1.3. SoA

Table 1 summarizes the relevant SoAs and dosing schedules for each treatment regimen. Except as noted, all assessments will occur predose. Evaluations for eligibility determination performed outside the screening window may need to be repeated unless specified otherwise.

Table 1: Guide to SoAs and Dosing

	Arm A (Tal-P) and Arm B (Tal-Tec)	**Arm C (EPd)**	**Arm C (PVd)**
Screening	Table 2		
SoA	Table 3	Table 7	Table 10
Dosing schedule (and pretreatment medications, as applicable)	Table 4 Table 5	Table 8	Table 11
PK, immunogenicity, and biomarker sampling (as applicable)	Table 6	Table 9	Table 12
Bone marrow testing	Table 34		

1.3.1. SoA for Screening

Table 2: SoA for Screening (≤28d Before Randomization, Unless Noted Otherwise) – All Participants

Assessments	Notes
STUDY PROCEDURES	
Informed consent	
Eligibility criteria	
Demography, medical history and prior cancer therapies	
Disease characteristics	See Section 8.1.1.1.1
ECOG performance status	See Section 8.3.9
Physical examination including height and weight	Complete examination; see Section 8.3.1
Neurologic examination including ICE Tool	See Section 8.3.8 and Appendix 14
Vital signs including oxygen saturation	See Section 8.3.2
12-lead ECG	See Section 8.3.3
LABORATORY ASSESSMENTS: See Appendix 1	
Hematology and chemistry and coagulation	Local laboratory; see Section 8.3.4
HIV assessment	For participants with known HIV, local HIV testing by PCR and CD4 count are required if not performed as part of standard of care within 3 months prior to C1D1 (see inclusion criteria #17 [Section 5.1]); see Section 8.3.6
HBV and HCV screening	HBV: see Section 8.3.5.1 HCV: local testing is required if not performed as part of standard of care within 3 months before C1D1; see Section 8.3.5.2
Serum/urine pregnancy test	Local laboratory – for POCBP only. • Serum pregnancy test within 10-14d prior to C1D1 and either serum or urine pregnancy test within 24 h prior to C1D1
DISEASE EVALUATIONS: See Section 8.2	
Serum β2-microglobulin/albumin	• Central laboratory. In exceptional circumstances, local laboratory assessments may be used to establish measurable disease at screening (see Section 5.1); see Section 8.2.1 • If the 24-h urine collection (UPEP) begins the day before informed consent is obtained as part of SoC, the sample can be used for this study if it is sent to the central laboratory for analysis after the informed consent was obtained
Serum quantitative Ig	
SPEP, 24-h UPEP	
Serum FLC and SIFE/UIFE	
Bone marrow aspirate	See Section 8.2.2; disease characterization (morphology and either IHC, immunofluorescence, or flow cytometry for PC clonality) performed locally. If a biopsy was done within 42d before randomization, no need to repeat for morphology; however, fresh aspirate samples need to be obtained and sent to central laboratory for MRD, cytogenetics, immunophenotype and molecular markers
Imaging for disease evaluation (including assessment of lytic bone lesions)	See Section 8.2.4 for acceptable modalities If performed within 42d before randomization, does not need to be repeated at screening
Assessment of bone lesions and soft-tissue plasmacytomas	See Section 8.2.4 and Section 8.2.5 for acceptable modalities and instructions regarding biopsies If performed within 42d before randomization, does not need to be repeated at screening
ONGOING REVIEW	
AEs	Continuous from the time of signing of ICF
SPM	
Concomitant therapy (see Section 6.9)	
RANDOMIZATION	
If eligible	Eligible participants must be randomized within 3 business days of sponsor approval for randomization and must receive the C1D1 dose ≤7 calendar days after date randomized Hematology and chemistry eligibility criteria must be met again within 72 h prior to first dose of study treatment (see Table 3, Table 7, Table 10, and Section 5.1)

Abbreviations: see ABBREVIATIONS AND DEFINITIONS OF TERMS.

1.3.2. SoA for Arm A (Tal-P) and Arm B (Tal-Tec)

Table 3: SoA for Treatment Phase, EOT Visit, and Posttreatment Follow-up Phase – Arm A (Tal-P) and Arm B (Tal-Tec)

Assessments	Notes	Treatment Phase (28-day cycle)									Follow-up Phase
Cycle		Cycle 1				Cycle 2		Cycle 3+		EOT	
Day		1	4 (+2d)	8 (+2d)	15 (+2d)	1 (±3d)	15 (±3d)	1 (±3d)	15 (±3d)	≤30d after last dose (+7d) or before SST	Pre-PD Q28d (±7d) Post-PD Q16W (±14d)
STUDY PROCEDURES											
ECOG performance status	See Section 8.3.9 and Appendix 15	On Day 1 of C1-C4; Day 1 of C7, C10, C13; and Day 1 every 6 cycles thereafter								X	
Physical examination	Symptom- and disease-directed	Once per cycle									
Weight		X				X		X			
Venous thromboembolism prophylaxis (Arm A [Tal-P] only)	See Section 6.9.2.4 and Appendix 20	As clinically indicated									
Neurologic examination	See Section 8.3.8, see ICE Tool in Appendix 14	X	As clinically indicated								
Vital signs including oxygen saturation[a]	See Section 8.3.2	X	X	X	X	X	X	X	C3+[c]	X	
12-lead ECG	See Section 8.3.3	As clinically indicated									
TTE or MUGA Scan	For patients receiving pomalidomide	As clinically indicated. Monitor subjects for clinical signs or symptoms of cardiac failure or cardiac ischemia. Evaluate promptly if cardiac toxicity is suspected.									
LABORATORY ASSESSMENTS: See Appendix 1											
Hematology	Ensure all values meet criteria in Section 5.1 prior to C1D1 (perform within 72 h before dosing). From C1D8 may be performed within 48 h before dosing.	X	X	X	X	X	X	X	C3+[c]	X	
Chemistry		X		X	X	X		X		X	
TLS-related laboratory assessments	May be performed within 72 h before dosing, including for C1D1	X				X					
Hemoglobin A1c	Local laboratory	X						C5D1, C9D1 and D1 of every 4th cycle (±1 week) thereafter			
HBV, HCV	See Section 8.3.5.3	Perform at C1D1 (±7d). PCR testing Q12W (±4 weeks) up to 6 months after last dose of study treatment for participants with history of HBV infection/HCV antibody positivity									
HIV PCR and CD4 count	For participants with history of HIV antibody positivity, see Section 8.3.6	C1D1, C5D1, C9D1 and D1 of every 4th cycle (±1 week) thereafter								3 and 6 months (±1 month) after last dose	
Coagulation		As clinically indicated (eg, CRS)									
Serum or urine pregnancy test (POCBP only)	Additional testing may be required per the global PPP or local PPP/REMS program (Arm A [Tal-P] only; see Appendix 4)	Both arms: • Serum pregnancy test within 10-14d prior to C1D1 and either serum or urine pregnancy test within 24 h prior to C1D1								X	Xb (until 6 months after last dose)

Assessments	**Notes**	**Treatment Phase (28-day cycle)**									**Follow-up Phase**
Cycle		**Cycle 1**				**Cycle 2**		**Cycle 3+**		**EOT**	
Day		**1**	**4** (+2d)	**8** (+2d)	**15** (+2d)	**1** (±3d)	**15** (±3d)	**1** (±3d)	**15** (±3d)	**≤30d after last dose** (+7d) **or before SST**	**Pre-PD** Q28d (±7d) **Post-PD** Q16W (±14d)
		• Within 24 h of D1 of each cycle Arm A (Tal-P) only: • Weekly for first 4 weeks from start of pomalidomide treatment, including within 24 h prior to start of pomalidomide administration • Thereafter, Q28d (Q14d for participants with irregular menses)									
DISEASE EVALUATIONS: See Section 8.2											
Serum quantitative Ig	Central laboratory; local laboratory assessments may be used under specified circumstances (see Section 8.2.6). Sample may be collected on or within 7 d prior to CnD1. **NOTE**: SPEP and UPEP assessments will continue until 30 d after the start of the first SST for participants with no PD or unconfirmed PD (ie, single instance of PD by laboratory assessment). For participants with measurable disease by light chain, serum FLC will also continue during this period. *In the event of treatment delays, disease evaluations should occur every 28 days (±7 days).	X				X*		X*			X (until PD or start of SST)
SPEP		X				X*		X*			X (until PD or start of SST)
24-h UPEP		X				X*		X*			X (until PD or start of SST)
Serum FLC and SIFE/UIFE		• For participants with measurable disease only by light chain: with every disease evaluation* and, if applicable, each pre-PD disease evaluation visit until PD or 30 d after the start of SST. • For participants with measurable disease by serum and/or urine M spike: at time of suspected CR or sCR.									
Bone marrow aspirate	For local assessments; see Section 8.2.6 (a portion of aspirate should be sent to the central laboratory for biomarker and MRD analysis)	• Whenever CR or sCR are suspected • For participants with confirmed CR or sCR, collect additional samples 12 months post C1D1 (±3 months) and 12 months (±3 months) after time of confirmed CR or sCR, then every 12 months (±3 months) until PD. • Time of PD (even if occurs after treatment is discontinued; should occur prior to SST)									
Imaging	Disease evaluation including assessment of lytic bone lesions; see Section 8.2.4 for acceptable modalities	• As clinically indicated to document response or disease progression before start of SST									
Assessment of soft-tissue plasmacytomas	See Section 8.2.5 for acceptable modalities	• For participants with a history of soft-tissue plasmacytoma until development of confirmed CR, PD or start of SST. ○ For assessment by physical examination (if applicable), Q28d (±7d) from C1D1. ○ For assessment by radiology, Q12W (±7d) from C1D1. • As clinically indicated for other participants.									

Assessments	**Notes**	**Treatment Phase (28-day cycle)**									**Follow-up Phase**
Cycle		**Cycle 1**				**Cycle 2**		**Cycle 3+**		**EOT**	
Day		**1**	**4** (+2d)	**8** (+2d)	**15** (+2d)	**1** (±3d)	**15** (±3d)	**1** (±3d)	**15** (±3d)	**≤30d after last dose** (+7d) **or before SST**	**Pre-PD** Q28d (±7d) **Post-PD** Q16W (±14d)
PRO AND MRU: PRO ASSESSMENTS SHOULD BE COMPLETED BEFORE ANY CLINICAL TESTS OR PROCEDURES (see Section 8.2.7)											
MySIm-Q, EORTC-QLQ-C30, EQ-5D-5L, PGI-S, Epstein Taste Survey	Window for PRO data collection is 2d prior to dosing during Treatment Phase. Should continue to be collected even if SST has begun	To be collected on Day 1 of C1 to C12, then on Day 1 of every 3rd cycle								X	MySIm-Q, EORTC-QLQ-C30, and EQ-5D-5L only Q16W ±14d
MRU	See Section 8.9	Collected continuously after first day of study treatment until PD or 30d after last dose or the SST, whichever is earlier.									
Symptomatic progression evaluation		From 30d prior, to until 30d after confirmed PD (or the start of SST, whichever is earlier), progression-associated symptoms and concomitant medications will be documented in eCRF									
Qualitative interview	Optional; see Section 8.2.7.6	Single interview to be conducted approximately 12 months (±3 months) after the start of study treatment									
ONGOING REVIEW											
AEs	See Section 8.4	Continuous from signing of ICF until 30d after last dose or until the start of SST, if earlier; thereafter, continue to report any AEs/SAEs related to study treatment until EOS									
SPM		Continuous until EOS									
Concomitant therapy	See Section 6.9	Continuous from signing of ICF until 30d after last dose or until the start of SST, if earlier; thereafter, continue to report concomitant therapy given for any AEs/SAEs considered related to study treatment until EOS									
SST	See Section 6.10										X
Survival	See Section 8.1.1.4										Q16W

Abbreviations: see ABBREVIATIONS AND DEFINITIONS OF TERMS.

a. Vital signs to only be collected in the eCRF during Cycle 1 (including the step-up doses), and thereafter at any repeat step-up dose(s) and any additional vital signs assessments supporting the start and end dates of an AE.
b. Serum or urine pregnancy tests to be performed, as determined necessary by the investigator, or as required by local regulation, to establish the absence of pregnancy.
c. For participants on Q4W schedule assessments are not required at Cycle n Day 15 but may be performed as clinically indicated.

Table 4: Dosing Schedule and Pretreatment Medications – Arm A (Tal-P)

Cycle / Day	Notes	Treatment Phase (28-day cycle)						
		Cycle 1				Cycle 2-6		Cycle 7+
		1	4	8	15	1 ±3d	15 ±3d	1 ±3d
REQUIRED PRETREATMENT MEDICATIONS: From Cycle 2 onwards, all PO pretreatment medications may be administered at home, provided they are taken within the time frames specified below. See Section 6.1.2.1 for event-driven required pretreatment medications.								
Dexamethasone 20 mg or equivalent (see Appendix 13)	• PO/IV: administer 1–3 h (±15 mins) prior to talquetamab SC/teclistamab SC • Prior to all step-up doses and first treatment dose in C1 • Diphenhydramine and acetaminophen: not required at Day 15 if the participant is in Q4W dosing schedule.	X	X	X	X	For participants who develop Grade ≥2 CRS/sARR related to talquetamab and/or teclistamab[a] (see Section 6.1.2.1).		
Diphenhydramine 25 to 50 mg, or equivalent		X	X	X	X			
Acetaminophen 650 to 1000 mg		X	X	X	X			
OPTIONAL PRETREATMENT MEDICATION: Additional pretreatment medications such as H_2 antagonists or antiemetics are optional and may be used at investigator discretion.								
STUDY DRUGS: See Section 6.1. Criteria for dose delays/skips and dose reductions are provided in Section 6.6. **Step-up and Treatment doses MUST be delayed until CRS and/or ICANS associated with prior dose have fully resolved** (see also criteria in Section 6.6.2.2).								
Talquetamab SC SU1 (0.01 mg/kg)[b,c]		X						
Talquetamab SC SU2 (0.06 mg/kg)[b,c]	• Administer ≥2d after SU1		X					
Talquetamab SC Treatment Dose (0.4 mg/kg)[b,c]	• Administer ≥2d after SU2			X				
Talquetamab SC Study Treatment Dose (0.8 mg/kg)[b,c]	• Administer ≥2d after first study treatment dose, between Days 7-15 • C2-C4 talquetamab SC must be administered 14d (±3d) after prior treatment dose *From C5, if confirmed VGPR or better, schedule can change to Q4W dosing (D1 only) per investigator discretion Change to Q4W dosing should occur on C5 or C6 Day 1 (±3d) #At C7 Day 1 (±3d), participants with response of confirmed PR or better must change to Q4W dosing. In exceptional cases only, participants can continue Q2W dosing after sponsor consultation and approval. For all participants who are not in confirmed PR or better at C7D1, continue with Q2W dosing until confirmed PR or better is achieved.				X	X	X*	X[#d]
Dexamethasone 40 mg or equivalent	• Administered weekly (Days 1, 8, 15, and 22) during C2-C4 only • For participants <75 years of age with BMI <18.5 or ≥75 years of age, the weekly dose of dexamethasone is 20 mg					X	X	
Pomalidomide[e]	• Administer ≥7d between the course of pomalidomide treatment for each cycle					Days 1-21[e]		Days 1-21[e]

Abbreviations: see ABBREVIATIONS AND DEFINITIONS OF TERMS.

a. Dispensing and compliance, as required for participants with at-home administration. Sites to confirm that any PO pretreatment medications dispensed for at-home administration were taken as directed before administration of study treatment, where applicable.
b. Participants receiving outpatient talquetamab/teclistamab are to check their body temperature (Section 6.1.3), and will receive daily phone call follow-up from after SU1 until 48 h after first treatment dose.
c. Participants receiving talquetamab/teclistamab may be hospitalized or receive outpatient clinic dosing with sponsor approval, if criteria are met (see Section 6.1.3.1.1 and Appendix 16). For outpatient clinic dosing, participants should remain in close proximity (within 30 min) to the site, in the company of a competent adult, starting after SU1 until 48 h after administration of the study treatment dose.
d. Participants will receive therapy with talquetamab/teclistamab (as appropriate) for up to 26 cycles if they have no sign of PD or toxicity. Participants can continue therapy with pomalidomide (Arm A [Tal-P] only) beyond Cycle 26 if no discontinuation criteria are met.
e. Pomalidomide (Arm A [Tal-P] only) will be initiated at 2 mg daily at C2D1, and may be increased to 4 mg daily per investigator discretion from C3D1. The selected dose regimen for pomalidomide is based on standard doses used in clinical practice for the treatment of multiple myeloma.

Table 5: Dosing Schedule and Pretreatment Medications – Arm B (Tal-Tec)

Cycle / Day	Notes	Treatment Phase (28-day cycle)						
		Cycle 1				Cycle 2-6		Cycle 7+
		1	4	8	15	1 ±3d	15 ±3d	1 ±3d
REQUIRED PRETREATMENT MEDICATIONS: From Cycle 2 onwards, all PO pretreatment medications may be administered at home, provided they are taken within the time frames specified below. See Section 6.1.2.1 for event-driven required pretreatment medications.								
Dexamethasone 20 mg or equivalent (see Appendix 13)	• PO/IV: administer 1–3 h (±15 mins) prior to talquetamab SC/teclistamab SC • Prior to all step-up doses and first treatment dose in C1	X	X	X	X	For participants who develop Grade ≥2 CRS/sARR related to talquetamab and/or teclistamab[a] (see Section 6.1.2.1).		
Diphenhydramine 25 to 50 mg, or equivalent		X	X	X	X			
Acetaminophen 650 to 1000 mg		X	X	X	X			
OPTIONAL PRETREATMENT MEDICATION: Additional pretreatment medications such as H_2 antagonists or antiemetics are optional and may be used at investigator discretion.								
STUDY DRUGS: See Section 6.1. Criteria for dose delays/skips and dose reductions are provided in Section 6.6. **Step-up and Treatment doses MUST be delayed until CRS and/or ICANS associated with prior dose have fully resolved** (see also criteria in Section 6.6.2.2).								
Talquetamab SC SU1 (0.01 mg/kg)[b,c]		X						
Talquetamab SC SU2 (0.06 mg/kg)[b,c]	• Administer ≥2d after SU1		X					
Talquetamab SC Treatment Dose (0.4 mg/kg)[b,c]	• Administer ≥2d after SU2			X				
Talquetamab SC Study Treatment Dose (0.8 mg/kg)[b,c]	• Administer ≥2d after first study treatment dose, between Days 7-15 • C2-C4 talquetamab SC must be administered 14d (±3d) after prior treatment dose *From C5, if confirmed VGPR or better, schedule can change to Q4W dosing (D1 only) per investigator discretion. Change to Q4W dosing should occur on Cycle 5 or Cycle 6 Day 1 (±3d) #At Cycle 7 Day 1 (±3d), participants with response of confirmed PR or better must change to Q4W dosing. In exceptional cases only, participants can continue Q2W dosing after sponsor consultation and approval. For all participants who are not in confirmed PR or better at C7D1, continue with Q2W dosing until confirmed PR or better is achieved.				X	X	X*	X[#d]
Teclistamab SC SU1[b,c] (0.06 mg/kg)		X						
Teclistamab SC SU2[b,c] (0.3 mg/kg)	• Administer ≥2d after SU1		X					
Teclistamab SC Treatment Dose (1.5 mg/kg)	• Administer ≥2d after SU2 • Administer ≥2d after first treatment dose, between Days 7-15			X	X			
Teclistamab SC Study Treatment Dose (3 mg/kg)	• From the study treatment at C2, Q4W dosing (D1 only) for all participants					X		X[d]

Abbreviations: see ABBREVIATIONS AND DEFINITIONS OF TERMS.

a. Dispensing and compliance, as required for participants with at-home administration. Sites to confirm that any PO pretreatment medications dispensed for at-home administration were taken as directed before administration of study treatment, where applicable.

b. Participants receiving outpatient talquetamab/teclistamab are to check their body temperature (Section 6.1.3), and will receive daily phone call follow-up from after SU1 until 48 h after first treatment dose.

c. Participants receiving talquetamab/teclistamab may be hospitalized or receive outpatient clinic dosing with sponsor approval, if criteria are met (see Section 6.1.3.1.1 and Appendix 16). For outpatient clinic dosing, participants should remain in close proximity (within 30 min) to the site, in the company of a competent adult, starting after SU1 until 48 h after administration of the study treatment dose.

Table 6: Sampling for PK, Immunogenicity, and Biomarkers for Treatment Phase, EOT Visit, and Posttreatment Follow-up Phase – Arm A (Tal-P) and Arm B (Tal-Tec)

Assessments		Time[a]	Treatment Phase (28-day cycle)							Follow-up Phase[c]
Cycle			Cycle 1		Cycle 2		Cycle 3-Cycle 7	Cycle 12	EOT[c]	
Day			1	15[f]	1	15	1	1	≤30d after last dose (+7d) or before SST	8 weeks after last dose
PK AND IMMUNOGENICITY SAMPLING[h]										
Talquetamab (Arm A [Tal-P] and Arm B [Tal-Tec]) Teclistamab (Arm B [Tal-Tec] only)		Predose on day of dosing	X		X		Collect sample at dose regimen change[d]	C12, then every 6 cycles	X	X
		Suspected sARR, CRS, or neurotoxicity/ICANS Grade ≥2	Collect additional PK/immunogenicity sample as soon as sARR, CRS, or neurotoxicity/ICANS Grade ≥2 is detected, if feasible.							
BIOMARKER SAMPLING[b]: See Section 8.7. For bone marrow aspirate, see Table 34 for Disease Evaluation										
Immunophenotyping[e] (whole blood)		Predose on day of dosing	X			X	C5, C7	C12 only	X	
		Response-based	Time of PD							
Circulating proteins (serum)	M-protein Mass Spectrometry	Predose on day of dosing	X				C3, C5			
		Response-based	• Time of suspected CR or sCR • For participants with confirmed CR or sCR, additional samples will be collected 6 (±3 months) and 12 months (±3 months) after time of confirmed CR or sCR, and then every 12 months (±3 months) until PD • Time of PD							
	Cytokines/ ferritin/ CRP	Predose on day of dosing	X	X[f]		X				
Molecular markers/ CyTOF[g] (whole blood)		Predose on day of dosing	X			X	C5		X	
Biopsy of soft-tissue plasmacytomas[e]		As clinically indicated	See Section 8.2.5							

Abbreviations: see ABBREVIATIONS AND DEFINITIONS OF TERMS.

a. If a dose is delayed or missed, then sample collection should be performed on the actual administration day, not on the originally scheduled administration day.
b. Predose sample window for biomarker samples: -4 to 0h.
c. Sample window +7d only for PK and immunogenicity sampling.
d. For intra-participant dose regimen change between C3 and C7, a PK/immunogenicity sample is to be collected prior to the administration of the changed dose regimen. This should be done each time the participant's talquetamab or teclistamab dose regimen is modified.
e. Immunophenotyping testing will be performed in approximately 50% of the participants.
f. Samples should be collected at the last step-up dose.
g. Molecular marker/CyTOF assessments and biomarker assessments for soft-tissue plasmacytomas will not be performed for participants enrolling in China.
h. Predose sample window for PK samples: -24 to 0h.

1.3.3. SoA for Arm C (EPd)

Table 7: SoA for Treatment Phase, EOT Visit, and Posttreatment Follow-up Phase – Arm C (EPd)

Assessments	Notes	Treatment Phase (28-day cycle)						Follow-up Phase
Cycle		Cycle 1-2				Cycle 3+	EOT	
Day		1 (±3d)	8 (±2d)	15 (±2d)	22 (±2d)	1 (±3d)	≤30d after last dose (+7d) or before SST	Pre-PD Q28d (±7d) Post-PD Q16W (±14d)
STUDY PROCEDURES								
ECOG performance status	See Section 8.3.9 and Appendix 15	On Day 1 of C1-C4 and Day 1 of C7, C10, C13, and D1 of every 6 cycles thereafter					X	
Physical examination	Symptom- and disease-directed	Once per cycle						
Weight		X				X		
Venous thromboembolism prophylaxis	See Section 6.9.2.4 and Appendix 20	As clinically indicated						
Vital signs including oxygen saturation	See Section 8.3.2	X	X	X	X	X	X	
12-lead ECG	See Section 8.3.3	As clinically indicated						
TTE or MUGA Scan		As clinically indicated. Monitor subjects for clinical signs or symptoms of cardiac failure or cardiac ischemia. Evaluate promptly if cardiac toxicity is suspected.						
LABORATORY ASSESSMENTS: See Appendix 1								
Hematology	Ensure all values meet criteria in Section 5.1 prior to C1D1 (perform within 72 h before dosing). From C1D8 may be performed within 48 h before dosing.	X	X	X	X	X	X	
Chemistry		X				X	X	
Uric acid	May be performed within 72 h before dosing, including for C1D1	X						
Hemoglobin A1c	Local laboratory	C1				C5D1, C9D1 and D1 of every 4th cycle (±1 week) thereafter		
HBV, HCV	See Section 8.3.5.3	Perform at C1D1 (±7d). PCR testing **Q12W** (±4 weeks) up to 6 months after last dose of study treatment for participants with history of HBV infection/HCV antibody positivity						
HIV PCR and CD4 count	For participants with history of HIV antibody positivity, see Section 8.3.6	C1D1, C5D1, C9D1 and D1 of every 4th cycle (±1 week) thereafter					3 and 6 months (±1 month) after last dose	
Coagulation		As clinically indicated						
Serum or urine pregnancy test (POCBP only)	Additional testing may be required per the global PPP or local PPP/REMS program (see Appendix 4)	• Serum pregnancy test within 10-14d prior to C1D1 and either serum or urine pregnancy test within 24 h prior to C1D1 • Within 24 h of D1 of each cycle • Weekly for the first 4 weeks of pomalidomide treatment, including within 24 h prior to start of pomalidomide administration • Thereafter, Q28d (or Q14d for participants with irregular menses)					X	X[a] (until 6 months after last dose)
DISEASE EVALUATIONS: See Section 8.2								
Serum quantitative Ig	Central laboratory; local laboratory assessments may be used under specified circumstances (see	X				X*	X	X (until PD or start of SST)
SPEP		X				X*	X	X (until PD or start of SST)

Assessments / Cycle / Day	Notes	Treatment Phase (28-day cycle)					Follow-up Phase
		Cycle 1-2				Cycle 3+	EOT
		1 (±3d)	8 (±2d)	15 (±2d)	22 (±2d)	1 (±3d)	≤30d after last dose (+7d) or before SST	Pre-PD Q28d (±7d) Post-PD Q16W (±14d)
24-h UPEP	Section 8.2.6); sample may be collected on or within 7d prior to CnD1 **NOTE**: SPEP and UPEP assessments will continue until 30d after the start of the first SST for participants with no PD or unconfirmed PD (ie, single instance of PD by laboratory assessment). For participants with measurable disease by light chain, serum FLC will also continue during this period. *In the event of treatment delays, disease evaluations should occur every 28 days (±7 days).	X				X*	X	X (until PD or start of SST)
Serum FLC and SIFE/UIFE		• For participants with measurable disease only by light chain: with disease evaluation* and, if applicable, each pre-PD disease evaluation visit until PD or 30 d after the start of SST. • For participants with measurable disease by serum and/or urine M spike: at time of suspected CR or sCR.						
Bone marrow aspirate	For local assessments; see Section 8.2.6 (a portion of aspirate should be sent to the central laboratory for biomarker and MRD analysis)	• Whenever CR or sCR are suspected • For participants with confirmed CR or sCR, collect additional samples 12 months post C1D1 (±3 months) and 12 months (±3 months) after time of confirmed CR or sCR, then every 12 months (±3 months) until PD. • Time of PD (even if occurs after treatment is discontinued; should occur prior to SST)						
Imaging	Disease evaluation including assessment of lytic bone lesions; see Section 8.2.4 for acceptable modalities	• As clinically indicated to document response or disease progression before start of SST						
Assessment of soft-tissue plasmacytomas	See Section 8.2.5 for acceptable modalities	• For participants with a history of soft-tissue plasmacytoma until development of confirmed CR, PD or start of SST ○ For assessment by physical examination (if applicable), Q28d (±7d) from C1D1 ○ For assessment by radiology, Q12W (±7d) from C1D1 • As clinically indicated for other participants						
PRO AND MRU: PRO ASSESSMENTS SHOULD BE COMPLETED BEFORE ANY CLINICAL TESTS OR PROCEDURES (see Section 8.2.7)								
MySIm-Q, EORTC-QLQ-C30, EQ-5D-5L, PGI-S, Epstein Taste Survey	Window for PRO data collection is 2d prior to dosing during Treatment Phase. Should continue to be collected even if SST has begun	To be collected on Day 1 of C1 to C12, then on Day 1 of every 3rd cycle					X	MySIm-Q, EORTC-QLQ-C30, and EQ-5D-5L only Q16W ±14d
MRU	See Section 8.9	Collected continuously from the start of study treatment until 30d after last dose or the start of SST, whichever is earlier.						
Symptomatic progression evaluation		From 30d prior, to until 30d after confirmed PD (or the start of SST, whichever is earlier), progression-associated symptoms and concomitant medications will be documented in eCRF						
Qualitative interview	Optional; see Section 8.2.7.6.	Single interview to be conducted approximately 12 months (±3 months) after the start of study treatment						
ONGOING REVIEW								
AEs	See Section 8.4	Continuous from signing of ICF until 30d after last dose or until the start of SST, if earlier; thereafter, continue to report any AEs/SAEs related to study treatment until EOS						
SPM		Continuous until EOS						

Assessments	Notes	Treatment Phase (28-day cycle)							Follow-up Phase
Cycle		Cycle 1-2				Cycle 3+		EOT	
Day		1 (±3d)	8 (±2d)	15 (±2d)	22 (±2d)	1 (±3d)		≤30d after last dose (+7d) or before SST	Pre-PD Q28d (±7d) Post-PD Q16W (±14d)
Concomitant therapy	See Section 6.9	Continuous from signing of ICF until 30d after last dose or until the start of SST, if earlier; thereafter, continue to report concomitant therapy given for any AEs/SAEs considered related to study treatment until EOS							
SST	See Section 6.10								X
Survival	See Section 8.1.1.4								Q16W

Abbreviations: see ABBREVIATIONS AND DEFINITIONS OF TERMS.
a. Serum or urine pregnancy tests to be performed, as determined necessary by the investigator, or as required by local regulation, to establish the absence of pregnancy.

Table 8: Dosing Schedule and Pretreatment Medications – Arm C (EPd)

	Notes	Treatment Phase (28-day cycle)											
Cycle		Cycle 1				Cycle 2				Cycle 3+			
Day		1	8	15	22	1	8	15	22	1	8	15	22
REQUIRED PRETREATMENT MEDICATIONS: From Cycle 2 onwards, all PO pretreatment medications may be administered at home, provided they are taken within the time frames specified below.													
Acetaminophen 650 to 1000 mg PO	• Administer 45–90 min before elotuzumab	X	X	X	X	X	X	X	X	X			
Diphenhydramine (25 to 50 mg IV or PO) or equivalent		X	X	X	X	X	X	X	X	X			
Locally available H2 blocker[a]		X	X	X	X	X	X	X	X	X			
Dexamethasone 8 mg IV/PO		X	X	X	X	X	X	X	X	X			
STUDY TREATMENT ADMINISTRATION: Criteria for dose delays/skips and dose modifications are provided in Section 6.6.													
Elotuzumab IV	10 mg/kg for Cycles 1 and 2, and 20 mg/kg for Cycles 3+	X	X	X	X	X	X	X	X	X			
Pomalidomide PO	4 mg/day There must be ≥7d between the course of pomalidomide for each cycle	Days 1-21				Days 1-21				Days 1-21			
Dexamethasone PO	≤75 years of age (between 3-24 h before elotuzumab)	28 mg	28 mg	28 mg	28 mg	28 mg	28 mg	28 mg	28 mg	28 mg	40 mg	40 mg	40 mg
Dexamethasone PO	>75 years of age (between 3-24 h before elotuzumab)	8 mg	8 mg	8 mg	8 mg	8 mg	8 mg	8 mg	8 mg	8 mg	20 mg	20 mg	20 mg

Abbreviations: see ABBREVIATIONS AND DEFINITIONS OF TERMS.
a. H2 blockers that can be used include famotidine 20 mg IV or ranitidine 50mg IV or other locally available H2 blockers.

Table 9: Sampling for Biomarkers for Treatment Phase, EOT Visit, and Posttreatment Follow-up Phase – Arm C (EPd)

Assessments		Time	Treatment Phase (28-day cycle)			Follow-up Phase
Cycle			Cycle 1-2	Cycle 3+	EOT	
Day			1	1	≤30d after last dose (+7d) or before SST	8 weeks after last dose
BIOMARKER SAMPLING: See Section 8.7. For bone marrow aspirate, see Table 34 for Disease Evaluation						
Immunophenotyping[a] (whole blood)		Predose on the day of dosing[c]	C1			
Circulating proteins (serum/plasma)	M-Protein Mass spectrometry	Predose on the day of dosing[c]	C1	C5	X	
		Response-based	• Time of suspected CR or sCR • For participants with confirmed CR or sCR, additional samples will be collected 6 months (±3 months) and 12 months (±3 months) after time of confirmed CR or sCR, and then every 12 months (±3 months) until PD			
Molecular markers/CyTOF[b] (whole blood)		Predose on the day of dosing[c]	C1	C5	X	

Abbreviations: see ABBREVIATIONS AND DEFINITIONS OF TERMS.
a. Immunophenotyping testing will be performed in approximately 50% of the participants in Arm C and only at C1D1.
b. Molecular marker/CyTOF assessments will not be performed for participants enrolling in China.
c. Predose sample window for biomarker samples: -4 to 0h.

1.3.4. SoA for Arm C (PVd)

Table 10: SoA for Treatment Phase, EOT Visit, and Posttreatment Follow-up Phase – Arm C (PVd)

Assessments	Notes	Treatment Phase (21-day cycle)							Follow-up Phase
Cycle		Cycle 1-8				Cycle 9+		EOT	
Day		1 (±3d from Cycle 2)	4 (+2d)	8 (+2d)	11 (+2d)	1 (±3d)	8 (±2d)	≤30d after last dose (+7d) or before SST	Pre-PD Q28d (±7d) Post-PD Q16W (±14d)
STUDY PROCEDURES									
ECOG performance status	See Section 8.3.9 and Appendix 15	X				X		X	
Physical examination	Symptom- and disease-directed	Once per cycle							
Weight		X				X			
Venous thromboembolism prophylaxis	See Section 6.9.2.4 and Appendix 20	As clinically indicated							
Vital signs including oxygen saturation	See Section 8.3.2	X		C1-C3	C1-C3	X		X	
12-lead ECG	See Section 8.3.3	As clinically indicated							
Chest imaging[b]	Prior to administration of bortezomib[b]								
TTE or MUGA Scan	Ejection fraction	As clinically indicated. Monitor subjects for clinical signs or symptoms of cardiac failure or cardiac ischemia. Evaluate promptly if cardiac toxicity is suspected.							
LABORATORY ASSESSMENTS: See Appendix 1.									
Hematology	Ensure all values meet criteria in Section 5.1 prior to C1D1 (perform within 72 h before	X	C1-C3	C1-C3	C1-C3	X		X	
Chemistry		X		C1	C1	X			

Assessments	Notes	Treatment Phase (21-day cycle)							Follow-up Phase
Cycle		Cycle 1-8				Cycle 9+		EOT	
Day		1 (±3d from Cycle 2)	4 (+2d)	8 (+2d)	11 (+2d)	1 (±3d)	8 (±2d)	≤30d after last dose (+7d) or before SST	Pre-PD Q28d (±7d) Post-PD Q16W (±14d)
	dosing). From C1D8 may be performed within 48 h before dosing.								
Uric acid	Perform ≤72 h before dosing	C1							
Hemoglobin A1c	Local laboratory	C1, C5				C9D1 and D1 of every 4th cycle (±1 week) thereafter			
HBV, HCV	See Section 8.3.5.3	Perform at C1D1 (±7d). PCR testing **Q12W** (±4 weeks) up to 6 months after last dose of study treatment for participants with history of HBV infection/HCV antibody positivity							
HIV PCR and CD4 count	For participants with history of HIV antibody positivity, see Section 8.3.6	C1, C5				C9D1 and D1 of every 4th cycle (±1 week) thereafter		3 and 6 months (±1 month) after last dose	
Coagulation		As clinically indicated							
Serum or urine pregnancy test (POCBP only)	Additional testing with sufficient sensitivity may be required per the global PPP or local PPP/REMS program (see Appendix 4)	• Serum pregnancy test within 10-14d prior to C1D1 and either serum or urine pregnancy test within 24 h prior to C1D1 • Within 24 h of D1 of each cycle • Weekly for the first 4 weeks of pomalidomide treatment, including within 24 h prior to start of pomalidomide administration • Thereafter, Q21d (or Q14d for participants with irregular menses)						X	Xa (until 6 months after last dose)
DISEASE EVALUATIONS									
Serum quantitative Ig	Central laboratory; local laboratory assessments may be used under specified circumstances (see Section 8.2.6); sample may be collected on or within 7d prior to CnD1 **NOTE**: SPEP and UPEP assessments will continue until 30d after the start of the first SST for participants with no PD or unconfirmed PD (ie, single instance of PD by laboratory assessment). For participants with measurable disease by light chain, serum FLC will also continue during this period. *In the event of treatment delays, disease evaluations should occur every 28 days (±7 days).	X				X*		X (until PD or start of SST)	
SPEP		X				X*		X (until PD or start of SST)	
24-h UPEP		X				X*		X (until PD or start of SST)	
Serum FLC and SIFE/UIFE		• For participants with measurable disease only by light chain: with every disease evaluation*and, if applicable, each pre-PD disease evaluation visit until PD or 30 d after the start of SST. • For participants with measurable disease by serum and/or urine M spike: at time of suspected CR or sCR.							
Bone marrow aspirate	For local assessments; see Section 8.2.6 (a portion of aspirate should be sent to the central laboratory for biomarker and MRD analysis)	• Whenever CR or sCR are suspected • For participants with confirmed CR or sCR, collect additional samples 12 months post C1D1 (±3 months) and 12 months (±3 months) after time of confirmed CR or sCR, then every 12 months (±3 months) until PD. • Time of PD (even if occurs after treatment is discontinued; should occur prior to SST)							
Imaging	Disease evaluation including assessment of lytic bone lesions; see Section 8.2.4 for acceptable modalities	• As clinically indicated to document response or progression before start of SST							

Assessments	Notes	Treatment Phase (21-day cycle)							Follow-up Phase
Cycle		Cycle 1-8				Cycle 9+		EOT	
Day		1 (±3d from Cycle 2)	4 (+2d)	8 (+2d)	11 (+2d)	1 (±3d)	8 (±2d)	≤30d after last dose (+7d) or before SST	Pre-PD Q28d (±7d) Post-PD Q16W (±14d)
Assessment of soft-tissue plasmacytomas	See Section 8.2.5 for acceptable modalities	• For participants with a history of soft-tissue plasmacytoma o For assessment by physical examination (if applicable), Q3W (±1 week) from C1D1 until development of confirmed CR or PD or start of SST o For assessment by radiology, Q12W (±1 week) from C1D1 until confirmed CR or PD or start of SST • As clinically indicated for other participants							
PRO AND MRU: PRO ASSESSMENTS SHOULD BE COMPLETED BEFORE ANY CLINICAL TESTS OR PROCEDURES (see Section 8.2.7)									
MySIm-Q, EORTC-QLQ-C30, EQ-5D-5L, PGI-S, Epstein Taste Survey	Window for PRO data collection is 2d prior to dosing during Treatment Phase. Should continue to be collected even if SST has begun	To be collected on Day 1 of C1 to C12, then on Day 1 of every 3rd cycle						X	MySIm-Q, EORTC-QLQ-C30, and EQ-5D-5L only Q16W ±14d
MRU	See Section 8.9	Collected continuously from the start of study treatment until 30d after last dose or the start of SST, whichever is earlier.							
Symptomatic progression evaluation		From 30d prior, to until 30d after confirmed PD (or the start of SST, whichever is earlier), progression-associated symptoms and concomitant medications will be documented in eCRF							
Qualitative interview	Optional; see Section 8.2.7.6	Single interview to be conducted approximately 12 months (±3 months) after the start of study treatment							
ONGOING REVIEW									
AEs	See Section 8.4	Continuous from signing of ICF until 30d after last dose or until the start of SST, if earlier; thereafter, continue to report any AEs/SAEs related to study treatment until EOS							
SPM		Continuous until EOS							
Concomitant therapy	See Section 6.9	Continuous from signing of ICF until 30d after last dose or until the start of SST, if earlier; thereafter, continue to report concomitant therapy given for any AEs/SAEs considered related to study treatment until EOS							
SST	See Section 6.10								X
Survival	See Section 8.1.1.4								Q16W

Abbreviations: see ABBREVIATIONS AND DEFINITIONS OF TERMS.

a. Serum or urine pregnancy tests to be performed, as determined necessary by the investigator, or as required by local regulation, to establish the absence of pregnancy.

b. Baseline before start of bortezomib for potential post-treatment pulmonary changes. Other imaging modality is acceptable per investigator discretion.

Table 11: Dose Schedule – Arm C (PVd)

Cycle	Notes	Treatment Phase (21-day cycle)											
		Cycle 1-8								Cycle 9+			
Day		1	2	4	5	8	9	11	12	1	2	8	9
Pomalidomide PO	4 mg/day There must be ≥7d between the course of pomalidomide for each cycle	Days 1-14								Days 1-14			
Bortezomib SC	1.3 mg/m^2 There must be ≥3d between doses of bortezomib	X		X		X		X		X		X	
Dexamethasone PO	20 mg/day (≤75 years of age) or 10 mg/day (>75 years of age)	X	X	X	X	X	X	X	X	X	X	X	X

Abbreviations: see ABBREVIATIONS AND DEFINITIONS OF TERMS.

Table 12: Sampling for Biomarkers for Treatment Phase, EOT Visit, and Posttreatment Follow-up Phase – Arm C (PVd)

Assessments		Time	Treatment Phase (21-day cycle)			Follow-up Phase
Cycle			Cycle 1-2	Cycle 3+	EOT	
Day			1	1	≤30d after last dose (+7d) or before SST	8 weeks after last dose
BIOMARKER SAMPLING: See Section 8.7. For bone marrow aspirate, see Table 34 for Disease Evaluation						
Immunophenotyping[a] (whole blood)		Predose on the day of dosing[c]	C1			
Circulating proteins (serum/plasma)	M-Protein Mass spectrometry	Predose on the day of dosing[c]	C1	C5	X	
		Response-based	• Time of suspected CR or sCR • For participants with confirmed CR or sCR, additional samples will be collected 6 (±3 months) and 12 months (±3 months) after time of confirmed CR or sCR, and then every 12 months (±3 months) until PD			
Molecular markers/CyTOF[b] (whole blood)		Predose on the day of dosing[c]	C1	C5	X	

Abbreviations: see ABBREVIATIONS AND DEFINITIONS OF TERMS.
a. Immunophenotyping testing will be performed in approximately 50% of the participants in Arm C and only at C1D1.
b. Molecular marker/CyTOF assessments will not be performed for participants enrolling in China.
c. Predose sample window for biomarker samples: -4 to 0h.