STATISTICAL ANALYSIS PLAN

A Phase 1/2 Open Label Study of SL-401 in Combination with Pomalidomide and Dexamethasone in Relapsed or Relapsed and Refractory Multiple Myeloma

Protocol Number:	STML-401-0414
Protocol Version and Date:	Amendment 2: 27 March 2018 Amendment 1: 29 June 2016 Original: 04 May 2015
Name of Test Drug:	SL-401 (Tagraxofusp)
Phase:	Phase 1/2
Methodology:	Non-randomized, open-label, dose escalation study.
Sponsor:	Stemline Therapeutics, Inc. 750 Lexington Avenue, 11th Floor New York, NY 10022 Tel: (646) 502-2310 Fax: (646) 389-0968
Sponsor Representative:	Debra Sieminski, MS, PA-C Vice President, Clinical and Medical Affairs
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APPROVAL SIGNATURE PAGE

Protocol Title: A Phase 1/2 Open Label Study of SL-401 in Combination with Pomalidomide and Dexamethasone in Relapsed or Relapsed and Refractory Multiple Myeloma

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750 Lexington Avenue, 11th Floor
New York, NY 10022

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Document Date / Version: 14 October 2021 / Final Version 1.0

Veristat, LLC Author:

Approval Signature	Job Title
[redacted]	[redacted]

Sponsor Approval

By signing this document, I acknowledge that I have read the document and approve of the planned statistical analyses described herein. I agree that the planned statistical analyses are appropriate for this study, are in accordance with the study objectives, and are consistent with the statistical methodology described in the protocol, clinical development plan, and all applicable regulatory guidances and guidelines.

I have discussed any questions I have regarding the contents of this document with the biostatistical author.

I also understand that any subsequent changes to the planned statistical analyses, as described herein, may have a regulatory impact and/or result in timeline adjustments. All changes to the planned analyses will be described in the clinical study report.

Sponsor Signatory:

Approval Signature	Job Title
[redacted]	[redacted]

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LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

Abbreviation	Definition
AE	Adverse event
AESI	Adverse event of special interest
ALT	Alanine aminotransferase
AML	Acute myeloid leukemia
AST	Aspartate aminotransferase
ATC	Anatomic therapeutic class
BM	Bone Marrow
BP	Blood Pressure
BUN	Blood Urea Nitrogen
CBC	Complete Blood Count
CPK	Creatine Phophokinase
CBR	Clinical Benefit Rate
CI	Confidence interval
CLS	Capillary leak syndrome
CR	Complete response
CSC	Cancer stem cell
CSR	Clinical study report
CTCAE	Common Terminology Criteria for Adverse Events
DEX	Dexamethasone
DLT	Dose-limiting toxicity
DOR	Duration of Response
DSRC	Data Safety Review Committee
DT	Diphtheria toxin
ECOG	Eastern Cooperative Oncology Group
ECG	Electrocardiogram
FLC	Free light chain
IL-3	Interleukin-3
IL-3R	Interleukin-3 receptor
MedDRA	Medical Dictionary for Regulatory Activities
mITT	Modified Intent-to-Treat
MM	Multiple Myeloma
MR	Minimal Response
MRD	Minimal residual disease

MTD	Maximum tolerated dose
ORR	Overall response rate

Abbreviation	Definition
OS	Overall survival
pDC	Plasmacytoid dendritic cell
PCS	Potentially clinically significant
PFS	Progression free survival
PFS-6	Progression free survival at 6 months
PK	Pharmacokinetic
PT	Preferred Term
SAP	Statistical analysis plan
sCR	Stringent Complete Response
SD	Standard deviation
SOC	System organ class
TEAE	Treatment-emergent adverse event
ULN	Upper limit of normal
WHO	World Health Organization

1. INFORMATION FROM THE STUDY PROTOCOL

1.1. Introduction and Objectives

The overall purpose of study STML-401-0414 is to support the development of tagraxofusp (SL-401), to evaluate the safety of the product as a single agent in an initial run-in cycle, and to assess the safety and clinical efficacy of tagraxofusp in combination with pomalidomide (POM) and dexamethasone (DEX) in the treatment of patients with relapsed or relapsed and refractory multiple myeloma (RRMM).

Multiple myeloma (MM) is a heterogeneous clonal B-cell malignancy characterized by the accumulation of abnormal antibody producing plasma cells in the bone marrow (BM). The disease is associated with a variety of clinical manifestations including lytic bone lesions, hypercalcemia, renal impairment, and anemia. MM is the second most common hematologic malignancy and accounts for approximately 11,000 deaths per year in the United States and 19,000 in Europe (ACS 2013).

The molecular mechanism by which MM cells evade drug–induced cytotoxicity and acquire drug resistant phenotypes include interaction of MM cells with the BM microenvironment which is composed of extracellular matrix (ECM) proteins such as fibronectin, collagen, and laminin, along with cellular elements such as hematopoietic stem cells, immune cells, BM endothelial cells, and bone marrow stromal cells (BMSCs). Adhesion of MM cells to ECM proteins and accessory cells leads to increased expression of factors such as IL-6, insulin-like growth factor (IGF-1), and vascular endothelial growth factor (VEGF), which in turn further stimulates growth and survival of the malignant clone (Chauhan 1996; Agarwal 2013).

In addition, early studies using both *in vitro* and *in vivo* MM models, have demonstrated increased numbers of plasmacytoid dendritic cells (pDCs) in the BM microenvironment, which promotes MM cell growth and survival (Chauhan et al. 2009). These studies also showed increased interleukin-3 (IL-3) levels resulting from pDCs and MM cell interaction, which in turn, trigger MM cell growth and pDC survival.

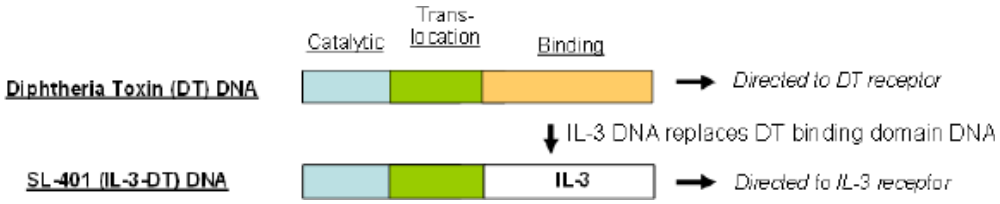
The field of cancer stem cells (CSCs) is a new area of cancer biology that may fundamentally alter the approach to oncology drug development. CSCs have been identified in virtually all major tumor types, including leukemia and cancers of the brain, breast, colon, prostate, and pancreas (Jordan et al. 2006). CSCs are the highly malignant “seeds” of a tumor that self-renew and generate more mature cells that comprise the bulk of the tumor, or “the tumor bulk.” As such, CSCs appear to be responsible for tumor initiation, propagation, and metastasis. Many of the characteristics of CSCs, such as their slow growth, anti-cell death mechanisms, and presence of multi-drug resistance proteins, may enable CSCs to resist therapeutic agents traditionally used to treat cancer. This may be due to the many challenging characteristics of CSCs, including slow growth, presence of multi-drug resistance proteins, anti-cell death mechanisms, and increased activity of cellular mechanisms that repair damaged deoxyribonucleic acid. CSCs are particularly resistant to chemotherapy, radiation, or targeted therapy relative to tumor bulk.

1.1.1. Tagraxofusp (SL-401)

Diphtheria toxin (DT) IL-3 fusion protein, named tagraxofusp following Biologics Licensing Application (designated SL-401 during clinical development by Stemline Therapeutics, Inc.), is

a novel biologic targeted therapy directed to the IL-3 receptor. Tagraxofusp is comprised of recombinant human IL-3 genetically fused to a truncated DT, in which the binding domain of DT has been replaced with IL-3. As depicted in Figure 1-1, the IL-3 domain of tagraxofusp is able to target the agent to leukemia blasts and CSCs that over-express IL-3R, leading to receptor-mediated endocytosis and localization of tagraxofusp to early endosomes. The translocation domain of DT changes conformation in the acidic environment of the endosome, and the RXRR motif (residues 191-194) located between the catalytic and translocation domains of DT is cleaved by endosomal furin. The translocation domain of DT then inserts into the endosomal membrane. As the TAT-like domain of DT (residues 201-230) interacts with cytosolic heat shock protein 90 (Hsp90) and thioreduxin reductase, the catalytic domain (A fragment) unfolds, is reduced, and translocates to the cytosol. Upon release into the cytosol, the A fragment refolds and catalytically inactivates cellular protein synthesis by ADP-ribosylating the diphthamide residue in domain IV of elongation factor 2, leading to apoptosis (Yamaizumi et al. 1978; Deng et al. 2008; FitzGerald et al. 1989; Perentesis et al. 1992; Louie et al. 1997; Ratts et al. 2005; Thorburn et al. 2004).

Figure 1-1 Schematic of Tagraxofusp Construction



1.1.2. Study Objectives

The following objectives are as defined in the Study Protocol (Amendment 2, 27 March 2018).

Primary Objectives

- Evaluate the safety of single agent tagraxofusp in an initial run-in cycle in patients with MM.
- Determine the maximum tolerated dose (MTD) or the maximum tested dose of tagraxofusp given in combination with POM/DEX for the treatment of relapsed or RRMM.
- Characterize the safety and tolerability profiles of tagraxofusp in combination with POM/DEX at the MTD

Secondary Objectives:

- Evaluate the immunogenicity of tagraxofusp in combination with POM/DEX.
- Evaluate the pharmacokinetics (PK) of tagraxofusp as single agent and when administered in combination with POM/DEX.
- Evaluate the activity of the combination of tagraxofusp/POM/DEX regiment in terms of:

- Overall response rate (complete response [CR]+ very good partial response [VGPR] + partial response [PR]) and clinical benefit rate (CBR) (CR + VGPR + PR + minimal response [MR]) based on the International Myeloma Working Group (IMWG) defined response criteria and the duration of response (DOR) in RRMM patients.

- Progression-free survival (PFS) and PFS at 6 months (PFS-6).

- Overall Survival (OS).

Exploratory objectives:

- Characterize expression of IL-3 receptor (IL-3R)/CD123 (and other potentially relevant markers) on MM cells, pDCs and associated cell populations in peripheral blood (PB) and BM prior to and during/following therapy.

- Evaluate the treatment effects on IL-3R/CD123-expressing pDCs in the BM microenvironment prior to, during, and following therapy. Specifically, assess (i) the relative abundance of tumor cells to pDCs; (ii) immunohistochemistry (IHC) on BM biopsy specimens and flow cytometry analysis using antibodies specific against pDCs, to evaluate potential reduction in the pDC population in MM BM; and (iii) MM cell growth-promoting activity of pDCs will be determined by assessment of their ability to stimulate MM cell proliferation *ex-vivo*.

- Evaluate therapy-related effects on the levels of circulating cytokines/factors (i.e., IL-3 and others) associates with pDCs and MM cell growth, survival, and immune dysfunction using serum and plasma samples prior to, during, and following therapy.

- Identify surrogate markers of therapy-related anti-osteolytic activity. Specifically, assess the levels of bone turnover markers (potentially to include N and C telopeptide, osteocalcin, and bone alkaline phosphatase) prior to, during, and following therapy.

1.1.3. Purpose of this Document

This statistical analysis plan (SAP) is designed to outline the methods to be used in the analysis of study data to answer the study objective(s). Populations for analysis, data handling rules, statistical methods, and formats for data presentation are provided. The statistical analyses and summary tabulations described in this SAP will provide the basis for the results sections of the clinical study report (CSR) for this trial.

This SAP will also outline any differences in the currently planned analytical objectives relative to those planned in the study protocol.

1.2. Study Design

1.2.1. Synopsis of Study Design

This study is a Phase 1/2 non-randomized, open-label, dose escalation, multicenter study of tagraxofusp in combination with standard doses of POM and DEX. The study will be conducted as a modified Fibonacci 3 + 3 dose escalation design to determine the MTD of tagraxofusp in

combination with standard doses of POM and DEX. The study will be conducted in 2 phases. Each evaluated tagraxofusp dose level will also incorporate an initial "Run-in Cycle" of single agent tagraxofusp in at least 3 patients; following the Run-in Cycle, patients who have not experienced a dose-limiting toxicity (DLT) will receive combination tagraxofusp/POM/DEX. All patients in phase 2 will initiate therapy with the combination of tagraxofusp/POM/DEX at the MTD or maximum tested dose established in phase 1.

Phase I

Run-In Cycle: Tagraxofusp will be administered as a single agent during a Run-in Cycle. Upon completion of the Run-in Cycle patients will be evaluated for safety and response.

- Patients who do not experience a DLT during the Run-in Cycle will have POM/DEX added to their regimen at the assigned cohort dose.
- Patients who experience a DLT during the Run-in Cycle will be discontinued from the study.

Table 1-1 details the Tagraxofusp/POM/DEX dose levels, beginning with dose level 1 to be evaluated.

Table 1-1 Dose Levels to be Tested

Dose Level	DLT EVALUTION PERIOD = RUN-IN CYCLE AND CYCLE 1			
	Run-In Cycle	Combination therapy Cycle 1 - 6		
	SL-401 (IV) Daily on Days 1 – 5	SL-401 (IV) Daily on Days 1 – 5	POM (oral) Daily on Days 1 – 21	DEX (oral) on Days 1, 8, 15 and 22
-1	5 µg/kg	5 µg/kg	4 mg	40 mg
1	7 µg/kg	7 µg/kg	4 mg	40 mg
2	9 µg/kg	9 µg/kg	4 mg	40 mg
3	12 µg/kg	12 µg/kg	4 mg	40 mg

Cohorts of 3-6 patients will be treated at each dose level. All patients within a cohort must complete the Run-in Cycle and the first cycle of combination therapy (Cycle 1) before patients can be enrolled into the subsequent cohort of tagraxofusp (single-agent) at the next higher dose. No intra-patient dose escalation is allowed. The first cohort of patients will receive tagraxofusp single agent at a dose of 7 µg/kg/day followed by tagraxofusp with POM/DEX.

The period for evaluation for DLT will include the Run-in Cycle and Cycle 1 (the first cycle of combination therapy).

A decision to allow treatment at the next higher does level will depend on the number of patients who experience a DLT during the first cycle of combination therapy.

If after 3 patients complete Cycle 1 of combination therapy:

- None of the initial 3 patients treated (0/3) experiences a DLT), then dose escalation will proceed, and 3 new patients will be treated at the next higher dose.
- If 1 of the initial 3 patients treated (1/3) experiences a DLT, the cohort will be expanded to include an additional 3 patients treated at the same dose.
    - If only 1 patient (1/6) from this expanded cohort experiences a DLT then 3 new patients will be treated at the next higher dose.
- If 2 or more patients within a cohort have a DLT, then the MTD will be exceeded, and further dose escalation will not occur.

If the highest planned treatment dose is completed and determined to be safe and the MTD is not exceeded, the available safety data will be reviewed to assess whether further dose escalation is justified.

The MTD of the combination therapy is defined as the dose preceding the dose level at which 2 or more patients experience a DLT during the Run-in Cycle and Cycle 1 of combination therapy. The MTD of the combination will be used in phase 2 of the study. If the highest planned treatment dose is completed and determined to be safe and the MTD is not exceeded, the available PK and safety data will be reviewed to assess whether further dose escalation is justified. A patient who does not complete the first cycle of treatment for reasons other than the occurrence of DLT will be replaced by another patient who will receive the same dose regimen if necessary to evaluate that cohort (e.g., if a patient is not evaluable for DLT but 2 others have experience a DLT within the cohort, there will be not a need to replace the patient as the MTD will have been exceeded).

In the event that a DLT occurs in 2 or more patients treated at the 7 μg/kg/day dose level, 5 μg/kg/day will be considered by the Data Safety Review Committee (DSRC) as an alternative starting dose. In this event, a new cohort of 3 patients will receive 5 μg/kg/day for the first cycle. The same DLT rules will apply to this does level. If 2 or more patients experience a DLT at the 5 μg/kg/day dose level, the study will be halted.

DLT Assessment

Run-in Cycle:

Patients are evaluable for DLT assessment during the Run-in Cycle of single agent tagraxofusp after receiving at least one dose of tagraxofusp. Patients who experience a DLT during the Run-in Cycle will not be further dosed.

Combination Therapy:

Patients who receive at least 1 infusion of tagraxofusp and 1 dose of POM during Cycle 1 are evaluable for DLT assessment of the combination therapy. Patients should receive a minimum of 8 doses of POM during Cycle 1 and complete the 28 days of observation unless the patient

experiences DLT (patients who discontinue prior to this juncture because of disease progression or for reasons unrelated to study therapy will be replaced).

During phase 1, DLT is defined as any of the following AEs that are possibly, probably, or definitely related to therapy:

- Any grade ≥4 neutropenia lasting greater than 7 days or grade ≥3 neutropenia associated with fever.
- Any grade ≥4 thrombocytopenia lasting greater than 7 days or grade ≥3 thrombocytopenia associated with bleeding.
- Any grade ≥3 non-hematologic toxicity except:
    - Grade 3 nausea, vomiting, or diarrhea lasting no longer than 48 hours (with resolution to grade ≤1 or baseline) with optimal supportive care.
    - Grade 3 arthralgia, myalgia, fever, in the absence of neutropenia, lasting no longer than 48 hours (with resolution to grade ≤1 or baseline).
    - Grade 3 fatigue lasting <7 days.
    - Grade 3 laboratory abnormalities that are asymptomatic and not considered clinically significant by the Investigator, that respond to or do not require intervention and resolve to grade ≤1 or baseline ≤28 days after the last infusion of tagraxofusp
- Grade 4 transaminase or creatine phosphokinase (CPK) elevation (confirmed within 24 hours of initial identification) regardless of duration or relationship to tagraxofusp.

Phase 2: Expansion

During phase 2, at least 14 additional patients (total 20 patients) will be treated at the MTD or maximum tested dose at which multiple DLTs are not observed (identified in phase 1). During phase 2, the Run-in Cycle will no longer be administered. However, the first 6 patients treated at the MTD without the Run-in Cycle will also be assessed for DLT during the first cycle of therapy. If more than one DLT is identified in these initial 6 patients, consideration will be given to the administration of a reduced tagraxofusp dose in the remainder of phase 2, or reinstitution of the tagraxofusp single agent Run-in Cycle for the remainder of phase 2.

1.2.2. Randomization Methodology

As this is a single-agent study, randomization is not applicable.

1.2.3. Treatment Discontinuation

Tagraxofusp treatment could be discontinued for any of the following reasons:

- Patient withdrawal of consent
- Occurrence of unacceptable toxicity, including DLT

- Tagraxofusp related anaphylaxis or grade ≥3 hypersensitivity reaction
- Tagraxofusp-related grade ≥3 CLS
- Disease recurrence/progression
- Intercurrent illness that prevents further administration of tagraxofusp
- Patient non-compliance
- Occurrence of pregnancy
- Completion of 6 cycles of treatment
- Investigator's decision

The reason for tagraxofusp discontinuation and the date of discontinuation are recorded in the electronic case report form (eCRF).

1.2.4. Study Procedures

The schedules of assessments, as outlined in the study protocol, are presented in Table 7-1.

1.2.5. Efficacy, Pharmacokinetic, Immunogenicity, and Safety Parameters

1.2.5.1. Efficacy Parameters

Efficacy assessments include M-protein determination, serum free light chain results, bone marrow aspirate/biopsy results, plasmacytoma evaluations, skeletal survey, tumor assessments, ORR, and clinical benefit rate (CR + VGPR+PR+MR) based on the IMWG defined response criteria, as well as DOR and OS. Definitions for each efficacy assessment are described in in Section 4.3.

1.2.5.2. Safety Parameters

Safety evaluations performed during the study included physical examinations, Eastern Cooperative Oncology Group (ECOG) performance status, measurement of vital signs, 12-lead electrocardiograms (ECGs), clinical laboratory evaluations (hematology, serum chemistry, coagulation, and urinalysis), and monitoring of adverse events (AE) (including serious AEs [SAEs]), DLTs, and concomitant medications (CM).

Further details on the definitions and analysis methods for safety endpoints are provided in Section 4.4.

1.2.5.3. Pharmacokinetic and Immunogenicity Parameters

Noncompartmental PK parameter summaries are described in a separate Modeling and Simulation Plan.

Summary of immunogenicity parameters are described in a separate plan.

2. PATIENT POPULATION

2.1. Population Definitions

The following patient populations will be evaluated and used for presentation and analysis of the data:

- Modified Intent-to-Treat (mITT) Population: All patients who are eligible based on the screening criteria, had baseline disease assessments, and had their disease re-evaluated, and who received at least 1 dose of tagraxofusp, POM, or DEX. Patients who meet the criteria for mITT will be considered "evaluable." Patients will be grouped according to the planned dose level at time of enrollment.

- Safety Population: All patients enrolled in the study who received at least 1 dose of tagraxofusp, POM, or DEX. Patients will be grouped according to the actual dose level received.

The mITT population is the primary population for the analysis of efficacy parameters. The safety population is the primary population for the analysis of safety parameters.

2.2. Protocol Violations

All protocol violations will be presented in a data listing.

3. GENERAL STATISTICAL METHODS

3.1. Sample Size Justification

The primary objectives of phase 1 of the study are to evaluate the safety of tagraxofusp as a single agent in an initial Run-in Cycle, to determine the MTD or the maximum tested dose where multiple DLTs are not observed, and to further characterize the safety profile of tagraxofusp/POM/DEX at the MTD. Based on such, a recommended dose for phase 2 studies will be defined. The number of patients to be enrolled in the dose-escalation portion of the study is dependent on the dose levels at which DLTs are seen, and the number of dose levels investigated to determine the MTD; 3 to 6 patients are planned to be treated at each dose level. The anticipated sample size is sufficient to evaluate these objectives. A secondary objective is to characterize the antitumor activity of tagraxofusp /POM/DEX in terms of ORR, CBR, PFS, and PFS-6.

During phase 2, if approximately 14 patients are enrolled at the recommended phase 2 dose as defined in phase 1 over 12 months and follow-up continues for 12 months after the last enrolled patient, the total of 20 patients treated at this dose has approximately 60% power with a 1-sided type I error rate of 6% to reject the null hypothesis that the PFS-6 is <40% if the true rate is 60%.

3.2. General Methods

All data listings that report an evaluation date will include a relative study day (Rel Day). Pre-treatment and on-treatment study days are numbered relative to the day of the first dose of Tagraxofusp which is designated as Day 1. The preceding day is Day -1, the day before that is Day -2, etc. The last day of any study drug is designated with an "L" (e.g., Day 26L). Post-treatment study days are numbered relative to the last dose and are designated as Day 1P, Day 2P, etc.

All output will be incorporated into Microsoft Word files, sorted, and labeled according to the International Council for Harmonisation (ICH) recommendations, and formatted to the appropriate page size(s).

Tabulations will be produced for appropriate demographic, baseline, efficacy, and safety parameters. For categorical variables, summary tabulations of the number and percentage of patients within each category (with a category for missing data) of the parameter will be presented. Two-sided 95% confidence intervals (CIs) will be computed using the Clopper Exact method. For continuous variables, the number of patients, mean, median, standard deviation (SD), minimum, and maximum values will be presented. Time-to-event data will be summarized using Kaplan-Meier methodology using 25^{th}, 50^{th} (median), and 75^{th} percentiles with associated 2-sided 95% CIs, as well as percentage of censored observations.

3.3. Computing Environment

All descriptive statistical analyses will be performed using SAS statistical software Version 9.4, unless otherwise noted. Medical history and AEs will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) Version 19.0 or higher. Concomitant medications will be coded using the World Health Organization (WHO) Drug Dictionary (December, 2016).

3.4. Baseline Definitions

For all analyses, baseline will be defined as the most recent measurement prior to the first administration of tagraxofusp or tagraxofusp/POM/DEX.

3.5. Methods of Pooling Data

Overall summaries of safety parameters will be presented by stage of enrollment for MM patient groups across all dose levels.

3.6. Adjustments for Covariates

Due to the small sample size, no formal statistical analyses that adjust for possible covariate effects are planned.

3.7. Multiple Comparisons/Multiplicity

Multiplicity is not of concern for this Phase 1 study.

3.8. Subgroup Analyses

No subgroup analyses will be performed.

3.9. Withdrawals, Dropouts, Loss to Follow-up

At the discretion of the Sponsor, additional patients may be enrolled to supplement patient data that are compromised due to premature study dropout or other reasons.

3.10. Missing, Unused, and Spurious Data

In general, there will be no substitutions made to accommodate missing data points. All data recorded on the eCRF will be included in data listings that will accompany the CSR.

When tabulating AE data, partial dates will be handled as follows: If the day of the month is missing, the onset day will be set to the first day of the month unless it is the same month and year as study treatment. In this case, to conservatively report the event as treatment-emergent, the onset date will be assumed to be the first day of treatment. If the onset day and month are both missing, the day and month will be assumed to be January 1, unless the event occurred in the same year as the study treatment. In this case, the event onset will be set to the first day of treatment in order to conservatively report the event as treatment emergent. A missing onset date will be set to the first day of treatment.

3.11. Visit Windows

It is expected that all visits should occur according to the protocol schedule. All data will be tabulated per the evaluation visit as recorded on the eCRF even if the assessment is outside of the visit window. In data listings, the relative day of all dates will be presented (see Section 3.2).

3.12. Timing of Analysis

Safety data were summarized in support of a Biologics Licensing Application (data cutoff: 07MAY2017) and in support of a Marketing Authorization Application (data cutoff: 31JAN2018) for the licensing of tagraxofusp in the United States and Europe, respectively. Efficacy data were not summarized at that time. The respective analyses were described in a separate SAP.

There were no planned interim efficacy analyses. The final, end of study analysis for the CSR using data from the locked database, will be supported from the analyses described in this document.

4. STUDY ANALYSES

4.1. Patient Disposition

Patient disposition will be tabulated and will include the number of patients screened, the number treated in total, the number in each patient population for analysis, and the number who withdrew prior to completing the study and reason(s) for withdrawal. The summary will be presented by dose level.

A data listing of study completion information, including the reason for premature study withdrawal, if applicable, will be presented.

4.2. Demographics and Baseline Characteristics

Demographics and baseline characteristics will be summarized and presented by disease and dose level. Age, height, and weight will be summarized using descriptive statistics (number of patients, mean, SD, median, minimum, and maximum). The number and percentage of patients in each gender, ethnicity, race, and ECOG performance status category will be presented.

Medical history will be tabulated. Disease history, including MM baseline diagnosis, time since MM diagnosis, prior MM treatment, response to prior treatment, and date of relapse, if applicable, will be summarized.

Demographic and baseline data for each patient will be provided in data listings.

4.3. Efficacy Evaluation

The study will evaluate the activity of the tagraxofusp/POM/DEX regimen.

Secondary efficacy endpoints will include PFS and PFS-6; ORR (CR + VGPR + PR) and clinical benefit rate (CR + VGPR + PR + MR) based on the IMWG defined response criteria, as well as DOR, and OS.

Data for all efficacy endpoints will be presented in by-patient listings.

Time to response, DOR, and survival will be estimated using the product-limit method of Kaplan and Meier. Exact 1-sided 95% CIs will be calculated for ORR and clinical benefit rates, and the distributions for DOR, PFS, PFS-6 and OS will be estimated by Kaplan-Meier methodology.

4.3.1. Progression Free Survival

Progression-free survival is defined as the time from the date of first infusion of tagraxofusp to the date of PD or death from any cause, whichever occurred first. Patients who do not progress and are still alive at the time of analysis will be censored on the date of the last disease assessment prior to the analysis cutoff date. The distribution for PFS will be estimated by Kaplan-Meier methodology and the 25^{th} percentile, median, 75^{th} percentile, number and percentage of events and censored observations, and appropriate CIs will be presented.

Progression-free survival at 6 months, PFS-6, will also be calculated for patients who do not progress and are still alive 6 months after the date of first treatment.

4.3.2. Response Rate

Response rates and depth of response will be calculated as the percent of evaluable patients that have confirmed sCR/CR/VGPR or PR. For CR, ORR, and CBR, Clopper Exact 95% CIs will be presented.

Complete response rate will be presented as the number and percentage of patients who achieved CR after treatment.

Overall Response (ORR) is defined as the percentage of evaluable patients that have confirmed CR, VGPR, or PR

- ORR = (CR+ VGPR + PR)

Clinical Benefit Rate is defined as the percentage of evaluable patients that have confirmed CR/VFPR/PR or MR

- CBR = (CR + VGPR + PR + minimal response [MR])

4.3.3. Duration of Response

Duration of response is defined as the time from when the criteria are first met for CR until the date that the criteria for relapse after CR are met. This could be the occurrence of PD or relapse. In the case that PR or SD follows CR and there is no evidence that response rebounds to CR, duration of CR will end at the time of first reduction of response to below CR. Patients who are lost to follow-up or who do not relapse after CR as of the cut-off for analysis will be censored on the latter of the date of last treatment with tagraxofusp or date of last disease assessment recorded prior to the analysis cutoff date.

4.3.4. Overall Survival

Overall survival is defined as the time from the date of first infusion of tagraxofusp/POM/DEX to the date of death from any cause. Patients who are still alive or lost to follow-up at the time of the analysis will be censored on the last date known to be alive prior to the analysis cutoff date, as determined by in-person visit or telephone contact. The overall distribution for OS will be estimated by Kaplan-Meier methodology in a similar manner as PFS.

4.3.5. Exploratory Efficacy Assessments

Exploratory efficacy assessment analyses will include:

- M-protein determination actual values and changes from baseline will be summarized over time by visit and included in by-patient data listings using both of the following procedures:
    - SPEP and serum protein immunofixation with quantitative immunoglobulins; and

- UPEP and urine protein immunofixation (all using the same 24-hour urine collection)

- Serum FLC results actual values and changes from baseline, including FLC Kappa, FLC Lambda, FLC Kappa/Lambda ratio, will be summarized over time by visit and included in a by-patient data listing

- BM to quantify percent MM cell involvement results actual values and changes from baseline will be summarized over time by visit and included in a by-patient data listing

- Plasmacytoma evaluation results will be included in a by-patient data listing only

- Skeletal survey, serum β2 microglobulin, and cytogenetic analysis/FISH from BM aspirate results will be included in by-patient data listings only

4.4. Safety Analyses

All safety tabulations will be presented by dose.

4.4.1. Study Drug Exposure

Duration of study drug exposure will be calculated as the number of days and number of cycles patients were administered each study drug.

$$\text{DDDDDDDDDDDDDDD DDoo SSDDDDSSSS DDDDDDDD EEEEEEDDssDDDDss} = (\text{DDDDDDss DDoo llDDssDD SSDDssss} - \text{DDDDDDss DDoo ooDDDDssDD SSDDssss}) + 1$$

Duration in cycles of drug exposure will be defined the total number of cycles of each study drug initiated while the patient is on study. Total dose administered will be summarized for each study drug overall and by cycle.

Relative Dose Intensity will be computed using the following definition:

$$\text{RRssllDDDDDDRRss DDDDssss IIDDDDssDDssDDDDSS (\%)} = 100 * \frac{\text{SSDDSS(CCDDSSDDllDDDDRRss AAAADDDDDDll DDDDssss RRssAAssDDRRssSS bbSS CCSSAAllss)}}{\text{SSDDSS(PPllDDDDDDssSS DDDDssss DDDD bbss AASSSSDDDDDDssDDssDDssSS bbSS CCSSAAllss)}}$$

Exposure to tagraxofusp, POM, and DEX will be presented in by-patient data listings.

4.4.2. Adverse Events

All AEs will be coded using the MedDRA coding system and displayed in tables and data listings using system organ class (SOC) and preferred term (PT).

Analyses of AEs will be performed for those events that are considered treatment-emergent, where treatment-emergent is defined per protocol as any AE with onset after the first administration of tagraxofusp or tagraxofusp/POM/DEX through 30 days after the last dose of tagraxofusp/POM/DEX, or any event that was present at baseline but worsened in intensity or was subsequently considered drug-related by the Investigator through 30 days after the last dose of Tagraxofusp/POM/DEX.

The number and percentage of patients with any treatment-emergent AE (TEAE), any TEAE assessed by the Investigator as related to any study treatment (definitely, probably, or possibly related), any Grade ≥3 TEAE as per the Common Terminology Criteria for Adverse Events (CTCAE), any SAE, any AE leading to discontinuation of any study treatment, and any AE leading to any dose modification will be summarized by dose group and overall. In these tabulations, each patient will contribute only once (i.e., the most related occurrence or the most intense occurrence) to each of the incidence rates in the descriptive analysis, regardless of the number of episodes. Summaries of related TEAEs will also be presented for relationship to each study drug (SL-401, Pomalidomide, and Dexamethasone).

Treatment-emergent AEs summarized by patient incidence rates are not tabulated by severity or relationship to study treatment; therefore, in such tabulations, a patient contributes only once to the count for a given AE SOC or PT. For tabulations that include classification by relationship to any study treatment, AEs with missing relationship to any study treatment will be considered related.

Adverse events of special interest (AESIs) will be determined using MedDRA version 19.0 standardized medical queries (SMQs), high-level terms, or PTs, as follows:

- Possible hypersensitivity events, based on the SMQ Hypersensitivity (broad search).
- Vascular capillary leak syndrome (CLS), based on the MedDRA SMQ (to be provided) in addition to PTs of hypoalbuminemia, blood albumin decreased, and proteinuria.
- Possible drug-induced liver injury events, based on the SMQ drug-related hepatic disorders (broad search).

Summary tables of AESIs will be presented as follows:

- AESIs overall and by PT,
- AESIs by PT overall and by grouped cycle (Run-in, Cycle 1, Cycle 2, Cycles ≥ 3),
- Grade ≥3 AESIs overall and by PT,
- Serious AESIs overall and by PT,
- AESIs resulting in any drug interruption overall and by PT,
- AESIs resulting in dose reduction overall and by PT,
- AESIs resulting in any study drug discontinuation overall and by PT,
- AESIs resulting in death overall and by PT.

These tabulations will be completed for all MM patients by dose group. AESIs will also be included in data listings.

4.4.2.1. Capillary Leak Syndrome

In addition to the summaries described in Section 4.4.2, a summary will be provided presenting the number and grade of CLS events, exposure to tagraxofusp prior to onset of CLS, and time to first onset, and time to resolution of CLS events.

4.4.3. Laboratory Data

Clinical laboratory values will be expressed in Système International (SI) units.

The actual value and change from baseline (Day 1) to each on-study evaluation through cycle 6 will be summarized for each clinical laboratory parameter, including hematology, clinical chemistry, coagulation, and urinalysis. In the event of repeat values, the last non-missing value per study day/time will be used.

Shift tables of change in CTCAE grade of laboratory parameters from baseline to worst value and from baseline to last value on study will be presented. Both scheduled and unscheduled visits will be included in shift tables.

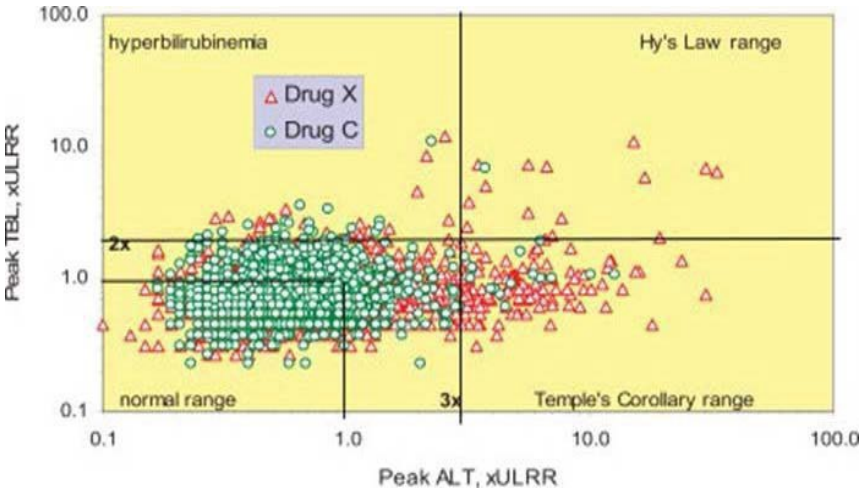
Results from pregnancy test results will be tabulated by patient.

To assess for possible drug-induced liver injury (FDA 2009), a figure plotting peak alanine aminotransferase (ALT) versus peak total bilirubin (both on a logarithmic scale × upper limit of normal [ULN]) will be produced similar to that recommended by Watkins et al (Watkins, et al. 2008) so that values within the normal reference range (<ULN) for ALT and total bilirubin are found in the left lower quadrant and Hy's Law case candidates are in the upper right quadrant (ALT >3 × ULN and total bilirubin >2 × ULN). Patients with Gilbert's syndrome or cholestasis are typically found in the upper left quadrant, and patients with ALT elevations without significant hepatic abnormality (i.e., without increased total bilirubin) are found in the lower right quadrant. The peak total bilirubin value plotted will be the peak within ± 7 days of the peak ALT value. If at least 5 patients are identified as potential Hy's Law Cases, a summary table will be produced for the number and percentage of patients who have values of aspartate aminotransferase (AST) (>3 to ≤5 × ULN, >5 to ≤10 × ULN, >10 to ≤20 × ULN, >20 × ULN), ALT (>3 to ≤5 × ULN, >5 to ≤10 × ULN, >10 to ≤20 × ULN, >20 × ULN), alkaline phosphatase (>1.5 × ULN), or total bilirubin (>1.5 to ≤2 × ULN, >2 × ULN) after initiation of study drug. In this table, a patient may be counted only once. For instance, a patient with a result of AST of 11 × ULN will be counted in the category of >10 to ≤20 × ULN.

This plot will be repeated for peak aspartate aminotransferase (AST) by total bilirubin.

An example of the scatterplot is provided in Figure 4-1.

Figure 4-1 Hy's Law Candidates Scatterplot



Time to first onset of elevated AST and ALT will be analyzed using Kaplan-Meier analyses and presented as figures.

All laboratory data will be provided in by-patient data listings. A by-patient listing will also be presented for all laboratory values with CTCAE Grade ≥3.

4.4.4. Vital Signs and Physical Examination

The actual value and change from baseline (Day 1) to each on-study evaluation and to the last on study evaluation will be summarized for vital signs.

A summary table of the number and percent of patients with treatment-emergent potentially clinically significant (PCS) vital signs parameters will be tabulated based on the following criteria:

	PCS – Low if:			**PCS – High if:**		
Variable Name	**Observed Value is:**	**AND**	**Decrease from Baseline is:**	**Observed Value is:**	**AND**	**Increase from Baseline is:**
Systolic Blood Pressure	<90 mmHg		≥20 mmHg	>180 mmHg		≥20 mmHg
Diastolic Blood Pressure	<50 mmHg		≥10 mmHg	>105 mmHg		≥10 mmHg
Heart Rate	<50 bpm		≥15 bpm	>120 bpm		≥15 bpm

PCS= potentially clinically significant.

All tables summarizing vital sign measurements only include visits in which at least 10% of the analysis population had measurements. Vital sign measurements will be presented for each patient in a data listing.

All physical examination findings and ECOG performance status findings will be tabulated by visit and presented in data listings.

4.4.5. Electrocardiogram

ECG results will be summarized descriptively, including the number and percentage of patients with normal, abnormal, and clinically significant abnormal results at baseline and each study visit. Actual values and change from baseline will be summarized for QTc intervals. All tables summarizing ECG measurements only include visits in which at least 10% of the analysis population had measurements.

The number and percentage of patients whose mean QTcF or QTcB value at any time point meets any of the following categories will be summarized:

- >450 msec
- >480 msec
- >500 msec
- increase from baseline >30 msec
- increase from baseline >60 msec

QTcF and QTcB will be derived using QT interval and heart rate using the formulas:

$$QQQQAAQQ = \frac{QQQQ\ IIDDDDssDDRRDDll}{HHssDDDDDD\ RRDDlss^{1/3}} \qquad QQQQAAQQ = \frac{QQQQ\ IIDDDDssDDRRDDll}{HHssDDDDDD\ RRDDlss^{1/2}}$$

ECG and echocardiogram/multigated acquisition scan (MUGA) data for each patient will be provided in data listings.

4.4.6. Concomitant Medications and Subsequent Treatments

Concomitant medications will be coded using the WHO Drug Dictionary. Results will be tabulated by anatomic therapeutic class (ATC) and PT.

Concomitant medications will be tabulated by dose group, where any medications that were not discontinued prior to the first dose of study drug will be included. If an end date is missing or the medication is ongoing at the time of first dose, the medication will be considered concomitant.

The use of concomitant medications and subsequent treatment(s) will be included in by-patient data listings.

4.4.7. Pre-Treatment Medications

Pre-treatment medications will be coded using the WHO Drug Dictionary. Results will be tabulated by ATC and PT. In addition, the number and percent of patients who receive pre-treatment medication at least once will be summarized by dose group.

Pre-treatment medications will be included in by-patient data listings.

5. CHANGES TO PLANNED ANALYSES

As of this date, there have been no changes between the protocol-defined statistical analyses and those presented in this SAP. All changes from procedures outlined in this SAP will be summarized in the study report. Decisions to deviate from planned analyses will be documented at the time they are made.

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7. STUDY FLOW CHARTS

The following Study Flow Chart is from Protocol Amendment 2.

Table 7-1 Schedule of Events

Evaluation	Screening Baseline	Run in Cycle Cycle is 28 days								Cycles 1 - 6 [v] Each Cycle is 28 days								EOT[w]	30-day Post-Tx F/U	F/U[x]
	D-21 to -1	D 1	D 2	D 3	D 4	D 5	D 8	D 15	D 22	D 1	D 2	D 3	D 4	D 5	D 8	D 15	D 22			
Informed Consent & Pomalyst REMS[a]	X																			
Entry Criteria Review	X																			
Medical and Myeloma History[b]	X																			
Physical Examination[c]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
Performance Status (ECOG)	X	X								X								X		
Height (Baseline only) / Weight	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
Vital Signs (HR, Temperature, RR, BP)[d]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
ECG	X									X								X		
ECHO/MUGA	X[e]																			
Pregnancy testing [FCBP) and counseling [f]	X								X[f]	X					X[f]	X[f]	X[f]	X		
Hematology[g]	X	X	X	X	X	X	X	X	X	X[g]	X	X	X	X	X	X	X	X		
Serum Chemistry[h]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
PT / INR aPTT	X									X								X		
Urinalysis [i]	X	X								X								X		
Plasmacytoma Evaluation [j]	X									X[j]								X		As needed
Skeletal Survey [k]	X																			As needed
Bone Marrow Aspiration and biopsy[l]	X									X[l]								X		
Peripheral blood for correlative studies[m]	X									X[m]								X		

Evaluation	Run in Cycle Cycle is 28 days								Cycles 1 - 6 [v] Each Cycle is 28 days								EOT[w]	30-day Post-Tx F/U	F/U[x]
	D 1	D 2	D 3	D 4	D 5	D 8	D 15	D 22	D 1	D 2	D 3	D 4	D 5	D 8	D 15	D 22			
Myeloma-specific Laboratory Tests[n]	X								X								X		As needed
PK (SL-401)[o]	X				X				X C2				X C2						
Immunogenicity (SL-401)[p]	X				X				X								X		
SL-401 Pre-medication[q]	X	X	X	X	X				X	X	X	X	X						
SL-401 Administration[r]	X	X	X	X	X				X	X	X	X	X						
Pomalidomide[s]									Days 1 - 21										
Dexamethasone									X					X	X	X			
Vision assessment								X								X	X		
Adverse Event monitoring[t]		← X →																	X
Prior/Concomitant Medication[u]		← X →																	X

a. **Informed consent** All patients must sign an IRB approved informed consent prior to screening and agree to enroll in the Pomalyst REMS program prior to starting POM.

b. **Medical History:** Includes relevant history of previous/associated pathologies other than the tumor. **Myeloma History:** Includes date of initial diagnosis, stage, and extent of the disease both at diagnosis and at study entry, previous anti-tumor therapy (including surgical, radiation and systemic therapy; for systemic therapy, includes approximate dates of administration, best response and approximate dates of disease progression).

c. **Physical Examination:** Consists of examination of major body systems including neurologic, digestive, respiratory, any evaluable sites of extramedullary disease. Physical examination is required at screening/baseline and Day 1 of each treatment cycle. Symptom directed physical examination may also be performed on other treatment days or mid-cycle evaluations if there are symptoms or vital sign abnormalities warranting examination.

d. **Vitals signs:** HR, temperature, RR, BP, and pulse oximetry to be taken pre- SL-401 infusion, end of SL-401 infusion, 30, 60 and 240 minutes post-infusion and as clinicallyindicated for all doses of the Run-in Cycle. Cycle 1 +, vital signs are to be taken pre-infusion, at end of infusion, and then every 30 minutes through 4 hours post-infusion, and as clinically indicated. For temperature ≥38°C, draw blood cultures ×2 and collect urine for urinalysis and culture.

e. ECHO/MUGA: may be performed within 28 days before baseline.

f. **Pregnancy tests** for FCBP at screening, test must be repeated within 10 – 14 days prior to initiation of POM therapy (before Cycle 1) and again within 24 hours prior to initiation of POM therapy (before Cycle 1). While on POM, repeat pregnancy test every week for the first 4 weeks and then every 28 days while on therapy and during interruptions in therapy and 28 days following discontinuation of POM. Women with irregular menstruation must have pregnancy testing every 14 days while on therapy and during interruptions and 14 and 28 days after discontinuation of POM. All patients enrolled into this study, must be registered in and must comply with all requirements of the POMALYST REMS™ program. A FCBP is a female of childbearing potential is a sexually mature woman who: 1) has not undergone a

hysterectomy or bilateral oophorectomy; or 2) has not been naturally postmenopausal for at least 24 consecutive months.

g. **Hematology:** CBC to be performed and reviewed by clinician prior to SL-401 dosing on Days 1 – 5 and Days 8, 15 and 22 or as clinically indicated. The Run in and Cycle1, Day 1, results must remain within the entry criteria values to initiate therapy.

h. **Serum Chemistry:** to be performed and reviewed by clinician prior to SL-401 dosing on Days 1 – 5 and Days 8, 15, and 22 or as clinically indicated. The Run in and Cycle1 Day 1 results must remain within the entry criteria values to initiate therapy. Chemistry includes: glucose (fasting at baseline), albumin, total protein, AST, ALT, bilirubin(total and direct), alkaline phosphatase, LDH, CPK, sodium, potassium, chloride, bicarbonate/carbon dioxide, calcium, magnesium, phosphate, uric acid, BUN, serum creatinine and estimated creatinine clearance (Cockroft-Gault formula Appendix 15.7). Albumin, transaminases (AST/ALT) and creatinine must be evaluated prior to each SL-401 dose.

i. **Urinalysis:** Appearance, color, pH, specific gravity, ketones, leukocytes, protein, glucose, bilirubin, urobilinogen, and occult blood. To be performed at baseline, Day 1 ofeach cycle, and EOT.

j. **Plasmacytoma Assessment Disease:** For patient with known or suspected plasmacytomas, assess by physical exam and/or radiologic evaluation at baseline and as clinicallyindicated. Disease that can be assessed by physical exam should be evaluated on Day 1 of each cycle. Disease that can be assessed by radiologic evaluation should be assessed according the IMWG criteria for evaluation of response. This may include computerized tomography (CT) scan, ultrasound, PET/CT or MRI. The same method ofassessment should be used at each evaluation for any individual patient. Assess the need to evaluate for suspected new, worsening, or improved plasmacytomas to confirm response or progression every cycle. Evaluations may be performed on Day 1 of a cycle or during the 7 days prior to Day 1 of the Cycle as needed for scheduling.

k. **Skeletal Survey:** Plain film X-rays to including skull, vertebrae, all long bones, pelvis and chest are required. PET/CT MRI may be done to supplement X-rays of any disease site at Investigators discretion. Also required at any time when clinically indicated, for suspected progression per IMWG response criteria.

l. **Bone Marrow Aspiration:** Bone marrow aspiration + biopsy for cytogenetic analysis both by FISH and standard karyotyping, and morphologic evaluation including assessment of plasma cell percentage is required at screening/baseline (within 21 days prior to study drug administration. Bone marrow aspirate should be repeated if CR or stringent complete response (sCR) is suspected to confirm achievement of response according to IMWG criteria, and at End of therapy. BM biopsy material should be fixed, and 10 unstained slides from sequential tissue sections should be shipped to the laboratory listed for further translational analysis. Additional BM aspirate material (10-15cc iffeasible) and biopsy for correlative studies are to be collected at baseline and any time a specimen is obtained to confirm response.

m. **Peripheral blood for correlative studies** should be obtained at baseline, for **phase 1** Day 1 of Cycles 1, 3, and 5 and for **phase 2** on Day 1 of Cycles 2, 4, and 6 and at EOTfor all patients. Four 10 mL tubes in total (2 green top, 1 lavender top; 1 red top/serum separator tube). Whole blood will be evaluated for circulating MM/plasma cells (and other mononuclear cells of interest); serum and plasma will be for evaluated for potentially relevant circulating cytokines, and surrogate markers of osteolytic activity.

n. **Myeloma-specific laboratory tests:** β2 Microglobulin (at baseline only), serum and 24-hour urine immunoelectrophoresis, serum immunoglobulin assay, serum/urine immunofixation and serum FLC with kappa/lambda ratio to be performed at baseline, every cycle prior to study drug administration thereafter and at end of treatment (if last tests were >4 weeks) and for patients who discontinue therapy for reasons other than disease progression. Myeloma laboratory tests will be repeated every month until disease progression or initiation of subsequent therapy. Response assessment will be done at the beginning of every cycle. Following pre-treatment evaluations on Day 1 of the first cycle evaluations may be performed on Day 1 of a subsequent cycle or during the 7 days prior to Day 1 of the Cycle as needed for scheduling. (Note that an evaluation performed during the final week of Cycle 1 should nonetheless be recorded as the evaluation for the beginning of Cycle 2, with similar assignments for subsequentcycles).

o. **Pharmacokinetic Assessment: phase 1 only**. PK samples (plasma) are to be obtained at the following time points: pre-infusion, immediately after infusion then 15, 30, 45, 60, 90, 120, 180, and 240 minutes post-infusion in Phase 1 on Days 1 and 5 of the Run-in Cycle and Cycle 2. See Table 8. Pomalidomide will be administered approximately 4-6 hours post SL-401 end of infusion for the purpose of obtaining PK samples on the day of infusion 1 and 5 of Cycle 2.

p. **Immunogenicity:** Serum for immunogenicity evaluation will be collected prior to the infusion during the run-in Cycle 1 on Days 1 and 5 and on Day 1 pre-infusion at thebeginning of all subsequent cycles, and at End-of-therapy. If infusions are held (postponed) for any reason, an immunogenicity sample must be collected within 3 ± 3 daysafter completion of the last SL-401 infusion for the cycle.

q. **Pre-medication:** Approximately 60 minutes prior to each dose of SL-401, patients shall receive pre-medication with acetaminophen, diphenhydramine, methylprednisolone,and ranitidine according to Section 7.3.3.1.

r. **SL-401 administration:** SL-401 will be given by iv infusion over 15 minutes on Days 1 – 5 of each 28 day cycle (Run-in Cycle and Cycles 1 – 6) with delays permitted as delineated in relevant protocol sections such that administration on days 6-10 of any cycle is also permitted (5 doses may be administered over 10 days, if necessary). Dose modifications are permitted following the Run-in Cycle and Cycle 1; 5 doses of SL-401 may be administered over the initial 10-day period of each cycle. See Protocol Section 7.3 for drug administration instructions and for Protocol Section 7.7 dose modification guidelines.

s. **Pomalidomide:** Pomalidomide will be administered approximately 4-6 hours post SL-401 end of infusion for the purpose of obtaining SL-401 PK samples on the days ofinfusion 1 and 5 of Cycle 2. Pomalidomide should be taken on an empty stomach 2 hours before or after a meal. Capsules should not be opened, broken or chewed.

t. **AE monitoring:** Patients to be observed for AEs at least 4 hours post each infusion. All AEs, including AEs of new onset as well as worsening of baseline signs and symptoms are to be reported from the signing of the informed consent to 30 days following the last administration of any study drug. After the 30-day follow-up all ongoing and new related AEs, and all the SAEs regardless of causal relationship are to be followed up to resolution or stabilization.

u. **Prior/concomitant medication** should be recorded including medications taken during the 28 days prior to initial study therapy, at any/all times during studytherapy/participation, and through approximately 30 days following the last dose of investigational therapy.

v. Patients with evidence of MM stabilization or response and without unacceptable toxicity will receive the Run-in Cycle and 6 cycles of SL-401/POM/DEX. If, following completion of these cycles, there is ongoing evidence of MM stabilization or response, patients may receive additional therapy on-study if the Investigator believes the potential risk/benefit of additional therapy is justifiable. During Cycle 7 and beyond, SL-401 will be administered on Day 1-5 of **every other cycle (every 56 days**), POMadministered on Days 1-21, and DEX administered on Days 1, 8, 15 and 22 of each cycle.

w. **EOT:** Evaluations should be completed at the time a decision is made to discontinue study therapy, and approximately 30 ±7 days following the last dose of study therapyregardless for the reason of discontinuation, unless patient withdraws consent and refuses further evaluation.

x. **Follow-up**: Patients who discontinue therapy for reasons other than MM progression will be followed for response every month until progression of disease or initiation of subsequent therapy. Patients who have discontinued study therapy and have had MM progression should be contacted approximately every 3 months (telephone contact is permitted) to assess overall survival status for 1 year; patients who discontinue therapy for reasons other than disease progression and are no longer willing to follow-up for evaluation of disease progression should also be contacted for survival status whenever feasible. Patients who undergo stem cell transplant will be followed for the occurrence of VOD as part of long-term follow-up.