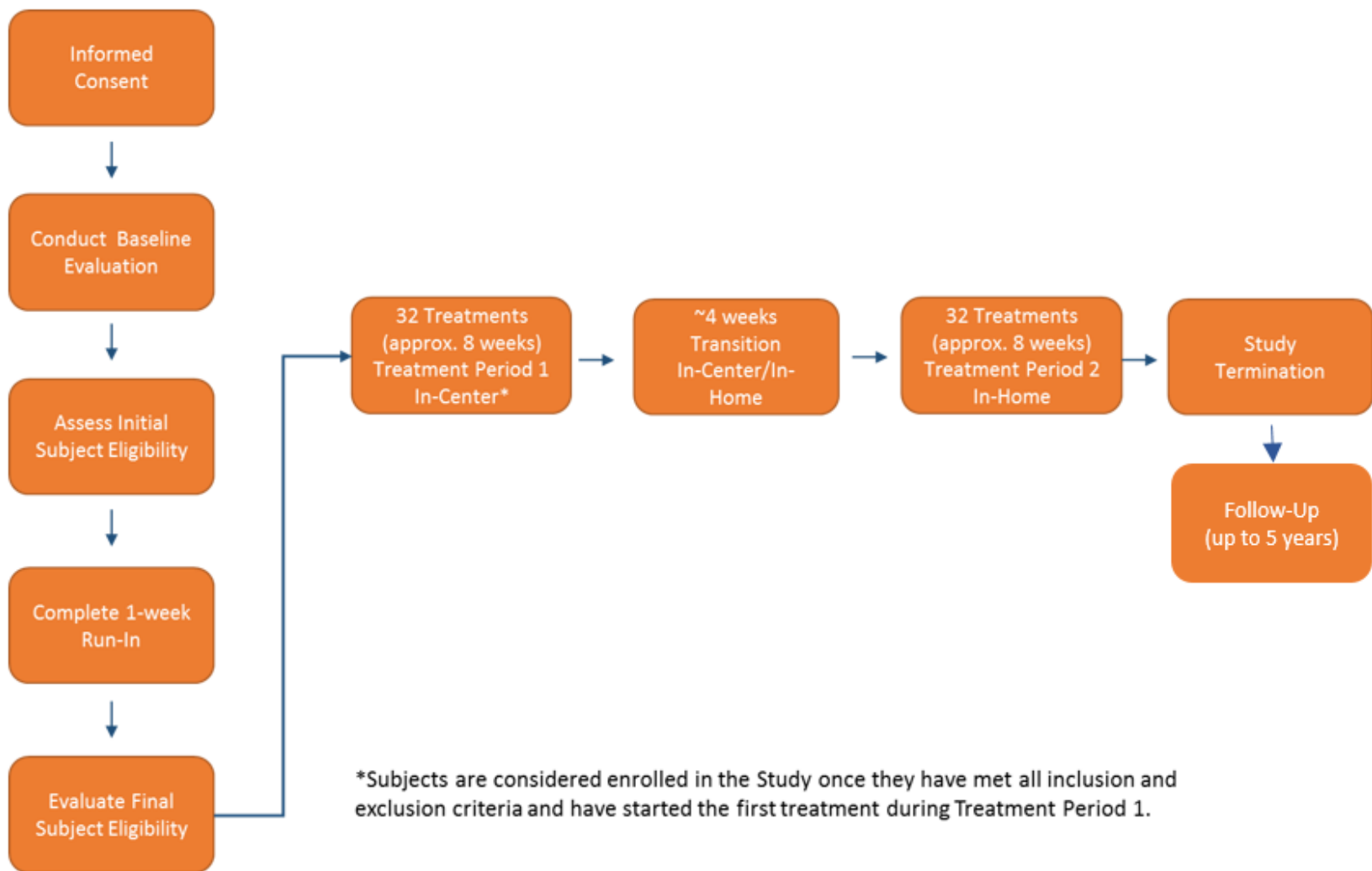
- Failure to obtain a written Informed Consent
- Significant non-adherence to Subject inclusion/exclusion criteria
- Repeated protocol deviations
- Inability to sustain appropriate Subject enrollment rates
- Repeated failure to complete case report forms in a timely manner
- Investigator debarment by regulatory agencies
- Disqualification or suspension by the IRB of this or another study

In the event a study site is suspended, the Subjects already enrolled at these sites will continue to have protocol-designated follow-up despite termination of further enrollment at the site.

#### **14.6.5 Publication Policy**

The data and results from the study are the sole property of the Sponsor. Outset shall have the right to access and use all data and results generated during the clinical study. The Investigators will not use the study related data without the written consent of Outset for any other purpose than for study completion or for generation of a multi-center publication, such as in a peer-reviewed journal deemed appropriate by the Sponsor.

APPENDIX A: SUBJECT STUDY FLOW



APPENDIX B: SCHEDULE OF ASSESSMENTS

Assessment	Dialysis Treatment Week																						Study Exit
	Baseline	Run-in	In-Center Treatment Period 1								Self-Care Transition				In-Home Treatment Period 2								
Study Week	1	1	2	3	4	5	6	7	8	1	2	3	4	1	2	3	4	5	6	7	8		
Informed Consent (≤90 days from Run-In Tx 1)	X																						
Inclusion /Exclusion Criteria Verification	X	X																					
Demographics/Medical/Vascular Access History (including assessment of historical lab values)	X																						
Physical Exam (≤90 days from Run-In Tx 1)	X																						
Concomitant Medications <sup>12</sup>	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Chemistry 20 <sup>13</sup> /CMP	X <sup>14</sup>		X				X								X				X				
CBC <sup>15</sup>	X <sup>15</sup>		X				X								X				X				
Iron Studies (TSAT, Ferritin, Transferrin)	X <sup>15</sup>		X												X								
Pre and Post BUN sample collection (Kt/V) <sup>16</sup>		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Signs and Symptoms <sup>13</sup>	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Subject Evaluation of Device <sup>13</sup>		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Adverse Event <sup>13</sup>		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Study Completion																						X	

<sup>12</sup>Data for each of these Assessments will be recorded at every treatment.

<sup>13</sup>Tests will include the following: Albumin, Alkaline Phosphatase, Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Bilirubin (total and direct), Blood Glucose, Blood Urea Nitrogen (BUN), Calcium (Ca) in blood, Carbon Dioxide (Bicarbonate), Chloride, Creatinine, Phosphate in blood, Potassium in blood, Sodium in blood, and total serum protein.

<sup>14</sup> Additional testing at baseline is not required if lab data on file is within 2 weeks of the Run-In Period and includes all protocol required tests.

<sup>15</sup> CBC includes: White Blood Cells (WBC), Hemoglobin (Hgb), Hematocrit (HCT), Mean Corpuscular Volume (MCV), and Platelets,

<sup>16</sup> Standard Kt/V (stdKt/V) = 168\*(1-exp(-Kt/V))/t/((1-exp(- t/V))/(Kt/V)+168/(N\*t) -1), where: N=number of treatments / week; t= treatment time in hours