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TRANSPLANT
CLINICAL TRIALS NETWORK

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STATISTICAL ANALYSIS PLAN

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TABLE OF CONTENTS

1 PROTOCOL 1
2 GENERAL REVIEW OF STUDY DESIGN AND PROCESS 1
2.1 Study Objectives 1
2.1.1 Primary Objective 1
2.1.2 Secondary Objective 1
2.2 Study Design and Procedures 2
2.2.1 Primary Hypothesis and Primary Endpoint 2
2.2.2 Accrual Plan and Randomization 2
2.2.3 Duration of Follow-Up 3
2.3 Inclusion/Exclusion Criteria and Treatment Description 3
2.4 Response Variables and Data Collection Time Points 3
3 GENERAL STATISTICAL CONSIDERATIONS 6
3.1 Sample Size and Power Calculations 6
3.2 Handling Missing Data 7
3.3 Multiple Comparisons 7
3.4 Interim Analysis and Stopping Guidelines 7
3.4.1 Monitoring Guideline: 100-Day Graft Failure Rate 8
3.4.2 Monitoring Guideline: Grade III-IV Acute GVHD by Day 100 Post Transplant 8
3.4.3 Monitoring Guideline: Overall Mortality by Day 180 Post Conditioning 9
3.4.4 Monitoring Guideline: 18-Month Severe Chronic GVHD 9
3.5 Timing of Analysis 9
3.6 Software 10
3.7 Analysis Populations 10
3.7.1 Primary Analysis Population (Transplant Population) 10
3.7.2 Enrollment Population 10
3.7.3 Conditioning Population 10
4 PARTICIPANT CHARACTERISTICS AND COMPLIANCE 11

4.1 Demographics and Baseline Characteristics 11
4.2 Paticipant Compliance 11
5 ANALYSIS PLAN 11
5.1 Analysis of the Primary Endpoint 11
5.2 Anaylsis of the Key Secondary Endpoints 12
5.3 Analysis of Other Secondary Endpoints 14
5.4 Safety Analysis 15
6 ASSESSMENT OF IMPACT OF COVID-19 ON TRIAL RESULTS 16
7 TEMPLATE OF PROPOSED TABLE/FIGURE/LISTING (TFL) SHELLS 16
8 REFERENCES 16
APPENDIX A 17
ADULT STRATUM DATA ANALYSIS SUMMARY 18
EXHIBIT 1507A-1: PARTICIPANT DISPOSITION AND FOLLOW-UP 18
EXHIBIT 1507A-2: PARTICIPANT DEMOGRAPHICS AND BASELINE CHARACTERISTICS 18
EXHIBIT 1507A-3: EVENT-FREE SURVIVAL (EFS) 20
EXHIBIT 1507A-4: OVERALL SURVIVAL (OS) 20
EXHIBIT 1507A-5: PRIMARY AND SECONDARY GRAFT FAILURE 22
EXHIBIT 1507A-6: DISEASE RECURRENCE 23
EXHIBIT 1507A-7: NEUTROPHIL RECOVERY POST-TRANSPLANT 24
EXHIBIT 1507A-8: PLATELET RECOVERY POST-TRANSPLANT 25
EXHIBIT 1507A-9: DONOR CHIMERISM POST-TRANSPLANT 26
EXHIBIT 1507A-10: ACUTE GVHD POST-TRANSPLANT 27
EXHIBIT 1507A-11: CHRONIC GVHD POST-TRANSPLANT 29
EXHIBIT 1507A-12: COMPLICATIONS AND EVENTS 30
EXHIBIT 1507A-13: SICKLE CELL DISEASE EVENTS OF SPECIAL INTEREST 32
EXHIBIT 1507A-14: SUMMARY OF HEMATOLOGICAL OUTCOMES 33
EXHIBIT 1507A-15: SUMMARY OF RENAL FUNCTION 35
EXHIBIT 1507A-16: SUMMARY OF SICKLE BRAIN DISEASE (BRAIN MRI/MRA) 37
EXHIBIT 1507A-17: SUMMARY OF LUNG FUNCTION TEST 37
EXHIBIT 1507A-18: SUMMARY OF CARDIAC FUNCTION (TRJV) 39
EXHIBIT 1507A-19: SIX MINUTE WALK DISTANCE 40

EXHIBIT 1507A-20: QUALITY OF LIFE (PROMIS) 41
EXHIBIT 1507A-21: PAIN INTENSITY FROM PAIN DIARY 42
EXHIBIT 1507A-22: ASSESSMENT OF COVID-19 IMPACT ON THE STUDY AND TRIAL RESULTS 42
SUPPLEMENTAL EXHIBIT 1507A-1: ENROLLMENT 43
SUPPLEMENTAL EXHIBIT 1507A-2: SIGNIFICANT PROTOCOL DEVIATIONS 43
SUPPLEMENTAL EXHIBIT 1507A-3: PRIMARY CAUSE OF DEATH 43
SUPPLEMENTAL EXHIBIT 1507A-4: ADVERSE EVENTS 43
SUPPLEMENTAL EXHIBIT 1507A-5: SERIOUS OR GRADES 3-5 ADVERSE EVENTS 43
SUPPLEMENTAL EXHIBIT 1507A-6: SAFETY MONITORING (SAFETY ENDPOINT) 43
SUPPLEMENTAL EXHIBIT 1507A-7: INCIDENCE OF TOXICITIES GRADE >2 (SAFETY ENDPOINT) 44
SUPPLEMENTAL EXHIBIT 1507A-8: INCIDENCE OF INFECTIONS GRADE >=2 45
SUPPLEMENTAL EXHIBIT 1507A-9: INCIDENCE OF HOSPITALIZATION POST-TRANSPLANT 46
PEDIATRIC STRATUM DATA ANALYSIS SUMMARY 47
EXHIBIT 1507P-1: PARTICIPANT DISPOSITION AND FOLLOW-UP 47
EXHIBIT 1507P-2: PARTICIPANT DEMOGRAPHICS AND BASELINE CHARACTERISTICS 47
EXHIBIT 1507P-3: EVENT-FREE SURVIVAL (EFS) 47
EXHIBIT 1507P-4: OVERALL SURVIVAL (OS) 47
EXHIBIT 1507P-5: PRIMARY AND SECONDARY GRAFT FAILURE 47
EXHIBIT 1507P-6: DISEASE RECURRENCE 47
EXHIBIT 1507P-7: NEUTROPHIL RECOVERY POST-TRANSPLANT 47
EXHIBIT 1507P-8: PLATELET RECOVERY POST-TRANSPLANT 47
EXHIBIT 1507P-9: DONOR CHIMERISM POST-TRANSPLANT 47
EXHIBIT 1507P-10: ACUTE GVHD POST-TRANSPLANT 47
EXHIBIT 1507P-11: CHRONIC GVHD POST-TRANSPLANT 47
EXHIBIT 1507P-12: COMPLICATIONS AND EVENTS 47
EXHIBIT 1507P-13: SICKLE CELL DISEASE EVENTS OF SPECIAL INTEREST 47
EXHIBIT 1507P-14: SUMMARY OF HEMATOLOGICAL OUTCOMES 47

EXHIBIT 1507P-15: SUMMARY OF RENAL FUNCTION 47
EXHIBIT 1507P-16: SUMMARY OF BRAIN DISEASE (BRAIN MRI/ MRA) 47
EXHIBIT 1507P-17: SUMMARY OF LUNG FUNCTION TEST 47
EXHIBIT 1507P-18: SUMMARY OF CARDIAC FUNCTION (TRJV) 47
EXHIBIT 1507P-19: SIX MINUTE WALK DISTANCE 47
EXHIBIT 1507P-20: ASSESSMENT OF COVID-19 IMPACT ON THE STUDY AND TRIAL RESULTS 47
SUPPLEMENTAL EXHIBIT 1507P-1: ENROLLMENT 48
SUPPLEMENTAL EXHIBIT 1507P-2: SIGNIFICANT PROTOCOL DEVIATIONS 48
SUPPLEMENTAL EXHIBIT 1507P-3: PRIMARY CAUSE OF DEATH 48
SUPPLEMENTAL EXHIBIT 1507P-4: ADVERSE EVENTS 48
SUPPLEMENTAL EXHIBIT 1507P-5: SERIOUS OR GRADES 3-5 ADVERSE EVENTS 48
SUPPLEMENTAL EXHIBIT 1507P-6: SAFETY MONITORING (SAFETY ENDPOINT) 48
SUPPLEMENTAL EXHIBIT 1507P-7: INCIDENCE OF TOXICITIES GRADE >2 (SAFETY ENDPOINT) 48
SUPPLEMENTAL EXHIBIT 1507P-8: INCIDENCE OF INFECTIONS GRADE >=2 48
SUPPLEMENTAL EXHIBIT 1507P-9: INCIDENCE OF HOSPITALIZATION POST-TRANSPLANT 48
APPENDIX B: STATISTICAL ANALYSIS PLAN APPROVAL SIGNATURE PAGE 49

1 PROTOCOL

BMT CTN 1507 is titled “Reduced Intensity Conditioning for Haploidentical Bone Marrow Transplantation in Patients with Symptomatic Sickle Cell Disease”.

This SAP is developed based off v5.0 of the protocol, which is dated May 19, 2021.

2 GENERAL REVIEW OF STUDY DESIGN AND PROCESS

2.1 STUDY OBJECTIVES

BMT CTN protocol 1507 is Phase II, multi-center trial designed to estimate the efficacy and toxicity of haploidentical bone marrow transplantation (BMT) in patients with sickle cell disease (SCD). Patients are stratified into two groups: (1) children between 5.00-14.99 years with SCD with strokes; and (2) adults between 15.00-45.99 years with severe SCD. Based on their age and entry criteria, participants are enrolled in these two strata.

2.1.1 PRIMARY OBJECTIVE

BMT CTN protocol 1507 is Phase II, multi-center trial designed to estimate the efficacy and toxicity of haploidentical bone marrow transplantation (BMT) in patients with sickle cell disease (SCD). Patients are stratified into two groups: (1) children between 5.00-14.99 years with SCD with strokes; and (2) adults between 15.00-45.99 years with severe SCD. Based on their age and entry criteria, participants are enrolled in these two strata.

2.1.2 SECONDARY OBJECTIVE

The secondary objectives of the study include following within each stratum:

1. Estimate overall survival at one year and two years after enrollment and after haploBMT.

2. Estimate EFS at one year after haploBMT.

3. Estimate incidence of primary and secondary graft rejection at one and two years after haploBMT.

4. Estimate incidence and severity of acute GVHD until Day 100 then chronic GVHD at six months, one year, 18 months, and two years post-transplant.

5. Characterize donor hematopoietic chimerism in peripheral blood at days 28, 42, 100, and 180 and at 1 and 2 years after haploBMT.

6. Characterize hematologic and non-hematologic toxicities of haploBMT, including the incidence and severity of acute and chronic graft-versus-host disease; time to and probability of red blood cell, neutrophil, and platelet recovery; hepatic veno-occlusive disease (VOD); idiopathic pneumonia syndrome (IPS); central nervous system (CNS) toxicity (reversible posterior leukoencephalopathy syndrome [RPLS], hemorrhage, and seizures); cytomegalovirus (CMV) infection; adenovirus infection; Epstein Barr virus post-transplant lymphoproliferative disease (EBV PTLD); invasive fungal infection.

7. Evaluate if cerebral vasculopathy is halted by successful transplantation as determined by comparing brain MRI pre- and 2 years post-haploBMT. Cerebral MRI/MRA is required for all pediatric patients to assess progression of CNS disease. For adults with where the indication for the transplant is a stroke, cerebral MRI/MRA is required after transplant to assess progression of CNS disease.

8. Estimate disease recurrence at one and two years after haploBMT.

9. Evaluate sickle-related events and end organ function in all recipients after haploBMT to determine if severe and debilitating vaso-occlusive events such as pain and cerebral infarction are stabilized after transplantation.

10. Evaluate patient-reported quality of life (pain and fatigue domains) pre- and 1 and 2 years post-haploBMT in the adult stratum for English and Spanish-speaking patients.

11. Lung function pre- and 2 years post-haploBMT

12. TRJV pre- and 1 and 2 years post-haploBMT

13. 6 min walk distance pre- and 1 and 2 years post-haploBMT

14. Pain intensity assessed by an electronic pain diary at baseline, 1 and 2 years post-haploBMT for English-speaking patients ≥ 15.00 years of age at time of enrollment

15. Hematological outcomes at 2 years (Hgb, retic, %HbS, LDH, bilirubin, last date of red blood cell transfusion)

16. Viral mold infections/bacterial or fungal sepsis at any time up to 2 years post-transplant

17. Proportion still receiving immunosuppression at 2 years post-haploBMT

2.2 STUDY DESIGN AND PROCEDURES

2.2.1 PRIMARY HYPOTHESIS AND PRIMARY ENDPOINT

This is designed as a Phase II single arm study to investigate the event-free survival (EFS) at 2 years after a reduced intensity conditioning regimen and human leukocyte antigen (HLA)-haploidentical bone marrow transplantation (haploBMT) in children with SCD and adults with severe SCD. The primary hypothesis of this study is that using pre-conditioning Hydroxyurea (HU) with a conditioning regimen that consists of a combination of rATG/CY/Flu/TT with post-grafting high-dose cyclophosphamide in patients with severe SCD who have HLA-haploidentical donors will achieve a high rate of event-free survival at 2 years post-transplant.

The primary endpoint is event-free survival (EFS) at 2 years post-transplant in each age-specific stratum of children with SCD and adults with severe SCD.

2.2.2 ACCRUAL PLAN AND RANDOMIZATION

The target sample size of the study is 40 transplanted participants per each of the two strata, children with SCD and adults with severe SCD.

The estimated accrual period is 4 years. If the safety monitoring for graft failure passes a stopping boundary within the first 12 evaluable participants, it is estimated that the accrual period will be extended up to an additional 15 months.

This is a single arm study with no randomization and no blinding.

2.2.3 DURATION OF FOLLOW-UP

Participants will be followed for the 28-day pain diary (prior to 70-day conditioning period) and for 2 years from date of infusion (post-transplant).

Final analysis report will include the actual accrual and follow up status of the study with actual timeline upon the study closure.

2.3 INCLUSION/EXCLUSION CRITERIA AND TREATMENT DESCRIPTION

Participant inclusion criteria (both common and age-specific stratum) and exclusion criteria can be found in protocol section 2.2.1 and 2.2.2, respectively. Section 2.3 of study protocol provide details of donor eligibility criteria.

The BMT preparative regimen will start on Day -70 with hydroxyurea 30mg/kg daily through Day -10. The conditioning regimen will also include Thymoglobulin (rATG) (0.5mg/kg on Day -9, 2mg/kg on Day -8, Day -7), Thiotepa 10mg/kg on Day -7, Fludarabine (30mg/m2 on Day -6 to Day -2), Cyclophosphamide 14.5mg/kg on Day -6 and Day -5, and TBI 200cGy on Day -1. Day 0 is the day of infusion with non T-cell depleted bone marrow. Cyclophosphamide 50 mg/kg and Mesna 40mg/kg is given on Days +3 and +4, and GVHD prophylaxis (sirolimus and mycophenolate mofetil) begin on Day +5. Section 2.4 of the study protocol provide details of treatment plan

2.4 RESPONSE VARIABLES AND DATA COLLECTION TIME POINTS

The response variables for this study include the primary and secondary endpoints. The primary endpoint is event-free survival at 2 years after a reduced intensity conditioning regimen and human leukocyte antigen (HLA)-haploidentical bone marrow transplantation (haploBMT) in children with SCD and adults with severe SCD. EFS is defined as survival without a qualifying event. Primary graft rejection, secondary graft rejection, second infusion of hematopoietic cells or death will count as events for this endpoint. A secondary endpoint will assess EFS at 1 year post-transplant.

All the primary endpoint and secondary endpoints are stratum-specific.

Other secondary endpoints include:

- Overall survival at one year and two years after enrollment and after haploBMT.
- EFS at one year after haploBMT.
- Engraftment post-transplant. Engraftment is defined as having greater than or equal to 5% donor cells post-transplant, from any molecular chimerism assessment (e.g., unsorted, myeloid, or T-cell) on a peripheral blood or bone marrow aspirate sample.
- Primary graft failure and secondary graft after haploBMT. Primary graft failure is defined as never achieving ≥ 5% donor whole blood or myeloid chimerism (myeloid is

preferable) assessed by bone marrow or peripheral blood chimerism assays by day +42 post-transplant. Second infusion of stem cells is also considered indicative of primary graft failure by day +42 post-transplant. Secondary graft failure is defined as < 5% donor whole blood or myeloid chimerism (myeloid is preferable) in peripheral blood or bone marrow beyond day +42 post-transplant in patients with prior documentation of hematopoietic recovery with >5% donor cells by day +42 post-transplant. Second infusion of stem cells is also considered indicative of secondary graft failure. Infusion of a second stem cell product will be considered graft rejection, and counted toward primary or, depending on timing of the second infusion, secondary graft rejection.

- Incidence and grade II-IV and grade III-IV acute GVHD until Day 100 post-transplant. Acute GVHD will be graded according to the BMT CTN MOP.

- Incidence and severity of chronic GVHD post-transplant. Incidence and severity of chronic GVHD will be scored according to the NIH consensus criteria.

- Donor hematopoietic chimerism in peripheral blood at days 28, 42, 100, and 180 and at 1 year and 2 years after haploBMT.

- Neutrophil recovery and platelet recovery post-transplant. Time to neutrophil recovery is defined as the first of 3 measurements on different days when the patient has an absolute neutrophil count of ≥500/μL after conditioning. Time to platelet recovery is defined as the first day of a minimum of 3 measurements on different days that the patient has achieved a platelet count > 50,000/μL AND did not receive a platelet transfusion in the previous 7 days.

- Hepatic veno-occlusive disease (VOD). Veno-occlusive disease (VOD) will be diagnosed and defined in accordance with either the modified Seattle or Baltimore criteria as outlined in Appendix J of the study protocol.

- Idiopathic pneumonia syndrome (IPS). IPS will be defined evidence of widespread alveolar injury and in which infectious etiologies and cardiac dysfunction, acute renal failure, or iatrogenic fluid overload have been excluded. Refer to Appendix K of the study protocol for complete IPS criteria.

- Central nervous system (CNS) toxicity. CNS toxicity will be defined as seizures, CNS hemorrhage, or Posterior reversible leukoencephalopathy syndrome (PRES or RPLS). Refer to Appendix I of the study protocol for details regarding PRES.

- Infections. Significant infections will be recorded including but not limited to bacterial or fungal sepsis, CMV reactivation with/without clinical disease, adenovirus infection, EBV PTLD, or other significant viral reactivations or community-acquired viral mold infections and invasive fungal infections.

- Cerebral vasculopathy. Evaluate if sickle-related cerebral vasculopathy is halted by successful transplantation by comparing brain MRA pre- and 2 years post-haploBMT.

- Disease recurrence. Disease recurrence is defined as the return of sickle erythropoiesis (in the absence of RBC transfusion, Hb S level > 70%), or primary or secondary graft rejection, as defined above, or second infusion of hematopoietic cells.

- Sickle-related events and end organ function in all recipients after haploBMT to determine if severe and debilitating vaso-occlusive pain and cerebral infarction are stabilized after transplantation.

- Patient-reported quality of life outcomes at baseline (prior to the initiation of hydroxyurea), 1 year and 2 years post-haploBMT in the adult stratum for English and Spanish-speaking participants. Quality of life will be described using the quality of life questionnaires (PROMIS) pain and fatigue domains.

- Electronic pain diary at baseline, 1 year and 2 years post-haploBMT for English-speaking patients ≥ 15.00 years of age at time of enrollment. The electronic pain diary is administered twice daily for 28 consecutive days for English-speaking patients ≥ 15.00 years of age at the time of enrollment. An average value will be computed for each day on which the diary shows two entries. If the diary reflects only a single entry for a day, then the single value will be used, and if a patient did not enter a value on a given day, that non-adherence will be tallied separately.

- Disease-related complications, including stroke and occurrence of sickle related events. SCD related events are expected events of special interest (SCD-EOSI) as outlined in section 3.8.2 of the study protocol.

- Lung function (PFTs) at baseline, 1 year and 2 years post-haploBMT.

- TRJV (Cardiac Function) at baseline, 1 year and 2 years post-haploBMT.

- 6-minute walk distance assessment at baseline, 1 year and 2 years post-haploBMT.

- Hematological outcomes at baseline, Day 28, 100, 180, 1 year and 2 years post-transplant, including Hgb, reticulocyte count, %HbS, LDH, bilirubin, and last date of red blood cell transfusion.

- Proportion on immunosuppression at 2 years post-haploBMT. Proportion of participants still receiving immunosuppressive therapy because of GVHD or concern about graft rejection will be determined.

Participants are expected to complete all the pre-enrollment, pre-transplant and post-transplant evaluations per protocol schedule (refer to details in section 4.2 of study protocol). Pre-transplant phase includes pre-HU (baseline) and should be performed < 30 days after enrollment, and prior to initiation of HU. The participants are evaluated at every week till week 13, Day 100, Day 180, 1 year, Day 540 and Day 730 (two years post-transplant). Pre-transplant conditioning assessments should be performed < 30-day prior to initiation of Thymoglobulin.

Participants complete quality of life questionnaires (PROMIS) at the baseline, and at the following time points: Day 365 and Day 730 post-transplant.

Infections, hospitalizations, and adverse events are reported on event-driven forms

3 GENERAL STATISTICAL CONSIDERATIONS

3.1 SAMPLE SIZE AND POWER CALCULATIONS

The sample size is 40 transplanted participants per each of the two strata in this trial. Ninety-five percent confidence intervals were calculated for varying probabilities based on the sample size. The primary endpoint, event-free survival (EFS), is considered for sample size determination. Table 2.1 provides confidence intervals for a variety of observed proportions based on the binomial proportion. Of particular interest is where the EFS probability is 80%. If the observed EFS probability is 80%, the width of the confidence interval is 24.8. The tabulated percentages and confidence intervals for observed probabilities above and below 80% are meant to represent other plausible EFS percentages.

TABLE 2.1A: Confidence Interval Lengths and Possible Confidence Intervals for Various Observed Event-Free Survival Probabilities

40 participants enrolled and transplanted				
N (per stratum)	Event-free survival %	Length of 95% Confidence Interval	Possible Confidence Intervals	
40	90	18.6	80.7	99.3
40	85	22.1	73.9	96.1
40	80	24.8	67.6	92.4
40	75	26.8	61.6	88.4

The EFS probability estimate will be based on the Kaplan-Meier product limit estimator using Greenwood's formula as the variance estimate. In the absence of censoring, the Kaplan-Meier estimate reduces to the simple binomial proportion. If the linear confidence intervals extend beyond 0 or 100, log-log confidence intervals may be used.

It is estimated that there may be more than 40 participants enrolled to reach 40 transplanted participants. For example, there may be 53 participants enrolled with 15% censored. The following table shows how the binomial confidence intervals would change based on 45 participants who were not censored for the primary endpoint.

TABLE 2.1B: Confidence Interval Lengths and Possible Confidence Intervals for Various Observed Event-Free Survival Probabilities

45 participants not censored for primary endpoint				
N (per stratum)	Event-free survival %	Length of 95% Confidence Interval	Possible Confidence Intervals	
45	88.9	18.4	79.7	98.1
45	84.4	21.1	73.9	95.0
45	80.0	23.4	68.3	91.7
45	75.6	25.1	63.0	88.1

3.2 HANDLING MISSING DATA

In general, Time to events endpoints should use censoring mechanism to count for missingness. Missing data on other types of endpoint will be treated as missing completely at random and no imputation will be performed since this is a phase II trial. However, imputation may be considered if the number of participants withdraw early from the study (i.e., before 2 year follow up post-transplant) exceeds 15% of the total number of participants in the transplant population. Further details may be added in future revisions of the SAP if deemed necessary.

3.3 MULTIPLE COMPARISONS

There are no groups being compared either on the primary or secondary endpoints, so no significance level and hence no multiplicity adjustment is been specified.

3.4 INTERIM ANALYSIS AND STOPPING GUIDELINES

There is no formal interim analysis planned for the study.

Monitoring of key safety endpoints will be conducted monthly within each stratum, and if rates significantly exceed pre-set thresholds, the NHLBI will be notified in order that the DSMB can be advised. Policies and composition of the DSMB are described in the BMT CTN's Manual of Procedures. The stopping guidelines serve as a trigger for consultation with the DSMB for additional review.

The key safety endpoint of 100-day graft failure will be monitored, with a planned protocol modification of the conditioning regimen planned if rates exceed 15% in the first 12 evaluable participants in a stratum. After the first 12 evaluable participants, if the stopping boundary has not been crossed, then the graft failure rate will continue to be monitored as a safety guideline for consultation with the DSMB but it is unlikely the conditioning regimen will change and accrual be restarted.

Within each stratum, the additional key safety endpoints to be monitored are the following rates:

- Acute, grade III-IV GVHD by 100 days post-transplant
- Overall mortality by 180 days post initiation of hydroxyurea
- Severe chronic GVHD by 18 months post-transplant

A truncated version of the sequential probability ratio test (SPRT) will be used for monitoring, as described in greater detail in Appendix H of the study protocol. This sequential testing procedure conserves type I error across all of the planned examinations for a treatment arm for a given stopping rule and stratum. Two versions of the SPRT will be used. For graft failure, a binomial SPRT will be used, and a plot will display the number of evaluable patients versus the number of observed events. Other safety endpoints will be monitored using an extension to the SPRT for censored exponential data. This extension will plot the observed time on study versus the number of observed events. The continuation region for both versions of the SPRT is defined by two parallel lines. Only the upper boundary will be used for monitoring to protect against excessive rates. If the graph crosses the upper boundary, the SPRT rejects the null hypothesis, and concludes that there are more events than predicted. Otherwise, the SPRT continues until the monitoring period is complete.

The usual measures of performance of an SPRT are the error probabilities □ and □ of rejecting H0 when □ = □0 and of accepting H1 when □ = □1, respectively, and the expected sample size E(N|□i).

3.4.1 MONITORING GUIDELINE: 100-DAY GRAFT FAILURE RATE

The monitoring of graft failure is a key safety endpoint for which a protocol modification for a change in the dose level of TBI is pre-planned in the event the boundary is crossed within the first 12 evaluable participants.

This monitoring procedure assumes a binary distribution for graft failure during the first 100 days post-transplant. If the participant has been transplanted but has had primary or secondary graft rejection by day 100, the participant is assumed to be a graft failure at day 100. Chimerism from samples collected within the D100 visit window will be used for evaluation of graft failure at Day 100. This monitoring guideline uses an SPRT contrasting a null hypothesis of 15% versus an alternative of 35% 100-day graft failure which results in decision boundaries with a common slope of 0.240 and an upper intercept of 2.59, with nominal type I and type II errors of 5% and 10%, respectively. Table 2.4.1 summarizes the stopping rule.

Table 2.4.1: Stopping Rule for 100-Day Graft Failure

Number of evaluable participants	Stop if graft failure occurs in
4-5	4
6-10	5
11-14	6
15-18	7
19-22	8
23-26	9
27-30	10
31-34	11
35-39	12

While participants are enrolled under the 200 cGy dose of TBI, if the stopping boundary is crossed before the end of the first 12 evaluable participants, then a planned protocol modification may be discussed by the DSMB. Refer to section 5.3.1.1 of the study protocol.

3.4.2 MONITORING GUIDELINE: GRADE III-IV ACUTE GVHD BY DAY 100 POST TRANSPLANT

The incidence of acute grade III-IV GVHD is approximately 15-17% after HLA-identical sibling BMT.i, ii, iii, iv. Each month, the null hypothesis that the 100-day acute GVHD rate is 20% is tested.

This monitoring procedure assumes a censored exponential distribution for the time until acute grade III-IV GVHD during the 100 days post-transplant, and censor's follow-up time after 100 days. Only events that occur after transplant and on or before the participant has been followed for 100 days post-transplant are counted. Total time on study is computed as time from transplant to acute grade III-IV GVHD, or to 100 days, whichever comes first, summed for all transplanted participants on study. This monitoring guideline uses an SPRT contrasting a null hypothesis of 20% versus an alternative of 40% 100-day acute grade III-IV GVHD which results in decision boundaries with a

common slope of 1.27 and an upper intercept of 2.94, with nominal type I and type II errors of 7% and 20%, respectively.

For the actual operating characteristics of this truncated test, refer to section 5.3.2 of the study protocol.

3.4.3 MONITORING GUIDELINE: OVERALL MORTALITY BY DAY 180 POST CONDITIONING

Overall mortality (OM) is defined as death with or without disease recurrence. The monitoring procedure assumes a censored exponential distribution for the time until death during the first 180 days, and censor's follow-up time after 180 days. Deaths that occur on or before the participant has been followed for 180 days are counted as events. Total time on study is computed as time from start of hydroxyurea (HU) at day -70 pre-BMT to death, loss to follow-up, or to 180 days, whichever comes first, summed for all participants on study. This monitoring guideline uses an SPRT contrasting a null hypothesis of 10% versus an alternative of 30% 180-day mortality, which results in decision boundaries with a common slope of 0.42 and an upper intercept of 2.05, with nominal type I and type II errors of 7% and 15%, respectively.

For the actual operating characteristics of this truncated test, refer to section 5.3.3 of the study protocol.

3.4.4 MONITORING GUIDELINE: 18-MONTH SEVERE CHRONIC GVHD

The incidence of severe chronic GVHD (defined as NIH severe chronic GVHD) is approximately 5-20% after HLA-identical sibling BMT.i, v, vi. The working hypothesis is that the overall toxicity of mini-haploBMT is not significantly greater than HLA-identical sibling BMT after myeloablative conditioning.

This monitoring procedure assumes a censored exponential distribution for the time until severe cGVHD during the eighteen months post-transplant, and censor's follow-up time after eighteen months. Only events that occur after transplant and on or before the participant has been followed for 18 months post-transplant are counted. Total time on study is computed as time from transplant to severe cGVHD, or to eighteen months, whichever comes first, summed for all transplanted participants on study. This monitoring guideline uses an SPRT contrasting a null hypothesis 20% versus an alternative hypothesis of 40% 18-month severe cGVHD which results in decision boundaries with a common slope of 0.23 and an upper intercept of 2.87, with nominal type I and type II errors of 8% and 14%, respectively.

For the actual operating characteristics of this truncated test, refer to section 5.3.4 of the study protocol**.**

3.5 TIMING OF ANALYSIS

All analyses are within stratum, and each stratum will follow its own timeline for the primary analysis.

For each stratum, a data lock will be used for the primary analysis. The data lock will occur upon the completion of 2-year follow up of all transplanted participants for the stratum. The data lock will include the mature data on the primary and key secondary endpoints for the study participants.

For each stratum, the protocol team will form Endpoint Review Committee (ERC) to review study data and adjudicate primary endpoint and secondary endpoints, then the timing of data lock for analysis will be after the completion of the ERC process. An ERC Charter will be developed to guide the ERC process before the ERC reviewers will review study data.

3.6 SOFTWARE

All statistical analyses will be conducted using SAS 9.4 or higher software, or R version 3.1.0 or higher.

3.7 ANALYSIS POPULATIONS

3.7.1 PRIMARY ANALYSIS POPULATION (TRANSPLANT POPULATION)

The primary analysis population is the transplant population. This includes all participants who consented and received transplantation for each stratum. The primary endpoint will use the primary analysis population. Some of the secondary analysis or secondary endpoints will also use the transplant population.

Time to event data for participants in this population will be derived with start time as start date of transplantation.

3.7.2 ENROLLMENT POPULATION

Enrollment population will include all participants who consented and enrolled to the study for each stratum.

Some of the secondary endpoints will use the enrollment population if needed.

Time to event data for participants in this population will be derived with start time as start date of enrollment.

3.7.3 CONDITIONING POPULATION

For continuous variables, descriptive statistics will include the number of subjects (n), mean, standard deviation, median, minimum, and maximum. Frequencies and percentages will be displayed for categorical data. Clopper-Pearson Exact test will be used for computation of 95% CI for binomial proportion. Estimation of cumulative incidence for both the stratum in presence of competing risk will be done using Aalen-Johansen estimator. No hypothesis testing is planned to compare the stratum in any of the analyses.

All analyses are within-stratum. If a new conditioning regimen is implemented for any strata, then for that stratum, descriptive statistics or listings will be provided using data from participants enrolled under the original dose of TBI; the stratum-specific analyses will be limited to the participants enrolled under the new conditioning regimen

Any changes to the planned analyses and ad hoc analysis will be documented and clarified in the final analysis report with detailed explanation/justifications for such changes. If it is changes to an existing endpoint, the changes e.g. on the definition or method, should be clearly stated in the exhibit. If it is a new endpoint or analysis performed, it should be included in a supplemental exhibit.

There is optional future research as defined in the protocol appendix C which will collect laboratory samples from the study participants and use clinical data from this trial. Details regarding these

ancillary studies or future research are available in the protocol Appendix C. Statistical consideration and analysis plan for these are NOT covered in this SAP. Presentation and publication of the primary results will not include any ancillary studies.

4 PARTICIPANT CHARACTERISTICS AND COMPLIANCE

4.1 DEMOGRAPHICS AND BASELINE CHARACTERISTICS

Descriptive statistics for demographics and baseline characteristics will be presented by strata. Characteristics to be examined include age, gender, race, ethnicity, Karnofsky/Lansky performance status, number and duration of prior transfusions, TRJV, disease risk characteristics, disease symptoms, donor characteristics, HLA match, serum bilirubin level, serum creatinine level, pulmonary function tests (O_2 saturation, DCLO), cardiac function (LVEF, LVSF), splenic function, hemoglobin electrophoresis, cerebral MRI/MRA, serum ferritin and PROMIS score (both pain and fatigue domains).

Donor data will include donor age, sex, relationship to patient (sibling/parent), SCD carrier status, ABO blood type and CMV status. Some baseline data will be retrieved from the Center for International Blood and Marrow Transplant Research (CIBMTR) data system.

4.2 PATICIPANT COMPLIANCE

A table listing significant protocol deviations/violations will be provided for each stratum (if applicable). Compliance with protocol interventions will be evaluated as appropriate. Premature withdrawals will be described for each case.

A consort diagram will be provided to illustrate study accrual, transplantation, and follow up.

In the tables/figures, the number of included participants will be provided/described for each analysis.

5 ANALYSIS PLAN

All analyses will be conducted and reported within each stratum, including primary endpoint and secondary endpoints. There is no comparison between the two strata.

5.1 ANALYSIS OF THE PRIMARY ENDPOINT

Event-Free Survival (EFS) at 2 years post-transplant:

The primary outcome of the trial is two-year post-transplant event-free survival in each stratum using the primary analysis population. EFS is defined as survival without a qualifying event. Events contributing to this endpoint are as below:

i) Primary graft rejection (Primary graft failure is defined as never achieving ≥ 5% donor whole blood or myeloid chimerism (myeloid is preferable) assessed by bone marrow or peripheral blood chimerism assays by day +42 post-transplant. Second infusion of stem cells is also considered indicative of primary graft failure by day +42 post-transplant).

ii) Secondary graft rejection (Secondary graft failure is defined as < 5% donor whole blood or myeloid chimerism (myeloid is preferable) in peripheral blood or bone marrow beyond day +42 post-transplant in patients with prior documentation of hematopoietic recovery

with >5% donor cells by day +42 post-transplant. Second infusion of stem cells is also considered indicative of secondary graft failure).

iii) Second infusion of hematopoietic cells (Infusion of a second stem cell product will be considered graft rejection, and counted toward primary or, depending on timing of the second infusion, secondary graft rejection).

iv) Death (from any cause by 2 years post-transplant)

The EFS probability estimates and its confidence interval for each stratum will be based on the Kaplan-Meier product limit estimator using Greenwood's formula as the variance estimates. Complimentary log-log transformation for confidence interval will be used. For the primary analysis, time to event will be calculated as follows:

Minimum (date of first qualifying event, date of lost to follow-up, date of two-years post-transplant) - Date of Transplant.

5.2 ANAYLSIS OF THE KEY SECONDARY ENDPOINTS

The primary analysis of the secondary endpoints will be limited to the participants enrolled under the TBI conditioning regimens in effect at the close of the study. The data from participants enrolled under the initial conditioning regimens that were subsequently modified as part of the planned protocol amendment will be provided using descriptive statistics or lists only. If the endpoint definitions indicate the endpoint is only for adults, the analysis will be restricted to those participants.

One-year Event-Free Survival (EFS):

For those with a transplant, EFS from day of transplant will be estimated using the Kaplan-Meier estimator. A point estimate and confidence interval will be provided for the rate of EFS at one year from the date of transplant.

Overall Survival (OS):

Death from any cause will be considered as event for this endpoint. Patient will be censored at the date of last contact or two years whichever comes first. OS at 1 year and 2 years post HU conditioning or post-HaploBMT will be estimated using the Kaplan-Meier method and 95% confidence interval using Greenwood's formula as the variance estimates.

Time to event for OS will be calculated as follows:

OS post HU conditioning: Minimum (date of death, date of lost to follow-up, date of two-years post-conditioning) - Date of conditioning).

OS post-transplant: Minimum (date of death, date of lost to follow-up, date of two-years post-transplant) - Date of transplant).

Note there are 2 sets of analysis for OS, one is from date of HU conditioning using the conditioning population and another is from date of transplant using the primary analysis population (transplant population). Analysis methods and report format will be the same for these two sets.

Graft Failure (primary and secondary):

Primary graft failure will be summarized by the frequency and proportion of participants experiencing primary graft failure at Day 42 post-transplant.

Secondary graft failure will be assessed in patient who engrafted. Secondary graft rejection will be estimated using the cumulative incidence function, treating death as a competing risk. A point estimate and confidence interval will be provided for the cumulative incidence at one year and two years post-transplant for secondary graft rejection. Events for secondary graft failure include 1) donor chimerism <5%; 2) second infusion/transplant, as defined in section 4.1 for secondary graft rejection.

Neutrophil Recovery:

The incidence of neutrophil recovery from transplant will be estimated using the cumulative incidence function, treating death or second transplant without neutrophil recovery as a competing risk. A point estimate and confidence interval will be provided for the cumulative incidence at Day 42 post-transplant.

Platelet Recovery:

The incidence of platelet recovery from transplant will be estimated using the cumulative incidence function, treating death or second transplant as a competing risk. A point estimate and confidence interval will be provided for the cumulative incidence at Day 100 post-transplant.

Lineage Specific Chimerism following HCT for SCD:

Lineage specific chimerism taking into account the genotype of the donor will be described. A point estimate and confidence interval will be provided for the mean percent donor chimerism at the time points specified in the Schedule of Evaluations Table, including Day 28, Day 42, Day 100, Day 180, 1 year and 2 years post-transplant. The proportions with low chimerism (<5%), mixed chimerism (5-95%), or full chimerism (>95%) will be tabulated and described.

Grade II-IV and Grade III-IV Acute GVHD:

The time of onset of acute grades II-IV and III-IV acute GVHD will be recorded, as well as the maximum grade achieved. This endpoint will be evaluated through Day 100 post-transplant. Cumulative incidence of acute GVHD will be estimated from the time of transplant using the cumulative incidence function, treating death and second transplant prior to acute GVHD as competing risks. Both grades II-IV acute GVHD and grades III-IV acute GVHD will be evaluated, respectively. Point estimates and 95% confidence intervals will be provided at Day 100 post-transplant.

Chronic GVHD:

Chronic GVHD will be tabulated and summarized by severity. The incidence of chronic GVHD will be computed using the cumulative incidence function, treating death prior to chronic GVHD and second transplant as competing risks. The event of interest is any chronic GVHD based on NIH Consensus Criteria. Cumulative incidence will be plotted for the event of interest. Pointwise estimates and 95% confidence intervals will be provided at 6 months, 1 year and 2 years post-transplant.

Complications and Events:

The frequency of the following complications and events will be tabulated, and the proportion of participants experiencing each at baseline, 1 year and 2 years post-transplant will be estimated, with confidence intervals provided for each estimate:

- Idiopathic pneumonia syndrome (IPS)
- Veno-occlusive disease (VOD)
- Various CNS toxicities
- Stroke
- Infection – bacterial/fungal sepsis, CMV reactivation with/without clinical disease, adenovirus, EBV PTLD, invasive fungal infection, CMV specified, viral mold infection
- Proportion of participants still on immunosuppression for GVHD at 2 years

The number of significant infections and number of participants experiencing infections will be tabulated by type of infection, severity, and time period post-transplant.

If the event date is available for the analysis, cumulative incidence analysis will be used for the endpoint.

Quality of Life:

Quality of life will be described using the PROMIS pain and fatigue domains. Descriptive statistics and confidence intervals for the change from baseline will be reported for each domain for English- and Spanish-speaking patients in the adult stratum. Exploratory models may be used to investigate the change over time adjusted for covariates using mixed effect model for repeated measures (MMRM) with baseline as continuous covariate.

Pain Intensity:

The mean pain intensity from the diary will be the sum of the reported daily pain intensities averaged over the number of days on which at least one pain intensity was reported. Descriptive statistics (mean, standard deviation) and confidence intervals for the change from baseline will be reported at each assessment time point. Change from baseline scores will be analyzed as an exploratory analysis using Mixed effect model for repeated measures (MMRM) with baseline as continuous covariate.

5.3 ANALYSIS OF OTHER SECONDARY ENDPOINTS

Sickle cell disease events of special interest are reported before hydroxyurea initiation and every 6 months post-transplant for the 2-year duration of the study. These events will be summarized in a descriptive way.

The following secondary endpoints will be analyzed for transplanted participants in a descriptive way, and all these analyses are considered as exploratory:

- Hematological outcomes

  Hgb, reticulocyte count, %HbS, LDH, bilirubin, and last date of red blood cell transfusion will be measured pre-transplant and on post-transplant days 28, 100 and 180 days, 365 and 730

- Renal function
- Cerebral vasculopathy as measured by brain MRI and neurological examination

  Evaluate if sickle cerebral infarct recurrence is halted by successful transplantation as determined by comparing brain MRI pre- and 2 years post-haploBMT. Cerebral MRI is required for all pediatric patients to assess progression of CNS disease. For adults with where the indication for the transplant is a stroke, cerebral MRI is required after transplant to assess progression of CNS disease.

- Lung function (PFT), including FEV1 and restrictive lung disease

  A complete set of pulmonary function tests (PFTs) will be obtained at baseline (prior to the initiation of hydroxyurea), 1 year and 2 years post-transplant. In addition to assessing change from baselines in FEV1 at 1 year and 2 years post BMT the proportion of participants with evidence of restrictive lung disease will be estimated. Restrictive lung disease is defined as TLC below the 5th percentile adjusted for age, gender, race and height.

- Cardiac function (TRJV)

  Tricuspid regurgitant jet velocity (TRJV) is a marker for the severity and progression of SCD. Changes in TRJV from baseline (prior to the initiation of hydroxyurea) to 1 year and 2 years post-transplant will be estimated.

- 6-minute walk distance

  The 6MWD will be summarized at baseline (prior to the initiation of hydroxyurea), 1 year and 2 years post-transplant. This endpoint will measure absolute change from baseline, with increased distance identified as positive change.

- Other SCD-EOSI (defined in Section 3.8.2 of protocol)

For binary outcomes, proportions and confidence intervals will be provided at each time point. For continuous outcomes, results will be summarized with descriptive statistics and confidence intervals will be provided where appropriate.

5.4 SAFETY ANALYSIS

The reporting of adverse events (AE) and serious adverse events (SAE) will be consistent with standard BMT CTN procedures. In addition to the standard BMT CTN SAE reporting, all deaths, central nervous system (CNS) events, diagnosis of posterior reversible encephalopathy syndrome (PRES)/reversible posterior leukoencephalopathy syndrome (RPLS), and/or events requiring advanced care interventions or admission/transfer to an intensive care unit (ICU) are required to be reported via the expedited AE reporting system in AdvantageEDC for this study. The type and severity of adverse events will be described. Safety data will be summarized using Medical Dictionary for Regulatory Activities (MedDRA) Coding Version 20.0 or above.

Descriptive analysis will be done for safety outcomes within each stratum.

AEs and toxicities will be reported and summarized.

Infections will be reported and summarized by infection severity and type.

Hospitalizations will be tabulated and summarized by the frequency, timing of hospitalization and diagnosis for hospital discharge.

6 ASSESSMENT OF IMPACT OF COVID-19 ON TRIAL RESULTS

This section is NOT pre-defined in the protocol. This section is added to address the potential impact of the Covid-19 pandemic starting during the ongoing accrual and follow up of patients enrolled on this trial. The BMT CTN considers the COVID-19 era to have potentially impacted trials effective March 10, 2020, unless otherwise specified. Data collection was adjusted, and guidance was given to centers to track the impact of COVID-19. Specifically, the following adjustments were made:

- Impact of COVID-19 on scheduled visits and assessments: Collection of information about whether visits were missed or scheduled out of the assessment window; the type of visit (clinic visit, telemedicine visit, phone contact, or combination); and if the visit was missed, what the reason for the missed visit was (which included COVID-19 as an option).
- COVID-19 infections: Guidance on the collection of COVID-19 infection occurrences was incorporated into the infection data collection form.
- COVID-19 related deaths: Addition of COVID-19 as a potential primary cause of death.

Frequencies and percentages will be provided on the number of missed visits, out of window visits, type of visits, and reasons for missed visits. The number of deaths attributed to COVID-19 and the number of COVID-19 infections will also be described.

Sensitivity analyses will be conducted using the additional data collection for COVID assessment on the primary endpoint and secondary endpoint if felt important based on the results. The goal of the sensitivity analyses is to assess the robustness of the primary analysis; the impact of various censoring schemes on the number of events and widths of the confidence intervals should be considered in interpreting these analyses.

7 TEMPLATE OF PROPOSED TABLE/FIGURE/LISTING (TFL) SHELLS

Table/Figure/Listing titles and layout are for illustration purposes only and may not be the final layout or wording chosen for publications or presentations. Actual format of the tables and figures may differ and will be subject to change in the final analysis report and/or publication.

See Appendix of this SAP for the exhibits title and shell. Analysis will be completed for the adult stratum and the pediatric stratum, respectively. The adult stratum and the pediatric stratum will have the same exhibits and report layout as outlined in Appendix, unless otherwise specified. TFL shells for pediatric stratum follows the same structure as the adult's stratum.

8 REFERENCES

i) Lucarelli G, Isgro A, Sodani P, et al. Hematopoietic SCT for the Black African and non-Black African variants of sickle cell anemia. Bone Marrow Transplantation. 2014 Nov;49(11):1376-81.

ii) Soni S, Gross TG, Rangarajan H, Baker KS, Sturm M, Rhodes M. Outcomes of matched sibling donor hematopoietic stem cell transplantation for severe sickle cell disease with myeloablative conditioning and intermediate-dose of rabbit anti-thymocyte globulin. Pediatric Blood and Cancer. 2014 Sep;61(9):1685-9.

iii) Hsieh M.M., Fitzhugh C.D., Weitzel R., et al: Nonmyeloablative HLA-matched sibling allogeneic hematopoietic stem cell transplantation for severe sickle cell phenotype. JAMA. 2014 Jul 2;312(1):48-56.

iv) Walters M.C., Patience M., Leisenring W., et al: Stable mixed hematopoietic chimerism after bone marrow transplantation for sickle cell anemia. Biology of Blood Marrow Transplantation. 2001;7(12):665-73.

v) Locatelli F., Kabbara N., Ruggeri A., et al: Outcome of patients with hemoglobinopathies given either cord blood or bone marrow transplantation from an HLA-identical sibling. Blood. 2013 Aug 8;122(6):1072-8.

vi) Panepinto J.A., Walters M.C., Carreras J., et al: Matched-related donor transplantation for sickle cell disease: report from the Center for International Blood and Transplant Research. British Journal of Haematology. 2007 Jun;137(5):479-85.

vii) Philip H. Quanjer, Sanja Stanojevic, Tim J. Cole, et al: Multi-ethnic reference values for spirometry for the 3–95-yr age range: the global lung function 2012 equations, Eur Respir J 2012; 40: 1324–1343 DOI: 10.1183/09031936.00080312 COPYRGHT @ERS 2012

viii) Implementation of the 2021 CKD-EPI GFR equations, CKD EPI Chronic Kidney Disease Epidemiology Collaboration, Version date: October 15, 2021

APPENDIX A

Analysis will be completed for the adult stratum and the pediatric stratum, respectively. The adult stratum and the pediatric stratum will have the same exhibits and report layout unless otherwise specified. The health-related Quality of Life (QOL) assessment is only applicable for the adult stratum so the pediatric stratum analysis will NOT include exhibits for QOL. Exhibit 1507A indicates Adult Stratum and exhibit 1507P indicates Pediatric Stratum. Supplemental Exhibits are provided to display additional data and information besides the protocol-defined endpoints.

ADULT STRATUM DATA ANALYSIS SUMMARY

EXHIBIT 1507A-1: PARTICIPANT DISPOSITION AND FOLLOW-UP

A consort diagram will be provided showing the number of participants enrolled, initiated HU conditioning, transplanted, and any noncompliance with study treatment per protocol as applicable. Descriptive statistics on length of follow-up will be provided. Withdrawal will be described for each case if applicable.

EXHIBIT 1507A-2: PARTICIPANT DEMOGRAPHICS AND BASELINE CHARACTERISTICS

Baseline characteristics and demographics will be described by frequencies and percentages for categorical covariates, and minimum, maximum, median, mean, and standard error for continuous covariates. The following covariates may be included:

- Age
- Gender
- Race
- Ethnicity
- Disease type
- Disease risk characteristics
- Disease symptoms
- Karnofsky/Lansky performance status
- HLA match score
- Number and duration of prior transfusions
- Donor characteristics

Below measurements at baseline will be included in each specific exhibit for the endpoint and also added to the baseline table for the baseline measurements.

- Serum bilirubin level
- Serum creatinine level
- Serum ferritin level
- Pulmonary function tests (PFTs)
- Cardiac Function (TRJV)
- Splenic function
- Hemoglobin electrophoresis
- Cerebral MRI/MRA
- PROMIS score (both pain and fatigue domains)

Other baseline covariates will be summarized at the request of the investigators.

	N	%
Gender		
Female		
Male		
Ethnicity		

	N	%
Hispanic or Latino		
Not Hispanic or Latino		
Not Answered /Unknown		
Race		
American Indian/Alaskan Native		
Asian		
Hawaiian/Pacific Islander		
Black or African American		
White		
More than One Race		
Other, Specify		
Not Answered/ Unknown		
Age, years		
Mean (Std Dev)		
Median (Range)		
Karnofsky Performance Score		
90 - 100		
60 - 80		
Disease Type		
Hemoglobin SS Disease		
Hemoglobin Sβ° Thalassemia		
Hemoglobin SC		
Hemoglobin Sβ+ Thalassemia		
HLA Match Score		
4/8		
5/8		
6/8		
Disease Risk		
Disease Symptoms		
Prior Transfusions		
Donor Characteristics		

(A) Baseline Characteristics for the Enrolled Population

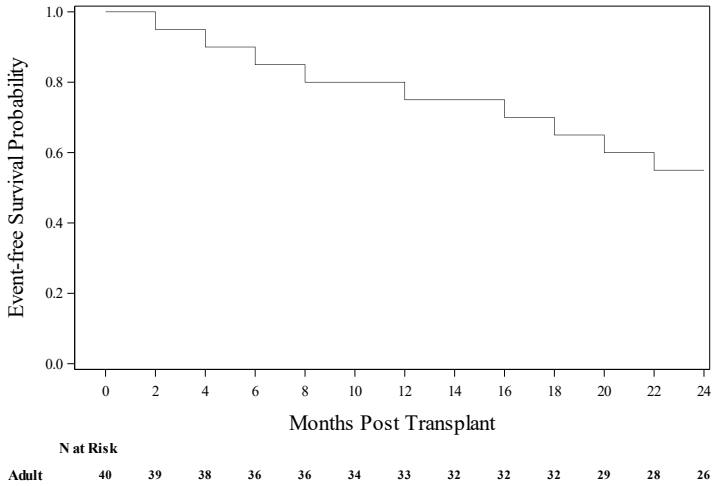
(B) Baseline Characteristics for the Transplant Population

EXHIBIT 1507A-3: EVENT-FREE SURVIVAL (EFS)

EFS is the primary endpoint of the study. Event free survival is a composite endpoint defined in section 4.1 of this SAP. The 2-year EFS is the primary endpoint of the study. 1-year EFS is one of the secondary endpoints of the study. Figure and summary table will be included in this exhibit.

EFS post-transplant

This endpoint will use the primary analysis population (Transplant population).



Kaplan Meier estimates and 95% confidence interval will be displayed in the table:

	Post-Transplant
1-year EFS	XX.X (XX.X, XX.X) %
2-year EFS	XX.X (XX.X, XX.X) %

EXHIBIT 1507A-4: OVERALL SURVIVAL (OS)

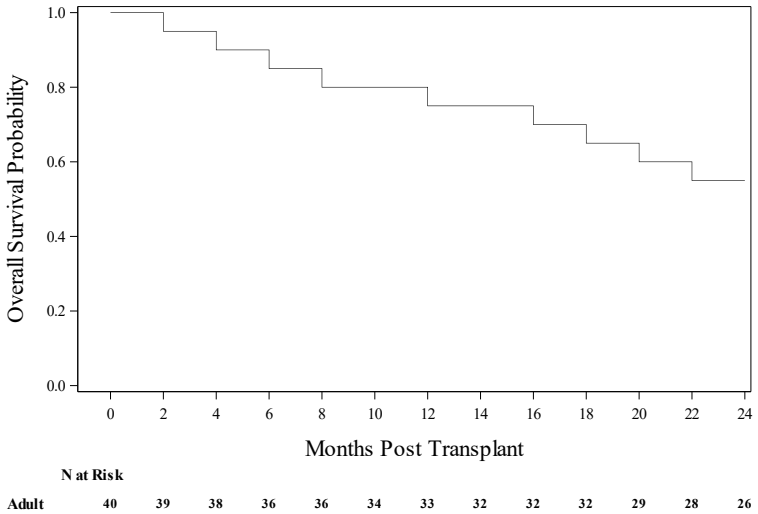
OS is one of the secondary endpoints of the study. Two figures and a summary table will be included in this exhibit.

(A) OS post HU conditioning

This endpoint will use the conditioning population and time will start from date of HU conditioning

(B) OS post-transplant

This endpoint will use the primary analysis population (Transplant population).



Kaplan Meier estimates and 95% confidence interval will be displayed in the table:

	Post Conditioning	Post-Transplant
1-year OS	XX.X (XX.X, XX.X) %	XX.X (XX.X, XX.X) %
2-year OS	XX.X (XX.X, XX.X) %	XX.X (XX.X, XX.X) %

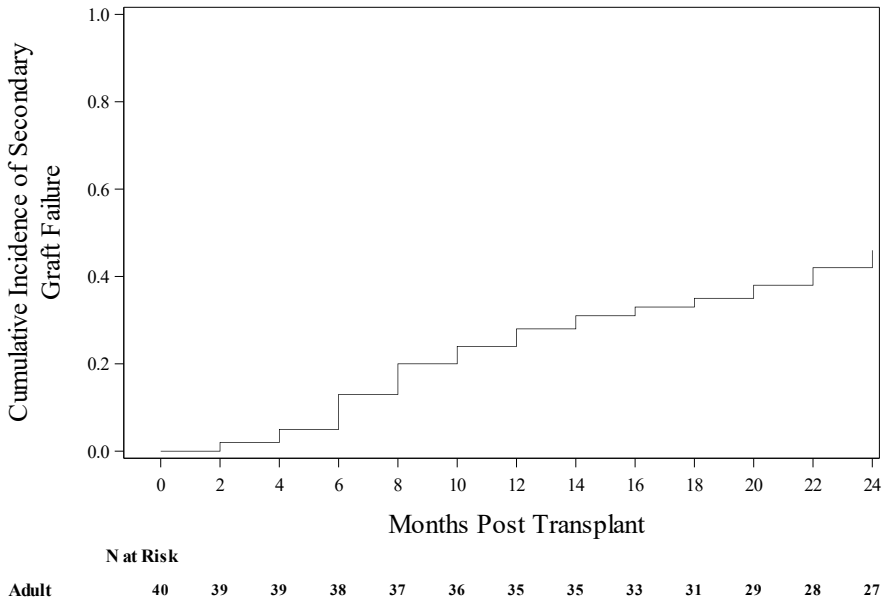
EXHIBIT 1507A-5: PRIMARY AND SECONDARY GRAFT FAILURE

This exhibit will include one summary table (A) for both primary and secondary graft failures, one figure (B) for secondary graft failure and another table (C) for secondary graft failure. Transplant population will be used for this endpoint. Second infusion or second transplant will be described if applicable.

(A) Graft Failure Summary

Graft Failure/Rejection	**N**	**%**
Primary Graft Failure (By Day 42)	X	XX.X
Secondary Graft Failure	X	XX.X
Total Graft Failures	XX	XX.X
Total Transplanted and Evaluable	XX	100.0

(B) Cumulative Incidence of Secondary Graft Failure



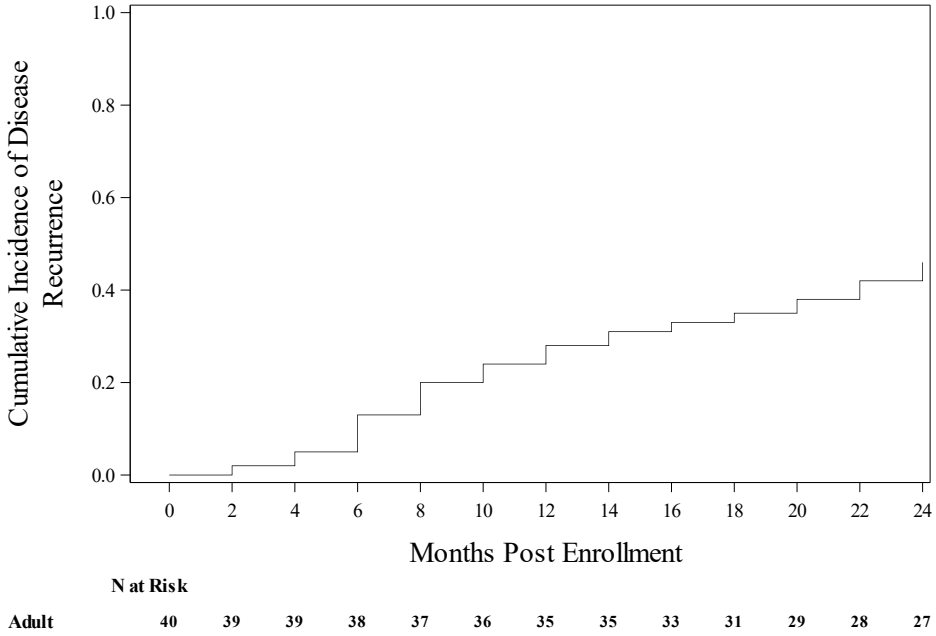
(C) Cumulative Incidence Estimates of Secondary Graft Failure and Confidence Interval

	CI Rate (95% CI)
1-year Secondary Graft Failure	XX.X (XX.X, XX.X) %
2-year Secondary Graft Failure	XX.X (XX.X, XX.X) %

EXHIBIT 1507A-6: DISEASE RECURRENCE

This exhibit will include one figure for cumulative incidence and one summary table to display estimates and confidence interval for disease recurrence. Enrollment population will be used for this endpoint.

Cumulative incidence of disease recurrence

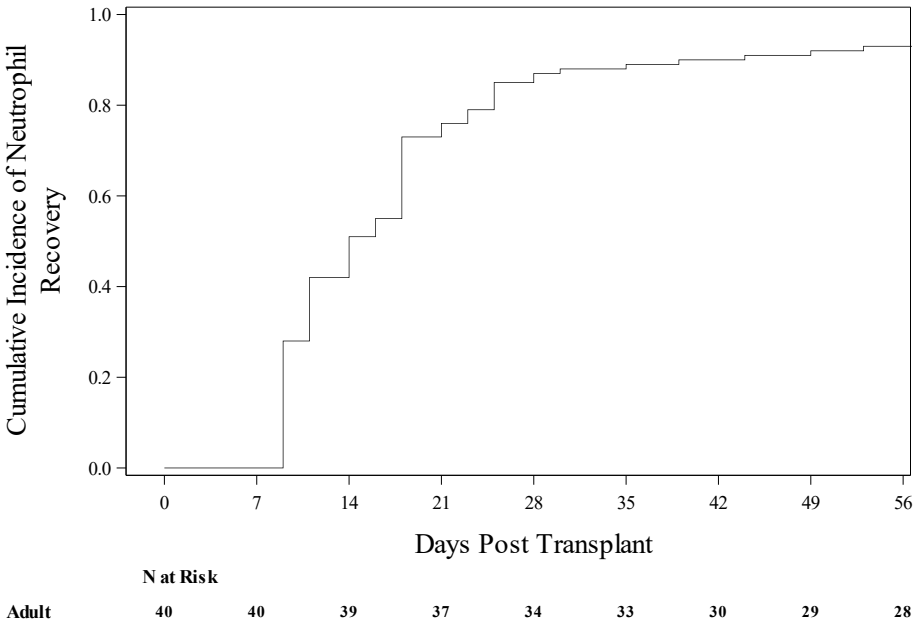


	CI Rate (95% CI)
1-year Disease Recurrence	XX.X (XX.X, XX.X) %
2-year Disease Recurrence	XX.X (XX.X, XX.X) %

EXHIBIT 1507A-7: NEUTROPHIL RECOVERY POST-TRANSPLANT

This exhibit will include one figure for cumulative incidence and one summary table to display estimates and confidence interval for neutrophil recovery. Transplant population will be used for this endpoint. Participants who never dropped neutrophil count below 500/μL will be described. Median time to neutrophil recovery for engrafted participants will be described.

Cumulative Incidence of Neutrophil Recovery Post-Transplant

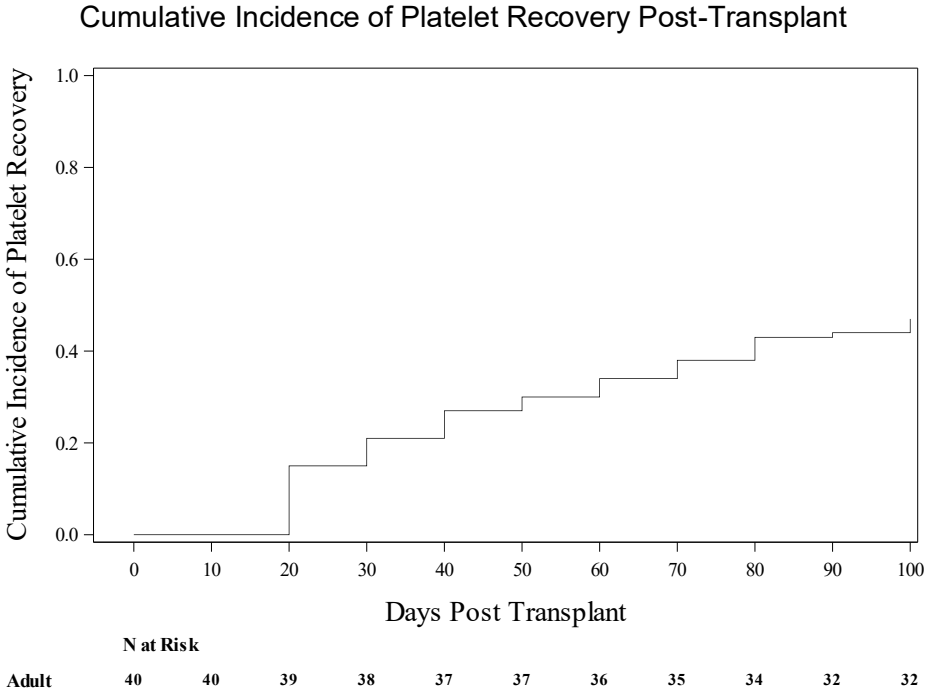


	CI Rate (95% CI)
Neutrophil Recovery at Day 42	XX.X (XX.X, XX.X) %

EXHIBIT 1507A-8: PLATELET RECOVERY POST-TRANSPLANT

This exhibit will include one figure for cumulative incidence and one summary table to display estimates and confidence interval for platelet recovery. Transplant population will be used for this endpoint. Participants who never dropped platelet count below 50,000/μL will be described. Median time to platelet recovery for engrafted participants will be described.

Data will be retrieved from CIBMTR data system for this endpoint.



	CI Rate (95% CI)
Platelet Recovery at Day 60	XX.X (XX.X, XX.X) %
Platelet Recovery at Day 100	XX.X (XX.X, XX.X) %

EXHIBIT 1507A-9: DONOR CHIMERISM POST-TRANSPLANT

This exhibit will include one summary table to display estimates and confidence interval for the mean percent of donor chimerism at the assessment time points, and also display the numbers and proportions of categories for donor chimerism. Transplant population will be used for this endpoint. Participants who missed chimerism assessment will be described.

Chimerism Assessment Time Post-Transplant	**Assay Evaluable N**	**Donor Percent Mean (95% CI)**	**Low Chimerism (Donor <5%)**	**Mixed Chimerism (Donor 5-95%)**	**Full Chimerism (Donor >95%)**
Day 28	XX	XX.X (XX.X, XX.X) %	XX.X **%**	XX.X **%**	XX.X **%**
Day 42	XX	XX.X (XX.X, XX.X) %	XX.X **%**	XX.X **%**	XX.X **%**
Day 100	XX	XX.X (XX.X, XX.X) %	XX.X %	XX.X %	XX.X %
Day 180	XX	XX.X (XX.X, XX.X) %	XX.X %	XX.X %	XX.X %
1 Year	XX	XX.X (XX.X, XX.X) %	XX.X %	XX.X %	XX.X %
2 Years	XX	XX.X (XX.X, XX.X) %	XX.X %	XX.X %	XX.X %

Figures can be added e.g. bar graph or box plot to facilitate visual presentation of the results, upon the request of the protocol team.

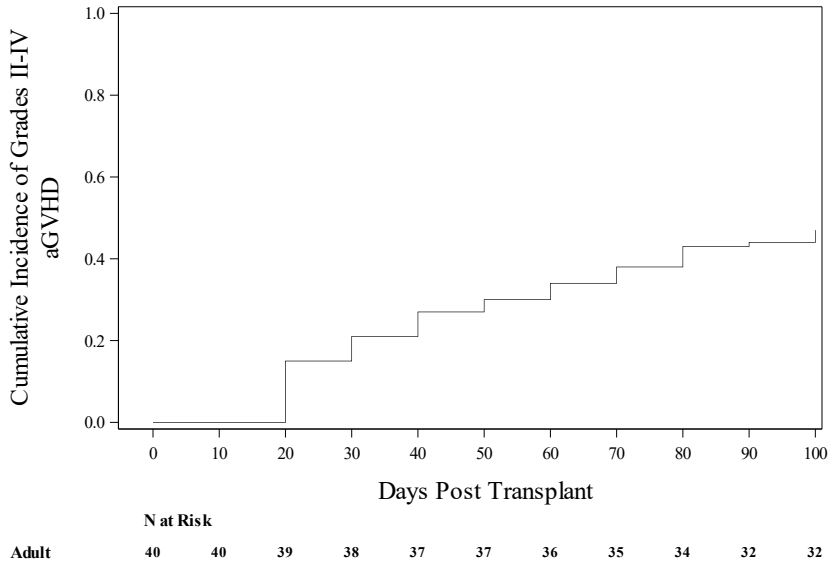
EXHIBIT 1507A-10: ACUTE GVHD POST-TRANSPLANT

This exhibit will include one summary table to display maximum acute GVHD grade, two figures to display cumulative incidence of acute GVHD (for grades II-IV acute GVHD and grades III-IV acute GVHD, respectively), and another table to display estimates and confidence intervals of the cumulative incidence rates. Transplant population will be used for this endpoint. Participants who missed acute GVHD assessment will be described.

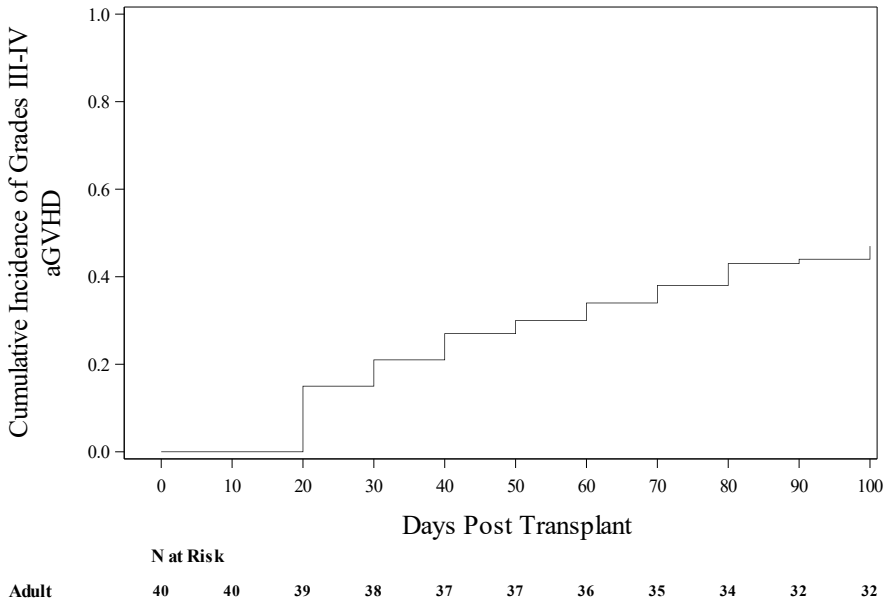
(A) Maximum Acute GVHD Grade through Day 100 Post-Transplant

Maximum Grade of Acute GVHD	Total	
	N	%
Grade 0, no aGVHD	XX	XX.X
Grade I	XX	XX.X
Grade II	XX	XX.X
Grade III	XX	XX.X
Grade IV	XX	XX.X
Total Transplanted and Evaluable	XX	100.0

(B) Cumulative incidence of Grades II-IV acute GVHD



(C) Cumulative incidence of Grades III-IV acute GVHD



(D) Acute GVHD Estimates and Confidence Intervals

	CI (95% CI)
Grade II-IV aGVHD at Day 100	XX.X (XX.X, XX.X) %
Grade III-IV aGVHD at Day 100	XX.X (XX.X, XX.X) %

Acute GVHD through Day 100 post-transplant will be summarized in tables and figures as above shown, any late GVHD events (acute GVHD occurred after Day 100) will be described.

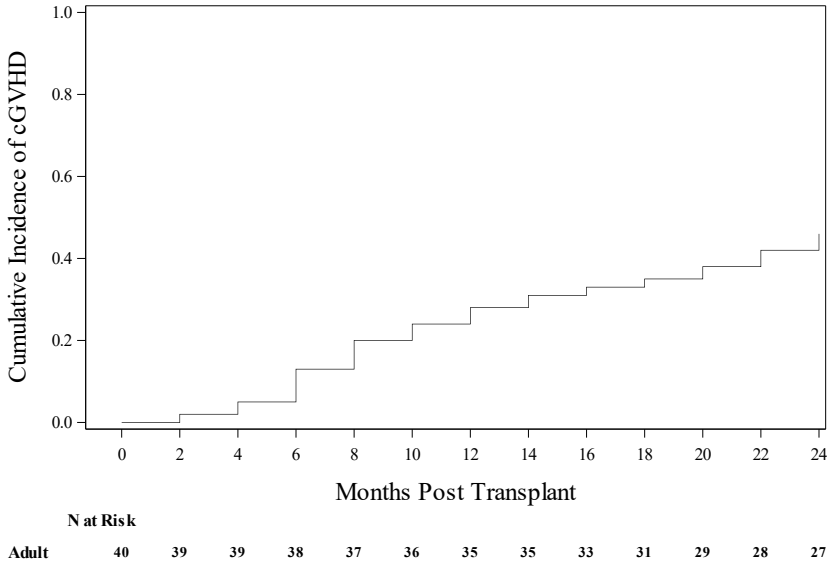
EXHIBIT 1507A-11: CHRONIC GVHD POST-TRANSPLANT

This exhibit will include one summary table to display maximum chronic GVHD severity post-transplant based on the NIH Chronic GVHD consensus criteria, one figure to display cumulative incidence of chronic GVHD and another table to display estimate and confidence interval of the cumulative incidence rates at various time points of interest. Transplant population will be used for this endpoint. Participants who missed chronic GVHD assessment will be described.

(A) Maximum Chronic GVHD Severity Post-Transplant

Maximum Severity of Chronic GVHD	Total	
	N	%
None, no chronic GVHD	XX	XX.X
Mild	XX	XX.X
Moderate	XX	XX.X
Severe	XX	XX.X
Total Transplanted and Evaluable	XX	100.0

(B) Cumulative incidence of Chronic GVHD Post-Transplant



(C) Chronic GVHD Estimate and Confidence Intervals

	CI (95% CI)
Chronic GVHD at 6 months post-transplant	XX.X (XX.X, XX.X) %
Chronic GVHD at 1 year post-transplant	XX.X (XX.X, XX.X) %
Chronic GVHD at 2 years post-transplant	XX.X (XX.X, XX.X) %

EXHIBIT 1507A-12: COMPLICATIONS AND EVENTS

This exhibit will include one summary table to display frequency and proportion of participants reporting complications and events at assessment time points: baseline, 1 year and 2 years post-transplant. Significant infections include any bacterial/fungal sepsis, CMV reactivation with/without clinical disease, adenovirus, EBV PTLD, invasive fungal infection, CMV specified, viral mold infections. Participants who are not evaluable at each assessment time point will be described.

Complications and Events Post-Transplant	**Assessment Time**					
	Baseline		**1 year**		**2 years**	
	N	**%**	**N**	**%**	**N**	**%**
Number of Evaluable Participants at each assessment	XX	100.0	XX	100.0	XX	100.0
Number of Patients reported complications/events	XX	XX.X	XX	XX.X	XX	XX.X
Idiopathic pneumonia syndrome (IPS)						
Yes	XX	XX.X	XX	XX.X	XX	XX.X
No	XX	XX.X	XX	XX.X	XX	XX.X
Veno-occlusive disease (VOD)						
Yes	XX	XX.X	XX	XX.X	XX	XX.X
No	XX	XX.X	XX	XX.X	XX	XX.X
Various CNS toxicities						

Complications and Events Post-Transplant	Assessment Time					
	Baseline		1 year		2 years	
	N	%	N	%	N	%
Yes	XX	XX.X	XX	XX.X	XX	XX.X
No	XX	XX.X	XX	XX.X	XX	XX.X
Stroke						
Yes	XX	XX.X	XX	XX.X	XX	XX.X
No	XX	XX.X	XX	XX.X	XX	XX.X
Participant on immunosuppression						
Yes	XX	XX.X	XX	XX.X	XX	XX.X
No	XX	XX.X	XX	XX.X	XX	XX.X
Significant Infections reported						
Yes	XX	XX.X	XX	XX.X	XX	XX.X
No	XX	XX.X	XX	XX.X	XX	XX.X
Reported any of the above complications/events						
Yes	XX	XX.X	XX	XX.X	XX	XX.X
No	XX	XX.X	XX	XX.X	XX	XX.X

EXHIBIT 1507A-13: SICKLE CELL DISEASE EVENTS OF SPECIAL INTEREST

Participants will be followed for the entire 2 year duration of their time on study for the recurrence of SCD related complications. These SCD related complications are referred to as SCD events of special interest (SCD-EOSI) and will be summarized in this exhibit. The SCD-EOSI are defined in protocol section 3.8.2. Per protocol each occurrence of any SCD-EOSI must be reported on the SCD-EOSI Form at each regularly scheduled follow up interval.

This exhibit will include one summary table to display sickle cell disease events of special interest SCD-EOSI at assessment time points: baseline, 6 months, 1 year, 18 months and 2 years post-transplant. Participants who are not evaluable at each assessment time point will be described.

	Assessment Time									
	Pre HU		6 Months		1 year		18 Months		2 years	
	N	%	N	%	N	%	N	%	N	%
Number of Participants for Evaluation	XX	100.0	XX	100.0	XX	100.0	XX	100.0	XX	100.0
Pulmonary Hypertension										
Yes	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
No	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
Unknown or Not evaluated	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
New Onset of a Significant Cerebrovascular Event										
Yes	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
No	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
Unknown or Not evaluated	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
Renal Function Compromise										
Yes	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
No	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
Unknown or Not evaluated	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
New Onset of Avascular Necrosis of Hip or Shoulder										
Yes	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X

	Assessment Time									
	Pre HU		6 Months		1 year		18 Months		2 years	
	N	%	N	%	N	%	N	%	N	%
No	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
Unknown or Not evaluated	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
New Onset of Leg Ulceration										
Yes	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
No	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
Unknown or Not evaluated	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
New Onset of Acute Chest Syndrome										
Yes	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
No	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
Unknown or Not evaluated	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
New Onset of Painful Vaso-occlusive Crisis Requiring Hospitalization or Parenteral Opioid Drug in the Outpatient Setting										
Yes	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
No	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
Unknown or Not evaluated	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
Participants Having Any of the Above Events										
Yes	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
No	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
Unknown or Not evaluated	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X

EXHIBIT 1507A-14: SUMMARY OF HEMATOLOGICAL OUTCOMES

This exhibit will include one summary table to display hematological outcomes measured at the assessment time points: pre-transplant, Day 28, Day 100, 6 months, 1 year and 2 years post-transplant. Hematological outcomes include Hgb, reticulocyte count, %HbS, LDH and bilirubin. Red blood cell transfusion at each assessment time point will also be described.

Outcome	Assessment Time																							
	Pre-transplant				Day 28				Day 100				6 months				1 year				2 years			
	N	Med	Mean	SD	N	Med	Mean	SD	N	Med	Mean	SD	N	Med	Mean	SD	N	Med	Mean	SD	N	Med	Mean	SD
Hgb																								
Reticulocyte count																								
%HbS																								
LDH																								
Bilirubin																								
Serum ferritin																								
Red blood cell transfusion (Yes or No)																								

Med: Median. SD: Standard Deviation.

EXHIBIT 1507A-15: SUMMARY OF RENAL FUNCTION

This exhibit will include one summary table to display renal function test at the assessment time points: pre-enrollment, pre-transplant, 1 year and 2 years post-transplant. Participants who missed the assessment will be described- see references below.

Renal Function	Assessment Time															
	Pre-enrollment				Pre-transplant				1 year post-transplant				2 years post-transplant			
	N	Med	Mean	SD	N	Med	Mean	SD	N	Med	Mean	SD	N	Med	Mean	SD
24-hour urine Creatinine Clearance																
Radionuclide GFR																
Estimate GFR (see references)																
Urine Albumin-to-Creatine Ratio																

Renal function test results will be summarized and displayed based on available data collection. If data on persistent albuminuria, kidney disease and Chronic Kidney Disease (CKD) will become available at the time of final analysis, they will be summarized, and description will be added to this exhibit.

The estimated GFR will be calculated, based on the site-reported creatinine level if data is available. The following equation to estimate children and adult eGFR will be used.

Adults equations:

- CKD-EPI Creatinine Equation (2021)
  - eGFR= 142 X $\min(S_{cr}/\kappa,1)^{\alpha}$ X $\max(S_{cr}/\kappa,1^{)-1.200}$ X 0.9938^{Age} X 1.012 [if female]

Abbreviations/Units

- eGFR (estimated glomerular filtration rate) = mL/min/1.73 m2
- S_{cr} (standardized serum creatinine) = mg/dL
- S_{cys} (standardized serum cystatin C) = mg/L
- κ = 0.7 (females) or 0.9 (males)
- α = -0.219 (females) or -0.144 (males)
- min = indicates the minimum of SCr/κ or 1
- max = indicates the maximum of SCr/κ or 1
- age = years

Peds equations:

- Creatinine-Based “Bedside Schwartz” Equation (2009)
  - eGFR = 0.413 x (height/S_{cr}) where height is expressed in centimeters
- Kidney.org reports that Bedside Schwartz is still the standard equation to use and currently the
- The Schwartz that came out in 2021 though it is not mentioned on kidney.org yet
  - https://www.sciencedirect.com/science/article/pii/S0085253820314198

EXHIBIT 1507A-16: SUMMARY OF SICKLE BRAIN DISEASE (BRAIN MRI/MRA)

CNS injury as measured by brain MRI/MRA is one of the secondary endpoints of the study. This exhibit will include one summary table to display cerebral MRI/MRA test at the assessment time points: pre-transplant, 1 year and 2 years post-transplant. Participants who missed the assessment will be described.

	Assessment Time					
	Pre-transplant		1 year post-transplant		2 years post-transplant	
MRI						
MRA						

Analysis plan for initial or recurrent cerebral infarct (overt or silent cerebral infarct):

A silent cerebral infarction could be either an enlargement of an existing infarct lesion or a new cerebral infarction, as long as there is no new focal neurologic deficit that is called an overt stroke by the treating team. An enlarged silent cerebral infarct will be defined as a previously identified silent cerebral infarct that increased by at least 3 mm along any linear dimension in any plane on MRI. A transient ischemic attack (TIA), which is included in secondary analyses of neurologic outcomes, is defined as an event that resulted in focal neurologic deficits that lasted less than 24 hours, did not result in abnormalities on T_2-weighted or FLAIR images that were indicative of an acute infarct, and had no other reasonable medical explanation. Members of neurology and neuroradiology committees will adjudicate MRI findings (N Engl J Med. 2014 Aug 21;371(8):699-710).

Time to the first or recurrent overt stroke or silent cerebral infarct will be noted as the time to the progression of the cerebral infarct after the first stroke or silent cerebral infarct. The date for progression of a silent infarction will be defined as the date of the MRI on which the new lesion is noted, whereas the date for second overt strokes is defined as the date of symptom onset or recognition.

Analysis plan for MRA:

For MRA studies, vessels examined will be the internal carotid artery and the first segments of the anterior, middle, and posterior cerebral arteries bilaterally; each vessel will be graded as normal, mild stenosis (25%-50%), moderate stenosis (50%-75%), severe stenosis (75%-99%), or occlusion. On the initial MRA, vasculopathy will be as defined as any presence of moderate or worse stenosis in any vessel segment scored.

Worsening vasculopathy will be defined as an increase in stenosis from one category to a higher category in any vessel segment, or any new vessel occlusion (*Blood* (2011) 117 (3): 772–779).

EXHIBIT 1507A-17: SUMMARY OF LUNG FUNCTION TEST

This exhibit will include one summary table to display pulmonary function tests (PFT) at the assessment time points: pre-enrollment, 1 year and 2 years post-transplant. Participants who

missed the assessment will be described. The reference for assessment of spirometry evaluation is the ERS Global Lung Function Initiative European Respiratory Journal 2012 40: 1324-1343.

PFTs	Assessment Time											
	Pre-enrollment				1 year post-transplant				2 years post-transplant			
	N	Med	Mean	SD	N	Med	Mean	SD	N	Med	Mean	SD
FEV1												
Value												
Percent Predicted												
FVC												
Value												
Percent Predicted												
FEV1/FVC												
Value												
Percent Predicted												
TLC												
Value												
Percent Predicted												
DLCO												
%												
Oxygen Saturation												
%												

Considering the variability of these assessments among multiple sites, this exhibit is very descriptive and exploratory. Results should be taken with caution. For the pulmonary function test, it is recommended to define the reference population and equation from the Global Lung Index reference, if data available.

If more data regarding lung function test will become available at the time of final analysis, they will be summarized, and description will be added to this exhibit.

EXHIBIT 1507A-18: SUMMARY OF CARDIAC FUNCTION (TRJV)

This exhibit will include one summary table to display cardiac function (TRJV) at the assessment time points: pre-enrollment, 1 year and 2 years post-transplant. Participants who missed the assessment will be described.

Cardiac Function	Assessment Time											
	Pre-enrollment				1 year post-transplant				2 years post-transplant			
	N	Med	Mean	SD	N	Med	Mean	SD	N	Med	Mean	SD
TRJV (m/sec)												
Current value												
Change from baseline	—	—	—	—								

Mixed model for the repeated TRJV measures may be run using some demographics and clinical data as covariates. Considering the small sample size of the study, such multivariate analysis will only be performed if deemed necessary and results will be considered as exploratory.

EXHIBIT 1507A-19: SIX MINUTE WALK DISTANCE

This exhibit will include one summary table to display 6-minute walk test at the assessment time points: pre-enrollment, 1 year and 2 years post-transplant. Participants who missed the assessment and reasons why the test was not performed will be described.

6-min Walk Test	Assessment Time											
	Pre-enrollment				1 year post-transplant				2 years post-transplant			
	N	Med	Mean	SD	N	Med	Mean	SD	N	Med	Mean	SD
Time												
Current value												
Change from baseline	—	—	—	—								

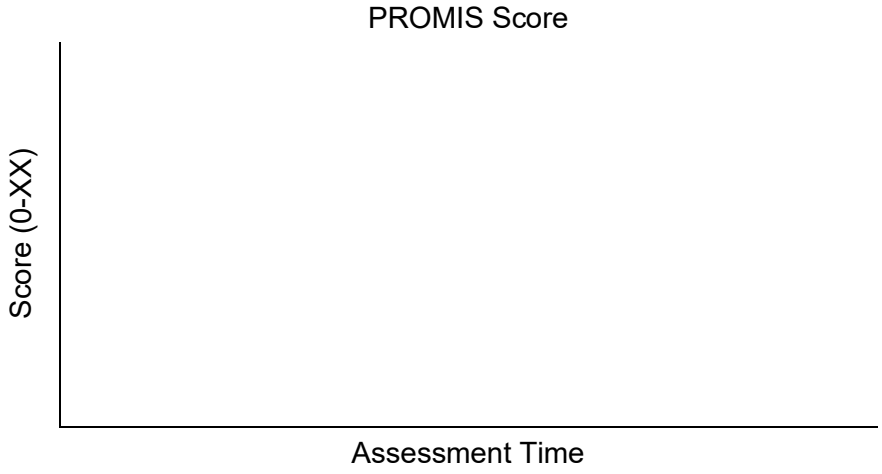
EXHIBIT 1507A-20: QUALITY OF LIFE (PROMIS)

This exhibit will include one summary table to display quality of life assessment using Patient Reported Outcome Measurement Information System (PROMIS) at assessment time points: baseline, 1 year and 2 years post-transplant. Participants who are not evaluable at each assessment time point will be described.

Only adult stratum will have the QOL assessments.

HQL score	**PROMIS Assessment Time**											
	Baseline				**1 year post-transplant**				**2 years post-transplant**			
	N	Median	Mean	StdErr	N	Median	Mean	StdErr	N	Median	Mean	StdErr
Domain 1 score	XX	XX	XX	XX.X	XX	XX	XX	XX.X	XX	XX	XX	XX.X
Domain 2 score	XX	XX	XX	XX.X	XX	XX	XX	XX.X	XX	XX	XX	XX.X
Total Score	XX	XX	XX	XX.X	XX	XX	XX	XX.X	XX	XX	XX	XX.X
Pain Intensity from the PROMIS short form	XX	XX	XX	XX.X	XX	XX	XX	XX.X	XX	XX	XX	XX.X

Figures will be included to illustrate PROMIS over time as below.



The primary analysis report will only include the exploratory analysis on descriptive statistics for the QOL measurements. All other analysis will be included in the secondary analysis e.g. the exploratory models to investigate change over time using mixed model for repeated measures adjusted for the baseline covariate.

EXHIBIT 1507A-21: PAIN INTENSITY FROM PAIN DIARY

This exhibit will include one summary table to pain intensity from the pain diary at assessment time points: baseline, 1 year and 2 years post-transplant. Participants who are not evaluable at each assessment time point will be described.

	Assessment Time											
	Baseline				1 year post-transplant				2 years post-transplant			
	N	Median	Mean	StdErr	N	Median	Mean	StdErr	N	Median	Mean	StdErr
Pain Intensity from the Pain Diary	XX	XX	XX	XX.X	XX	XX	XX	XX.X	XX	XX	XX	XX.X
Change from Baseline	–	–	–	–	XX	XX	XX	XX.X	XX	XX	XX	XX.X

The primary analysis report will only include the exploratory analysis on descriptive statistics for pain intensity if data is available at the time of primary analysis. All other analysis will be included in the secondary analysis e.g. the exploratory models to investigate change over time using mixed model for repeated measures adjusted for the baseline covariate.

EXHIBIT 1507A-22: ASSESSMENT OF COVID-19 IMPACT ON THE STUDY AND TRIAL RESULTS

To evaluate COVID-19 impact on the study and trial results, frequencies and percentages will be provided in this exhibit on the number of missed visits, out of window visits, type of visits, and reasons for missed visits. The number of deaths attributed to COVID-19 and the number of COVID-19 infections will also be described.

Sensitivity analyses will be conducted using the additional data collection for COVID assessment on the primary endpoint and secondary endpoint if felt important based on the results.

SUPPLEMENTAL EXHIBIT 1507A-1: ENROLLMENT

A table will be provided showing actual monthly accrual for each participating center from study initiation to accrual closure.

A figure will be provided showing projected and actual accrual from study initiation to accrual closure on a quarterly basis.

SUPPLEMENTAL EXHIBIT 1507A-2: SIGNIFICANT PROTOCOL DEVIATIONS

A listing of significant protocol deviations will be provided to describe each deviation.

SUPPLEMENTAL EXHIBIT 1507A-3: PRIMARY CAUSE OF DEATH

A table summarizing the primary cause of death for each participant expired on the study will be provided.

SUPPLEMENTAL EXHIBIT 1507A-4: ADVERSE EVENTS

A listing to display the adverse events reported on the study using MedDRA-coded System Organ Class (SOC) will be provided.

SUPPLEMENTAL EXHIBIT 1507A-5: SERIOUS OR GRADES 3-5 ADVERSE EVENTS

A listing to display the serious adverse events reported on the study using MedDRA-coded System Organ Class (SOC) will be provided.

SUPPLEMENTAL EXHIBIT 1507A-6: SAFETY MONITORING (SAFETY ENDPOINT)

Figure of SPRT to illustrate safety monitoring for each of the 4 stopping guidelines as defined in the protocol.

SUPPLEMENTAL EXHIBIT 1507A-7: INCIDENCE OF TOXICITIES GRADE >2 (SAFETY ENDPOINT)

A summary table to display grade 3 or higher toxicities reported at each assessment time points (6 months, 1 year, 18 months, 2 years) as well as the maximum toxicity grade post-transplant per participant level using NCI's Common Terminology Criteria for Adverse Events (CTCAE) Version 4.02 will be provided.

Additional tables for different toxicities (organ system) of interest will be provided.

Additional tables for toxicity grade breakdowns of interest – Grade 3, Grade 4, Grade 5 will be provided.

Toxicity	Assessment Time Period Post-Transplant				
	Day 0 to 6 months N %	6 months to 1 year N %	1 year to 18 months N %	18 months to 2 years N %	Overall (within 2 years) N %
Transfusion Reaction					
Abnormal Liver Symptoms					
Alkaline Phosphatase					
Bilirubin					
AST					
ALT					
Mucositis					
Cystitis Noninfective					
Acute Kidney Injury					
Chronic Kidney Disease					
Receive Dialysis					
Hemorrhage					
Cardiac Arrhythmia					
Left Ventricular Systolic Dysfunction					
Somnolence					
RPLS/PRES					
Thrombotic Thrombocytopenic Purpura					
Capillary Leak Syndrome					
Hypertension					
Dyspnea					
Anemia					
Neutropenia					
Thrombocytopenia					
Nausea					
Diarrhea					
Constipation					
Oligospermia					
Any Grades 3-5 as listed above					

Figures can be added e.g. bar graph or box plot to facilitate visual presentation of the results, upon the request of the protocol team.

SUPPLEMENTAL EXHIBIT 1507A-8: INCIDENCE OF INFECTIONS GRADE >=2

A summary table to display grade 2 or higher infections during the study period will be provided, including the number of participants with infections reported, infection type, infection severity and reporting period.

	Total
	N %
# Participants transplanted	
# Participants with Infections	
# Participants with Infection Reports =1 =2 =3 =4 >=5	
Total Infection Events	
Infection Period Within Day 100 of Transplant From Day 100 to 1 Year of Transplant From 1 year to 2 years of Transplant	
Maximum Severity by Participant None Grade 2 Grade 3	
Infection by Type (# of Participants) Bacterial Viral Fungal Protozoal Other	

SUPPLEMENTAL EXHIBIT 1507A-9: INCIDENCE OF HOSPITALIZATION POST-TRANSPLANT

This exhibit will include three tables to summarize the hospital re-admissions post-transplant. All data summary is descriptive.

(A) Distribution of Re-admissions

	Total (N = XX)	
Number of Re-admissions	**N**	**%**
0	XX	XX.X
1	XX	XX.X
2	XX	XX.X
3	XX	XX.X
>=4	XX	XX.X

(B) Readmissions by Visit Period

	Total (N = XX)		
Time of Re-admission Post Transplantation	**N Pts with Admit**	**% Pts with Admit**	**Total Admit**
1-100 Days	XX	XX.X	XX
101-365 Days	XX	XX.X	XX
>365 Days	XX	XX.X	XX
Ever	XX	XX.X	XX

Note: % is calculated using subjects at risk during time interval.

(C) Primary Reason for Re-admissions

	Total	
Primary Reason for Re-admission	**N**	**%**
Total Number of Re-admissions	XX	100.0
Fever	XX	XX.X
Infection	XX	XX.X
Nausea/Vomiting	XX	XX.X
Diarrhea	XX	XX.X
Psychiatric	XX	XX.X
Other	XX	XX.X

PEDIATRIC STRATUM DATA ANALYSIS SUMMARY

EXHIBIT 1507P-1: PARTICIPANT DISPOSITION AND FOLLOW-UP

EXHIBIT 1507P-2: PARTICIPANT DEMOGRAPHICS AND BASELINE CHARACTERISTICS

EXHIBIT 1507P-3: EVENT-FREE SURVIVAL (EFS)

EXHIBIT 1507P-4: OVERALL SURVIVAL (OS)

EXHIBIT 1507P-5: PRIMARY AND SECONDARY GRAFT FAILURE

EXHIBIT 1507P-6: DISEASE RECURRENCE

EXHIBIT 1507P-7: NEUTROPHIL RECOVERY POST-TRANSPLANT

EXHIBIT 1507P-8: PLATELET RECOVERY POST-TRANSPLANT

EXHIBIT 1507P-9: DONOR CHIMERISM POST-TRANSPLANT

EXHIBIT 1507P-10: ACUTE GVHD POST-TRANSPLANT

EXHIBIT 1507P-11: CHRONIC GVHD POST-TRANSPLANT

EXHIBIT 1507P-12: COMPLICATIONS AND EVENTS

EXHIBIT 1507P-13: SICKLE CELL DISEASE EVENTS OF SPECIAL INTEREST

EXHIBIT 1507P-14: SUMMARY OF HEMATOLOGICAL OUTCOMES

EXHIBIT 1507P-15: SUMMARY OF RENAL FUNCTION

EXHIBIT 1507P-16: SUMMARY OF BRAIN DISEASE (BRAIN MRI/ MRA)

EXHIBIT 1507P-17: SUMMARY OF LUNG FUNCTION TEST

EXHIBIT 1507P-18: SUMMARY OF CARDIAC FUNCTION (TRJV)

EXHIBIT 1507P-19: SIX MINUTE WALK DISTANCE

EXHIBIT 1507P-20: ASSESSMENT OF COVID-19 IMPACT ON THE STUDY AND TRIAL RESULTS

SUPPLEMENTAL EXHIBIT 1507P-1: ENROLLMENT

SUPPLEMENTAL EXHIBIT 1507P-2: SIGNIFICANT PROTOCOL DEVIATIONS

SUPPLEMENTAL EXHIBIT 1507P-3: PRIMARY CAUSE OF DEATH

SUPPLEMENTAL EXHIBIT 1507P-4: ADVERSE EVENTS

SUPPLEMENTAL EXHIBIT 1507P-5: SERIOUS OR GRADES 3-5 ADVERSE EVENTS

SUPPLEMENTAL EXHIBIT 1507P-6: SAFETY MONITORING (SAFETY ENDPOINT)

SUPPLEMENTAL EXHIBIT 1507P-7: INCIDENCE OF TOXICITIES GRADE >2 (SAFETY ENDPOINT)

SUPPLEMENTAL EXHIBIT 1507P-8: INCIDENCE OF INFECTIONS GRADE >=2

SUPPLEMENTAL EXHIBIT 1507P-9: INCIDENCE OF HOSPITALIZATION POST-TRANSPLANT

APPENDIX B:
STATISTICAL ANALYSIS PLAN APPROVAL SIGNATURE PAGE

BMT CTN 1507 Statistical Analysis Plan Prepared and Accepted by:

BMT CTN 1507 Protocol Chair:

Signature: _____ Date: _____

Print Name: Michael DeBaun, MD dd / Mmm / yyyy

Title: BMT CTN 1507 Protocol Chair

BMT CTN 1507 Protocol Officer:

Signature: _____ Date: _____

Print Name: Mary Eapen, MD dd / Mmm / yyyy

Title: BMT CTN 1507 Protocol Officer

BMT CTN Statistical Leadership:

Signature: _____ Date: _____

Print Name: Brent Logan dd / Mmm / yyyy

Title: BMT CTN Statistical Leadership

BMT CTN Protocol Statistician:

Signature: _____ Date: _____

Print Name: Maggie Wu dd / Mmm / yyyy

Title: BMT CTN Protocol Statistician