STATISTICAL ANALYSIS PLAN

A Phase 1/2, Open-label, Single-arm Study to Assess the Safety, Tolerability, and Efficacy of ST-400 Autologous Hematopoietic Stem Cell Transplant for Treatment of Transfusion-dependent β-thalassemia (TDT)

Investigational Product:	ST-400
Protocol Number:	ST-400-01
Development Phase:	1/2
Sponsor:	Sangamo Therapeutics, Inc. Point Richmond Tech Center II 501 Canal Blvd., Suite A100 Richmond, CA 94804
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Protocol: A Phase 1/2, Open-label, Single-arm Study to Assess the Safety, Tolerability, and Efficacy of ST-400 Autologous Hematopoietic Stem Cell Transplant for Treatment of Transfusion-dependent β-thalassemia (TDT)

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This Statistical Analysis Plan has been reviewed and approved by:

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VERSION HISTORY

Version	Date	Description
V1.0	20 December 2017	Original Final Version
V2.0	20 December 2021	Update corresponding sections per protocol Version 6.0/Amendment 5.

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LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

ABBREVIATION	DEFINITION
ACTH	Adrenocorticotropic Hormone
AE	Adverse event
ALP	Alkaline phosphatase
ALT	Alanine aminotransferase
ANC	Absolute neutrophil count
AST	Aspartate aminotransferase
ATC	Anatomic therapeutic class
BMI	Body mass index
BUN	Blood urea nitrogen
CBC	Complete blood count
CRF	Case report form
CTCAE	Common Terminology Criteria for Adverse Events
DXA	Dual-energy X-ray absorptiometry
ECG	Electrocardiogram
ECHO	Echocardiogram
ETV	Early termination visit
G-CSF	Granulocyte colony-stimulating factor
Hb	Hemoglobin
HbF	Fetal hemoglobin ($\alpha 2\gamma 2$)
HEENT	Head, eyes, ears, nose, and throat
HSCT	Hematopoietic stem cell transplantation
HSPC	Hematopoietic stem/progenitor cell
IV	Intravenous
KPS	Karnofsky performance scor
LDH	Lactate dehydrogenase
LVEF	Left ventricular ejection fraction
MedDRA	Medical Dictionary for Regulatory Activities
MRI	Magnetic resonance imaging
NCI	National Cancer Institute
PFT	Pulmonary function test
PRBC	Packed red blood cell
RBC	Red blood cell
SAE	Serious adverse event
SAP	Statistical Analysis Plan
SF-36	36-Item Short Form Health Status Survey
SMC	Safety Monitoring Committee
SOC	System organ class
TDT	Transfusion-dependent β-thalassemia
TEAE	Treatment-emergent adverse event
TESAE	Treatment-emergent serious adverse event

WBC	White blood cell
WHO	World Health Organization
ZFN	Zinc finger nuclease

1 INTRODUTION

This Statistical Analysis Plan (SAP) provides a description of the statistical methodology to be implemented for the analyses of data collected in the study described in Sangamo Therapeutics, Inc., Protocol ST-400-01. This document is based on the original protocol dated 15AUG2017, and protocol amendments dated 28JUN2018, 10OCT2018, 22FEB2019, 10MAR2020 and 9APR2021. If the protocol is amended, or if circumstances arise during the study such that more appropriate analytic procedures become available, the SAP may be revised. Any deviations from the final analysis plan will be substantiated by sound statistical rationale and will be documented in the final clinical study report.

Unless otherwise specified, all statistical analyses and output will be produced using SAS® version 9.3 or later version.

2 STUDY OBJECTIVES

2.1 Primary Objective

The primary objective of this study is to evaluate the safety and tolerability of ST-400 infusion in patients with TDT.

2.2 Secondary Objective

The secondary objective of this study is to assess the efficacy of ST-400 in patients with TDT.

2.3 Exploratory Objectives

The exploratory objectives of this study are to assess the following:

- Evaluate the gene modification characteristics (% and durability) at the erythroid-specific enhancer of the BCL11A gene after ST-400 treatment.
- Assess the impact of ST-400 on the biochemical, imaging, functional, and bone marrow evaluations related to β-thalassemia and hematopoietic stem cell transplantation (HSCT).

3 STUDY OVERVIEW

3.1 Overall Study Design and Plan

This is a Phase 1/2, open-label, multi-center, single-arm study to assess the safety, tolerability, and efficacy of ST-400 Autologous HSCT for TDT. Subjects who satisfy all eligibility criteria will be enrolled and undergo apheresis to collect autologous CD34+ hematopoietic stem/progenitor cells (HSPCs). The CD34+ HSPCs will be treated *ex vivo* by transfection with zinc finger nuclease (ZFN) mRNAs SB-mRENH1 and SB-mRENH2 to manufacture the study drug, ST-400. ST-400 will be cryopreserved until the subject is ready for conditioning.

Subjects will receive conditioning therapy with IV busulfan before being infused with ST-400. Clinical and laboratory data will be collected for a total of 156 weeks post-infusion of ST-400.

Due to the invasive nature of the apheresis procedure and the potential toxicity of IV busulfan, no treatment control group is included in this study. A minimum of 2 years of retrospective clinical and hematological data will be collected for each subject, thus each subject will serve as their own control to provide reference data for evaluation of change from baseline of the study assessments, including transfusion requirements, clinical laboratory measurement of Hb fractions (A and F in g/dL) HbF levels.

Five subjects who satisfy all eligibility criteria will be enrolled and treated in this study. Subjects who do not receive ST-400 or who are lost to follow-up or withdraw from the study before the Week 26 visit in the Primary Study Period (which begins with ST-400 infusion) will be replaced. The first three subjects will be considered sentinel subjects, and the second and third sentinel subjects will not begin conditioning with IV busulfan until the previous subject treated with ST-400 has achieved successful hematopoietic reconstitution. Upon hematopoietic reconstitution of the third sentinel subject, the study's independent Safety Monitoring Committee will convene and advise the future dosing of subjects four, five and six.

To reduce the risk of graft failure, the minimal dose of ST-400 required in this study exceeds the generally recommended minimum cell dose of 2.0×10^6 CD34+ HSPCs/kg for autologous HSCT. To achieve the highest likelihood of efficacious ST-400 engraftment, the target dose of ST-400 is 10×10^6 cells/kg, and the maximum dose that may be given is 20×10^6 cells/kg.

3.2 Study Population

The study population will comprise male and non-pregnant, non-lactating female subjects with TDT between 18 and 40 years old, who are willing and able to undergo autologous HSCT. Detailed inclusion and exclusion criteria are available in Section 5 of the protocol.

3.3 Study Outcome Measures

3.3.1 Primary Outcome Measures

Safety and tolerability will be assessed by incidence of adverse events (AEs) and serious AEs (SAEs) during the Primary Study Period, defined as the date of ST-400 infusion through the date of the Week 52 study visit or date of the early termination visit (ETV) for subjects withdrawing prior to Week 52, inclusive. Additional safety and tolerability evaluations will include:

- Routine hematology and chemistry laboratory testing, vital signs, physical exam, electrocardiogram (ECG), echocardiogram (ECHO), pulmonary function tests (PFTs), bone marrow aspiration, and concomitant medications.
- Kinetics and success of hematopoietic reconstitution.

- Duration of hospitalization after conditioning.
- Screening for potential development of hematological malignancies.

3.3.2 Secondary Outcome Measures

The secondary objectives of this study are to assess efficacy by evaluating change from baseline in:

- Hb fractions (HbA and HbF in g/dL) and percent HbF.
- Annualized frequency and volume (when baseline volume data are available) of PRBC transfusions.

3.3.3 Exploratory Outcome Measures

The exploratory endpoints are to assess the following:

- Percentage and durability of gene modification at the erythroid-specific enhancer of the BCL11A gene.
- Change from baseline in
    - thalassemia-related disease biomarkers.
    - endocrine function by lab testing.
    - cardiac function by ECHO.
    - iron content by magnetic resonance imaging (MRI) (liver and heart).
    - bone mineral density by dual-energy X-ray absorptiometry (DXA).
    - quality-of-life by 36-Item Short Form Health Status Survey (SF-36).
    - overall function by Karnofsky performance score (KPS).
    - Percentage of F-cells.
- Efficiency of apheresis procedure.
- Difference between % indels in ST-400 product and indels detected in bone marrow and blood following ST-400 infusion.

3.4 Study Assessments

A detailed schedule of study visits and procedures is presented in Appendix 1 of the Protocol.

4 ANALYSIS POPULATIONS

4.1 Safety Population

The Safety Population consists of all subjects who receive any amount of ST-400 in the study.

4.2 All Enrolled Subjects Population

The All Enrolled Subjects Population consists of all subjects enrolled into the study. That is, all subjects who meet all eligibility criteria and who proceed to mobilization and apheresis.

5 GENERAL STATISTICAL CONSIDERATIONS

5.1 Evaluation of Center Effect

The center effect will not be considered for this study.

5.2 Multiple Comparisons

Not applicable to this study.

5.3 Examination of Subgroups

No subgroup analyses are planned for the study.

5.4 Definition of Baseline

Baseline is defined as the last non-missing assessment value obtained prior to the first administration of IV busulfan. The day of the ST-400 infusion will be defined as Visit Day 1. Study days prior to Visit Day 1 will be expressed as negative integers relative to Day 1.

5.5 Assessment Windows

The protocol visit names will be mapped to Analysis Study Days for analysis and reporting of selected data. The protocol-allowed windowing of subject visitsand the corresponding Analysis Study Days are provided in schedule of events.

Unscheduled and early termination assessments that occur outside of the protocol visit window will not be mapped to a protocol-specified visit. Otherwise, data within the Visit Window that is closest in time to the scheduled Analysis Study Day will be utilized. The latest time will be used in case of ties.

5.6 Study Periods

Analysis study periods will be assigned as described in the Table 2.

TABLE 2: STUDY PERIODS

Study Period	Period Start
Screening	Date of informed consent
Mobilization, Apheresis and Conditioning	Date of first study treatment (G-CSF, plerixafor, busulfan)
Primary	Date of ST-400 infusion
Follow Up	First day after the Week 52 visit date

Each period commences at the date shown in the table. Study assessments will be assigned to a period based on the assessment date; adverse events will be assigned to a period based on the event start date.

If the Week 52 procedures are not all performed on the same day, the day after the last Week 52 assessment will be used as the start of the Follow Up period.

5.7 Handling of Dropouts and Missing Data

Missing Dates: Dates will be presented in ISO 8601 date format (YYYY-MM-DD). If only year and month are available, date will be displayed as YYYY-MM. If only year is available, then just YYYY. Dates that are missing because they are not applicable for the subjects are output as "NA". In general, data will be analyzed and presented as observed and will not be imputed for the analysis of efficacy or safety data in this study unless otherwise specified.

In cases of missing or incomplete dates (e.g., AE and concomitant medications), the missing component(s) will be assumed as the most conservative value possible. For example, AEs with missing start dates, but with stop dates either overlapping into the treatment period or missing, will be counted as treatment-emergent, taking the worst-case approach. When partial dates are present in the data, both a partial start date and/or a partial stop date will be evaluated to determine whether it can be conclusively established that the AE started prior to the start of study drug or ended prior to the start of study drug. If the above cannot be conclusively established based on the partial and/or present dates, then the AE will be considered as treatment-emergent. Actual data values as they appear in the original case report forms (CRFs) will be presented in the data listings.

If the analysis study period cannot be determined due to insufficient date information, the following algorithm will be applied. If date is missing entirely, the record will be assigned to Screening. If the date is partial but definitively prior to the ST-400 infusion, the record will be assigned to Mobilization, Aphresis, Conditioning (MAC) period. If the date is partial but definitively after the Week 52 visit, the record will be assigned to Follow Up. In all other cases, the record will be assigned to Primary. As with evaluating treatment-emergence of AEs, any available end date information will also be utilized to help determine study period.

Other Missing Data: Unrecorded data values will be recorded as missing. Only recorded (e.g., non-missing) data values will be used for reporting of descriptive statistics unless otherwise stated.

5.8 Other Data Handling Approaches

For continuous variables, the estimated mean and median for a set of values will be printed out to one more decimal place than the individual units of measurement, and the standard deviation will be printed out to 1 additional place.

All fractional numeric values will be printed with a zero to the left of the decimal point (e.g., 0.12, 0.3 etc.). Percentage values will be printed with 1 digit to the right of the decimal point (e.g., 52.3%, 8.9% etc.).

6 STATISTICAL ANALYSIS

The statistical analyses will be performed by Medpace Inc.

Statistical analyses will primarily be descriptive, and no formal hypothesis testing will be conducted.

Unless otherwise stated, descriptive statistics including the count of available observations (n), mean, standard deviation, median, minimum and maximum will be presented for continuous variables. Categorical variables will be summarized with counts and percentages per category. Some summaries may be presented as graphs.

6.1 Subject Disposition

Subject disposition will be summarized for all screened subjects. The following subject disposition categories will be included in the summary:

- Subjects who were screened;
- Subjects who were screen failure;
- Subjects who completed the Primary Study Period (Week 52);
- Subjects who completed the Follow-up Study Period (Week 156);
- Subjects who underwent CD34+ HSPC mobilization;
- Subjects who underwent conditioning;
- Subjects who received ST-400 infusion;
- Subjects who did not receive ST-400 infusion;
- Subjects who withdrew or discontinued from the study.

For subjects who were screen failure, subjects who did not receive ST-400 infusion and subjects who withdrew or discontinued from the study, a summary will be provided for the primary reason. In addition, the total number of subjects for each defined analysis population will be tabulated.

All subject disposition data will be listed by subject.

6.2 Protocol Deviations

All deviations related to study inclusion or exclusion criteria, conduct of the trial, patient management or patient assessment should be described. All protocol deviations including CSR reportable and non-CSR reportable will be listed by subject.

6.3 Demographics

Demographic characteristics will be summarized for the Safety Population and All Enrolled Subjects Population.

Demographic characteristics for age, sex, race, and ethnicity at screening will be summarized. Age will be calculated by using *date informed consent signed by subject - date of birth of subject*. Descriptive statistics will be presented for age; gender, race and ethnicity will be summarized with contingency tables (count and percentage per category).

All demographic data will be listed by subject.

6.4 Baseline and Disease Characteristics

Summaries for baseline and disease characteristics will be summarized for the Safety Population.

Baseline characteristics will be summarized and will include weight, height and body mass index (BMI). Descriptive statistics will be presented for weight, height, and BMI.

Baseline disease characteristics will be summarized for Baseline KPS, KPS at Screening and time from the date of initial diagnosis to the date of informed consent (months). Descriptive statistics will be presented for time from initial diagnosis; frequency counts and percentages will be presented for all other baseline disease characteristics.

All baseline and disease characteristics data will be listed by subject.

6.5 Medical and Surgery History

A complete medical history, including prior surgeries and procedures, will be recorded for each subject at the screening visit. The reported medical history terms will be coded using the Medical Dictionary for Regulatory Activities (MedDRA, version 20.1 or higher). Medical and Surgery history will be summarized for the Safety Population by MedDRA system organ class (SOC) and preferred term.

All reported medical history conditions and surgeries will be listed by subject.

6.6 Transfusion History

History of RBC transfusions (mL packed RBC/kg, volume, date, units transfused, etc.) will be recorded for each subject at the screening visit based on medical documentation as available.

A minimum of 2 years of transfusion frequency history prior to Screening is required to be eligible to participate in this study; however up to 3 years of history will be recorded if available. Frequency and, if available, volume of transfusion and packed RBC units transfused will be annualized. The annualized number of transfusions and, as available, the total volume transfused and packed RBC units transfused in the 2 (or 3, if available) years prior to the date of informed consent will be summarized.

All reported transfusion history will be listed by subject.

6.7 Concomitant Medications

All prior and concomitant medications will be coded using the latest version of the World Health Organization Drug Dictionary (WHO Drug, Version March 2017 or later). Prior medications include medications that were taken prior to and stopped before the time of consent. Concomitant medications include medications that were taken on or after the time of consent.

The count and percentage of subjects taking concomitant medications will be summarized by the highest level of anatomic therapeutic class (ATC) and preferred name for the Safety Population. Prior medications will be summarized in the same manner.

All prior and current concomitant medications will be listed by subject.

6.8 COVID-19 Impact

The count and percentage of subjects impacted by COVID-19 will be summarized by the visit and number of subjects visit impacted by COVID-19 for the Safety Population.

All COVID-19 impacted visits will be listed by subjects.

7 EFFICACY ANALYSES

Efficacy analyses will be based on the Safety Population.

Efficacy analyses in general will be descriptive and will be presented in tabular format with the appropriate summary statistics. No formal statistical tests will be performed for the efficacy parameters.

7.1 Primary Efficacy Endpoint Analysis

Not applicable to this study.

7.2 Secondary Efficacy Endpoint Analyses

Baseline levels of Hb fractions (A and F in g/dL) and percent HbF will be determined based on the last assessment prior to the date of first administration of IV busulfan. Clinical laboratory measurement of Hb fractions (A and F in g/dL) and percent HbF will be quantified

for all subjects at Screening, Baseline, and throughout this study. HbF levels and change from baseline will be summarized by study visit.

Baseline annualized frequency and volume, if available, of PRBC transfusions will be based on the 2 year period prior to Screening. Frequency and volume of transfusion will be annualized by study period and overall, and compared descriptively to the baseline values. RBC transfusions will be closely monitored in this study.

The annualized number of PRBC units transfused will be summarized and compared by before consent versus after infusion, as well as annualized before consent versus after hematopoietic reconstitution.

The annualized volume of PRBC transfusions will be summarized and compared by annualized before consent versus after infusion, as well as annualized before consent versus after hematopoietic reconstitution.

The annualized number of PRBC transfusions will be summarized and compared by annualized before consent versus after infusion, as well as annualized before consent versus after hematopoietic reconstitution. If there are multiple PRBC transfusions in a day, it will be counted as one transfusion.

All laboratory results and transfusion details (including phlebotomy) will be listed by subject.

7.3 Exploratory Efficacy Endpoint Analyses

All exploratory endpoints will be summarized for the Safety Population, unless otherwise noted. The exploratory efficacy parameters will be descriptive and will be presented in tabular format with the appropriate summary statistics.

7.3.1 BCL11A Gene Modification Assay

The proposed mechanism of action of ST-400 is to produce precise genetic modification of the erythroid-specific enhancer of the BCL11A gene through the use of engineered ZFNs. The percentage, durability, and allelic distribution of gene modification at the BCL11A locus by ST-400 will be monitored at the time of product release and throughout the study. Analysis of the percentage of insertions/deletions (indels) at the targeted alleles, as well as dominance and frequency of any given indel will be reported using high-throughput sequencing technology.

All gene modification data will be listed by subject.

7.3.2 Subset Analysis of BCL11A Gene Modification

The analysis of this assay is the same as the BCL11A Gene Modification, but is performed on lineage-specific hematopoietic cells, which have been previously been sorted from the clinical sample.

7.3.3 Thalassemia-related Disease Biomarkers

Thalassemia-related disease biomarkers will be tested throughout this study to evaluate the effect of ST-400 on erythropoiesis and iron overload. These exploratory biomarker tests may include but are not limited to iron metabolism, erythropoietin, haptoglobin, and hepcidin levels. Descriptive statistics will be used to summarize thalassemia-related disease biomarkers and change from baseline by scheduled visit/timepoint for Safety Population.

All thalassemia-related disease biomarkers data will be listed by subject.

7.3.4 Endocrine Lab Testing

Chronic iron overload in TDT leads to iron deposition in endocrine organs and subsequent endocrine dysfunction. Endocrine laboratory testing may include but is not limited to thyroid studies, IGF-1, morning cortisol, adrenocorticotropic hormone (ACTH), HbA1C, and Vitamin D studies. Descriptive statistics will be used to summarize endocrine laboratory testing and change from baseline by scheduled visit/timepoint for Safety Population.

All endocrine laboratory testing data will be listed by subject.

7.3.5 Cardiac Function by ECHO

A standard 2-dimensional Doppler ECHO will be obtained at the specified visits to evaluate cardiac function, including left ventricular ejection fraction (LVEF), regional wall motion, and valvular morphology and function. Descriptive statistics will be used to summarize cardiac function and change from baseline by scheduled visit/timepoint for Safety Population.

All cardiac function data will be listed by subject.

7.3.6 Liver and Heart MRI

The following descriptive statistics will be used to summarize liver and heart MRI results and change from baseline by scheduled visit/timepoint for Safety Population:

- Mean Value of R2 in Cross-Section of the Liver – MVCSL 1/sec
- Average LIC Value in Cross-section of the Liver – LIC mg FE/g dw
- Standard Deviation of R2 in Cross-Section of the Liver – STDCSL ± SD
- Mean Value of R2* in Cross-Section of the Heart – MVHR2 1/sec
- Mean Value of T2* in Cross-Section of the Heart – MVHT ms

All liver and heart MRI data will be listed by subject.

7.3.7 DXA

Osteoporosis and fractures are common complications of TDT. DXA is a convenient and reliable method to determine bone mineral density and evaluate for the presence of

osteoporosis and fracture risk with low exposure to radiation. Descriptive statistics will be used to summarize DXA (T-score, Z-score) and change from baseline by scheduled visit/timepoint for Safety Population.

All DXA data will be listed by subject.

7.3.8 SF-36 Survey

The SF-36 is a quality-of-life questionnaire for assessing quality of life that is widely-accepted, validated, and easily administered. It is commonly utilized in clinical drug development, and has been studied in patient populations with TDT. The SF-36 survey dataset and analysis will be extracted and run through Pro Core software by Optum®. Descriptive statistics will be used to summarize SF-36 (8 domains: physical functioning, role physical, role emotional, bodily pain, vitality, mental health, social functioning, and general health) scores both in in 0-100 scores and norm-based scoreds, and change from baseline by scheduled visit for the Safety Population.

All SF-36 data will be listed by subject.

7.3.9 Karnofsky Performance Scale (KPS)

Each subject will be evaluated and scored at the specified visit using the KPS Definitions Rating Criteria. Descriptive statistics will be used to summarize KPS and change from baseline by scheduled visit for Safety Population.

All KPS data will be listed by subject.

7.3.10 Percentage of F-cells

F-cells are red blood cells that contain measurable amounts of HbF. Blood samples will be collected for analysis of percentage of F-cells. Descriptive statistics will be used to summarize Hi HbF+, Mid HbF+, Total HbF+ and percentage of F-cells and change from baseline by scheduled visit/timepoint for the Safety Population.

All F-cell data will be listed by subject.

7.3.11 Efficiency of Apheresis Procedure

Apheresis start time, apheresis stop time, total volume at the end, WBC in peripheral blood (pre-apheresis), % CD34+ of WBC in peripheral blood pre apheresis, absolute CD34+ count in peripheral blood (pre-apheresis), WBC in product, % CD34+ of WBC in product, weight, total CD34+ cells collected per body weight (10^6 CD34+ HSPCs/kg) will be listed by subject.

Total volume collected and total number of CD34+ cells collected over all apheresis procedures for a subject will be summarized for All Enrolled Subjects Population and listed by subject.

7.3.12 Difference between % indels in ST-400 product and indels detected in bone marrow and blood following ST-400 infusion

The % indels difference will be summarized by visit and sample tested.

8 SAFETY ANALYSES

Safety will be evaluated by presenting summaries of extent of exposure, AEs, safety clinical laboratory parameters, vital signs, ECG findings, physical examination findings and other safety parameters. All safety analyses will be performed for the Safety Population.

Safety analyses in general will be descriptive and will be presented in tabular format with the appropriate summary statistics. No formal statistical tests will be performed for the safety parameters.

8.1 Extent of Exposure

All ST-400 infusion data will be listed by subject.

8.2 Adverse Events

An AE is defined as any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug-related. A treatment-emergent adverse event (TEAE) is defined as an AE that started during the Primary Study Period, defined as the date of ST-400 infusion through the date of the Week 52 study visit (or date of early termination visit [ETV] for subjects withdrawing prior to Week 52), inclusive and Follow-up Study Period. The Investigator is responsible for classifying an AE and SAE as either Related or Not Related to ST-400.

AEs will be coded using the most updated version of the MedDRA (version 20.1 or higher). The severity of all AEs will be graded according to the revised National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) Version 5.0.

A pre-primary AE is defined as an AE that started prior to the Primary Study Period. A post-primary AE is defined as an AE that started after the Primary Study Period. Except as noted, reported AEs starting prior to the Primary Study Period or starting after the Primary Study Period will be summarized or listed separately.

An overview of AEs will be provided which summarizes subject incidence of the following information:

AEs starting during the MAC period:

- All AEs
- Mobilization-related AEs
- Apheresis-related AEs

- Conditioning-related AEs
- SAEs

TEAEs:

- All TEAEs, ST-400-related TEAEs, Busulfan-related TEAEs
- Grade 3/4/5 TEAEs, ST-400-related Grade 3/4/5 TEAEs
- Treatment-emergent serious adverse events (TESAEs), ST-400-related TESAEs
- TEAEs leading to death, TEAEs leading to study discontinuation

AEs, Mobilization-related AEs, Apheresis-related AEs, Conditioning-related AEs and SAEs startings during the MAC period will be summarized separately by SOC and preferred term.

The incidence of TEAEs will be summarized by analysis study period (Primary period, Follow-up period and Overall) by SOC and preferred term. ST-400-related TEAEs, Busulfan-related TEAEs, TESAEs, Grade 3/4/5 TEAEs, ST-400-related TESAE, TEAEs leading to death and TEAEs leading to study discontinuation will be summarized in the same manner. For these summaries, although a subject may have had two or more adverse events, the subject is counted only once within a SOC category. The same subject may contribute to two or more preferred terms within same SOC category.

By-subject listings will be provided for all AEs, SAEs, Grade 3/4/5 AEs, and AEs leading to study discontinuation, AEs leading to death. A by-subject AE listing including, but not limited to, verbatim term, preferred term, SOC, NCI-CTCAE grade, seriousness and relationship to ST-400 treatment will be provided.

8.3 Safety Laboratory Parameters

Standard clinical laboratory profiles for safety assessments (serum chemistry, hematology, liver function, and urine) will be evaluated.

- **Serum Chemistry**: includes sodium (Na), potassium (K), chloride (Cl), carbonate (CO_3^{2-}), calcium (Ca), Phosphate (PO_4^{3-}), magnesium (Mg^{2+}), blood urea nitrogen (BUN), creatinine, glucose and lactate dehydrogenase (LDH).
- **Hematology**: includes complete blood count (CBC) with differential, reticulocyte count, and peripheral smear.
- **Liver Function**: includes bilirubin (total and direct), alkaline phosphatase (ALKP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), albumin, total protein and ferritin.
- **Urine** (with microscopic examination): glucose, protein, bilirubin, blood, pH and specific gravity.

Descriptive statistics will be provided for serum chemistry, hematology, liver function, and urine parameters based on the laboratory results. Both actual values and changes from baseline relative to each scheduled visit will be presented. Changes in selected laboratory parameters will also be summarized for a subgroup of subjects based on use of concomitant medications.

Abnormal laboratory results will be graded according to NCI CTCAE version 5.0, if applicable. Shift tables from baseline to the highest post-baseline grade according to the NCI CTCAE grade will be provided for selected parameters using frequency counts and percentages. Both scheduled and unscheduled visits will be considered.

All clinical laboratory data will be listed by subject. Values outside the normal ranges will be flagged.

8.4 Kinetics and Success of Hematopoietic Reconstitution

The incidence of of neutrophil recovery and platelet recovery will be provided. Time to neutrophil recovery and time to platelet recovery will be summarized using descriptive statistics.

Hematopoietic reconsitituition data will be listed by subject.

8.5 Duration of Hospitalization

After release of ST-400 for clinical use, subjects will be hospitalized at the study center until clinical recovery and neutrophil recovery (ANC $\geq$ 500 cells/uL x 3 consecutive days) following conditioning with IV busulfan. The estimated duration of the hospitalization is approximately 2 to 4 weeks, but the actual duration shall be determined by the Investigator depending upon a subject's clinical course. The total number of days in the hospital from the ST-400 infusion date to the first date of discharge will be summarized using descriptive statistics.

Duration of hospitalization following ST-400 administration will also be listed by subject.

8.6 Development of Hematological Malignancies

Subject incidence of development of hematological malignancies listed below will be provided:

- Any new or worsened unexplained lymphadenopathy.
- Any new or worsened unexplained hepatosplenomegaly.
- Have unexplained WBC > 30000/uL or ANC < 500 cells/uL confirmed on repeat testing.
- Have unexplained platelet count < 50000/uL confirmed on repeat testing.
- Have a clinical suspicion of malignancy based on Investigator's judgement.

- Have clinically-significant abnormality on bone-marrow aspiration suggestive of a malignant transformation.

The development of hematological malignancies will be listed by subject.

8.7 Vital Signs

Vital signs includes measurement of height (cm), weight (kg), systolic blood pressure (mmHg), diastolic blood pressure (mmHg), heart rate (bpm), temperature (°C), respiratory rate (bpm), and oxygen saturation (%) will be recorded at specified study visits for each subject. Descriptive statistics will be used to summarize vital signs measurements and change from baseline by scheduled visit/timepoint for Safety Population. For vital signs that are collected 3 times per day at a treatment visit, the median value will be used in the summary.

Vital signs will be listed by subject.

8.8 Physical Examination

A physical examination will be conducted on each subject at the specified visits and will include at a minimum: general appearance; head, eyes, ears, nose, and throat (HEENT); as well as cardiovascular, dermatologic, respiratory, gastrointestinal, musculoskeletal, and neurologic systems at screening. If any new clinically significant abnormality or worsening of a previous condition is observed, it will be recorded as an Adverse Event.

All physical examination findings will be listed by subject.

8.9 ECG

A 12-lead ECG will be obtained for each subject at specified visits as a safety assessment to provide a baseline and to monitor for potential AEs on cardiac function/conduction.

12-lead ECGs will be summarized and listed by scheduled visit/timepoint. Descriptive statistics will be provided for ECG interval data (PR, QRS, and QTcF.) The corrected QT intervals using Fridericia's formula will be calculated as follows: $QTcF = QT/(RR)^{1/3}$.

Descriptive statistics presented will contain both actual values and changes from baseline relative to each on-study evaluation and to the last evaluation on study.

The number and percentage of patients with elevated QTcF over post baseline period will be presented for the following categories: QTcF worsening to >450 msec, >480 msec, and >500 msec from baseline, and increase in QTcF from baseline >30 msec and >60 msec.

All triplicate ECG measurements at a particular time point will be averaged prior to analysis and summarization.

All 12-lead ECG measurements and the Investigator interpretation of findings including details of any abnormalities will be listed by subject.

8.10 PFTs

Pulmonary function testing is a common method to evaluate respiratory function and oxygen transfer prior to myeloablative conditioning. Each subject will undergo diffusing capacity for carbon monoxide (DLCO) test at the screening visit and Week 52.

All PFT data will be listed by subject.

8.11 Bone Marrow Aspiration

Bone marrow aspiration will be conducted at Baseline, Day 90, Week 52, Week 104 and ETV. Bone marrow aspiration at the Day 90 visit may be waived at the Investigator's discretion. Bone marrow aspirate may be performed at either the Week 26 or the Week 39 visit; it should not be performed at both. Both of these procedures (at both Week 26 and Week 39) may be waived at the Investigator's discretion. Unscheduled bone marrow aspiration may also be conducted at any time if clinically indicated, such as to evaluate the potential development of hematological malignancy. Any clinically significant abnormality or worsening of a previous condition from a previous visit will be reported as an adverse event.

All bone marrow aspiration data will be listed by subject.

8.12 Other Safety Endpoints

Other safety endpoints will be summarized, and shifts from baseline will be evaluated where appropriate. All other variables (e.g., pregnancy test, chest X-ray, infectious disease panel, hepatic function, immunological assays, etc.) may be listed by subject.

9 INTERIM ANALYSIS

No formal interim analyses are planned for this study, however, informal interim analyses may be performed at the Sponsor's discretion.

10 SAMPLE SIZE DETERMINATION

This study will enroll and treat a total of 5 to 6 subjects. The sample size for this single-arm study is not based on providing statistical power for hypothesis testing. However, for an AE with a true rate of 20%, a sample size of 6 subjects provides an approximately 74% likelihood that the event will be observed during the study. Subjects who do not receive ST-400 or are lost to follow-up or who withdraw from the study before the Week 26 visit in the Primary Study Period (beginning with ST-400 infusion) may be replaced.

11 GENERAL INFORMATION

11.1 Statistical Software

The creation of analysis datasets and statistical analyses will be done using SAS® version 9.3 or higher. The Medpace standard operating procedures (Medpace documents GL-DS-02-S2.2 and GL-DS-03-S1.1) will be followed for the validation of all SAS programs and outputs.

11.2 Format of Tables, Listings, and Figures

The format of tables, listings, and figures will be described in a stand-alone programming specifications document and will be finalized before database lock for the study. Additional analyses determined after database lock may be performed on an ad hoc basis.

12 CHANGES FROM PROTOCOL SPECIFIED ANALYSIS

No changes or plans to deviate from the analysis described in the protocol have been made.