



A PHASE 1b/2 STUDY OF PF-07901801, A CD47 BLOCKING AGENT, WITH
TAFASITAMAB AND LENALIDOMIDE FOR PARTICIPANTS WITH
RELAPSED/REFRACTORY DIFFUSE LARGE B CELL LYMPHOMA NOT ELIGIBLE
FOR STEM CELL TRANSPLANTATION

Study Intervention Number: PF-07901801
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EU CT Number: NA
ClinicalTrials.gov ID: NCT05626322
Pediatric Investigational Plan Number NA
Protocol Number: C4971003
Phase: 1b/2
Sponsor Legal Address: Pfizer Inc.
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United States

Brief Title: Phase 1b/2 Study of PF-07901801, Tafasitamab, and Lenalidomide in
Transplant Ineligible Relapsed/Refractory Diffuse Large B Cell Lymphoma Participants

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Document History

Document	Version Date
Amendment 2	09 Dec 2024
Amendment 1	14 March 2023
Original protocol	18 Aug 2022

This amendment incorporates all revisions to date, including amendments made at the request of country health authorities and IRBs/ECs and any protocol administrative change letter(s).

Protocol and Amendment Summary of Changes Table

Amendment 2 (09 Dec 2024)

Overall Rationale for the Amendment:

The purpose of Amendment 2 is to move the secondary objectives and endpoints for PK of tafasitamab and lenalidomide, as well as immunogenicity of tafasitamab, to exploratory objectives and endpoints. Amendment is also to confirm study termination due to business decision made by Pfizer. As a result of this decision, Phase 1b will be discontinued after the last participant last visit and Phase 2 of the study will not be initiated.

Description of Change	Brief Rationale	Section # and Name
Substantial Modification(s)		
Moved the secondary objectives and endpoints for PK of tafasitamab and lenalidomide, as well as immunogenicity of tafasitamab to exploratory objectives and endpoints.	The PK of tafasitamab and lenalidomide, as well as immunogenicity of tafasitamab will not be analyzed due to the limited number of samples collected in Phase 1b and the decision to discontinue development of this drug combination across the program.	Section 1.1 Synopsis Section 3 Objectives, Endpoints, and Estimands Section 9.3.3.3 Pharmacokinetic Analyses for PF-07901801 Section 9.3.3.4 Immunogenicity Analyses for PF-07901801 Section 9.3.4 Tertiary/Exploratory Endpoint(s) Analysis

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Description of Change	Brief Rationale	Section # and Name
<p>Added statements about the study termination decision</p>	<p>Study to be terminated due to strategic business decision.</p>	<p>Section 1.1 Synopsis Section 1.2 Schema Section 2.1 Study Rationale Section 2.3.1 Risk Assessment Section 3 Objectives, Endpoints and Estimands Section 4.1 Overall Design Section 4.3.1. Dosing Regimens of PF-07901801 Section 6.3 Assignment to Study Intervention Section 9 Statistical Considerations Section 9.5 Sample Size Determination Section 10.10.2 Country-specific Requirements (Japan)</p>
<p>Non-Substantial Modification(s)</p>		
<p>Updated the EU CT number to NA; Added ClinicalTrials.gov ID</p>	<p>The study was not submitted to the EU and no EU participants were enrolled.</p>	<p>Title Page, Section 1.1 Synopsis</p>

Description of Change	Brief Rationale	Section # and Name
Updated the text to align with the latest protocol template sections	As required by Pfizer SOP to align with the respective protocol template sections	Section 10.1.1 Regulatory and Ethical Considerations Section 10.1.4 Data Protection Section 10.1.6 Dissemination of Clinical Study Data Section 10.1.7 Data Quality Assurance Section 10.1.10. Study and Site Start and Closure Section 10.1.11 Publication Policy Section 10.1.12 Sponsor’s Medically Qualified Individual
Addition of Appendix 15.	Relocated the summary of changes for prior amendments to align with the current protocol template processes.	Appendix 15: Protocol Amendment History
Clarification that blood sample for CD47 receptor occupancy will not be collected from participants in Japan. (PACL 30 Jun 2023)	This change is due to logistical challenges and limitations.	Section 1.3 Schedule of Activities: Blood sample for CD47 receptor occupancy
Clarified that blood sample for CD47 receptor occupancy will only be collected from participants in the United States and its territories. (PACL 17 Nov 2023)	This change is due to logistical challenges/ limitations.	Section 1.3 Schedule of Activities: Blood sample for CD47 receptor occupancy
The following sentence was removed: “Approximately 60 minutes must elapse after the completion of PF-07901801 prior to the start of infusion of tafasitamab.” (PACL 17 Nov 2023)	To provide clarity and consistency with the language that was previously updated in Section 6.1.1.1.	Section 6.1.1 Administration
Added text for Pfizer review of eligibility data. (PACL 17 Nov 2023)	To reduce risk for enrollment of non-	Section 5. Study Population

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Description of Change	Brief Rationale	Section # and Name
	eligible participants, due to the complexities of the inclusion/exclusion criteria.	
Added text Fluorescence in situ hybridization (FISH) testing is required prior to enrollment if historical results are not available. (PACL 17 Nov 2023)	Clarified that if these tests were not done as part of primary diagnosis or results are not available in medical history, detection of MYC and BCL2 and/or BCL6 rearrangements should be conducted prior to enrollment to verify exclusion criteria 3 high-grade lymphoma.	Section 5.2 Exclusion Criteria, for Exclusion Criteria 3
Added text for timing of blood collection for laboratory tests, vital signs and ECGs. (PACL 06 Feb 2024)	This change is due to logistical challenges with timing of collection for laboratory tests, vital signs and ECGs	Section 8.3.2.1 Blood Pressure and Pulse Rate Section 8.3.3. Electrocardiograms
The Emergency Contact Card is being replaced by a study information card and will no longer be referenced. (PACL 02 Apr 2024)	The process for contacting a medically qualified individual has changed from a medical escalation process via a Pfizer Call Center to direct clinical team contact using a Study Team Contact List.	Table 1: Schedule of Assessments Section 10.1.12 Sponsor's Medically Qualified Individual Appendix 16: Abbreviations
Editorial and formatting changes and clarifications	For document accuracy and consistency.	Throughout the document

090177e1a258b721\Approved\Approved On: 13-Dec-2024 05:57 (GMT)

TABLE OF CONTENTS

LIST OF TABLES	13
LIST OF FIGURES	13
1. PROTOCOL SUMMARY	14
1.1. Synopsis	14
1.2. Schema	22
1.3. Schedule of Activities	23
2. INTRODUCTION	37
2.1. Study Rationale	39
2.2. Background	39
2.2.1. Drug Mechanism of Action - PF-07901801	39
2.2.2. Nonclinical Overview of PF-07901801	40
2.2.3. Clinical Overview	41
2.2.3.1. Clinical Safety	41
2.2.3.2. Clinical Activity	42
2.2.3.3. Clinical Pharmacology	43
2.3. Benefit/Risk Assessment	45
2.3.1. Risk Assessment	46
2.3.2. Benefit Assessment	50
2.3.3. Overall Benefit/Risk Conclusion	50
3. OBJECTIVES, ENDPOINTS, AND ESTIMANDS	51
4. STUDY DESIGN	54
4.1. Overall Design	54
4.2. Scientific Rationale for Study Design	55
4.2.1. Diversity of Study Population	55
4.2.2. Dose Level Review Meeting	55
4.2.3. Choice of Contraception/Barrier Requirements	55
4.2.4. Collection of Retained Research Samples	56
4.3. Justification for Dose	56
4.3.1. Dosing Regimens of PF-07901801	56
4.3.2. Dosing regimen of Tafasitamab and Lenalidomide	56
4.3.3. Criteria for Dose Escalation	57

4.3.4. Dose Limiting Toxicity Definition	58
4.3.4.1. Hematological DLTs	58
4.3.4.2. Non-Hematologic DLTs.....	59
4.3.5. Maximum Tolerated Dose	59
4.4. End of Study Definition	59
5. STUDY POPULATION	59
5.1. Inclusion Criteria.....	60
5.2. Exclusion Criteria.....	62
5.3. Lifestyle Considerations.....	64
5.3.1. Contraception.....	64
5.3.2. Photosensitivity.....	65
5.4. Screen Failures	65
6. STUDY INTERVENTION(S) AND CONCOMITANT THERAPY	65
6.1. Study Intervention(s) Administered.....	65
6.1.1. Administration	67
6.1.1.1. PF-07901801	68
6.1.1.2. Tafasitamab	68
6.1.1.3. Lenalidomide.....	69
6.2. Preparation, Handling, Storage and Accountability.....	70
6.2.1. Preparation and Dispensing	71
6.3. Assignment to Study Intervention.....	71
6.4. Blinding.....	72
6.5. Study Intervention Compliance.....	72
6.6. Dose Modification.....	73
6.6.1. Dose-Modification Guidelines.....	73
6.6.2. Re-Treatment After Toxicity	81
6.7. Continued Access to Study Intervention After the End of the Study.....	81
6.8. Treatment of Overdose.....	82
6.9. Prior and Concomitant Therapy	82
6.9.1. Prohibited Inhibitors/Inducers	82
6.9.1.1. PF-07901801	82
6.9.1.2. Tafasitamab	82

6.9.1.3. Lenalidomide.....	82
6.9.2. Other Prohibited and/or Limited Use of Anti-Tumor/Anti-Cancer or Experimental Drugs or Procedures	83
6.9.3. Supportive Care	83
6.9.4. Hematopoietic Growth Factors and Blood Product Transfusions	84
6.9.5. Corticosteroids.....	84
6.9.6. Infection Prophylaxis and Vaccines	85
6.9.7. Surgery.....	85
6.9.8. Radiotherapy.....	85
7. DISCONTINUATION OF STUDY INTERVENTION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL.....	85
7.1. Discontinuation of Study Intervention	85
7.1.1. COVID-19	86
7.2. Participant Discontinuation/Withdrawal From the Study	86
7.2.1. Withdrawal of Consent	87
7.3. Lost to Follow-Up	87
8. STUDY ASSESSMENTS AND PROCEDURES.....	87
8.1. Administrative Procedures	87
8.1.1. Screening and Baseline Procedures	88
8.1.2. Follow-Up Visits and LTFU.....	88
8.2. Efficacy Assessments.....	89
8.2.1. Computed Tomography Scans.....	90
8.2.2. Positron Emission Tomography Scans	91
8.3. Safety Assessments	91
8.3.1. Physical Examinations.....	91
8.3.2. Vital Signs	91
8.3.2.1. Blood Pressure and Pulse Rate.....	92
8.3.2.2. Temperature and Respiratory Rate.....	92
8.3.3. Electrocardiograms	92
8.3.4. Clinical Safety Laboratory Assessments	93
8.3.4.1. Alternative Facilities for Clinical Safety Laboratory Assessment	94
8.3.5. Pregnancy Testing	94

8.3.6. B-Symptoms	94
8.4. Adverse Events, Serious Adverse Events, and Other Safety Reporting	94
8.4.1. Time Period and Frequency for Collecting AE and SAE Information.....	95
8.4.1.1. Reporting SAEs to Pfizer Safety	96
8.4.1.2. Recording Nonserious AEs and SAEs on the CRF	96
8.4.2. Method of Detecting AEs and SAEs	96
8.4.3. Follow-Up of AEs and SAEs.....	96
8.4.4. Regulatory Reporting Requirements for SAEs.....	97
8.4.5. Environmental Exposure, Exposure During Pregnancy or Breastfeeding, and Occupational Exposure	97
8.4.5.1. Exposure During Pregnancy.....	97
8.4.5.2. Exposure During Breastfeeding	99
8.4.5.3. Occupational Exposure	99
8.4.6. Cardiovascular and Death Events	100
8.4.7. Disease-Related Events and/or Disease-Related Outcomes Not Qualifying as AEs or SAEs.....	100
8.4.8. Adverse Events of Special Interest	100
8.4.8.1. Lack of Efficacy	100
8.4.9. Medical Device Deficiencies	100
8.4.10. Medication Errors	100
8.5. Pharmacokinetics	101
8.6. Genetics	102
8.6.1. Specified Genetics	102
8.6.2. Retained Research Samples for Genetics	102
8.7. Biomarkers	102
8.7.1. Blood Sample for Circulating Biomarker Analysis.....	103
8.7.2. Blood Sample for CD47 Receptor Occupancy Analysis.....	103
8.7.3. Blood Sample for T-cell Receptor Sequencing	103
8.7.4. Blood Sample for Immune Cell Profiling.....	103
8.7.5. Blood Sample for Specified Genetic Research.....	104
8.7.6. Saliva Sample for Matched Control and Specified Genetic Research	104
8.7.7. Blood Sample for Cell-Free DNA (cfDNA) Analysis.....	104
8.7.8. Tumor Tissue for Genetic/Biomarker Analysis.....	104

8.8. Immunogenicity Assessments	105
8.8.1. Anti-PF-07901801 Antibody (ADA) and Neutralizing Anti-PF-07901801 Antibody (NAb).....	105
8.8.2. Anti-Tafasitamab Antibody (ADA) and Neutralizing Anti-Tafasitamab Antibody (NAb)	106
8.9. Pharmacodynamics.....	106
9. STATISTICAL CONSIDERATIONS	106
9.1. Health Economics	107
9.2. Statistical Hypothesis	107
9.2.1. Primary Estimands.....	107
9.2.1.1. Phase 1b Primary Estimand.....	107
9.2.1.2. Phase 2 Primary Estimand.....	108
9.3. Analysis Sets	108
9.4. Statistical Analyses	109
9.4.1. General Considerations.....	109
9.4.2. Primary Endpoints/Analysis	109
9.4.2.1. Phase 1b.....	109
9.4.2.2. Phase 2.....	109
9.4.3. Secondary Endpoints/Analysis	110
9.4.3.1. Efficacy Analyses.....	110
9.4.3.2. Safety Analyses	111
9.4.3.3. Pharmacokinetic Analyses for PF-07901801.....	112
9.4.3.4. Immunogenicity Analyses for PF-07901801	112
9.4.4. Tertiary/Exploratory Endpoint(s) Analysis	112
9.4.5. Other Safety Analyses	113
9.4.5.1. Electrocardiogram Analyses.....	113
9.4.6. Other Analyses.....	113
9.5. Interim Analyses	113
9.6. Sample Size Determination.....	113
9.7. Statistical Methods and Decision Criteria.....	115
10. SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS.....	117
10.1. Appendix 1: Regulatory, Ethical, and Study Oversight Considerations	117

10.1.1. Regulatory and Ethical Considerations	117
10.1.1.1. Reporting of Safety Issues and Serious Breaches of the Protocol or ICH GCP.....	117
10.1.2. Financial Disclosure	118
10.1.3. Informed Consent/Assent Process	118
10.1.4. Data Protection	119
10.1.5. Committees Structure	119
10.1.6. Dissemination of Clinical Study Data	120
10.1.7. Data Quality Assurance	121
10.1.8. Source Documents	122
10.1.9. Use of Medical Records.....	122
10.1.10. Study and Site Start and Closure	123
10.1.11. Publication Policy	124
10.1.12. Sponsor’s Medically Qualified Individual.....	125
10.2. Appendix 2: Clinical Laboratory Assessments	126
10.3. Appendix 3: Adverse Events: Definitions and Procedures for Recording, Evaluating, Follow-Up, and Reporting	128
10.3.1. Definition of AE	128
10.3.2. Definition of an SAE	129
10.3.3. Recording/Reporting and Follow-Up of AEs and/or SAEs During the Active Collection Period.....	131
10.3.4. Reporting of SAEs.....	134
10.4. Appendix 4: Contraceptive and Barrier Guidance	135
10.4.1. Male Participant Reproductive Inclusion Criteria	135
10.4.2. Female Participant Reproductive Inclusion Criteria.....	135
10.4.3. Woman of Childbearing and Non-Childbearing Potential	136
10.4.4. Contraception Methods.....	137
10.4.5. Lenalidomide Pregnancy Prevention Program	138
10.5. Appendix 5: Genetics	142
10.6. Appendix 6: Liver Safety: Suggested Actions and Follow-Up Assessments	143
10.7. Appendix 7: Kidney Safety: Monitoring Guidelines	145
10.7.1. Laboratory Assessment of Change in Kidney Function and Detection of Kidney Injury	145

10.7.2. Age-Specific Kidney Function Calculation Recommendations	146
10.7.2.1. Adults (18 Years and Above)—2021 CKD-EPI Equations	146
10.7.3. Adverse Event Grading for Kidney Safety Laboratory Abnormalities.....	146
10.8. Appendix 8: ECG Findings of Potential Clinical Concern	147
10.9. Appendix 9: Prohibited Concomitant Medications That May Result in DDI.....	149
10.10. Appendix 10: Country-Specific Requirements	150
10.10.1. France	150
10.10.2. Japan	150
10.11. Appendix 11: Lugano Modification of Ann Arbor Staging System (for Primary Nodal Lymphomas)	154
10.12. Appendix 12: Lugano Criteria.....	155
10.13. Appendix 13: ECOG Performance Status	156
10.14. Appendix 14: International Prognostic Index (IPI).....	157
10.15. Appendix 15: Protocol Amendment History.....	158
10.16. Appendix 16: Abbreviations	163
11. REFERENCES	169

LIST OF TABLES

Table 1.	Study Schedule of Assessment	23
Table 2.	Clinical Activity with PF-07901801 Monotherapy at Doses Ranging from 0.8-18 mg/kg - Study C4971001 (as of 12 April 2021)	42
Table 3.	Provisional Dose Levels PF-07901801 in Dose-Escalation	57
Table 4.	Study Intervention(s) - IMP	65
Table 5.	Study Interventions Classified as NIMPs/AxMPs.....	67
Table 6.	Dose Modifications for Related Hematologic Toxicities	75
Table 7.	Dose Modifications for Non-Hematologic Toxicities	77
Table 8.	Dose Modifications for Lenalidomide Toxicities.....	79
Table 9.	Dose Modifications for Infusion-Related Reactions	80
Table 10.	Reductions for Lenalidomide	81
Table 11.	Sample Size and 95% CI for ORR based on Wilson Method (with Continuity Correction).....	115
Table 12.	mTPI-2 Decision Rules (pT=0.3, e1=0.05, e2=0.05)	116
Table 13.	Study-Specific Clinical Laboratory Assessments.....	126

LIST OF FIGURES

Figure 1.	PF-07901801 Structure and Mechanism of Action	39
Figure 2.	PF-07901801 Binds Minimally to Human Red Blood Cells.....	40
Figure 3.	In Vitro and In Vivo Anti-Tumor Activity of PF-07901801	41
Figure 4.	Pregnancy Prevention Plan Algorithm	141

1. PROTOCOL SUMMARY

1.1. Synopsis

Protocol Title:

A Phase 1b/2 study of PF-07901801, a CD47 blocking agent, with tafasitamab and lenalidomide for participants with relapsed/refractory diffuse large B cell lymphoma not eligible for stem cell transplantation

Brief Title:

Phase 1b/2 study of PF-07901801, tafasitamab, and lenalidomide in transplant ineligible relapsed/refractory diffuse large B cell lymphoma participants

Regulatory Agency Identification Number(s):

US IND Number:	IND 135421
EU CT Number:	NA
ClinicalTrials.gov ID:	NCT05626322
Pediatric Investigational Plan Number:	Not applicable
Protocol Number:	C4971003
Phase:	1b/2

Rationale:

The purpose of this Phase 1b/2 study is to evaluate the safety, tolerability and potential clinical benefits of PF-07901801 in combination with standard doses of tafasitamab and lenalidomide in participants with relapsed-refractory diffuse large B cell lymphoma (R/R DLBCL) not eligible for high dose chemotherapy followed by autologous stem cell transplantation (ASCT).

A business decision was made by Pfizer to terminate the C4971003 study. The reason for study termination is not due to any safety concerns or requests from regulatory authorities. As a result of this decision, Phase 1b will be discontinued after the last participant last visit and Phase 2 of the study will not be initiated.

Objectives, Endpoints, and Estimands:

PHASE 1b		
Objectives	Endpoints	Estimands
Primary		
To assess dose limiting toxicity (DLTs), safety and tolerability of PF-07901801 in combination with tafasitamab and lenalidomide in adult participants with R/R DLBCL in order to select up to 2 doses of PF-07901801 for further evaluation in Phase 2 of the study.	DLTs during the DLT observation period (28 days following C1D1).	DLT rate estimated based on data from DLT-evaluable participants during the DLT observation period (28 days following C1D1).
Secondary		
To evaluate the overall safety profile of the combination.	<ul style="list-style-type: none"> Adverse events (AEs) as characterized by type, frequency, severity (as graded by National Cancer Institute Common Terminology Criteria for Adverse Events [NCI CTCAE] v5.0), timing, seriousness, and relationship to study treatment. Laboratory abnormalities as characterized by type, frequency, severity (as graded by NCI CTCAE v5.0), and timing. 	Not Applicable
To evaluate the anti-tumor activity of PF-07901801 in combination with tafasitamab and lenalidomide.	Objective response (OR), duration of response (DoR), complete response (CR), duration of complete response (DoCR), and progression-free survival (PFS) per Lugano Response Classification Criteria 2014 as assessed by the investigator.	Not applicable
To evaluate the pharmacokinetics (PK) of PF-07901801.	Pre- and post-dose concentration of PF-07901801.	Not applicable
To evaluate immunogenicity of PF-07901801.	Antidrug antibodies (ADAs) and neutralizing antibodies (Nabs) against PF-07901801.	Not applicable

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PHASE 2		
Objectives	Endpoints	Estimands
Primary		
To assess the clinical anti-tumor activity of PF-07901801 in combination with tafasitamab and lenalidomide.	OR per Lugano Response Classification Criteria 2014 as assessed by the investigator.	The treatment effect of PF-07901801 in combination with tafasitamab and lenalidomide on OR per the Lugano 2014 response criteria as determined by investigator assessment from the date of first dose until the first documentation of PD, death, or start of new anticancer therapy. Participants who do not have a post-baseline disease assessment due to early PD, who receive anticancer therapies other than the study intervention prior to achieving an objective response, or who die, experience PD, or stop disease assessments for any reason prior to achieving an objective response will be counted as non-responders.
Secondary		
To assess additional efficacy outcomes of PF-07901801 in combination with tafasitamab and lenalidomide.	DoR, CR, DoCR and PFS by investigator per Lugano Response Classification Criteria 2014.	Not applicable
Select the RP3D for PF-07901801 in combination with tafasitamab and lenalidomide.	All endpoints in this study.	Not applicable
To further evaluate the overall safety profile and tolerability of PF-07901801 in combination with tafasitamab and lenalidomide.	<ul style="list-style-type: none"> • AEs as characterized by type, frequency, severity (as graded by NCI CTCAE v5.0), timing, seriousness, and relationship to study treatment. • Laboratory abnormalities as characterized by type, frequency, severity (as graded by NCI CTCAE v5.0), and timing. 	Not applicable
To evaluate the PK of PF-07901801.	Pre- and post-dose concentrations of PF-07901801.	Not applicable
To evaluate immunogenicity of PF-07901801.	ADAs and NAbs against PF-07901801.	Not applicable

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Overall Design

This is a multicenter, international, Phase 1b/2 study of different doses of PF-07901801 in combination with tafasitamab and lenalidomide in participants with R/R DLBCL who have completed at least 1 line of systemic treatment (at least 1 containing an anti-CD20 therapy), and who are not candidates for high dose therapy/ASCT.

An escalation/de-escalation approach will be used in Phase 1b to determine the PF-07901801 recommended Phase 2 dose (RP2D) (2 dose levels) in combination with tafasitamab and lenalidomide; the two dose levels will be further evaluated in Phase 2.

Number of Participants

Approximately 70 participants will be enrolled in the study: approximately 20 participants in the Phase 1b and 50 participants in the Phase 2.

Note: "Enrolled" means a participant's, or their legally authorized representative's, agreement to participate in a clinical study following completion of the informed consent process and assignment to study intervention.

Study Population

Adult participants (≥ 18 years of age) with histologically confirmed measurable relapsed or refractory DLBCL not eligible for stem cell transplantation will be enrolled in the study.

Key Inclusion Criteria

- Histologically confirmed DLBCL; relapsed or refractory disease.
- Participant is not a candidate for or is unwilling to undergo high dose chemotherapy and subsequent stem cell transplant or is unable to receive approved chimeric antigen receptor (CAR-T) therapy.
- Prior treatment with at least 1 line of systemic therapy (for phase 2: at least 1 and no more than 2 lines of systemic therapy). Prior therapy must include an anti-CD20 containing regimen.
- Adequate hematologic, hepatic and renal function.
- Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2 .
- Participants are able to provide a tumor tissue sample collected before start of treatment (fresh or archival).

Key Exclusion Criteria

- Prior treatment with an anti-CD47 or anti-CD19 (other than CAR-T) or immunomodulatory agents.

- Primary refractory DLBCL
- High-grade lymphoma (formerly known as ‘double’ or ‘triple hit’ DLBCL) or CNS lymphoma involvement.
- Prior allogeneic stem cell transplantation; autologous stem cell transplantation within 12 weeks prior to enrollment.
- Significant cardiac/cardiovascular/thromboembolic disease.
- Participants with active, uncontrolled bacterial, fungal, or viral infection.

Study Arms and Duration Study Intervention(s)			
Intervention Name	PF-07901801	Tafasitamab	Lenalidomide
Arm Name (group of participants receiving a specific treatment or no treatment)	Administered to all participants	Administered to all participants	Administered to all participants
Unit Dose Strength(s)	10 mg/mL solution for injection; 14 mL/vial	200 mg/vial	2.5 mg, 5 mg, 10 mg, 15 mg, 20 mg, 25 mg
Route of Administration	Intravenous (IV) infusion	IV infusion	By mouth (PO)
Use	Experimental	Experimental when combined with PF-07901801	Experimental when combined with PF-07901801
Investigational medicinal product (IMP) or non-IMP (NIMP)/auxiliary medicinal product (AxMP)	IMP	IMP	IMP
Dose Formulation	Single-use vials	Single-use vials	Capsules

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Study Interventions Classified as NIMPs/AxMPs

Intervention Name	Fludeoxyglucose (¹⁸F) (FDG)	Paracetamol^a	Diphenhydramine hydrochloride^a	Cimetidine^a	Methylprednisolone^a
ARM Name (group of participants receiving a specific treatment)	May be administered to all participants for use with PET scan	May be administered to all participants as premedication ^a	May be administered to all participants as premedication ^a	May be administered to all participants as premedication ^a	May be administered to all participants as premedication ^a
Dose Formulation	As per SmPC	As per SmPC	As per SmPC	As per SmPC	As per SmPC
Unit Dose Strength(s)	As per SmPC	As per SmPC	As per SmPC	As per SmPC	As per SmPC
Route of Administration	IV injection	PO	PO or IV	PO	IV injection or infusion
Use	For use with PET	Premedication	Premedication	Premedication	Premedication
IMP or NIMP/AxMP	AxMP	AxMP	AxMP	AxMP	AxMP

a. Premedications that may be given as per MINJUVI SmPC [equivalent premedication(s) includes variations to the stated ones, depending on the formulations available locally and or in accordance with institutional guidelines].

Administration

Study interventions will be administered in 28-day cycles. Lenalidomide will be administered up to C12 while PF-07901801 and tafasitamab will be administered until PD, non-tolerable toxicity, or death. PF-07901801 will be administered by intravenous (IV) infusion weekly for the first three cycles and then every two weeks for Cycle 4 and beyond. Participants will receive different dose levels as per assigned cohort.

Tafasitamab will be administered 12 mg/kg IV on Days 1, 4, 8, 15 and 22 in Cycle 1, weekly for Cycle 2 and 3 and then every 2 weeks for Cycle 4 and beyond. Lenalidomide will be administered 25 mg PO daily on Days 1 through 21 of each 28-day cycle for up to 12 cycles.

Statistical Methods:

There is no formal hypothesis testing for the study. All analyses will be performed for the Phase 1b and Phase 2 of the study separately. All efficacy analyses and safety analyses will be performed using the Safety Analysis Set (if not otherwise specified).

Phase 1b:

The primary endpoint of the Phase 1b of the study is the DLTs during the DLT observation period. The target number of participants per cohort is 2-4, and a minimum of 2-4 DLT-evaluable participants is required at each tested dose level of PF-07901801. Approximately 6 to 9 DLT-evaluable participants will be treated at the MTD or highest safe tested dose level for PF-07901801 before proceeding to Phase 2. The number and proportion

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of participants experiencing DLTs during the DLT observation period will be summarized and listed by dose level.

Phase 2:

Up to 2 doses will be selected for further evaluation in Phase 2 of the study. Approximately 25 participants will be treated for each selected dose.

The primary endpoint in the Phase 2 of the study is OR per Lugano Response Classification Criteria 2014 as assessed by the investigator. OR is defined as a BOR of CR or PR according to Lugano Response Classification Criteria 2014.

ORR will be calculated along with the 2-sided 95% CI using the Wilson method.

For both phases:

- Secondary efficacy endpoints (OR [Phase 1b only], DoR, CR, DoCR, and PFS per Lugano Response Classification Criteria 2014 as assessed by the investigator) will be summarized by dose levels.
- Secondary safety endpoints (AEs, laboratory abnormalities):
 - AEs will be graded by the investigator according to the CTCAE v5.0 and coded using MedDRA. AE data will be reported in tables and listings and will be presented by dose levels.
 - The laboratory results will be graded according to the NCI CTCAE v5.0 severity grade and will be analyzed using summary statistics.
- Secondary PK endpoints will be analyzed and presented using descriptive summary statistics.
- Secondary immunogenicity (ADAs and Nabs): the percentage of participants with positive ADA will be summarized. Listings and summary tabulations of the ADA data at baseline and post-first dose will be generated.

Ethical Considerations

Patients with R/R DLBCL who are not candidates for ASCT due to age or co-morbidities have limited treatment options and poor prognosis. The combination of tafasitamab and lenalidomide has shown increased response and progression-free survival in patients with R/R DLBCL, leading to conditional approval. By engaging overlapping as well as different mechanisms with the combination of tafasitamab and lenalidomide, PF-07901801 is expected to increase anti-tumor activity in patients with R/R DLBCL. Further, available safety data of PF-07901801 as a single agent in patients with DLBCL suggest that it may be combined with other approved agents without significantly increasing their toxicity. Possible overlapping toxicity with the proposed regimens include neutropenia and thrombocytopenia; to minimize

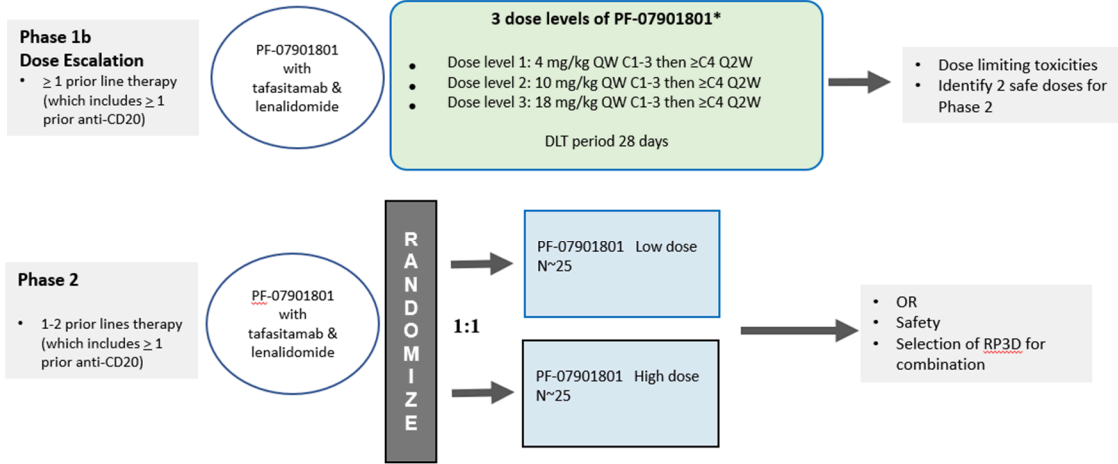
risks, participants will be monitored frequently, including weekly blood tests for their first 8 weeks of treatment.

Therefore, taking into consideration the complementary mechanisms of action of PF-07901801 with tafasitamab and lenalidomide as well as the safety profile of PF-07901801, this combination may offer a more efficacious and tolerable treatment option for older patients or patients with co-morbidities that are not candidates for high dose chemotherapy and/or ASCT.

1.2. Schema

Phase 2 of the study will not be initiated per business decision made by Pfizer (protocol amendment 2).

PF-07901801 Combined With Tafasitamab and Lenalidomide for R/R DLBCL



*A minimum of 2 to 4 participants is required at each dose level.
 Approximately 6 to 9 participants will be treated at the MTD or highest safe tested dose level before proceeding to Phase 2.

090177e1a258b721\Approved\Approved On: 13-Dec-2024 05:57 (GMT)

1.3. Schedule of Activities

The SoA table provides an overview of the protocol visits and procedures. Refer to the [STUDY ASSESSMENTS AND PROCEDURES](#) section of the protocol for detailed information on each assessment required for compliance with the protocol.

The investigator may schedule visits or tests (unplanned visits/tests) in addition to those listed in the SoA table, in order to conduct evaluations or assessments required to protect the well-being of the participant.

Table 1. Study Schedule of Assessment

Visit Identifier	Screen	On-Treatment Period (28-day Cycle)										FU visits			Notes		
		Cycle 1					Cycle 2-3					≥Cycle 4	EOT	FU visits		LTFU	
Cycle Day	≤28d	D1	D4	D8	D15	D22	D1	D8	D15	D22	D1	D15	7d	28d	90d	Q12W	
Visit Window			(±1d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d post-last TX)	(28-35d post-last TX)	(+7 post-last TX)	(±14d post 90d FU)	<ul style="list-style-type: none"> After 1 year of study intervention, cycle visit date windows are ±7d.
Informed consent	X															<ul style="list-style-type: none"> Consent obtained within 28 days prior to C1D1. See Section 10.1.3 for additional information. 	
Registration/randomization		X															<ul style="list-style-type: none"> At registration, which must be before the first study-related activity at D1, the participant enrollment number and dose level allocation are assigned. For randomized cohorts: Allocation of participants to treatment groups will proceed through the use of an IRT System. Study intervention must start preferably the same day or within 3 days after randomization.

Table 1. Study Schedule of Assessment

Visit Identifier	Screen	On-Treatment Period (28-day Cycle)											FU visits			LTFU	Notes		
		Cycle 1					Cycle 2-3				≥Cycle 4		EOT	28d	90d			Q12W	
Cycle Day	≤28d	D1	D4	D8	D15	D22	D1	D8	D15	D22	D1	D15	7d	28d	90d				
Visit Window			(±1d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d post-last TX)	(28-35d post-last TX)	(+7 post-last TX)	(±14d post 90d FU)			<ul style="list-style-type: none"> After 1 year of study intervention, cycle visit date windows are ±7d.
Disease characteristics/treatment history	X																		<ul style="list-style-type: none"> Including cancer history, disease staging (Ann Arbor), risk assessment (IPI score), prior cancer treatments, and inclusion/exclusion criteria.
Demographics/medical history	X																		<ul style="list-style-type: none"> See Section 8.1.1.
Physical examination	X	X			X		X		X		X		X	X					<ul style="list-style-type: none"> A complete PE will be conducted at Screening Visit only; targeted/symptom-directed PEs will be conducted at other visits. See Section 8.3.1 for additional information.
Body weight	X	X					X				X								<ul style="list-style-type: none"> See Section 8.3.1 for additional information. Also see Section 6.1.1 for dose calculation with weight.

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Table 1. Study Schedule of Assessment

Visit Identifier	On-Treatment Period (28-day Cycle)															Notes	
	Screen	Cycle 1					Cycle 2-3				≥Cycle 4		EOT	FU visits			LTFU
Cycle Day	≤28d	D1	D4	D8	D15	D22	D1	D8	D15	D22	D1	D15	7d	28d	90d	Q12W	
Visit Window			(±1d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d post-last TX)	(28-35d post-last TX)	(+7 post-last TX)	(±14d post 90d FU)	<ul style="list-style-type: none"> After 1 year of study intervention, cycle visit date windows are ±7d.
Vital signs	X	X	X	X	X	X	X	X	X	X	X	X	X	X			<ul style="list-style-type: none"> On days of infusion: as per local guidelines for monoclonal antibodies, with a minimum as follows for each infusion of PF-07901801 and tafasitamab. <ul style="list-style-type: none"> PF-07901801: C1D1: pre (within 15 min prior), EOI (±15 min), (end of): 2h (±15 min). ≥C1D8: pre and EOI (±15 min). Tafasitamab: pre, 15 (±5), 30 (±10), and then every 60 (±15) minutes during infusion and at EOI (± 20 min). After 3 infusions: pre and EOI (±15 min). See Section 8.3.2 for additional information.
12-Lead ECG	X	X					X					X	X	X			<ul style="list-style-type: none"> C1D1, C2D1, C3D1: Pre-PF-07901801 dose, PF-07901801 EOI (window for EOI: +30 min). C4D1, C5D1, C6D1: pre PF-07901801 dose See Section 8.3.3 for additional information.
B-symptoms	X	X					X					X	X				<ul style="list-style-type: none"> See Section 8.3.6.
ECOG assessment	X																<ul style="list-style-type: none"> Per Appendix 13.

Table 1. Study Schedule of Assessment

Visit Identifier	On-Treatment Period (28-day Cycle)															Notes	
	Screen	Cycle 1					Cycle 2-3				≥Cycle 4	EOT	FU visits		LTFU		
Cycle Day	≤28d	D1	D4	D8	D15	D22	D1	D8	D15	D22	D1	D15	7d	28d	90d	Q12W	
Visit Window			(±1d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d post-last TX)	(28-35d post-last TX)	(+7 post-last TX)	(±14d post 90d FU)	<ul style="list-style-type: none"> After 1 year of study intervention, cycle visit date windows are ±7d.
Diary card (lenalidomide)	X	X					X						X				<ul style="list-style-type: none"> See Section 6.5. To be collected through Cycle 12 or EOT, whichever occurs first.
AEs/SAEs	Continuously active collection															<ul style="list-style-type: none"> See Section 8.4 for additional information. 	
Medications	Concomitant medications										Subsequent anticancer therapy(ies)				<ul style="list-style-type: none"> Concomitant medications to be collected continuously from the time of ICD through EOT. 		
CD19 expression (if post CAR-T)	X																<ul style="list-style-type: none"> CD19 expression to be measured in participants with prior CAR-T treatment: local lab test (if available) and tissue for future central testing (both must be a sample after CAR-T and prior to C1D1). See also Section 8.7.8.
Survival status														X	X	<ul style="list-style-type: none"> May be conducted by phone. 	
Local Laboratory Assessments																	<ul style="list-style-type: none"> See Section 8.3.4 for additional information. See Appendix 2 for a list of clinical laboratory tests to be done.

090177e1a258b721\Approved\Approved On: 13-Dec-2024 05:57 (GMT)

Table 1. Study Schedule of Assessment

Visit Identifier	On-Treatment Period (28-day Cycle)															Notes	
	Screen	Cycle 1					Cycle 2-3				≥Cycle 4		EOT	FU visits			LTFU
Cycle Day	≤28d	D1	D4	D8	D15	D22	D1	D8	D15	D22	D1	D15	7d	28d	90d	Q12W	
Visit Window			(±1d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d post-last TX)	(28-35d post-last TX)	(+7 post-last TX)	(±14d post 90d FU)	
HIV status	X																<ul style="list-style-type: none"> For participants with known history of HIV: CD4 count and viral load
Hepatitis B/C panel	X																<ul style="list-style-type: none"> Monitor participants for HBV reactivation throughout the study, if applicable. See Appendix 2, Appendix 10, and REVLIMID SmPC.
Pregnancy test (WOCBP only)	X	X		X	X	X	X		X*		X	X*		X			<ul style="list-style-type: none"> Pregnancy test will be done weekly at C1; and monthly at C2 and beyond. *: WOCBP participants with irregular cycles should have the test done every 2 weeks. See Section 8.3.5 for additional information.
Contraception check	X	X					X				X			X	X		<ul style="list-style-type: none"> Only required for WOCBP and men with WOCBP partner. See Section 4.2.3 and Appendix 4 for additional information.
FSH	X																<ul style="list-style-type: none"> For confirmation of postmenopausal status.
Hematology	X	X	X	X	X	X	X	X	X	X	X	X	X	X			<ul style="list-style-type: none"> May be collected up to 72 hours prior to dosing visit date. See Appendix 2.

Table 1. Study Schedule of Assessment

Visit Identifier	On-Treatment Period (28-day Cycle)															Notes	
	Screen	Cycle 1					Cycle 2-3				≥Cycle 4	EOT	FU visits		LTFU		
Cycle Day	≤28d	D1	D4	D8	D15	D22	D1	D8	D15	D22	D1	D15	7d	28d	90d	Q12W	
Visit Window			(±1d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d post-last TX)	(28-35d post-last TX)	(+7 post-last TX)	(±14d post 90d FU)	
Serum chemistries	X	X			X		X		X		X		X	X			<ul style="list-style-type: none"> May be collected up to 72 hours prior to dosing visit date. See Appendix 2.
Coagulation panel	X	X					X					X					<ul style="list-style-type: none"> May be collected up to 72 hours prior to dosing visit date. See Appendix 2.
Urinalysis (dipstick)	X																<ul style="list-style-type: none"> May be collected up to 72 hours prior to dosing visit date. See Appendix 2.
Serum Immunoglobulin concentrations	X	X					X					X		X			<ul style="list-style-type: none"> May be collected up to 72 hours prior to dosing visit date. See Appendix 2.
Study Intervention and Other Treatments																	
Premedications		X	X	X	X	X	X	X	X	X	X	X					<ul style="list-style-type: none"> See Section 6.1.1 for additional information.
PF-07901801 IV infusion		X		X	X	X	X	X	X	X	X	X					<ul style="list-style-type: none"> See Section 6.1.1.1 for additional information.
Tafasitamab IV infusion		X	X	X	X	X	X	X	X	X	X	X					<ul style="list-style-type: none"> See Section 6.1.1.2 for additional information.

090177e1a258b721\Approved\Approved On: 13-Dec-2024 05:57 (GMT)

Table 1. Study Schedule of Assessment

Visit Identifier	Screen	On-Treatment Period (28-day Cycle)														Notes		
		Cycle 1					Cycle 2-3				≥Cycle 4		EOT	FU visits			LTFU	
Cycle Day	≤28d	D1	D4	D8	D15	D22	D1	D8	D15	D22	D1	D15	7d	28d	90d	Q12W		
Visit Window			(±1d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d post-last TX)	(28-35d post-last TX)	(+7 post-last TX)	(±14d post 90d FU)	<ul style="list-style-type: none"> After 1 year of study intervention, cycle visit date windows are ±7d. 	
Lenalidomide		Administer PO on D1-D21					Administer PO on D1-D21				Administer PO on D1-D21 through C12						<ul style="list-style-type: none"> See Section 6.1.1.3 for additional information. 	
Disease Assessment (Lugano Criteria 2014: Appendix 12)																		
Imaging: PET/CT or PET/MRI	X						C3 D1						C6D1, C9D1, C12D1, C18D1, C24D1 then yearly until PD.	X			(X)	<ul style="list-style-type: none"> Scans may be repeated at any time if progressive disease is suspected, to confirm the occurrence of a CR or to make important treatment related decisions. Window for imaging during study is ±7 days. See Section 8.2 for additional information.

090177e1a258b721\Approved\Approved On: 13-Dec-2024 05:57 (GMT)

Table 1. Study Schedule of Assessment

Visit Identifier	Screen	On-Treatment Period (28-day Cycle)											FU visits			LTFU	Notes		
		Cycle 1					Cycle 2-3				≥Cycle 4		EOT	28d	90d			Q12W	
Cycle Day	≤28d	D1	D4	D8	D15	D22	D1	D8	D15	D22	D1	D15	7d	28d	90d				
Visit Window			(±1d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d post-last TX)	(28-35d post-last TX)	(+7 post-last TX)	(±14d post 90d FU)			<ul style="list-style-type: none"> After 1 year of study intervention, cycle visit date windows are ±7d.
Blood for PF-07901801 PK		X		X			X					X	X						<ul style="list-style-type: none"> C1D1 and C2D1: pre-dose, EOI (approx. 60 min from start of infusion, within 5 min of PF07901801 infusion ends), 5h (± 2h) post-dose (relative to the start of infusion). C1D8, C3D1, C4D1 and C5D1: pre-dose. Starting C7 up to C13, collect pre-dose only every 3rd cycle (ie, C7D1, C10D1, C13D1) and then every 6th cycle thereafter (C19D1, C25D1, etc.).
Blood for tafasitamab PK		X					X					X	X						<ul style="list-style-type: none"> C1D1, C2D1, C3D1, and C4D1: pre-dose. Starting C7 up to C13, collect pre-dose only every 3rd cycle (ie, C7D1, C10D1, C13D1) and then every 6th cycle thereafter (C19D1, C25D1, etc.).
Blood for lenalidomide PK		X					X					C4 only							<ul style="list-style-type: none"> C1D1, C2D1, C3D1, C4D1: pre-dose.

090177e1a258b721\Approved\Approved On: 13-Dec-2024 05:57 (GMT)

Table 1. Study Schedule of Assessment

Visit Identifier	Screen	On-Treatment Period (28-day Cycle)											FU visits			LTFU	Notes	
		Cycle 1					Cycle 2-3				≥Cycle 4		EOT	28d	90d			Q12W
Cycle Day	≤28d	D1	D4	D8	D15	D22	D1	D8	D15	D22	D1	D15	7d	28d	90d	Q12W		
Visit Window			(±1d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d post-last TX)	(28-35d post-last TX)	(+7 post-last TX)	(±14d post 90d FU)		
ADA/NAb for PF-07901801 (PB)		X					X					X	X	See Notes				<ul style="list-style-type: none"> C1D1, C2D1, C3D1, C4D1 and C5D1: pre-dose. Starting C7 up to C13, collect pre-dose only every 3rd cycle (ie, C7D1, C10D1, C13D1) and then every 6th cycle thereafter (C19D1, C25D1, etc.). FU visits and LTFU: Participants with an unresolved AE at the end of study treatment considered possibly related to ADA formation may be asked to return to the clinic for ADA blood sampling at approximately 3-month intervals (if feasible given the underlying disease) until the AE or its sequelae resolve or stabilize at a level acceptable to the investigator and sponsor up to a maximum of 9 months from the last study treatment.

090177e1a258b721\Approved\Approved On: 13-Dec-2024 05:57 (GMT)

Table 1. Study Schedule of Assessment

Visit Identifier	On-Treatment Period (28-day Cycle)															Notes	
	Screen	Cycle 1					Cycle 2-3				≥Cycle 4		EOT	FU visits			LTFU
Cycle Day	≤28d	D1	D4	D8	D15	D22	D1	D8	D15	D22	D1	D15	7d	28d	90d	Q12W	
Visit Window			(±1d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d post-last TX)	(28-35d post-last TX)	(+7 post-last TX)	(±14d post 90d FU)	<ul style="list-style-type: none"> After 1 year of study intervention, cycle visit date windows are ±7d.
ADA/NAb for tafasitamab (PB)		X					X						X		See Notes		<ul style="list-style-type: none"> C1D1, C2D1, C3D1, C4D1: pre-dose. Starting C7 up to C13, collect pre-dose only every 3rd cycle (ie, C7D1, C10D1, C13D1) and then every 6th cycle thereafter (C19D1, C25D1, etc.). FU visits and LTFU: Participants with an unresolved AE at the end of study treatment considered possibly related to ADA formation may be asked to return to the clinic for ADA blood sampling at approximately 3-month intervals (if feasible given the underlying disease) until the AE or its sequelae resolve or stabilize at a level acceptable to the investigator and sponsor up to a maximum of 9 months from the last study treatment.
Genetics and Biomarker Assessments																	<ul style="list-style-type: none"> Pre-dose samples are to be collected before any pre-medication or study treatment administration on indicated visits. See Section 8.6 and Section 8.7 for additional information.

090177e1a258b721\Approved\Approved On: 13-Dec-2024 05:57 (GMT)

Table 1. Study Schedule of Assessment

Visit Identifier	Screen	On-Treatment Period (28-day Cycle)											FU visits			LTFU	Notes		
		Cycle 1					Cycle 2-3				≥Cycle 4		EOT	28d	90d			Q12W	
Abbreviations used in this table may be found in Appendix 16		≤28d	D1	D4	D8	D15	D22	D1	D8	D15	D22	D1	D15	7d	28d	90d			<ul style="list-style-type: none"> All screening should be done ≤28 days before the first dose, unless noted otherwise.
Cycle Day																			<ul style="list-style-type: none"> Day relative to start of study intervention (Day 1).
Visit Window			(±1d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d post-last TX)	(28-35d post-last TX)	(+7 post-last TX)	(±14d post 90d FU)		<ul style="list-style-type: none"> After 1 year of study intervention, cycle visit date windows are ±7d.
Tumor Tissue	X	At relapse/PD/EOT (strongly recommended), and as clinically indicated.															<ul style="list-style-type: none"> See Section 8.7.8 for additional information. 		
Blood sample for circulating biomarker analysis		X	X	X				C2 only	C2 only										<ul style="list-style-type: none"> Collect whole blood for processing into serum as indicated: <ul style="list-style-type: none"> C1D1 and C2D1: pre-dose; PF-07901801 EOI (within 5 min from the end of PF-07901801 infusion); 5h (±2h window) post dose of PF-07901801 (5h relative to the start of PF-07901801 infusion, preferably not collected during tafasitamab infusion). C1D4, C1D8, C2D8: pre-dose.
Blood sample for CD47 receptor occupancy		X		X				X					C4, C5 only						<ul style="list-style-type: none"> Collect whole blood as indicated: <ul style="list-style-type: none"> C1D1, C2D1: pre-dose and EOI [end of PF-07901801 infusion (+5 min window)]. C1D8, C3D1, C4D1, C5D1: pre-dose. Will be collected only in the United States and its territories.

090177e1a258b721\Approved\Approved On: 13-Dec-2024 05:57 (GMT)

Table 1. Study Schedule of Assessment

Visit Identifier	Screen	On-Treatment Period (28-day Cycle)											FU visits			LTFU	Notes
		Cycle 1					Cycle 2-3				≥Cycle 4		EOT	28d	90d		
Cycle Day	≤28d	D1	D4	D8	D15	D22	D1	D8	D15	D22	D1	D15	7d	28d	90d	Q12W	
Visit Window			(±1d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d post-last TX)	(28-35d post-last TX)	(+7 post-last TX)	(±14d post 90d FU)	<ul style="list-style-type: none"> After 1 year of study intervention, cycle visit date windows are ±7d.
Blood sample for TCR sequencing		X			X		X						X				<ul style="list-style-type: none"> Collect whole blood as indicated: <ul style="list-style-type: none"> ○ C1D1, C1D15, C2D1, C3D1: pre-dose. ○ EOT: sampling is not required for participants who are active on treatment for >1 year.
Blood sample for immune cell profiling		X		X	X		X					C5 only	X				<ul style="list-style-type: none"> Collect whole blood as indicated: <ul style="list-style-type: none"> ○ C1D1, C1D8, C1D15, C2D1, C3D1 and C5D1: pre-dose. ○ EOT: sampling is not required for participants who are active on treatment for >1 year.
Blood sample for specified genetic research		X															<ul style="list-style-type: none"> Collect whole blood pre-dose.
Saliva sample for matched control and specified genetic research		X															<ul style="list-style-type: none"> Collect saliva pre-dose.

090177e1a258b721\Approved\Approved On: 13-Dec-2024 05:57 (GMT)

Table 1. Study Schedule of Assessment

Visit Identifier	Screen	On-Treatment Period (28-day Cycle)											FU visits			LTFU	Notes
		Cycle 1					Cycle 2-3				≥Cycle 4		EOT	28d	90d		
Cycle Day	≤28d	D1	D4	D8	D15	D22	D1	D8	D15	D22	D1	D15	7d	28d	90d	Q12W	
Visit Window			(±1d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d)	(±2d post-last TX)	(28-35d post-last TX)	(+7 post-last TX)	(±14d post 90d FU)	<ul style="list-style-type: none"> After 1 year of study intervention, cycle visit date windows are ±7d.
Blood sample for cfDNA analysis		X					X						C6D1, at CR and at time of relapse/PD	X			<ul style="list-style-type: none"> Collect whole blood as indicated for processing into plasma: <ul style="list-style-type: none"> C1D1, C2D1, C3D1, C6D1: pre-dose. At CR and at time of relapse/PD: pre-dose. EOT: sampling is not required for participants who are active on treatment for >1 year.
Retained research sample for genetics (Prep D1)		X															<ul style="list-style-type: none"> Collect whole blood pre-dose. If not collected on the designated collection day, collect at the next available time point when biospecimens are being collected in conjunction with a participant visit.

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2. INTRODUCTION

DLBCL is the most common type of lymphoma encompassing around 30% to 40 % of the newly diagnosed cases of NHL.¹ R-CHOP has been the standard treatment for newly diagnosed patients for over 2 decades curing approximately 60% of the patients.¹ In older patients mini R-CHOP (a reduced intensity regimen for patients over 80 years old) may be used as first line treatment.²

Patients refractory to or relapsing after first line treatment may proceed to induction chemotherapy treatment (eg, R-ICE or R-DHAP) followed by ASCT. Patients not eligible to transplant due to age or co-morbidities may proceed to less invasive treatments like R-GemOx (rituximab, gemcitabine and oxaliplatin).

Polatuzumab vedotin, an antibody drug conjugate targeting CD79b on the B cells surface, in combination with bendamustine and rituximab received accelerated/conditional approval in R/R DLBCL after at least 2 prior lines of therapies.³ Reported response in the pola+BR arm was 45% (CRR 40%);⁴ and updated data showed median PFS was 9.2 (95% CI, 6.0-13.0) months and median OS was 12.4 (95% CI, 9.0-32.0) months.³ A confirmatory Phase 3 trial run in untreated DLBCL patients with intermediate or high-risk disease compared the PFS of R-CHOP versus a modified R-CHOP regimen where polatuzumab vedotin was administered instead of vincristine (pola-R-CHP), and after a median follow up of 28.2 months, pola-R-CHP was superior when compared to R-CHOP in terms of PFS (76.7% [95% CI, 72.7%-80.8%] vs 70.2% [95% CI, 65.8%-74.6%]).⁵

In 2020 tafasitamab in combination with lenalidomide received accelerated/conditional approvals for patients with R/R DLBCL who are not candidates for ASCT. Efficacy of tafasitamab with lenalidomide was evaluated in a single arm Phase 2 study (L-MIND) in patients with relapsed refractory DLBCL not eligible for high dose chemotherapy or ASCT.⁶ Primary refractory patients (defined as relapse within 6 months of first-line treatment) were excluded. Prior therapies had to include a CD20-directed therapy. The ORR reported in 80 patients was 60% (95% CI, 48%-71%) with a CRR of 43% (95% CI, 32%-54%) and a median PFS of 12.1 (95% CI, 5.7-not reached) months. The most common ($\geq 10\%$) $\geq G3$ AEs include neutropenia (48%), thrombocytopenia (17%), and febrile neutropenia (12%). Lenalidomide as a single agent has modest activity in patients with DLBCL; the combination of tafasitamab and lenalidomide, however, showed increased ADCC activity in DLBCL cells compared to tafasitamab or lenalidomide alone and led to better clinical outcome compared to real-world data of lenalidomide as a single agent.⁷

CAR-T cell therapies (eg, axicabtagene ciloleucel, tisagenlecleucel and lisocabtagene maraleuce) are new treatment options for patients with R/R DLBCL. Axicabtagene ciloleucel, an autologous anti-CD19 CAR-T cell therapy, was first explored in the ZUMA-1 trial. In this study, enrolling patients with R/R DLBCL after failure of conventional therapy, 83% of the patients had an OR, 58% achieved a CR and the median PFS was 5.9 (95% CI, 3.3-15.0) months.⁸ Axicabtagene ciloleucel has been approved in the US for patients with R/R DLBCL after at least 2 prior lines of systemic therapy and more recently in patients with DLBCL refractory to first line chemoimmunotherapy or with relapse within 12 months of first line chemoimmunotherapy.⁹ CAR-T cell therapy still presents challenges for patients'

access, including being available only at major academic institutions, turn-around time required for leukapheresis, and presenting with significant toxicities (48% of the patients reported \geq G3 AEs, including 11% cytokine release syndrome and 32% neurological events) which are currently limiting their use.⁸ Therefore, new treatments are urgently needed as this constitutes an area of unmet medical need with currently limited available treatment options.

CD47 is an innate immune checkpoint that binds SIRP α and delivers a “don’t eat me” signal to suppress macrophage phagocytosis. Overexpression of CD47 in solid and hematological malignancies, including in DLBCL, is associated with poor prognosis for patients’ outcome.¹⁰

PF-07901801 (previously referred to as TTI-622) is a fusion protein consisting of the CD47-binding domain of human SIRP α linked to the Fc region of human IgG4. It is designed to enhance phagocytosis and antitumor activity by preventing CD47 from delivering its inhibitory signal as well as generating a moderate pro-phagocytic signal via IgG4 Fc. Preclinical studies demonstrate that PF-07901801 induces macrophage-mediated phagocytosis of different malignant cell lines, including DLBCL cells, decreases tumor growth and improves survival in a DLBCL xenograft tumor model.

By blocking CD47, it is expected that the combination of PF-07901801 with a FcR-activating antibody, like tafasitamab, would prevent an inhibitory signal and deliver a positive stimulus to macrophages, resulting in the synergistic phagocytosis and elimination of target cells. Indeed, it has been demonstrated that the combination with tafasitamab and an anti-CD47-blocking antibody potentiated the anti-tumor activity of tafasitamab in a pre-clinical Burkitt lymphoma tumor model.¹¹

In addition to the potential synergy in ADCP, tafasitamab can provide anti-tumor activities through induction of NK mediated antibody-dependent cytotoxicity, and direct tumor cytotoxicity via induction of apoptosis.¹²

On the other hand, lenalidomide, a second generation immunomodulatory agent, has been shown to cause proliferation and activation of T and NK cells.¹³ By activating NK cells, lenalidomide has shown to enhance tafasitamab mediated ADCC activity.¹⁴ In addition, lenalidomide also has the potential to increase PF-07901801-mediated ADCP activity by induction of “eat” signals through cellular stress.

Therefore, by engaging overlapping and different mechanisms, the combination of PF-07901801, tafasitamab and lenalidomide is expected to result in increased anti-tumor activity in patients with R/R DLBCL.

In the ongoing Phase 1 Study C4971001, heavily pretreated participants with R/R lymphoma including R/R DLBCL have been treated with different doses of single agent PF-07901801. As of 12 April 2021, PF-07901801 has been administered to 43 participants at dose levels of up to 18 mg/kg QW and has been well-tolerated. Activity has been shown in R/R lymphoma.

Therefore, considering the different and non-redundant, though complementary mechanisms of action of PF-07901801, tafasitamab, and lenalidomide and the safety profile of

PF-07901801 from Study C4971001 this combination may offer a more efficacious and tolerable treatment option for older patients or patients with co-morbidities that are not candidates for high dose chemotherapy and/or ASCT.

2.1. Study Rationale

The purpose of this Phase 1b/2 study is to evaluate the safety, tolerability and potential clinical benefits of PF-07901801 in combination with standard doses of tafasitamab and lenalidomide in participants with R/R DLBCL not eligible for or not willing to undergo high dose chemotherapy followed by ASCT. Phase 1b will assess DLTs to select up to 2 fixed doses of PF-07901801 to be administered in combination with tafasitamab and lenalidomide in the randomized Phase 2 of the study. The Phase 2 of the study will determine the recommended Phase 3 dose of PF-07901801 to be administered in combination with tafasitamab and lenalidomide.

Phase 2 of the study will not be initiated per business decision made by Pfizer (protocol amendment 2).

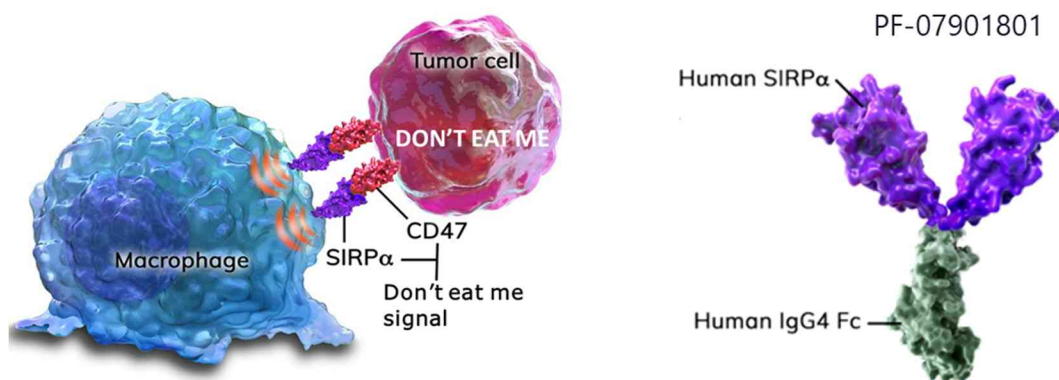
2.2. Background

2.2.1. Drug Mechanism of Action - PF-07901801

PF-07901801 is a novel fusion protein consisting of the CD47-binding domain of human SIRP α linked to the Fc region of human IgG4. It is designed to enhance phagocytosis and antitumor activity by preventing CD47 from delivering its inhibitory signal as well as generating a moderate pro-phagocytic signal via IgG4 Fc (Figure 1).

PF-07901801 has reported single agent activity in lymphoid malignancies and with CRs in hematologic malignancies through CD47/SIRP α blocking. The current clinical dataset includes monotherapy responses after IV administration in different types of lymphomas (DLBCL, FL, CTCL, PTCL) over a wide dose range, with a prolonged DoR (in responders, median 106 [71-880+] days on treatment).

Figure 1. PF-07901801 Structure and Mechanism of Action



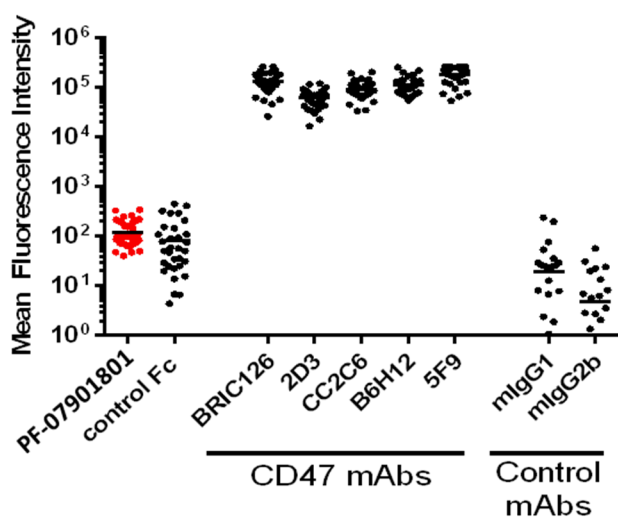
High levels of CD47 have been found to correlate with poor clinical prognosis in participants with a number of cancer types, including most hematologic malignancies.^{15,16,17,18} High

CD47 expression correlates with more aggressive disease and poorer clinical outcomes.¹⁹ For example, overall survival was significantly lower for participants with DLBCL or mantle cell lymphoma who had elevated CD47 expression.¹⁶ These findings are consistent with tumor cells exploiting the suppressive CD47-SIRP α axis to evade macrophage-mediated destruction. Blockade of CD47 by PF-07901801 is expected to enhance the anti-tumor activity of tafasitamab and lenalidomide in DLBCL.

2.2.2. Nonclinical Overview of PF-07901801

Extensive in vitro testing demonstrated that PF-07901801 bound to human hematopoietic tumor cell lines and primary tumor samples as well as normal human blood cells, with the exception of human red blood cells. Unlike anti-CD47 antibodies (eg, magrolimab, previously named 5F9), PF-07901801 binds minimally to human RBC (Figure 2). Due to this property, PF-07901801 is not expected to cause anemia, or to interfere with blood transfusion compatibility testing.

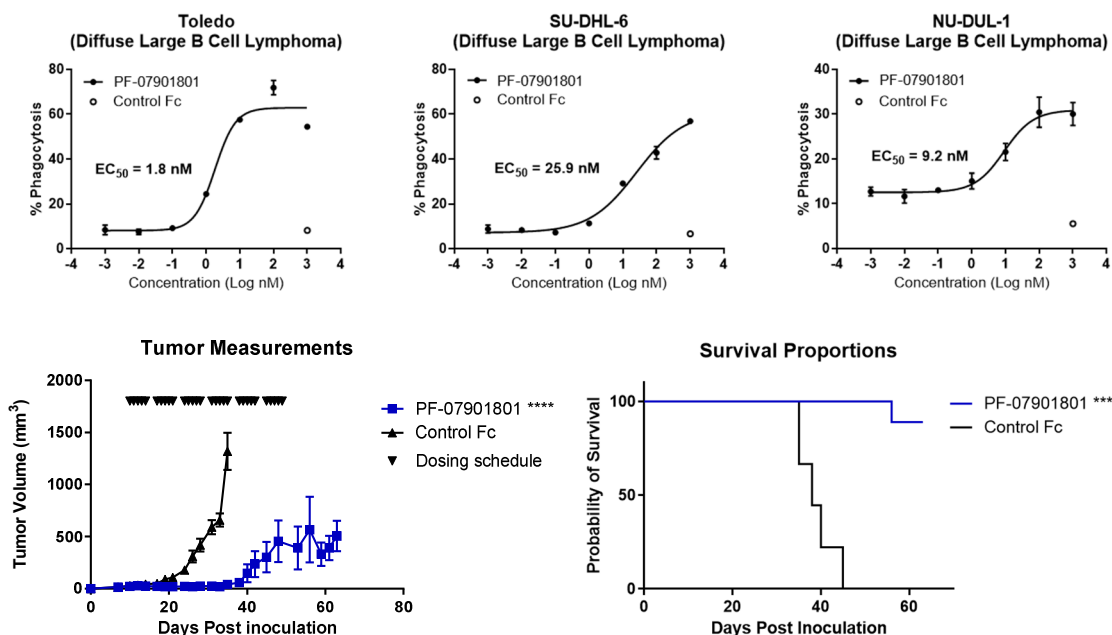
Figure 2. PF-07901801 Binds Minimally to Human Red Blood Cells



RBCs from healthy human donors (n=43) were incubated with saturating concentrations of PF-07901801, anti-CD47 monoclonal antibodies (clones BRIC126, 2D3, CC2C6, B6H12, 5F9) or controls, washed, followed by biotinylated anti-human IgG or anti-mouse IgG and streptavidin-PE. Cells were washed, fixed, and analyzed by flow cytometry.

Preclinical studies have demonstrated that PF-07901801 was effective in promoting macrophage-mediated phagocytosis of various B cell lymphoma cells in vitro. Furthermore, when in vivo efficacy was assessed in a Toledo DLBCL xenograft model, treatment of PF-07901801 resulted in a significant reduction in tumor growth and improved overall survival, compared to a control Fc (Figure 3).

Figure 3. In Vitro and In Vivo Anti-Tumor Activity of PF-07901801



Phagocytosis of DLBCL cell lines was assessed in the presence of PF-07901801 or control Fc in vitro (top). Activity of PF-07901801 was assessed in a DLBCL xenograft model (bottom). Mice were dosed intraperitoneally 5 times per week with PF-07901801 at 10 mg/kg or control Fc (6.67 mg/kg) starting on Day 10 for a total of 6 weeks. Mean tumor volumes \pm standard error of the mean were recorded only for timepoints at which $\leq 25\%$ mice per group were sacrificed (bottom left panel). Survival plot of the tumor-bearing mice is shown in the bottom right panel.

2.2.3. Clinical Overview

PF-07901801 is being evaluated in an ongoing Phase 1, two-part, multi-center, 1a/1b study in participants with advanced hematologic malignancies, including lymphoma, leukemia, and MM (Protocol C4971001 [previously referred as TTI-622-01]). In the Phase 1a dose-escalation part of the study, participants with advanced lymphoma are enrolled in sequential dose cohorts to receive PF-07901801 monotherapy QW to characterize safety, tolerability, and PK of PF-07901801. In the Phase 1b of the study, participants with DLBCL, MM and AML are treated in combination with selected approved anti-cancer agents in several cohorts to further define safety and to characterize efficacy.

2.2.3.1. Clinical Safety

As of 12 April 2021, PF-07901801 had been administered in Study C4971001 to 43 participants with R/R lymphoma in eight different dose-escalation, single-therapy cohorts, at doses ranging from 0.05 mg/kg to 18.0 mg/kg QW. A total of 37/43 (86%) participants experienced TEAEs, and in 20/43 (47%) of whom the TEAEs were assessed as treatment-related by the investigator. The most frequent ($\geq 9\%$) treatment-related TEAEs included thrombocytopenia (n=9, 21%), neutropenia (n=5, 12%), and anemia and fatigue (n=4 each, 9%).

Most TEAEs have been G1 or G2 and reversible. G3-4 TEAEs (neutropenia and thrombocytopenia [5 participants, 12% each], and pneumonia [2 participants, 5%]) were reported in 16 (37%) participants, and in 6 (14%) were assessed as treatment-related by the investigator (neutropenia [4 participants, 9%], thrombocytopenia [2 participants, 5%], and pneumonia [1 participant, 2%]). A single DLT of reversible, asymptomatic G4 thrombocytopenia has been observed in a participant treated in the 8 mg/kg QW cohort; the cohort was expanded and no other dose-limiting observation of thrombocytopenia was observed. G3 and G4 hematologic events occurred in dose levels ranging from 0.8 to 18 mg/kg without apparent dose relationship. Mild to moderate platelet decreases seen in the majority of participants generally occurred on dosing days and recovered to baseline levels. Updated information can be found in the current IB.

2.2.3.2. Clinical Activity

PF-07901801 has demonstrated single agent clinical activity in some of the 43 participants with advanced R/R lymphoma enrolled in Study C4971001. As of 12 April 2021, a 33% ORR has been observed in 27 response-evaluable participants enrolled across doses ranging from 0.8-18 mg/kg weekly. There appears to be a rapid onset of response, with PR or CR typically noted by Week 8 of treatment in this patient population.

In responding participants, there were 2 with CR and 1 with near-CR:

- One participant with DLBCL and four prior lines of therapy treated with PF-07901801 at 0.8 mg/kg weekly experienced PR at Week 8 and CR at Week 36. At more than 22 months since initiation of treatment, the participant remains on study in CR without PD under a modified treatment regimen of a single infusion per month.
- One participant with CTCL with large cell transformation and six prior lines of therapy treated with PF-07901801 at 18 mg/kg weekly experienced a CR at Week 8; the participant continues on study under a reduced schedule of one infusion every 21 days.
- A third participant with DLBCL and three prior regimens treated with PF-07901801 at 4 mg/kg weekly, had a 100% reduction in target lesions at Week 8 but was declared PR due to minimal residual signal on PET imaging. The participant continued on study and developed PD at Week 24.

Clinical activity with PF-07901801 as of the data cut-off of 12 April 2021 is summarized in Table 2. Updated information can be found in the current IB.

Table 2. Clinical Activity with PF-07901801 Monotherapy at Doses Ranging from 0.8-18 mg/kg - Study C4971001 (as of 12 April 2021)

Indication	Response-Evaluable Patient Population (N)	CR	PR	ORR
DLBCL	11	1 (9%)	2 (18%)	3 (27%)
PTCL	6	0 (0%)	2 (33%)	2 (33%)

Table 2. Clinical Activity with PF-07901801 Monotherapy at Doses Ranging from 0.8-18 mg/kg - Study C4971001 (as of 12 April 2021)

Indication	Response-Evaluable Patient Population (N)	CR	PR	ORR
CTCL	4	1 (25%)	2 (50%)	3 (75%)
FL	3	0 (0%)	1 (33%)	1 (33%)
HL	3	0 (0%)	0 (0%)	0 (0%)
Total	27	2 (7%)	7 (26%)	9 (33%)

2.2.3.3. Clinical Pharmacology

2.2.3.3.1. PF-07901801

Single- and multiple-dose PK of PF-07901801 are being evaluated in the ongoing Study C4971001. As of the data cutoff of 02 November 2021, preliminary PK data of PF-07901801 were available from 46 participants that received 0.05 mg/kg to 18 mg/kg QW as a 1-hour continuous IV infusion in the dose escalation part. PF-07901801 exhibited a greater than dose-proportional increase in systemic exposures due to target mediated drug clearance. PF-07901801 is eliminated via non-specific FcRn-mediated proteolytic degradation and target mediated clearance. Population PK analyses using data from 49 participants showed that a 2-compartment model with simultaneous linear and non-linear clearance adequately described the PK of PF-07901801 across all doses. Immunogenicity data from 46 participants suggests low (9%) overall incidence of ADAs against PF-07901801 (as of 19 November 2021). Evaluation of the impact of ADA on the PK of PF-07901801 is still ongoing.

2.2.3.3.2. Tafasitamab

Mean trough concentrations (\pm SD) were 179 (\pm 53) μ g/mL following administration of tafasitamab at 12 mg/kg on Days 1, 8, 15, and 22 in C1-C3 (plus an additional dose on C1D4), and 153 (\pm 68) μ g/mL following administration of tafasitamab at 12 mg/kg on Days 1 and 15 from C4 onwards. Overall maximum tafasitamab serum concentrations were 483 (\pm 109) μ g/mL. The total volume of distribution for tafasitamab-cxix was 9.3 L (95% CI: 8.6, 10). The clearance of tafasitamab was 0.41 L/day (CV: 32%) and $t_{1/2}$ was 17 days (95% CI: 15, 18).

Body weight (40 to 163 kg) has a significant effect on the PK of tafasitamab, with higher clearance and volume of distribution expected with higher body weight. No clinically meaningful differences in the PK of tafasitamab were observed based on age (16 to 90 years), sex, mild to moderate renal impairment (CrCl 30-89 mL/min estimated by the Cockcroft-Gault equation), or mild hepatic impairment (T bili \leq ULN and AST $>$ ULN, or T bili $>$ 1-1.5 \times ULN with any AST).

No clinically meaningful differences in tafasitamab PK were observed when used concomitantly with lenalidomide.

In 245 patients treated with tafasitamab, no treatment-emergent or treatment-boosted anti-tafasitamab antibodies were observed. Pre-existing anti-tafasitamab antibodies were detected in 17/245 patients (6.9%) with no impact on pharmacokinetics, efficacy or safety of tafasitamab.²²

2.2.3.3.3. Lenalidomide

Lenalidomide is rapidly absorbed following oral administration with a median serum T_{max} ranging from 0.5 to 1 hour with >90% oral bioavailability. Lenalidomide AUC and C_{max} values increased proportionally with dose from 5 mg to 400 mg indicating linear PK. Coadministration of lenalidomide with a high-fat meal reduced the extent and rate of lenalidomide oral absorption, however, the effect of food was considered not clinically significant, and thus lenalidomide can be taken with or without food. The mean half-life of lenalidomide is 3 to 5 hours in participants with MM.^{20,21}

Lenalidomide binding to plasma proteins is approximately 30% and the apparent volume of distribution is 74-91 L. Lenalidomide is also present in semen after the administration of a 25 mg QD dose. However, the lenalidomide total amount of drug presented in semen over 72 hours was <0.01%.²¹

Lenalidomide is eliminated primarily via renal clearance with ~82% of the dose excreted in urine, predominantly as unchanged drug. Lenalidomide renal excretion was not saturable over the dose range of 5 mg to 400 mg. Dose adjustment is needed for patients with renal impairment. As creatinine clearance decreases, half-life increases, and drug clearance decreases linearly.²¹ In a dedicated renal impairment study, participants with moderate and severe impairment had a 3-fold increase in half-life and a 66% to 75% decrease, respectively, in drug clearance compared to healthy participants. For Phase 2 participants with moderate renal impairment (creatinine clearance ≥ 30 mL/min and <60 mL/min), lenalidomide will be started (and/or reduced) to 10 mg daily (see Section 6.1.1.3).

Lenalidomide undergoes limited metabolism. Mild hepatic impairment ($T_{bili} > 1-1.5 \times ULN$ or $AST > ULN$) did not have a clinically significant effect on the PK of lenalidomide. Additionally, age (39 to 85 years), body weight (33 to 135 kg), sex, and race did not have a clinically relevant effect on lenalidomide clearance in adult participants.²¹

2.2.3.3.4. Drug-Drug Interactions Between PF-07901801 and Tafasitamab or Lenalidomide

Overall, the risk of clinically relevant DDI between PF-07901801 and tafasitamab or lenalidomide is considered low.

PF-07901801 is eliminated via non-specific FcRn-mediated proteolytic degradation and target mediated clearance. Due to the nature of the large molecule (PF-07901801 is a fusion protein), tafasitamab or lenalidomide are not expected to alter PF-07901801 PK.

Tafasitamab is a monoclonal antibody, which is expected to be eliminated via non-specific catabolic degradation. Lenalidomide is mainly eliminated via renal clearance. Therefore, PF-07901801 is not expected to impact the PK of tafasitamab or lenalidomide. In addition,

per the USPI of tafasitamab, no clinically meaningful differences in tafasitamab PK were observed when used concomitantly with lenalidomide.

Collection of PK samples for PF-07901801, tafasitamab and lenalidomide is planned in this study.

2.3. Benefit/Risk Assessment

The combination of PF-07901801 with the proposed agents (tafasitamab and lenalidomide) is expected to provide benefit to patients with R/R DLBCL that have previously been treated with standard of care due to the non-redundant MoA of the different combination molecules, all leveraging on enhanced activation of immune system effectors.

PF-07901801 reported single agent activity in patients with advanced R/R DLBCL and is generally well tolerated. Therefore it is suggested that it may be a relevant candidate to be combined with other active agents without significantly increasing the toxicity while enhancing the activity of other treatment regimens, including already approved therapies. Based on PF-07901801 clinical data from the Phase 1 Study C4971001, and the reported AEs from the information in SmPCs of the combination molecules (tafasitamab and lenalidomide), neutropenia and thrombocytopenia are possible overlapping toxicities. To minimize risks patients will be monitored with weekly hematologic blood tests for at least their first 3 cycles of treatment (see Section 2.3.1 for identified risks and mitigations) and subsequently twice monthly as per the [SoA](#) and the toxicity management Section 6.6.1.

More detailed information about the known and expected benefits and risks and reasonably expected AEs of PF-07901801 may be found in the IB, which is the SRSD for this study. The SRSDs for tafasitamab and lenalidomide are the current EU MINJUVI[®] and REVLIMID[®] SmPCs, respectively.^{20,22} The SRSD for fludeoxyglucose (¹⁸F) is the EU SmPC. The SRSDs for the pre-medications are the Ireland SmPCs for paracetamol, diphenhydramine hydrochloride, cimetidine and methylprednisolone.

2.3.1. Risk Assessment

Phase 2 of the study will not be initiated per business decision made by Pfizer (protocol amendment 2).

Potential Risk of Clinical Significance	Summary of Data/Rationale for Risk*	Mitigation Strategy
PF-07901801+tafasitamab+ lenalidomide		
Thrombocytopenia	<p>G3-4 thrombocytopenia was observed in 17.3% of the patients treated with tafasitamab and lenalidomide.⁶</p> <p>Treatment-related G3-4 thrombocytopenia (5%) has been reported with PF-07901801 in the ongoing Phase 1 Study C4971001. The combination may increase the risk of G3-4 thrombocytopenia.</p>	<p>Participants must have adequate hematological functions (including platelet counts with no transfusions for at least 2 weeks prior to C1D1) to be eligible to participate in this study. Participants will have weekly hematology blood tests for the first 3 cycles and thereafter every two weeks (or more frequently if clinically indicated).</p> <p>Platelet transfusion is allowed to manage severe thrombocytopenia, to prevent and minimize bleeding according to institutional guidelines (see Section 6.9.4).</p> <p>Dose interruption and dose modification are described in Section 6.6.1.</p>
Neutropenia	<p>G3-4 neutropenia was reported in 48.1% of the patients treated with tafasitamab and lenalidomide.⁶</p> <p>Treatment related, G3-4 neutropenia (9%) has been reported with PF-07901801 in the ongoing Phase 1 Study C4971001. The combination may increase the risk of G3-4 neutropenia.</p>	<p>Participants must have adequate hematological functions (including neutrophil counts, with no growth factor for at least 2 weeks prior to C1D1) to be eligible to participate in this study. Participants will have weekly hematology blood tests for the first 3 cycles and thereafter every two weeks (or more frequently if clinically indicated).</p> <p>Prophylactic use of granulocyte-colony stimulating factors is not permitted during the DLT period of Phase 1b but can be used in later cycles and in Phase 2 of the study. G-CSF may be used to treat treatment emergent neutropenia as per institutional guidelines.</p> <p>Any symptoms or signs of developing infection should be anticipated, evaluated and treated.</p> <p>Dose interruption and dose modification are described in Section 6.6.1.</p>

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Potential Risk of Clinical Significance	Summary of Data/Rationale for Risk*	Mitigation Strategy
PF-07901801+tafasitamab+ lenalidomide		
Anemia	<p>G3-4 anemia was observed in 7.4% of the patients treated with tafasitamab and lenalidomide.⁶</p> <p>Decreases in hemoglobin and hematocrit were observed in preclinical animal studies with PF-07901801, however, given the low affinity of PF-07901801 for human RBCs relative to monkey RBCs, serious treatment-emergent anemia is not expected in human participants. In clinical data as of 12 April 2021, 1 of 43 treated participants experienced G3 anemia that was assessed by the investigator as related to PF-07901801. No incidence of anemia was assessed by the investigator as an SAE and anemia did not appear to be associated with increased destruction of erythrocytes.</p>	<p>Participants must have adequate hematological functions (including hemoglobin, with no transfusion or erythropoiesis-stimulating agent for at least 2 weeks prior to C1D1) to be eligible to participate in this study.</p> <p>All participants will be closely monitored for anemia. Participants will have weekly hematology blood tests for the first 3 cycles and thereafter every two weeks (or more frequently if clinically indicated).</p> <p>Prophylactic use of erythropoietin or transfusions are not permitted during the DLT period of Phase 1b but can be used in later cycles and in Phase 2 of the study, per institutional guidelines (note: erythropoietin is not approved for the treatment related anemia in Japan).</p> <p>Blood transfusion is allowed to manage severe anemia according to institutional guidelines (see Section 6.9.4).</p> <p>Dose interruption and dose modification are described in Section 6.6.1.</p>
IRR	<p>In the L-MIND study, tafasitamab IRRs (all G1) were observed in 5 (6%) patients, and all occurred once during the first infusion and no discontinuation of infusion was required.⁶</p> <p>IRR with PF-07901801 has not been prevalent in the ongoing Study C4971001, when administered with premedications (see IB for current data).</p>	<p>Tafasitamab: Premedications to reduce the risk of IRRs are to be administered 30 minutes to 2 hours prior to tafasitamab infusion. For participants not experiencing IRRs during the first 3 infusions, pre-medication is optional for subsequent infusions.</p> <p>PF-07901801: no pre-medications are required (unless required by institutional guidelines or if previous IRR has been experienced).</p> <p>See Table 9 for treatment of IRRs.</p>
Infections	<p>Fatal and serious infections (10%), including opportunistic infections, occurred in patients during treatment with tafasitamab and lenalidomide. Urinary tract infections were common [G3 (4%) and G4 (1%)].⁶</p>	<p>Study intervention(s) may be administered to participants with an active infection only if the infection is treated appropriately and well controlled. Infections at time of screening that require systemic treatment is an exclusion criterion.</p>

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Potential Risk of Clinical Significance	Summary of Data/Rationale for Risk*	Mitigation Strategy
PF-07901801+tafasitamab+ lenalidomide		
	Neutropenia (an overlapping toxicity with PF-07901801 and lenalidomide) may increase risk for infections.	<p>Participants with a history of recurring or chronic infections may be at increased risk of infection and should be monitored appropriately.</p> <p>Participants will be advised to contact their healthcare professionals if fever or other evidence of potential infection, such as chills, cough or pain on urination, develops. Sites may use prophylaxis agents for infections per institutional guidelines (Section 6.9.6).</p> <p>There is no data available in HIV patients. Continue HIV antiretroviral therapy and monitor HIV patients for HIV-related signs and symptoms suggesting viral re-activation. Laboratory monitoring (eg, CD4 counts and HIV viral load) may be required as per standard of care at the institution.</p>
Teratogenicity	Lenalidomide is structurally related to thalidomide. Thalidomide is a known human teratogenic active substance that causes severe life-threatening birth defects. If lenalidomide is taken during pregnancy, a teratogenic effect of lenalidomide in humans is expected.	<p>Follow protocol guidelines for contraception requirements and the PPP set by the manufacturer for lenalidomide. See Section 5.3.1 and Section 10.4.5.</p> <p>Mandatory contraception will be implemented in WOCBP and males (see Section 10.4).</p> <p>In addition, any other PPP or applicable program required per local regulations must be followed.</p>
Venous and arterial thromboembolism	<p>DLBCL is associated with increased venous thromboembolism, particularly in the elderly.²³</p> <p>Lenalidomide has demonstrated a significantly increased risk of DVT and PE, as well as of arterial thromboembolism (predominantly myocardial infarction and cerebrovascular event). In the L-MIND study, 4% of patients experienced G3-4 pulmonary embolism.⁶</p>	<p>Monitor for and advise participants about signs and symptoms of thromboembolism. Advise participants to seek immediate medical care if they develop symptoms such as shortness of breath, chest pain, or arm or leg swelling.</p> <p>Thromboprophylaxis is recommended to be administered per REVLIMID® SmPC and institutional guidelines, tailored to the participant's individual risk/benefit profile by taking into account the individual thrombotic and</p>

Potential Risk of Clinical Significance	Summary of Data/Rationale for Risk*	Mitigation Strategy
PF-07901801+tafasitamab+ lenalidomide		
		bleeding risk or medical history and the quality of compliance with VTE prophylaxis. See Table 8 for dose modifications for lenalidomide.
Allergic reactions and severe skin reactions	Cases of allergic reactions including angioedema, anaphylactic reaction and severe cutaneous reactions including SJS, TEN, and DRESS have been reported in participants treated with lenalidomide. ^{24, 25}	Monitor for and advise participants about signs and symptoms of these severe reactions. Diagnostic procedures may need to be performed as indicated. Advise participants to seek medical attention immediately if they develop symptoms. See Table 8 for dose modifications for lenalidomide and SmPC ²⁰ for further details.
TLS	Patients with high tumor burden and rapidly proliferative tumor may be at increased risk of tumor lysis syndrome. In patients with DLBCL, TLS during treatment with tafasitamab has been observed. TLS is also a known side-effect of lenalidomide (under 1%).	Appropriate monitoring measures/prophylaxis in accordance with local guidelines should be implemented; allopurinol/rasburicase may be administered as per REVLIMID® SmPC ²⁰ or institutional guidelines for tumor lysis prophylaxis or treatment ²⁶ .
Reactivation of Hepatitis B virus	Cases of viral reactivation have been reported in patients receiving lenalidomide, including serious cases of HBV reactivation. See current Prescribing Information for lenalidomide. ²⁰	Hepatitis B virus status must be established before initiating treatment with lenalidomide. Caution must be exercised when lenalidomide is used in participants previously infected with HBV, including participants who are anti-HBcAb positive but HBsAg negative. These participants must be closely monitored for signs and symptoms of active HBV infection throughout therapy.
Reactivation of herpes zoster virus	Cases of viral reactivation have been reported in patients receiving lenalidomide, including serious cases of herpes zoster reactivation. See current Prescribing Information for lenalidomide. ²⁰	Consider temporary hold or permanent discontinuation of the treatment with lenalidomide and adequate antiviral treatment.

* Reference current SRSD for incidence of risks

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2.3.2. Benefit Assessment

By engaging overlapping as well as different mechanisms with the combination of tafasitamab and lenalidomide, PF-07901801 is expected to increase anti-tumor activity in patients with R/R DLBCL. As CD47 predicts poor prognosis for patients' outcome, there is potential for the addition of PF-07901801 to address significant unmet medical needs, particularly in combinations where enhanced clinical effect is expected for improved efficacy outcomes with an anticipated acceptable safety profile.

Patients with R/R DLBCL who are not candidates for ASCT due to age or co-morbidities have limited treatment options and poor prognosis. The combination of tafasitamab and lenalidomide has shown increased response and progression-free survival in patients with R/R DLBCL leading to accelerated and conditional approval. The combination with PF-07901801 has the potential to further enhance clinical benefit with an acceptable and manageable safety profile.

2.3.3. Overall Benefit/Risk Conclusion

Taking into account the potential risks identified combining PF-07901801 with tafasitamab and lenalidomide and the measures to minimize the anticipated risks to study participants this study is justified by the potential benefits in participants with R/R DLBCL.

3. OBJECTIVES, ENDPOINTS, AND ESTIMANDS

Phase 2 of the study will not be initiated per business decision made by Pfizer (protocol amendment 2).

PHASE 1b		
Objectives	Endpoints	Estimands ^a
Primary		
To assess DLTs, safety and tolerability of PF-07901801 in combination with tafasitamab and lenalidomide in adult participants with R/R DLBCL in order to select up to 2 doses of PF-07901801 for further evaluation in Phase 2 of the study.	DLTs during the DLT observation period (28 days following C1D1).	DLT rate estimated based on data from DLT-evaluable participants during the DLT observation period (28 days following C1D1).
Secondary		
To evaluate the overall safety profile of the combination.	<ul style="list-style-type: none"> AEs as characterized by type, frequency, severity (as graded by NCI CTCAE v5.0), timing, seriousness, and relationship to study treatment. Laboratory abnormalities as characterized by type, frequency, severity (as graded by NCI CTCAE v5.0), and timing. 	NA
To evaluate the anti-tumor activity of PF-07901801 in combination with tafasitamab and lenalidomide.	OR, DoR, CR, DoCR, and PFS per Lugano Response Classification Criteria 2014 as assessed by the investigator.	NA
To evaluate the PK of PF-07901801.	Pre- and post-dose concentration of PF-07901801.	NA
To evaluate immunogenicity of PF-07901801.	ADAs and NAbs against PF-07901801.	NA
Tertiary/Exploratory		
To evaluate the PK of tafasitamab and lenalidomide.	Pre-dose concentrations of tafasitamab and lenalidomide.	NA
To evaluate immunogenicity of tafasitamab.	ADAs and NAbs against tafasitamab.	NA
To understand the relationship between the therapeutic intervention(s) being studied and the biology of the participant's disease.	Measurements of biomarkers, which may consist of DNA, RNA, protein or defined cell types, resulting from analyses of peripheral blood, saliva and/or tumor tissue biospecimen obtained at baseline, on treatment and/or at end of study.	NA

a. See details of the estimand in [Section 9.2.1.1](#).

PHASE 2		
Objectives	Endpoints	Estimands ^a
Primary		
To assess the clinical anti-tumor activity of PF-07901801 in combination with tafasitamab and lenalidomide.	OR per Lugano Response Classification Criteria 2014 as assessed by the investigator.	The treatment effect of PF-07901801 in combination with tafasitamab and lenalidomide on OR per the Lugano 2014 response criteria as determined by investigator assessment from the date of first dose until the first documentation of PD, death, or start of new anticancer therapy. Participants who do not have a post-baseline disease assessment due to early PD, who receive anticancer therapies other than the study intervention prior to achieving an objective response, or who die, experience PD, or stop disease assessments for any reason prior to achieving an objective response will be counted as non-responders.
Secondary		
To assess additional efficacy outcomes of PF-07901801 in combination with tafasitamab and lenalidomide.	DoR, CR, DoCR and PFS by investigator per Lugano Response Classification Criteria 2014.	NA
Select the RP3D for PF-07901801 in combination with tafasitamab and lenalidomide.	All endpoints in this study.	NA
To further evaluate the overall safety profile and tolerability of PF-07901801 in combination with tafasitamab and lenalidomide.	<ul style="list-style-type: none"> • AEs as characterized by type, frequency, severity (as graded by NCI CTCAE v5.0), timing, seriousness, and relationship to study treatment. • Laboratory abnormalities as characterized by type, frequency, severity (as graded by NCI CTCAE v5.0), and timing. 	NA
To evaluate the PK of PF-07901801.	Pre- and post-dose concentrations of PF-07901801.	NA
To evaluate immunogenicity of PF-07901801.	ADAs and NAbs against PF-07901801.	NA
Tertiary/Exploratory		
To evaluate the PK of tafasitamab and lenalidomide.	Pre-dose concentrations of tafasitamab and lenalidomide	NA

PHASE 2		
Objectives	Endpoints	Estimands ^a
To evaluate immunogenicity of tafasitamab.	ADAs and NAbs against tafasitamab.	NA
To understand the relationship between the therapeutic intervention(s) being studied and the biology of the participant's disease.	Measurements of biomarkers, which may consist of DNA, RNA, protein or defined cell types, resulting from analyses of peripheral blood, saliva and/or tumor tissue biospecimen obtained at baseline, on treatment and/or at end of study.	NA

a. See details of the estimand in [Section 9.2.1.2](#).

4. STUDY DESIGN

4.1. Overall Design

A business decision was made by Pfizer to terminate the C4971003 study. The reason for study termination is not due to any safety concerns or requests from regulatory authorities. As a result of this decision, Phase 1b will be discontinued after the last participant last visit and Phase 2 of the study will not be initiated.

This is a multicenter, international, Phase 1b/2 study of different doses of PF-07901801 in combination with tafasitamab and lenalidomide in participants with R/R DLBCL who have completed at least 1 line of systemic treatment (at least 1 containing an anti-CD20 therapy), who are not candidates for high dose therapy/ASCT. See [Section 1.2](#) for design schema.

The Phase 1b will be conducted in approximately 20 participants. The objectives of the Phase 1b are to evaluate the safety and tolerability, PK, PD of PF-07901801 in combination with standard doses of tafasitamab and lenalidomide and to select doses for Phase 2.

An escalation/de-escalation approach guided by mTPI-2 will be used in Phase 1b to determine the PF-07901801 MTD or RP2D (2 dose levels) in combination with tafasitamab and lenalidomide, for further evaluation of the fixed doses for efficacy and safety in Phase 2.

A minimum of 2 to 4 DLT-evaluable ([Section 4.3.4](#)) participants is required at each tested dose level of PF-07901801. Approximately 6 to 9 DLT-evaluable participants will be treated at the MTD or highest safe tested dose level for PF-07901801 before proceeding to Phase 2.

Following completion of Phase 1b of the study, if at least 2 doses of PF-07901801 are considered tolerable, 2 doses will be selected for further evaluation in the Phase 2. In Phase 2 of the study, participants must have been exposed to 1 but no more than 2 lines of prior therapies. Approximately 50 participants will be randomized 1:1 into 2 selected doses of PF-07901801 in combination with standard doses of tafasitamab and lenalidomide to further characterize the safety and tolerability of the combination and assess the efficacy of each dose level.²⁷

If only 1 dose of PF-07901801 is considered tolerable after Phase 1b because of safety or other reasons, approximately 25 participants will be treated at the selected fixed dose in the Phase 2 of the study.

Enrollment of participants with prior CAR-T will initially be limited to approximately 3 to 6 participants; after review of all available safety data and determined safe, enrollment of further participants will continue. Post CAR-T participants are to provide local CD19 expression result (if available) and tissue for future central testing (both must be a sample after CAR-T and prior to C1D1).

At the sponsor's discretion proceeding to Phase 2 will be determined upon completion of Phase 1b. The totality of data including efficacy, safety, PK, PD, biomarker, and other considerations will be used to determine the recommended doses for further development in the Phase 2.

For Phase 1b and Phase 2, PF-07901801 and tafasitamab treatment will continue until PD, non-tolerable toxicity or death while lenalidomide will be administered for up to 12 cycles; if a participant with documented PD per Lugano criteria²⁷ continues to experience clinical benefit, study treatment with PF-07901801 and tafasitamab may continue until no longer clinically benefiting as per a risk-benefit assessment by the investigator (see [Section 8.2](#)).

4.2. Scientific Rationale for Study Design

4.2.1. Diversity of Study Population

Although the incidence of DLBCL is higher in Caucasians versus African-Americans (82% vs 7.33%), African-Americans are diagnosed at an average age 10 years younger compared to Whites, are more likely to have more advanced disease at the time of diagnosis, and have a worse overall survival rate.²⁸ To ensure African-Americans are adequately represented in this trial, efforts will be made to include sites that serve African-American communities. In addition, efforts will be made to initiate educational and recruitment campaigns focused on the African-American community if needed.

4.2.2. Dose Level Review Meeting

During the Phase 1 DLT period, a DLR team, composed by sponsor personnel, including at least one medically qualified member, together with the investigators that have enrolled treated study participants in the specific cohort will review cumulative safety data after the last participant in each cohort has been followed for at least 28 days from the first dose of the combination therapy. This review is separate from the ongoing safety assessments routinely performed by the sponsor (Section [9.4.5](#)).

4.2.3. Choice of Contraception/Barrier Requirements

There are no data on the use of tafasitamab in pregnant women. However, IgG is known to cross the placenta and tafasitamab may cause fetal B-cell depletion based on pharmacological properties.

Studies to evaluate the developmental toxicity of PF-07901801 have not been conducted.

Lenalidomide is known to cause risk for severe manifestations of developmental toxicity in humans. Therefore, the use of a highly effective method of contraception is required (see [Appendix 4](#)). The conditions of the PPP for lenalidomide that have been set by the manufacturer ([Section 10.4.5](#)) must be fulfilled for all participants unless there is reliable evidence that the participant does not have childbearing potential. Refer also to the local prescribing information for contraception guidelines for lenalidomide.²⁰

The duration of the contraception required after the last dose of study intervention is 4 weeks for male participants and 90 days for female participants; and contraception should be initiated 4 weeks before the start of study intervention (see [Appendix 4](#) for details).

4.2.4. Collection of Retained Research Samples

Retained Research Samples will be collected and stored for further analyses which may, for example, provide greater understanding of the study intervention.

4.3. Justification for Dose

4.3.1. Dosing Regimens of PF-07901801

Phase 2 of the study will not be initiated per business decision made by Pfizer (protocol amendment 2).

As of 12 December 2021 (Data Safety Update Report cut-off date), in the FIH Study C4971001, PF-07901801 has been administered to 67 participants with advanced R/R lymphoma as monotherapy in 8 different dose-escalation cohorts. Dose cohorts ranging from 0.05 mg/kg to 18 mg/kg (equivalent to 3.75 mg to 1350 mg for a 75 kg person, respectively) QW were well-tolerated with no MTD reached. The combination of PF-07901801 and tafasitamab plus lenalidomide has not previously been evaluated. The proposed starting dose of PF-07901801 (4 mg/kg QW for C1 to C3 then Q2W for C4 and onwards) in combination with full dosing of tafasitamab and lenalidomide is expected to provide limited target engagement for PF-07901801 antitumor activity while it is 4.5 times lower relative to the maximum administered dose of PF-07901801 (18 mg/kg QW) for monotherapy in the FIH Study C4971001. Preliminary analyses showed sustained target engagement at higher dose levels with dose-dependent increase in receptor occupancy durability at the end of dosing interval. For example, receptor occupancy for doses below 4 mg/kg QW decreased to substantially lower levels at the end of the dosing interval, eg, below 10% at 1.0/2.0 mg/kg QW dose level.

In Phase 2 of the current study C4971003, a fixed dosing approach will be used instead of body weight (BWT) based dosing approach used in the FIH study C4971001 based on the following rationales:

- BWT was found not to be a significant covariate on linear and non-linear clearance in the Population PK model.

AUC_{tau} normalized by total dose (mg) provided a lower inter-patient variability (2-31%) compared to the observed AUC_{tau} (23-48%) based on BWT dosing, suggesting a potential lower inter-patient variability in PK with fixed dosing compared to BWT based dosing. Fixed doses to be explored in the Phase 2 will be determined upon completion of Phase 1b. The totality of data including efficacy, safety, PK, PD, biomarkers, and other considerations will be used to determine the recommended doses (Low dose and High dose) for further dose optimization in the Phase 2.

4.3.2. Dosing regimen of Tafasitamab and Lenalidomide

Tafasitamab will be administered at 12 mg/kg IV according to the following schedule; each cycle has 28 days.

- C1: Days 1, 4, 8, 15 and 22.

- C2 and C3 (QW): Days 1, 8, 15 and 22.
- \geq C4 (Q2W): Days 1 and 15.

This is the recommended dosage and dosing schedule in the USPI and EU SmPC of tafasitamab in combination with lenalidomide for the treatment of adult patients with R/R DLBCL, who are not eligible for ASCT.

Lenalidomide will be administered 25 mg PO daily on Days 1 through 21 of each 28-day cycle for up to 12 cycles. This is the dosage regimen used in the L-MIND study, which supported the accelerated and conditional approval of tafasitamab in combination with lenalidomide for the treatment of adult patients with R/R DLBCL NOS, including DLBCL arising from low grade lymphoma, and who are not eligible for ASCT. To reduce PK and safety assessment variability, participants with creatinine clearance <60 mL/min will be excluded in the Phase 1b of the study since lenalidomide exposure and the risk for higher hematological adverse reactions or hepatotoxicity increase in this population.

4.3.3. Criteria for Dose Escalation

The provisional dose levels of PF-07901801 to be evaluated are listed in Table 3.

Table 3. Provisional Dose Levels PF-07901801 in Dose-Escalation

Cohort	Dose (mg/kg)	Increment (%)
1 (DL1)	4 mg/kg QW for C1 to C3 then Q2W	X
2 (DL2)	10 mg/kg QW for C1 to C3 then Q2W	150%
3 (DL3)	18 mg/kg QW for C1 to C3 then Q2W	80%

Additional PF-07901801 doses, dose levels and/or dosing frequency or schedule may be explored. Each cycle is 28 days. QW = Days 1, 8, 15 and 22. Q2W = Days 1 and 15.

The dosing schedule may also be adjusted to expand a dosing cohort to further evaluate safety, PK, and/or PD findings at a given dose level or to add cohorts to evaluate additional dose levels. The study procedures for these additional participant(s)/cohort(s) will be the same as that described for other study participants/cohorts.

If a participant experiences a non-DLT event that requires a dose held per dose-modification guideline additional participants may be enrolled. If DL3 is not tolerated an additional cohort (DL4) may be explored at a dose intermediate to DL2 and DL3.

If after one cohort dose level has been determined safe and the subsequent dose cohort is pending completion of its DLT period, new eligible participants may be enrolled and 'backfilled' into the safe, prior cohort. For these additional participants, their data will contribute to safety and efficacy analyses but they will not participate in the DLT algorithm.

4.3.4. Dose Limiting Toxicity Definition

The DLT observation period will be the first 28-day cycle of treatment in each participant. A DLT is defined as any of the following TEAEs that are considered by the investigator at least possibly related to any or all of the combination study treatments. Note that any AEs for which the relationship to study treatment cannot be ruled out should be considered possibly related. All toxicities that occur during the study will be actively managed following the standard of care per local institutional practice unless otherwise specified in the protocol.

A participant is classified as DLT evaluable if they either 1) receive at least 80% of the planned dose of PF-07901801 and at least 75% of the planned dose of tafasitamab and lenalidomide and have received the majority of scheduled safety assessments during the DLT observation period; or 2) have experienced a DLT. The percentage of drug received is calculated as the percentage of the actual total amount of drug(s) administered during the DLT observation period in relation to the planned total amount of drug(s) to be administered for the DLT observation period.

- A participant failing to meet these criteria may be replaced. If the participant has missed a minority of safety assessments due to emergency situations (eg, site accessibility issues, inability to go to an external lab, etc.), the DLR team may judge the participant evaluable, depending on the abundance of the available data.

For the purpose of dose escalation, any of the treatment-related AEs defined in Section 4.3.4.1, occurring in the first 28 days of treatment that in the opinion of the investigator cannot be reasonably attributed to the participant's underlying disease, concomitant medications or preexisting conditions are considered DLTs.

Severity of AEs will be graded according to CTCAE v5.0. For those events involving a worsening of a baseline abnormality, a DLT must represent a clinically significant (in the opinion of the investigator after discussion with the sponsor) shift from baseline:

4.3.4.1. Hematological DLTs

- G4 thrombocytopenia ($<25,000/\mu\text{L}$) lasting ≥ 72 hours or a platelet count $\leq 10,000/\mu\text{L}$ at any time, unexplained by underlying disease.
- $\geq G3$ thrombocytopenia associated with $\geq G2$ bleeding, unexplained by underlying disease.
- G4 anemia, unexplained by underlying disease.

Prophylactic use of erythropoietin or blood products are not allowed during the DLT period in Phase 1b.

- G4 neutropenia lasting ≥ 7 days, unexplained by underlying disease.
- G3 febrile ($\geq 38.3^\circ\text{C}$) neutropenia lasting ≥ 7 days, unexplained by underlying disease.

- G4 febrile neutropenia unexplained by underlying disease.

Note: Prophylactic use of granulocyte-colony stimulating factors is not permitted during the DLT period of Phase 1b, but they may be used to treat treatment emergent neutropenia as per prescribing information.

4.3.4.2. Non-Hematologic DLTs

- Any treatment-related \geq G3 non-hematologic toxicity (see below for specifications applying to special circumstances) with the following exceptions:
 - G3 nausea, vomiting and diarrhea that improve to G2 or better within 72 hours after supportive care;
 - Transient G3 fatigue lasting \leq 7 days;
 - G3 AEs that recover to baseline or G1 within 3 days;
 - Transient asymptomatic \geq G3 laboratory abnormalities considered not clinically significant following agreement between investigators and the sponsor's medical monitor and starting to recover within 72 hours of their onset with standard supportive care;
 - Hypersensitivity that can be controlled with medical treatment and resolves to asymptomatic (\leq G1) within 72 hours.
- Other \geq G2 PF-07901801-related non-hematologic toxicities that, in the opinion of the investigator, require a dose reduction or discontinuation of PF-07901801 may be considered a DLT.

4.3.5. Maximum Tolerated Dose

MTD is defined as the highest dose with true DLT rate within the EI of the target DLT rate. The target DLT rate is 0.3, the EI is (0.25, 0.35).

4.4. End of Study Definition

The end of the study is defined as the date of the last follow-up visit of the last participant in the global study.

A participant is considered to have completed the study if they have completed all periods of the study, including the last follow-up visit.

5. STUDY POPULATION

This study can fulfill its objectives only if appropriate participants are enrolled, including participants across diverse and representative racial and ethnic backgrounds. A prescreening tool for study recruitment purposes will include collection of information that reflects the enrollment of a diverse participant population including, where permitted under local

regulations, age, sex, and race, and ethnicity. The following eligibility criteria are designed to select participants for whom participation in the study is considered appropriate. All relevant medical and nonmedical conditions should be taken into consideration when deciding whether a particular participant is suitable for this protocol.

Prospective approval of protocol deviations to recruitment and enrollment criteria, also known as protocol waivers or exemptions, is not permitted.

Pfizer will review eligibility criteria verified by the investigator or qualified designee to confirm that participants meet study eligibility criteria before they are randomized into the study. The randomization approval process will be initiated for a participant after an Informed Consent Document has been signed and the investigator or qualified designee has assessed the participant as eligible. The randomization approval will be based on review of CRF/system data.

5.1. Inclusion Criteria

Participants are eligible to be included in the study only if all of the following criteria apply:

Age and Sex:

1. Participants aged 18 years of age or older (or the minimum age of consent in accordance with local regulations) at Screening.
 - Refer to [Appendix 4](#) for reproductive criteria for male ([Section 10.4.1](#)) and female ([Section 10.4.2](#)) participants, and PPP ([Section 10.4.5](#)).

Disease Characteristics:

2. Histologically confirmed, measurable relapsed and/or refractory DLBCL NOS, T cell/histiocyte rich large B-cell lymphoma; or EBV positive DLBCL, according to the 5th edition of the WHO Classification of Lymphoid Neoplasms.²⁹ Further, follicular lymphoma grade 3b, or composite lymphoma with a DLBCL component with a subsequent DLBCL relapse.
 - Participants with evidence of histological transformation to DLBCL from an earlier diagnosis of low grade lymphoma (ie, an indolent pathology such as follicular lymphoma, marginal zone lymphoma, chronic lymphocytic leukemia) are eligible if relapsed or refractory to at least one line of therapy for DLBCL (for primary refractory, see exclusion criterion #2 below).
3. Participant characteristics:
 - Not a candidate per investigator or unwilling to undergo high dose chemotherapy and subsequent autologous stem cell transplant or unable to receive approved CAR-T therapy (eg, logistical limitations).

- Measurable disease: at least 1 site of measurable, PET-avid disease per Lugano 2014 classification (index lesion: >1.5 cm in the longest diameter for nodal, >1.0 cm in the longest diameter for extranodal disease).

4. Prior systemic treatment regimen:

- Must include an anti-CD20 containing regimen:
 - Phase 1b: at least 1 prior line of systemic therapy.
 - Phase 2: at least 1 but no more than 2 prior lines of systemic therapy.

For both phases: induction, ASCT and consolidation will be considered one line of therapy; bridging therapy prior to CAR-T and CAR-T treatment will be considered together as one line of therapy.

- If exposed to prior CD19-targeting CAR-T therapy:
 - Last CAR-T infusion must have been completed >90 days prior to C1D1.
 - Provide CD19 expression test at Screening as per local lab, if available, and must provide a tissue sample for retrospective central testing (see also inclusion criterion #8 and [Section 8.7.8](#)). CD19 positivity is not required.

5. Adequate organ function:

- Hematology (with no transfusion or growth factor support for at least 2 weeks prior to C1D1):
 - ANC $\geq 1,000/\mu\text{L}$.
 - Platelet count $\geq 90,000/\mu\text{L}$.
 - Hemoglobin ≥ 8 g/dL.
- Hepatic function:
 - T bili $\leq 2.0 \times \text{ULN}$. Participants with documented Gilbert's syndrome are eligible for this study providing the direct bilirubin is $\leq \text{ULN}$.
 - ALT and AST $\leq 2.5 \times \text{ULN}$.
- Renal function:
 - Phase 1b: Estimated creatinine clearance ≥ 60 mL/min per local assessment.
 - Phase 2: Estimated creatinine clearance ≥ 30 mL/min per local assessment.

Note for Phase 2: for creatinine clearance ≥ 30 mL/min and < 60 mL/min, lenalidomide is to be started with a reduced dose of 10 mg daily.

6. ECOG performance status ≤ 2 .

Other Inclusion Criteria:

7. Resolution of acute effects of any prior therapy to either baseline severity or CTCAE v5.0 \leq G1 (except for AEs not constituting a safety risk in the investigator's judgment).
8. Participants are able to provide tumor tissue collected before C1D1 (fresh or archival) for biomarker analysis, unless not permitted by local regulations.

5.2. Exclusion Criteria

Participants are excluded from the study if any of the following criteria apply:

Medical Conditions:

1. Prior treatment with anti-CD47 or anti-CD19 (other than CAR-T) or immunomodulatory agents like thalidomide or lenalidomide.
2. Primary refractory DLBCL:
 - Primary refractory definition for this protocol: response less than a PR to first-line therapy or progression during or within 6 months after completion of first line of therapy.
3. High-grade lymphoma (formerly known as 'double' or 'triple hit' DLBCL) or CNS lymphoma (primary or secondary).
 - Simultaneous detection of MYC with BCL2 and/or BCL6 translocation(s) defined by fluorescence in situ hybridization. MYC, BCL2, BCL6 testing prior to study enrollment is not required. FISH testing is required prior to enrollment if historical results are not available.
 - CNS lymphoma involvement – present or past medical history
4. Any history of malignancies other than DLBCL except for:
 - Basal cell or squamous cell carcinoma of the skin or Bowen's disease that has adequately been treated.
 - Any prior malignancies ≥ 3 years before randomization with no subsequent evidence of recurrence or progression without treatment regardless of stage of disease.

- Any prior malignancies in situ, stage 0 – 1 cancer <3 years before randomization that has a remote probability of recurrence or progression per investigator.
5. Prior cancer treatment, radiotherapy within 2 weeks or major surgery within 2 weeks.
 6. Prior allogeneic stem cell transplantation; autologous stem cell transplantation within 12 weeks prior to enrollment.
 7. Significant cardiac/cardiovascular/thromboembolic disease, such as
 - Symptomatic congestive heart failure (New York Heart Association Class III or IV), symptomatic coronary artery disease, myocardial infarction, unstable angina within the last 6 months or known LVEF <40% (as determined by a MUGA scan or Echo)
 - Prolonged QTcF interval >470 msec at screening.
 - History of symptomatic ventricular or supraventricular arrhythmia (intermittent or permanent atrial fibrillation is not an exclusion criterion), inherited arrhythmia, or bradycardia
 - History of deep venous thrombosis or pulmonary embolism. Known, acquired, or hereditary thrombophilia.
 8. Participants with active, uncontrolled bacterial, fungal, or viral infection, including (but not limited to) COVID-19/SARS-CoV-2, HBV, HCV, or AIDS related illness.
 - For Phase 2, HIV: Participants with an undetectable viral load and a CD4 count \geq 400 μ L are eligible (they are not eligible for Phase 1b).
 - Hepatitis B: This criterion excludes participants with a positive HBsAg (ie, either acute or chronic active hepatitis). Participants with positive anti-HBcAb but negative HBsAg and anti-HBsAb profile or viral DNA negative are eligible.³⁰
 - Hepatitis C: Positive HCV Ab is indicative of infection but may not necessarily render a potential candidate ineligible, depending on clinical circumstances. If exposure to HCV is recent, HCV Ab may not have yet turned positive. In these circumstances test for HCV RNA. If HCV RNA is detected the participant is not eligible. Refer to CDC website for further details.³¹
 - COVID-19/SARS-CoV-2: While SARS-CoV-2 testing is not mandated for entry into this study, testing should follow local clinical practice standards. If a participant has a positive test result for SARS-CoV-2 infection, is known to have asymptomatic infection or is suspected of having SARS-CoV-2, the participant is excluded until a negative antigen test and resolution of symptoms if applicable.

9. Gastrointestinal abnormalities including the inability to take oral medication, requiring intravenous alimentation, or prior surgical procedure or condition affecting absorption.
10. Other medical or psychiatric condition including recent (within the past year) or active suicidal ideation/behavior or laboratory abnormality that may increase the risk of study participation or, in the investigator's judgment, make the participant inappropriate for the study.

Prior/Concomitant Therapy:

11. Live attenuated vaccines within 4 weeks prior to randomization and while on trial.
12. Use of corticosteroids except for the following:
 - Intranasal, inhaled, eye drops, topical steroids, or local steroid injection (eg, intraarticular injection).
 - Systemic corticosteroids ≤ 10 mg/day of prednisone or equivalent.

Prior/Concurrent Clinical Study Experience:

13. Participation in other studies involving study intervention within 28 days prior to study entry. A participant may be eligible even if they are in the follow-up phase of an investigational study as long as they haven't received investigational treatment in the study for 28 days.

Other Exclusion Criteria:

14. Investigator site staff directly involved in the conduct of the study and their family members, site staff otherwise supervised by the investigator, and sponsor and sponsor delegate employees directly involved in the conduct of the study and their family members.

5.3. Lifestyle Considerations

5.3.1. Contraception

The investigator or their designee, in consultation with the participant, will confirm that the participant is using an appropriate method of contraception for the individual participant and their partner(s) from the permitted list of contraception methods (see [Section 10.4.4](#)) and will confirm that the participant has been instructed in its consistent and correct use. At time points indicated in the [SoA](#), the investigator or designee will inform the participant of the need to use highly effective contraception consistently and correctly and document the conversation and the participant's affirmation in the participant's chart. Participants need to affirm their consistent and correct use of the selected method(s) of contraception, considering that their risk for pregnancy may have changed since the last visit.

In addition, the investigator or designee will instruct the participant to call immediately if the selected contraception method is discontinued and document the requirement to use an alternate protocol-specified method, including if the participant will no longer use abstinence as the selected contraception method, or if pregnancy is known or suspected in the participant or partner.

5.3.2. Photosensitivity

Photosensitivity has been reported as an adverse drug reaction (uncommon: $\geq 1/1000$ to $< 1/100$) with lenalidomide. Participants will be advised to report any reaction to sun exposed skin. If a photosensitivity reaction occurs in a participant, special precautions should then be taken to limit any potential photo irritation effect, by minimizing the participants' exposure to light including sunlight, and exposure to high intensity UVB light sources such as tanning beds, tanning booths and sunlamps. Furthermore, for photosensitive participants, these individuals should be encouraged to apply sunscreen/sunblock daily and to wear clothing that covers areas of exposed skin when outdoors during daylight hours.

5.4. Screen Failures

Screen failures are defined as participants who consent to participate in the clinical study but are not subsequently enrolled in the study. A minimal set of screen failure information is required to be entered into the CRF to ensure transparent reporting of screen failure participants to meet the CONSORT publishing requirements and to respond to queries from regulatory authorities. Minimal information includes demography, informed consent, Inclusion/Exclusion, screen failure details (disposition), and any S/AE.

Individuals who do not meet the criteria for participation in this study (screen failure) may be rescreened once. These participants will be provided a new SSID. Previously collected samples or exams may be utilized if within the requirements of the SoA (eg, previously collected screening samples were done between -D28 to -D1 or as noted in SoA).

6. STUDY INTERVENTION(S) AND CONCOMITANT THERAPY

Study interventions are all prespecified investigational and auxiliary medicinal products (AxMP), medical devices, and other interventions (eg, surgical and behavioral) intended to be administered to the study participants during the study conduct. For the purposes of this protocol, study intervention refers to PF-07901801, combination drugs tafasitamab and lenalidomide, and auxiliary medicinal products used for PET scan and as pre-medications.

6.1. Study Intervention(s) Administered

Table 4. Study Intervention(s) - IMP

Intervention Name	PF-07901801	Tafasitamab	Lenalidomide
Arm Name (group of participants receiving a specific treatment or no treatment)	Administered to all participants	Administered to all participants	Administered to all participants

Table 4. Study Intervention(s) - IMP

Intervention Name	PF-07901801	Tafasitamab	Lenalidomide
Type	Biologic: CD47 targeting Fc-fusion protein	Biologic: CD19 targeting monoclonal antibody	Drug: IMiD
Dose Formulation	Single-use vials	Single-use vials	Capsules
Unit Dose Strength(s)	10 mg/mL solution for injection; 14 mL/vial	200 mg/vial	2.5 mg, 5 mg, 10 mg, 15 mg, 20 mg, 25 mg
Dosage Level(s)	Section 6.1.1.1	Section 6.1.1.2	Section 6.1.1.3
Route of Administration	IV infusion	IV infusion	PO
Use	Experimental	Experimental when combined with PF-07901801	Experimental when combined with PF-07901801
IMP or NIMP/AxMP	IMP	IMP	IMP
Sourcing	Provided centrally by the sponsor. Refer to IP Manual.	Provided centrally by the sponsor. Refer to IP Manual.	Provided centrally by the sponsor. Refer to IP Manual.
Packaging and Labeling	Carton containing 1 vial. Each vial and carton will be open labeled as required by each country. Additional dosing details will be provided in the IP Manual.	Carton containing 1 vial. Each vial and carton will be open labeled as required by each country. Additional dosing details will be provided in the IP Manual.	Will be provided as blister packs. Each blister pack will be open labeled as required by each country. Additional details will be provided in the IP Manual.
Current/Former Name(s) or Alias(es)	PF-07901801	Tafasitamab	Lenalidomide

Table 5. Study Interventions Classified as NIMPs/AxMPs

Intervention Name	Fludeoxyglucose (¹⁸ F) (FDG)	Paracetamol ^a	Diphenhydramine hydrochloride ^a	Cimetidine ^a	Methylprednisolone ^a .
ARM Name (group of participants receiving a specific treatment)	May be administered to all participants for use with PET scan	May be administered to all participants as premedication ^a	May be administered to all participants as premedication ^a	May be administered to all participants as premedication ^a	May be administered to all participants as premedication ^a
Type	Drug (diagnostic)	Drug	Drug	Drug	Drug
Dose Formulation	As per SmPC	As per SmPC	As per SmPC	As per SmPC	As per SmPC
Unit Dose Strength(s)	As per SmPC	As per SmPC	As per SmPC	As per SmPC	As per SmPC
Dosage Level(s)		See MINJUVI SmPC and institutional guidelines	See MINJUVI SmPC and institutional guidelines	See MINJUVI SmPC and institutional guidelines	See MINJUVI SmPC and institutional guidelines
Route of Administration	IV injection	PO	PO or IV	PO	IV injection or infusion
Use	For use with PET	Premedication	Premedication	Premedication	Premedication
IMP or NIMP/AxMP	AxMP	AxMP	AxMP	AxMP	AxMP
Sourcing	Site Sourced	Site Sourced	Site Sourced	Site Sourced	Site Sourced
Packaging and Labeling	Site Sourced	Site Sourced	Site Sourced	Site Sourced	Site Sourced
Current/Former Name(s) or Alias(es)	Per local site sourcing	Per local site sourcing	Per local site sourcing	Per local site sourcing	Per local site sourcing

a. Premedications that may be given as per MINJUVI SmPC [equivalent premedication(s) includes variations to the stated ones, depending on the formulations available locally and or in accordance with institutional guidelines].

6.1.1. Administration

For this study, a cycle is defined as 28 days, regardless of missed doses or dose interruptions.

Administration of PF-07901801 and tafasitamab may be performed on an outpatient basis. There is a risk of allergic reactions, including anaphylaxis shock, thus these infusions are to be administered in a setting that allows for immediate access to an intensive care unit or equivalent environment and administration of therapy for anaphylaxis, such as the ability to implement immediate resuscitation measures.

PF-07901801 and tafasitamab drug products will be diluted and administered as per the IP Manual.

Body weight for dosing of PF-07901801 (in part 1b of the study) and tafasitamab can be measured up to 72 hours prior to administration on Day 1 of each cycle. This baseline weight will be used to calculate the subsequent dose(s) during the given cycle provided the weight does not deviate more than $\pm 10\%$ from baseline during the course of this cycle. In cases

where the participant's body weight changes more than $\pm 10\%$ from baseline, the current weight will be used to calculate the next and subsequent doses of drug. Using body weight prior to each infusion is also allowed, if this is the investigator's usual standard of care.

Pre-infusion safety laboratory test results must be reviewed prior to dosing, per dosing schedule.

Qualified and trained investigator site personnel will administer PF-07901801 and tafasitamab to participants by IV infusion. During and following each infusion, the participants will be monitored closely for signs and symptoms of an IRR. In case of IRRs or other adverse reactions, consult the recommended dose modifications provided in [Table 9](#).

On days in which PF-07901801 and tafasitamab are administered on the same day, PF-07901801 is administered first.

6.1.1.1. PF-07901801

Phase 1b: The initial dose levels PF-07901801 are as follows:

Cohort 1 (DL1): 4 mg/kg, C1 to C3 QW then \geq C4 Q2W.

Cohort 2 (DL2): 10 mg/kg, C1 to C3 QW then \geq C4 Q2W.

Cohort 3 (DL3): 18 mg/kg, C1 to C3 QW then \geq C4 Q2W.

Phase 2: if at least 2 doses from Phase 1b are considered tolerable, approximately 50 participants will be randomized to one of 2 selected fixed doses based on Phase 1b data. If only 1 dose from Phase 1b is considered tolerable, approximately 25 participants will be treated at that one selected fixed dose.

Premedications are not required for PF-07901801 but may be administered per institutional guidelines at the investigator's discretion and/or if a prior IRR has been experienced.

For at least the first 4 infusions of PF-07901801, the participant is to remain in the clinic for observation for at least 1 hour after the infusion (and this 1 hour must complete prior to starting the subsequent tafasitamab infusion).

6.1.1.2. Tafasitamab

Tafasitamab will be administered 12 mg/kg IV with the following schedule:

- C1: Days 1, 4, 8, 15 and 22.
- C2 and C3 (QW): Days 1, 8, 15 and 22.
- \geq C4 (Q2W): Days 1 and 15.

On days in which PF-07901801 and tafasitamab are administered on the same day, PF-07901801 is administered first.

As per MINJUVI (tafasitamab) SmPC:

- A premedication to reduce the risk of IRRs should be administered 30 minutes to 120 minutes prior to tafasitamab infusion; for participants not experiencing IRRs during the first 3 infusions, premedication is optional for subsequent infusions. The premedication may include paracetamol/acetaminophen, diphenhydramine, cimetidine, or methylprednisolone [or their respective equivalent(s)]. The investigator may repeat doses of individual agents as required and use other agents, doses and/or formulations in accordance with institutional guidelines. Any premedication given should be reported in the eCRF.
- For the first infusion on C1, the intravenous infusion rate should be 70 mL/h for the first 30 minutes. Afterwards, the rate should be increased to complete the first infusion within a 2.5-hour period. All subsequent infusions should be administered within a 1.5 to 2-hour period. In case of IRRs or other adverse reactions, consult the recommended dose modifications provided in [Table 9](#).

For at least the first 3 infusions, the participant is to remain in the clinic for observation for at least 1 hour (or as per institutional guidelines) after the tafasitamab infusion.

6.1.1.3. Lenalidomide

Lenalidomide will be administered according to instructions in the current Revlimid SmPC.²⁰

Starting on C1D1, lenalidomide will be administered 25 mg PO daily on Days 1 through 21 of each 28-day cycle for up to 12 cycles.

On C1D1, C2D1, C3D1, C4D1, the daily dose of lenalidomide is to be taken at the clinic after the blood draw for lenalidomide PK and prior to the PF-07901801 IV infusion (See [SoA](#)).

Lenalidomide is primarily excreted by the kidney; participants with greater degrees of renal impairment can have impaired treatment tolerance. For participants with moderate renal impairment (creatinine clearance ≥ 30 mL/min and < 60 mL/min), lenalidomide will be started (and/or reduced) to 10 mg daily. The dose may be escalated to 15 mg QD after 2 cycles if participant is not responding to treatment and is tolerating the treatment.

Participants may take their oral doses of lenalidomide without regard to food.

For take home study intervention administration (lenalidomide):

Participants must be instructed to take their medication at approximately the same time each day and to not take more than the prescribed dose at any time.

If a participant misses a scheduled dose of study intervention, and it is within 12 hours of the scheduled dose, the participant should immediately administer the missed dose and resume study intervention in accordance with the normal administration schedule. If more than 12 hours have elapsed since the time of scheduled administration, the participant should be

instructed not to administer the missed dose and to resume study intervention as prescribed. Participants should not take 2 doses together to “make up” for a missed dose.

If a participant vomits any time after taking a dose, he/she must be instructed not to “make it up” but to resume subsequent doses the next day as prescribed.

If a participant inadvertently takes 1 extra dose during a day, the participant should not take the next dose of lenalidomide.

A dosing diary will be provided to the participant to aid in compliance with the dosing instructions.

6.2. Preparation, Handling, Storage and Accountability

1. The investigator or designee must confirm appropriate temperature conditions (eg, temperature) have been maintained during transit for all study interventions received and any discrepancies are reported and resolved before use of the study intervention.
2. Only participants enrolled in the study may receive study intervention and only authorized site staff may supply or administer study intervention.
3. All study interventions must be stored in a secure, environmentally controlled, and monitored (manual or automated recording) area in accordance with the labeled storage conditions with access limited to the investigator and authorized site staff. At a minimum, daily minimum and maximum temperatures for all site storage locations must be documented and available upon request. Data for nonworking days must indicate the minimum and maximum temperatures since previously documented for all site storage locations upon return to business.
4. Any excursions from the study intervention label storage conditions should be reported to Pfizer upon discovery along with any actions taken. The site should actively pursue options for returning the study intervention to the storage conditions described in the labeling, as soon as possible. Once an excursion is identified, the study intervention must be quarantined and not used until Pfizer provides permission to use the study intervention. Specific details regarding the definition of an excursion and information the site should report for each excursion will be provided to the site in the IP Manual.
5. Any storage conditions stated in the SRSD will be superseded by the storage conditions stated on the label.
6. Study interventions should be stored in their original containers.
7. Site staff will instruct participants on the proper storage requirements for take home study intervention.

8. See the IP Manual for storage conditions of the study intervention once prepared for administration.
9. The investigator, institution, or the head of the medical institution (where applicable) or authorized site staff is responsible for study intervention accountability, reconciliation, and record maintenance (ie, receipt, reconciliation, and final disposition records), such as the IPAL or Sponsor-approved equivalent. All study interventions will be accounted for using a study intervention accountability form/record.
10. All study interventions provided by the site that is taken home by the participant, both used and unused, must be returned to the investigator by the participant. Returned study intervention must not be re-dispensed to the participants.
11. Further guidance and information for the final disposition of unused study interventions are provided in the IP Manual. All destruction must be adequately documented. If destruction is authorized to take place at the investigator site, the investigator must ensure that the materials are destroyed in compliance with applicable environmental regulations, institutional policy, and any special instructions provided by Pfizer.

Upon identification of a product complaint, notify the Sponsor within 1 business day of discovery as described in the IP Manual.

6.2.1. Preparation and Dispensing

A qualified staff member will dispense the centrally sourced study intervention using the IRT system via unique container numbers in the bottles, vials, or blister cards provided, in quantities appropriate according to the [SoA](#). Refer to IP Manual for dispensation of products. A second staff member will verify the dispensing. The participant/caregiver should be instructed to maintain the product in the bottles, or blister cards, as appropriate provided throughout the course of dosing and return the bottles, or blister cards, as appropriate to the site at the next study visit.

See the IP Manual, for instructions on how to prepare the study intervention for administration. Study intervention should be prepared and dispensed by an appropriately qualified and experienced member of the study staff (eg, physician, nurse, physician's assistant, nurse practitioner, pharmacy assistant/technician, or pharmacist) as allowed by local, state, and institutional guidance. A second staff member will verify the dispensing.

For PF-07901801 and tafasitamab, vials are single use.

6.3. Assignment to Study Intervention

Phase 2 of the study will not be initiated per business decision made by Pfizer (protocol amendment 2).

The study intervention will be assigned using an IRT system. The site will utilize the IRT system to assign the Dispensable Unit or container number(s) prior to the start of study intervention administration for each participant.

This is an open-label study. The investigator's knowledge of the treatment assignment must not influence the decision to enroll a particular participant or affect the order in which participants are enrolled. Potential bias in phase 2 of the study will be reduced by the following steps: central randomization.

Study intervention will be dispensed on the Day 1 Visit of each cycle.

The study specific IRT reference manual and IP Manual will provide the contact information and further details on the use of the IRT system.

6.4. Blinding

This is an open-label study.

6.5. Study Intervention Compliance

When participants are dosed at the site (PF-07901801 and tafasitamab), they will receive study intervention directly from the investigator or designee, under medical supervision. The date and time of each dose administered in the clinic will be recorded in the source documents and recorded in the CRF. The dose of study intervention and study participant identification will be confirmed at the time of dosing by a member of the study site staff other than the person administering the study intervention.

The site will complete the required dosage Preparation Record located in the IP Manual. The use of the Preparation Record is preferred, but it does not preclude the use of an existing appropriate clinical site documentation system. The existing clinical site's documentation system should capture all pertinent/required information on the preparation and administration of the dose. This may be used in place of the Preparation Record after approval from the sponsor and/or designee.

When participants self-administer study lenalidomide at home, compliance with study intervention will be assessed at each visit. Compliance will be assessed by direct questioning, dosing diary (to be maintained while on lenalidomide), and counting returned tablets/capsules during the site visits and documented in the source documents and CRF. Participants will be required to return the completed patient dosing diary for lenalidomide on Day 1 of every cycle through Cycle 12 or EOT for timely review by site personnel and discussion of missed doses and/or compliance issues to ensure accurate data entry for the Dosing CRF.

A record of the number of PF-07901801 vials, tafasitamab vials, and lenalidomide capsules dispensed to and taken by each participant must be maintained and reconciled with study intervention and compliance records. Intervention start and stop dates, including dates for intervention interruptions and/or dose reductions, will also be recorded in the CRF.

6.6. Dose Modification

Criteria for dose modification due to toxicity and efficacy are presented in the following sections. PF-07901801 dose escalation/de-escalation is described in [Section 4.3.3](#).

Every effort should be made to administer study intervention on the planned dose and schedule. In the event of significant toxicity, dosing of PF-07901801 and tafasitamab may be modified as described below. In the event of multiple toxicities, dose modification should be based on the worst toxicity observed and attribution for the combination treatment.

Dosing modifications should be assigned to each product based on attribution to each component (ie, when compound A and B are combined and toxicity occurs and is attributed to compound A, a dose modification of compound A may be applicable but not necessarily to compound B). When toxicity may be attributed to all compounds (eg, neutropenia and thrombocytopenia), all therapies will be interrupted and upon recovery only lenalidomide will be re-started at a lower dose.

Participants are to be instructed to notify investigators at the first occurrence of any adverse symptom. In addition to dose modifications, investigators are encouraged to employ best supportive care according to local institutional clinical practices.

6.6.1. Dose-Modification Guidelines

All dose modifications should be based on the worst preceding toxicity and must be recorded on the CRF. Dose modifications for tafasitamab are further described in MINJUVI (tafasitamab) SmPC; for dose modifications regarding lenalidomide consult the Revlimid® SmPC.^{20,22}

[Table 6](#) through [Table 9](#) provide dose modifications in case of hematologic and non-hematologic toxicities. Permitted dose reductions for lenalidomide are outlined in [Table 10](#). When dosing is withheld based on the following criteria outlined below, clinical and laboratory re-evaluation should be repeated at least weekly or more frequently per institutional guidelines until the toxicity resolves as per toxicity recommendation; see also [Appendix 6](#) (Hy's law). In events where there are transient lab value abnormalities that, based on investigator assessment, are not clinically significant or are related to disease and not the drug, continuation of therapy without following the dose-modification guidelines is permissible.

No specific dose adjustments are recommended for grade 1 or 2 treatment-related toxicity. However, investigators should always manage their participants according to their medical judgment based on the particular clinical circumstances.

Once a lenalidomide dose has been reduced for a given participant, all subsequent cycles will be administered at that dose level, unless further dose reduction is required. Intraparticipant dose re-escalation is not allowed.

Participants in Phase 1b experiencing a DLT may reduce PF-07901801 dosing and resume at the next lower dose level (if applicable) once adequate recovery is achieved, and in the

opinion of the investigator and sponsor, the participant is benefiting from therapy. In Phase 2, PF-07901801 toxicities are managed only with dose interruption (not reduction, unless expressly agreed otherwise following discussion between the investigator and the sponsor).

Appropriate follow-up assessments must be done until adequate recovery occurs as assessed by the investigator. Criteria required before treatment can resume are described in [Section 6.6.2](#).

If the AE that led to the treatment interruption recovers within the same cycle, then re-dosing in that cycle is allowed. Doses omitted for toxicity are not replaced within the same cycle. The need for a lenalidomide dose reduction at the time of treatment resumption should be based on the criteria defined in the tables below, unless expressly agreed otherwise following discussion between the investigator and the sponsor. If a dose reduction of lenalidomide is applied in the same cycle, the participant will need to return to the clinic to receive new drug supply.

Table 6. Dose Modifications for Related Hematologic Toxicities

Criteria	Severity	Dosage modification
Neutropenia ANC <1000/ μ l for at least 7 days or ANC <500/ μ l or ANC <1000/ μ l with a single temperature of >38.3 °C or a sustained temperature of \geq 38 °C for more than one hour	G3/4	Withhold PF-07901801, tafasitamab and lenalidomide and monitor CBC at least weekly until ANC is \geq 1000/ μ l, then: <ul style="list-style-type: none"> • Resume PF-07901801 and tafasitamab at the same dose; • Reduce lenalidomide by one dose level: <ul style="list-style-type: none"> ○ See Section 6.9.4 regarding use of hematopoietic growth factors. ○ Repeat as above for a subsequent event. After second dose reduction of lenalidomide and a subsequent event, discuss with sponsor for further dose modification options.
Thrombocytopenia	G3/4	Withhold PF-07901801, tafasitamab and lenalidomide and monitor CBC at least weekly until platelet count is \geq 50000/ μ l or baseline, then: <ul style="list-style-type: none"> • Resume PF-07901801 and tafasitamab at the same dose; • Reduce lenalidomide by one dose level: <ul style="list-style-type: none"> ○ Repeat as above for a subsequent event. After second dose reduction of lenalidomide and a subsequent event, discuss with sponsor for further dose modification options.
Thrombocytopenia \geq G3 with \geq G2 bleeding	\geq G3	Withhold PF-07901801, tafasitamab and lenalidomide and monitor CBC at least weekly until platelet count is \geq 50000/ μ l or baseline and bleeding has stopped, then: <ul style="list-style-type: none"> • Resume PF-07901801 and tafasitamab at the same dose; • Reduce lenalidomide by one dose level: <ul style="list-style-type: none"> ○ Repeat as above for a subsequent event. After second dose reduction of lenalidomide and a subsequent event, discuss with sponsor for further dose modification options.

Table 6. Dose Modifications for Related Hematologic Toxicities

Criteria	Severity	Dosage modification
Anemia	G3/4	Withhold PF-07901801, tafasitamab and lenalidomide and monitor CBC at least weekly until hemoglobin is ≥ 8 g/dL, then: <ul style="list-style-type: none"> • Resume PF-07901801 and tafasitamab at the same dose; • Reduce lenalidomide by one dose level: <ul style="list-style-type: none"> ○ See Section 6.9.4 regarding use of hematopoietic growth factors. ○ Repeat as above for a subsequent event. After second dose reduction of lenalidomide and a subsequent event, discuss with sponsor for further dose modification options.

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Table 7. Dose Modifications for Non-Hematologic Toxicities

Criteria	Severity	Dosage modification
Non-hematologic laboratory events considered related to study treatment(s)	≥G3	<ul style="list-style-type: none"> Hold suspected therapy(ies) until resolution to ≤G2 or baseline or to a level determined to be acceptable by the investigator. Lenalidomide may be reduced by one dose level. See also SmPCs for MINJUVI (tafasitamab) and REVLIMID (lenalidomide). Transient, asymptomatic, G4 laboratory abnormalities considered not clinically significant may not require a dose reduction following agreement between investigator and the sponsor.
Abnormal liver tests (related or unrelated)	≥G2	<ul style="list-style-type: none"> Participants who present with elevated AST/ALT and bilirubin must be evaluated further as potential DILI (Hy's law) cases to definitively determine the etiology of the abnormal laboratory values; evaluation is to occur as soon as possible, preferably within 48 hours of the abnormal results. See Liver Safety Guidelines for follow-up of possible DILI (Appendix 6).
Abnormal liver tests (related or unrelated)	≥G3	<ul style="list-style-type: none"> Hold suspected therapy(ies) until resolution to ≤G2 or baseline or to a level determined to be acceptable by the investigator. Lenalidomide may be reduced by one dose level. See also SmPCs for MINJUVI (tafasitamab) and REVLIMID (lenalidomide). Participants who present with elevated AST/ALT and bilirubin must be evaluated further as potential DILI (Hy's law) cases to definitively determine the etiology of the abnormal laboratory values; evaluation is to occur as soon as possible, preferably within 48 hours of the abnormal results. See Liver Safety Guidelines for follow-up of possible DILI (Appendix 6).

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Table 7. Dose Modifications for Non-Hematologic Toxicities

Criteria	Severity	Dosage modification
Other Non-hematologic AEs (related)	G3	<ul style="list-style-type: none"> • Hold suspected therapy(ies) until resolution to \leqG1 or baseline or to a level determined to be acceptable by the investigator. • Lenalidomide may be reduced by one dose level. See also SmPCs for MINJUVI (tafasitamab) and REVLIMID (lenalidomide). <p>Exceptions (do not require dose modifications, manage symptoms as per institutional standard of care):</p> <ul style="list-style-type: none"> ○ G3 nausea, vomiting, and diarrhea resolved to \leqG1 or baseline within 48 hours with supportive care; ○ Transient G3 fatigue (lasting <72 hours).
Other Non-hematologic AEs (related)	G4	<ul style="list-style-type: none"> • Consider permanently discontinuing the suspected therapy(ies). In the case where the investigator determines the participant is obtaining a clinical benefit, discuss with sponsor for further dose modification options. • Hold suspect therapy(ies) until resolution to \leqG1 or baseline or to a level determined to be acceptable by the investigator. When resumed after interruption, lenalidomide is to be reduced by one dose level. See also SmPCs for MINJUVI (tafasitamab) and REVLIMID (lenalidomide).

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Table 8. Dose Modifications for Lenalidomide Toxicities

Criteria	Severity	Dosage modification
Thromboembolic events (related)	G3/4	<ul style="list-style-type: none"> Interrupt lenalidomide dosing. Start anticoagulation as per local guidelines. Continue other study interventions after discussion with the sponsor.
	Toxicities resolve to \leq G2	<ul style="list-style-type: none"> Restart lenalidomide at investigator's discretion
Allergic reaction or hypersensitivity (related)	>G2	<ul style="list-style-type: none"> Interrupt lenalidomide dosing. Follow at least every 7 days. Continue other study interventions as per protocol.
	Toxicities resolve to \leq G2	<ul style="list-style-type: none"> Restart lenalidomide at next lower dose level.
Allergic reaction or hypersensitivity (including but not limited to SJS, TEN, exfoliative or bullous rash, angioedema) (related)	G3/4	<ul style="list-style-type: none"> Discontinue lenalidomide permanently. Continue other study interventions after discussion with the sponsor.
Desquamating (blistering) rash \geq G3 or non-desquamating rash G4 considered to be related to lenalidomide		<ul style="list-style-type: none"> Discontinue lenalidomide permanently. Continue other study interventions after discussion with the sponsor.
Non-desquamating rash (related)	G3/4	<ul style="list-style-type: none"> Interrupt lenalidomide dosing. Continue other study interventions after discussion with the sponsor.
	Toxicities resolve to \leq G1	<ul style="list-style-type: none"> Restart lenalidomide at next lower dose level.
Tumor flare reaction (related)	G1/2	<ul style="list-style-type: none"> Provide symptomatic treatment as per local guidelines. Continue lenalidomide without dose modifications or interrupt as per investigator's discretion. Continue other study interventions as per protocol.

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Table 8. Dose Modifications for Lenalidomide Toxicities

Criteria	Severity	Dosage modification
Tumor flare reaction (related)	G3/4	<ul style="list-style-type: none"> Interrupt lenalidomide dosing. Provide symptomatic treatment as per local guidelines. Continue other study interventions after discussion with the sponsor.
	Toxicities resolve to \leq G1	<ul style="list-style-type: none"> Restart lenalidomide (maintain same dose level).
Kidney toxicities as per CTCAE v5.0 (test can be repeated after proper hydration, if needed) (related or unrelated)	G2	<ul style="list-style-type: none"> Reduce lenalidomide to 10 mg once daily.
	G3 not requiring dialysis	<ul style="list-style-type: none"> Administer lenalidomide at 15 mg every other day. Discontinue lenalidomide if dialysis is required.
	G4	<ul style="list-style-type: none"> Discontinue lenalidomide.

Table 9. Dose Modifications for Infusion-Related Reactions

Severity	Dosage modification for PF-07901801 or tafasitamab
G1 to 3	<ul style="list-style-type: none"> If a participant has experienced a G1 to G3 IRR, premedication maybe administered before subsequent infusions with the study intervention that has caused the IRR (as per investigator discretion and institutional guidance).
G2	<ul style="list-style-type: none"> Interrupt infusion immediately and manage signs and symptoms as per institutional guidelines with an antihistamine and/or acetaminophen (paracetamol). If clinically indicated, a glucocorticoid can be used. Once signs and symptoms resolve or reduce to G1, resume infusion at no more than 50% of the rate at which the reaction occurred. If the participant does not experience further reaction within 1 hour and vital signs are stable, the infusion rate may be increased every 30 minutes as tolerated to the rate at which the reaction occurred.
G3	<ul style="list-style-type: none"> Interrupt infusion immediately and manage signs and symptoms. The participant is to receive appropriate treatment as per institutional guidelines with an antihistamine and/or acetaminophen (paracetamol) or a glucocorticoid and, if necessary, further medications (ie, epinephrine, bronchodilator). Once signs and symptoms resolve or reduce to G1, resume infusion at no more than 25% of the rate at which the reaction occurred. If the participant does not experience further reaction within 1 hour and vital signs are stable, the infusion rate may be increased every 30 minutes as tolerated to a maximum of 50% of the rate at which the reaction occurred. If after rechallenge the reaction returns, stop the infusion immediately. If signs and symptoms do not reduce to G1, stop the current infusion. The investigator and Sponsor's medical monitor will decide whether to continue treating participants who experienced a G3 IRR on a case-by-case basis.

Table 9. Dose Modifications for Infusion-Related Reactions

Severity	Dosage modification for PF-07901801 or tafasitamab
	<ul style="list-style-type: none"> As with all potential risks, the medical monitor should be apprised of any \geqG3 IRR that occurs during the study.
G4	Stop the infusion immediately and permanently discontinue tafasitamab and/or PF-07901801. The participant must receive appropriate treatment with an antihistamine and/or acetaminophen (paracetamol) or a glucocorticoid and, if necessary, further medications (ie, epinephrine, bronchodilator).

Table 10. Reductions for Lenalidomide

Starting dose	25 mg
DL1	20 mg
DL2	15 mg
DL3 (starting dose for moderate renal impairment)	10 mg
DL4	5 mg
DL5 ^a	2.5 mg

a. Patients who cannot tolerate DL5 are to be discontinued from lenalidomide treatment in the study but should continue PF-07901801 and tafasitamab.

6.6.2. Re-Treatment After Toxicity

Re-treatment following treatment interruption for treatment-related toxicity or at the start of any new cycle may not occur until all of the following parameters have been met:

- ANC \geq 1000/ μ L;
- Platelet count \geq 50000/ μ L;
- Hemoglobin is \geq 8 g/dL;
- Recovery of treatment-related non-laboratory toxicities to baseline or \leq G1 severity.
- Recovery of treatment-related non-hematologic laboratory toxicities to baseline or \leq G2 severity.

If a treatment interruption results from worsening of hematologic or biochemical parameters, the frequency of relevant blood tests is to be increased as clinically indicated.

6.7. Continued Access to Study Intervention After the End of the Study

No intervention will be provided per protocol to study participants beyond the end of the study. Availability of PF-07901801 following closure of the study (through expanded access/compassionate/continued use mechanism, if the investigator and participant desire to continue treatment) would be at the discretion of the sponsor and subject to local conditions and regulations.

6.8. Treatment of Overdose

There is no specific treatment for an overdose of PF-07901801. The Investigator must take symptom-directed actions with regard to supportive measures. An overdose for this study is defined as exceeding the planned dose by more than 20%.

In the event of an overdose, the investigator should:

1. Contact the study medical monitor within 24 hours.
2. Closely monitor the participant for any AEs/SAEs and laboratory abnormalities as medically appropriate and at least until the next scheduled follow-up.
3. Document the quantity of the excess dose as well as the duration of the overdose in the CRF (in the dosing pages and as medication error).
4. Overdose is reportable to Pfizer Safety only when associated with an SAE.

Refer to the prescribing information for overdose guidance for tafasitamab and lenalidomide.

6.9. Prior and Concomitant Therapy

Hormonal contraceptives that meet the requirements of this study are allowed to be used in participants who are WOCBP (see [Appendix 4](#)).

Concomitant treatment considered necessary for the participant's well-being may be given at discretion of the treating physician.

See [Section 6.9.4](#) regarding limitations on prophylactic use of colony stimulating factors or erythropoiesis-stimulating agents during the DLT period.

All concomitant treatments, blood products, as well as nondrug interventions received by participants from screening until the EOT visit will be recorded on the CRF.

6.9.1. Prohibited Inhibitors/Inducers

6.9.1.1. PF-07901801

PF-07901801 is eliminated via non-specific FcRn-mediated proteolytic degradation and target mediated clearance; therefore, other concomitant medications are unlikely to alter the PK of PF-07901801.

6.9.1.2. Tafasitamab

Investigators should consult the EU SmPC for tafasitamab for information regarding medication that is prohibited for concomitant use during the study.

6.9.1.3. Lenalidomide

Investigators should consult the EU SmPC for lenalidomide for information regarding medication that is prohibited for concomitant use during the study.

6.9.2. Other Prohibited and/or Limited Use of Anti-Tumor/Anti-Cancer or Experimental Drugs or Procedures

No additional anticancer therapy will be permitted while participants are receiving study intervention and prior to documented progression.

6.9.3. Supportive Care

Palliative and supportive care for disease related symptoms may be administered at the investigator's discretion and according to the specific supportive care product Prescribing Information or the current ASCO guidelines.

TLS results from the rapid breakdown of tumor cells and the release of their intracellular content into the bloodstream. The release of large amounts of potassium, phosphorus, and nucleic acids overwhelms normal homeostatic mechanisms, resulting in hyperkalemia, hyperphosphatemia, hyperuricemia, and secondary hypocalcemia. Elevated LDH and elevated AST are potential indicators for TLS. The onset of TLS is rapid, usually within 24 to 48 hours of receipt of the first dose of anticancer medication, but can also occur after the first week of treatment. Left untreated, TLS can lead to acute renal failure, cardiac dysrhythmia, neurologic complications, and seizures. Bulky disease, moderate renal insufficiency, a high number of circulating lymphoma cells and high uric acid levels (>8 mg/dL) prior to therapy, increase the likelihood of TLS. In patients with high risk of TLS (eg, patients with large tumor burden, elevated LDH, or high proliferation rate of tumor cells), TLS prophylaxis is to be considered. All approaches to mitigate the risk of developing TLS, such as adequate hydration or hypouricemic agents (eg, allopurinol or rasburicase), may be used in high risk patients as per institutional guidelines (see also REVLIMID SmPC). Patients should be monitored closely for TLS during treatment with tafasitamab and lenalidomide.

Cytokine release syndrome is not an expected risk with the combination therapies of this study. If suspected, symptoms and severity of CRS will be assessed according to the ASTCT criteria described by Lee et al.²⁸ For CRS management, published treatment guidelines are recommended, but they may be modified as needed by the responsible investigator according to the best practices at their institute.^{32,33}

Infusion related reaction is characterized by fever and chills, and less commonly hypotension, either experienced by a particular participant or if seen in other participants, pretreatment medication should be administered to reduce the incidence and severity. In the event of infusion related reactions, Investigators should institute treatment measures according to best medical and nursing practice. A suggested treatment algorithm for the management of IRR is provided in the [Table 9](#); however, if local standard of care is a different regimen this should be utilized.

Type 1 hypersensitivity or allergic (eg, shortness of breath, urticaria, anaphylaxis, angioedema) reactions are theoretically possible in response to any injected protein. Immune complex mediated Type 3 hypersensitivity reactions are similar to the AEs of Type 1 reactions but are likely to be delayed from the time of infusion and may include symptoms

such as rash, urticaria, polyarthritis, myalgia, polysynovitis, fever, and, if severe, glomerulonephritis.

All participants should be closely observed while receiving study intervention infusions and monitoring for clinical signs of a systemic reaction will continue thereafter for clinical signs of allergic reactions/hypersensitivity.

In the case of a hypersensitivity reaction, the participant will be treated symptomatically with supportive care, further monitoring, and treatment with anti-histamines and/or corticosteroids. Study infusions may be stopped and the participant will be followed until the end of the study.

Hypersensitivity reactions, IRR, TLS, CRS are to be reported as AEs (all grades).

6.9.4. Hematopoietic Growth Factors and Blood Product Transfusions

Participants must have adequate hematological function with no transfusion or colony stimulating factor or erythropoiesis-stimulating agent for at least 2 weeks prior to C1D1 to be eligible to participate in this study.

Primary prophylactic use of colony stimulating factors or erythropoiesis-stimulating agents is not permitted during the first 28 days of Phase 1b C1, ie, DLT observation period.

If hematopoietic growth factors or blood product transfusions are required to manage an AE that did not meet DLT criteria, the DLR team may determine if the AE is a DLT or that the participant is not DLT-evaluable (and may need to be replaced).

6.9.5. Corticosteroids

The use of systemic corticosteroids is generally discouraged because their potential anti-lymphoma activity in patients with DLBCL may confound interpretation of antitumor effects mediated by study drug treatment. However chronic systemic corticosteroids in doses up to 10 mg/day prednisone or equivalent (ie, equipotent corticosteroid) are permitted, provided the dosing is stable (not increased within the last month), but only for the treatment of non-neoplastic comorbid indications (eg, rheumatoid arthritis).

- Chronic systemic corticosteroid use (prednisone >10 mg/day or equivalents) for palliative or supportive purposes is not permitted.
- Acute emergency administration of systemic corticosteroids (\geq equivalent of prednisone 10 mg/day) is discouraged, but permitted if no alternative therapy is available.
- Acute emergency administration of topical applications, inhaled sprays, eye drops, or local injections of corticosteroids are allowed.
- Corticosteroids may be given prior to tafasitamab as per SmPC and when indicated for IRR or toxicity management.

6.9.6. Infection Prophylaxis and Vaccines

Investigators should follow institutional guidelines concerning infection prophylaxis for participants regarded to be at high risk for infection.

Live vaccines must not be administered to participants in this study.

COVID-19 vaccines (approved or given by emergency use authorization, including but not limited to mRNA vaccines, and excluding attenuated virus vaccines) are permitted and should be recorded as concomitant medications in the CRF. All doses of vaccine and type of vaccine administered will be recorded in the CRF. The timing of vaccine administration relative to study intervention is at the discretion of the investigator although, if possible, it is best to avoid vaccine administration within 48 hours before or after the first and second doses of study intervention.

6.9.7. Surgery

Caution is advised for any surgical procedures during the study. The appropriate interval of time between surgery and study treatment required to minimize the risk of impaired wound healing and bleeding has not been determined. Postoperatively, the decision to reinitiate study treatment should be based on a clinical assessment of satisfactory wound healing and recovery from surgery.

6.9.8. Radiotherapy

After the baseline PET/CT scan, radiotherapy is to be discussed with the Sponsor prior to initiation.

7. DISCONTINUATION OF STUDY INTERVENTION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1. Discontinuation of Study Intervention

It may be necessary for a participant to permanently discontinue study intervention. Reasons for permanent discontinuation of study intervention may include the following:

- Objective disease progression;
- Global deterioration of health status requiring discontinuation;
- Unacceptable toxicity;
- Pregnancy;
- Significant protocol violation;
- Lost to follow-up;
- Participant refused further treatment;

- Study terminated by sponsor;
- Death.

Note that discontinuation of study intervention does not represent withdrawal from the study. If study intervention is permanently discontinued, the participant should remain in the study to be evaluated for safety. See the [SoA](#) for data to be collected at the time of discontinuation of study intervention and follow-up for any further evaluations that need to be completed.

In the event of discontinuation of study intervention, it must be documented on the appropriate CRF/in the medical records whether the participant is discontinuing further receipt of study intervention or also from study procedures, posttreatment study follow-up, and/or future collection of additional information.

7.1.1. COVID-19

If a participant has COVID-19 during the study, this must be reported as an AE or SAE (as appropriate) and appropriate medical intervention provided. Temporary discontinuation of the study intervention may be medically appropriate until the participant has recovered from COVID-19. Participants with COVID-19 symptoms or exposed to COVID-19 should be tested and treated as allowed by local regulations.

It is recommended that the investigator discuss temporary or permanent discontinuation of study intervention with the study medical monitor.

7.2. Participant Discontinuation/Withdrawal From the Study

A participant may withdraw from the study at any time at their own request. Reasons for discontinuation from the study may include:

- Withdrawal by participant;
- Lost to follow-up;
- Death;
- Study terminated by sponsor.

If a participant withdraws from the study, they may request destruction of any remaining samples taken and not tested, and the investigator must document any such requests in the site study records and notify the sponsor accordingly.

If the participant withdraws from the study and also withdraws consent (see [Section 7.2.1](#)) for disclosure of future information, no further evaluations will be performed and no additional data will be collected. The sponsor may retain and continue to use any data collected before such withdrawal of consent.

7.2.1. Withdrawal of Consent

Participants who request to discontinue receipt of study intervention will remain in the study and must continue to be followed for protocol-specified follow-up procedures. The only exception to this is when a participant specifically withdraws consent for any further contact with them or persons previously authorized by the participant to provide this information. Participants should notify the investigator in writing of the decision to withdraw consent from future follow-up, whenever possible. The withdrawal of consent should be explained in detail in the medical records by the investigator, as to whether the withdrawal is only from further receipt of study intervention or also from study procedures and/or posttreatment study follow-up, and entered on the appropriate CRF page. In the event that vital status (whether the participant is alive or dead) is being measured, publicly available information should be used to determine vital status only as appropriately directed in accordance with local law.

7.3. Lost to Follow-Up

A participant will be considered lost to follow-up if the participant repeatedly fails to return for scheduled visits and is unable to be contacted by the study site.

The following actions must be taken if a participant fails to attend a required study visit:

- The site must attempt to contact the participant and reschedule the missed visit as soon as possible. Counsel the participant on the importance of maintaining the assigned visit schedule and ascertain whether the participant wishes to and/or should continue in the study.
- Before a participant is deemed lost to follow-up, the investigator or designee must make every effort to regain contact with the participant (where possible, 3 telephone calls and, if necessary, a certified letter to the participant's last known mailing address or local equivalent methods). These contact attempts should be documented in the participant's medical record.
- Should the participant continue to be unreachable, the participant will be considered to have withdrawn from the study.

8. STUDY ASSESSMENTS AND PROCEDURES

8.1. Administrative Procedures

The investigator (or an appropriate delegate at the investigator site) must obtain a signed and dated ICD before performing any study-specific procedures.

Study procedures and their timing are summarized in the [SoA](#). Protocol waivers or exemptions are not allowed.

Adherence to the study design requirements, including those specified in the [SoA](#), is essential and required for study conduct.

All screening evaluations must be completed and reviewed to confirm that potential participants meet all eligibility criteria. The investigator will maintain a screening log to record details of all participants screened and to confirm eligibility or record reasons for screening failure, as applicable.

Procedures conducted as part of the participant's routine clinical management (eg, blood count, scans) and obtained before signing of the ICD may be utilized for screening or baseline purposes provided the procedures met the protocol-specified criteria and were performed within the time frame defined in the [SoA](#).

Every effort must be made to ensure that protocol-required tests and procedures are completed as described. However, it is anticipated that from time to time there may be circumstances outside the control of the investigator that make it unfeasible to perform the test. In these cases, the investigator must take all steps necessary to ensure the safety and well-being of the participant. When a protocol-required test cannot be performed, the investigator will document the reason for the missed test and any corrective and preventive actions that they have taken to ensure that required processes are adhered to as soon as possible. The study team must be informed of these incidents in a timely manner.

For samples being collected and shipped, detailed collection, processing, storage, and shipment instructions and contact information will be provided to the investigator site prior to initiation of the study.

8.1.1. Screening and Baseline Procedures

Demographic data and medical history will be collected at Screening by the investigator or qualified designee, including relevant medical and surgical history, and current illnesses. The medical history of DLBCL, including baseline symptoms as well as a detailed history of prior cancer therapies for DLBCL, with start and stop dates, number of therapy line(s), PD during or after therapy, as well as discontinuations due to intolerability or any other clinically significant illness. Any previous therapy (eg, chemotherapy, immunotherapy, or radiation therapy) for DLBCL should be recorded in the eCRF. Also, examinations leading to the diagnosis of the latest progression of DLBCL should be documented in the participant's source documents. This may include, for example, results of laboratory examinations, imaging results, or clinical symptoms related to DLBCL. The assessment of the lymphoma should include staging.

In order to reflect the participant's status at the time of enrollment, the standard staging system used for DLBCL reflecting the number of sites of involvement and their relation to the diaphragm, the existence of B-symptoms, and the presence of extranodal disease, will be used (see [Appendix 11](#) for Lugano Modification of Ann Arbor Staging). Disease risk as per IPI (see [Appendix 14](#)) and ECOG performance status (see [Appendix 13](#)) will be recorded in the CRF.

8.1.2. Follow-Up Visits and LTFU

At least 28 calendar days, and no more than 35 calendar days after discontinuation of study intervention, participants will return to undergo review of concomitant treatments, vital signs,

and assessment for resolution of any treatment related AEs. Participants continuing to experience AEs at this point following discontinuation of treatment will continue to be followed at least every 4 weeks until resolution or determination, in the clinical judgment of the investigator, that no further improvement is expected.

If the unresolved AE is considered by the investigator as possibly related to or associated with ADA formation, the participant may be asked to return for ADA blood sampling at up to 3 month intervals (if feasible given the underlying disease), until the AE or its sequelae resolve or stabilize at a level acceptable to the investigator and sponsor up to a maximum of 9 months from the last study treatment.

The 90-day post-dose follow-up visit for AEs, contraception check, and subsequent anticancer therapy(ies) may be performed via remote contact (eg, telephone). The investigator may complete these follow-up visits in clinic if any concerns are noted during the remote contact.

Participants discontinued from study interventions before disease progression will enter the LTFU phase and be contacted until disease progression, the start of a new anti-cancer therapy or death, whichever comes first. Participants will be contacted by telephone every 12 weeks from the 90-day follow-up visit (24 weeks from the last dose) to confirm survival status and to collect any new anti-cancer therapies. Onsite visits may be required to conduct follow-up assessments described in the [SoA](#) (Section 1.3), including scans.

8.2. Efficacy Assessments

All disease responses will be assessed according to the Lugano Response Classification Criteria ([Appendix 12](#)), with interpretation according to the 5 point scale.

Pseudo-progression, which has been observed in lymphoma patients on lenalidomide and other immune therapies, will be managed as per refined Lugano criteria 2016 (LYRIC). In cases where pseudo-progression is suspected, when meeting Lugano 2016 criteria for ‘indeterminate response’, the participant may continue to receive study treatment. As per Lugano 2016, a biopsy (if safe and feasible), or a repeat scan within 12 weeks may be indicated ([Appendix 12](#)); for this study, it is recommended that only new lesions (presenting after baseline) are biopsied (to be discussed with sponsor as needed). PD will be entered in the CRF only upon confirmation of PD on subsequent scan. Tumor flare/pseudo-progression will be reported as an AE.

Radiological assessment will be performed at Screening, during treatment as specified in the [SoA](#), whenever PD is suspected (eg, symptomatic deterioration), and at the time of withdrawal from study treatment (if not done in the previous cycle). All scans/assessments, including unplanned scans (or scans in addition to the [SoA](#)) are to be recorded in the CRF.

Radiographic imaging evaluation should include diagnostic quality CT/MRI and FDG PET per Lugano criteria. And the following should be noted:

- Imaging done up to 42 days prior to dosing (before ICD is signed) can be used for screening and as baseline assessment if it is performed per standard of care as per protocol requirements.
- Imaging schedule is to be maintained irrespective of dose delays or interruption.
- Imaging is required at the EOT visit if the participant has withdrawn from treatment for reason other than progression and imaging has not performed in the cycle before the EOT visit.
- If study intervention is discontinued prior to PD, scans are to continue irrespective of other intervening treatment until PD is documented.

All participants' files and radiologic images and pathology samples must be available for source verification and for potential peer review; radiographic images utilized for efficacy assessments may be collected and stored by an independent third party imaging laboratory, (see Imaging Manual for details).

If a participant with documented PD per Lugano criteria²⁷ continues to experience clinical benefit, per investigator's clinical judgment the study treatment with PF-07901801 and tafasitamab may continue until no longer clinically benefiting as per a risk-benefit assessment by the investigator. The first observation of PD, prior to continuation of therapy, will be documented in the CRF and considered the date of PD.

8.2.1. Computed Tomography Scans

CT scans of the chest, abdomen, and pelvis (neck should be included, if appropriate and as clinically indicated) will be performed to assess disease at Screening and per assessment schedule in the [SoA](#). All CT scans should be performed with IV contrast and abdominal and pelvic CT scans should be performed with oral or IV contrast unless contraindicated (see Imaging Manual for details). Hybrid PET-CT scanners may be used to acquire the required CT images only if CT produced by the scanner is of diagnostic quality, adheres to specified scan parameters, and includes IV contrast (unless medically contraindicated). Non-diagnostic CT images acquired for attenuation purposes during PET-CT are NOT acceptable as the only CT scan for the time point. Diagnostic CT images with contrast (unless medically contraindicated) with a standalone CT scanner must be acquired if PET-CT is unable to acquire diagnostic CT images. If the diagnostic CT and PET are acquired on the same day, it is strongly recommended that the PET is performed prior to the CT with IV contrast as to not compromise PET results. MRI or PET/MRI can be used in place of CT if a participant cannot tolerate CT contrast agent or as clinically indicated. The same imaging modality should be used for a given participant throughout the study duration.

8.2.2. Positron Emission Tomography Scans

A PET scan with FDG extending from the neck through the mid thighs will be performed to assess baseline disease at Screening and to assess disease response as per the [SoA](#); in addition to the FDG-PET imaging a diagnostic quality contrast-enhanced CT scan must be included for lesion measurements. Examinations should be consistent across all time points, including amount of tracer, location of injection, arm position, and scan delay. Note that if a participant achieves a metabolic CR, PET scans are not required at subsequent assessments. Additional PET/CT or CT or MRI examinations may be performed by the investigator in the course of the study, if deemed necessary (eg, if PD is suspected, to confirm the occurrence of a CR or to make important treatment-related decisions). If the participant discontinues from study intervention, a PET/CT scan is only required at the EOT if it was not performed in the cycle prior to the EOT. CT may be performed in lieu of PET/CT if the participant discontinues from study intervention within C1.

8.3. Safety Assessments

Planned time points for all safety assessments are provided in [SoA](#). Unscheduled safety measurements may be obtained at any time during the study to assess any perceived safety issues.

8.3.1. Physical Examinations

A complete PE will be performed at Screening and is to include, at a minimum, assessments of the cardiovascular, respiratory, gastrointestinal, and neurological systems. Targeted/symptom-directed PEs, including signs and symptoms of the disease under study, will be conducted at other visits as per the [SoA](#). Height will be collected at baseline and weight will be measured and recorded as per the [SoA](#).

PEs may be conducted by a physician, trained physician's assistant, or nurse practitioner as acceptable according to local regulation.

PE findings collected during the study will be considered source data and will not be required to be reported, unless otherwise noted. Any untoward PE findings that are identified during the active collection period and meet the definition of an AE or SAE ([Appendix 3](#)) must be reported according to the processes in Sections [8.4.1](#) to [8.4.3](#).

When should it be done:

PE is to be performed prior to infusion of study intervention.

8.3.2. Vital Signs

Pre-dose vital signs will be reported on the CRF. All other vital signs collected during the course of the study will be considered source data only and will not be required to be reported on the CRF.

Any untoward vital sign findings that are identified during the active collection period and meet the definition of an AE or SAE ([Appendix 3](#)) must be reported according to the processes in [Section 8.4.1](#) to [Section 8.4.3](#).

8.3.2.1. Blood Pressure and Pulse Rate

BP and PR measurements will be assessed per institutional standards with a completely automated device. Manual techniques will be used only if an automated device is not available.

Vital signs will be taken before blood collection for laboratory tests.

In case of logistical issue, the vitals can be taken after blood collection for laboratory tests after the participant has rested as per standard of care.

Vital signs consist of a single measurement of PR and single BP measurement.

8.3.2.2. Temperature and Respiratory Rate

Temperature and respiratory rate findings collected during the study will be considered source data and will not be required to be reported, unless associated with an AE/SAE or otherwise noted.

8.3.3. Electrocardiograms

Standard 12-lead ECGs utilizing limb leads (with a 10-second rhythm strip) should be collected at times specified in the [SoA](#) section of this protocol using an ECG machine that automatically calculates the heart rate and measures PR interval, QT interval, QTcF, and QRS complex. For ECG machines that do not report QTcF, calculation of QTcF from QT and heart rate, for example using online tools, is required. Alternative lead placement methodology using torso leads (eg, Mason-Likar) should not be used given the potential risk of discrepancies with ECGs acquired using standard limb lead placement. All scheduled ECGs should be performed after the participant has rested quietly for at least 5 minutes in a supine position.

If a) a post-dose QTcF interval remains ≥ 60 ms from the baseline **and** is >450 ms; or b) an absolute QT value is ≥ 500 ms for any scheduled ECG for greater than 4 hours (or sooner, at the discretion of the investigator); or c) QTcF intervals get progressively longer, the participant should undergo continuous ECG monitoring.

A cardiologist should be consulted if QTcF values do not return to less than the criteria listed above after 8 hours of monitoring (or sooner, at the discretion of the investigator).

In some cases, it may be appropriate to repeat abnormal ECGs to rule out improper lead placement as contributing to the ECG abnormality. It is important that leads be placed in the same positions each time in order to achieve precise ECG recordings. If a machine-read QTcF value is prolonged, as defined above, repeat measurements may not be necessary if a

qualified medical provider's interpretation determines that the QTcF values are in the acceptable range.

ECG values of potential clinical concern are listed in [Appendix 8](#).

When should it be done:

ECG assessments should precede blood collection for clinical laboratory tests. In case of logistical issue, ECG can be performed after blood collection for clinical laboratory tests after the participant has rested quietly for at least 5 minutes in a supine position.

8.3.4. Clinical Safety Laboratory Assessments

See [Appendix 2](#) for the list of clinical safety laboratory tests to be performed and the [SoA](#) for the timing and frequency. All protocol-required laboratory assessments, as defined in [Appendix 2](#), must be conducted in accordance with the Laboratory Manual and the [SoA](#). Unscheduled clinical laboratory measurements may be obtained at any time during the study to assess any perceived safety issues and results recorded in the CRF.

The investigator must review the laboratory report prior to the infusions, document this review, and record any clinically significant changes occurring during the study in the AE section of the CRF. Clinically significant abnormal laboratory test findings are those that are not associated with the underlying disease, unless judged by the investigator to be more severe than expected for the participant's condition.

All laboratory tests with values considered clinically significant and abnormal during participation in the study or within 28 calendar days after the last administration of PF-07901801 and/or lenalidomide or 90 days after the last administration of tafasitamab should be repeated until the values return to normal or baseline or are no longer considered clinically significant by the investigator or study medical monitor.

If such values do not return to normal/baseline within a period of time judged reasonable by the investigator, the etiology should be identified and the sponsor notified.

See [Appendix 6](#) for suggested actions and follow-up assessments in the event of potential DILI.

See [Appendix 7](#) for instructions for laboratory testing to monitor kidney function and reporting laboratory test abnormalities.

Screening laboratories may be used as pre-dose baseline if they are within 3 days of C1D1, and therefore there is no need to repeat clinical laboratory assessments on C1D1 in this case. If laboratory values are not within eligibility, blood test may be repeated once.

All safety laboratory results must be available prior to dosing to determine if dose modifications are necessary; may be drawn up to 72 hours prior to dosing visit date.

8.3.4.1. Alternative Facilities for Clinical Safety Laboratory Assessment

Protocol-specified safety laboratory evaluations (refer to [SoA](#)) may be conducted at a local laboratory, during a mobile visit, or at home if permitted by local regulations. The local laboratory may be a standalone institution or within a hospital.

If a local laboratory is used, qualified study site personnel must order, receive, and review results. Site staff must collect the local laboratory reference ranges and certifications/accreditations for filing at the site. Laboratory test results are to be provided to the site staff as soon as possible. The local laboratory reports should be filed in the participant's source documents/medical records. Relevant data from the local laboratory report should be recorded on the CRF.

8.3.5. Pregnancy Testing

Pregnancy tests will be performed in WOCBP at the times listed in the [SoA](#). A serum pregnancy test is required at Screening. Following screening, pregnancy tests may be urine or serum tests, and must have a sensitivity of at least 25 mIU/mL β -HCG. Following a negative pregnancy test result at Screening, appropriate contraception must be commenced and a second negative pregnancy test result will be required at the baseline visit prior to the participant's receiving the study treatment. Pregnancy tests will also be done whenever 1 menstrual cycle is missed during the active treatment period (or when potential pregnancy is otherwise suspected) and at the end of the study. Additional pregnancy tests must be performed per the local lenalidomide label.

Pregnancy tests may also be repeated if requested by IRBs/ECs or if required by local regulations. If a urine test cannot be confirmed as negative (eg, an ambiguous result), a serum pregnancy test is required. In such cases, the participant must be excluded if the serum pregnancy result is positive.

Consult also the lenalidomide PPP ([Section 10.4.5](#)).

8.3.6. B-Symptoms

Assessment of the presence or absence of B-symptoms will be performed at Screening and on Day 1 for all cycles, as well as the EOT.

B-symptoms are defined as the presence of: (a) unintentional weight loss of more than 10% within the previous 6 months, and/or (b) persistent or recurrent fevers of $>38.0^{\circ}\text{C}$ without other evidence of infection, and/or (c) drenching night sweats without evidence of infection.

8.4. Adverse Events, Serious Adverse Events, and Other Safety Reporting

The definitions of an AE and an SAE can be found in [Appendix 3](#).

AEs may arise from symptoms or other complaints reported to the investigator by the participant (or, when appropriate, by a caregiver, surrogate, or the participant's legally authorized representative), or they may arise from clinical findings of the investigator or other healthcare providers (clinical signs, test results, etc).

The investigator and any qualified designees are responsible for detecting, documenting, and recording events that meet the definition of an AE or SAE and remain responsible to pursue and obtain adequate information both to determine the outcome and to assess whether the event meets the criteria for classification as an SAE or caused the participant to discontinue the study intervention (see [Section 7.1](#)).

During the active collection period as described in Section 8.4.1 each participant will be questioned about the occurrence of AEs in a nonleading manner.

In addition, the investigator may be requested by Pfizer Safety to obtain specific follow-up information in an expedited fashion.

8.4.1. Time Period and Frequency for Collecting AE and SAE Information

The time period for actively eliciting and collecting AEs and SAEs (“active collection period”) for each participant begins from the time the participant provides informed consent, which is obtained before undergoing any study-related procedure and/or receiving study intervention, through and including a minimum of 28 calendar days after the last administration of PF-07901801 and/or lenalidomide or 90 days after the last administration of tafasitamab, whichever is longer.

Follow-up by the investigator continues throughout and after the active collection period and until the AE or SAE or its sequelae resolve or stabilize at a level acceptable to the investigator.

When a clinically important AE remains ongoing at the end of the active collection period, follow-up by the investigator continues until the AE or SAE or its sequelae resolve or stabilize at a level acceptable to the investigator and Pfizer concurs with that assessment.

For participants who are screen failures, the active collection period ends when screen failure status is determined.

If the participant withdraws from the study and also withdraws consent for the collection of future information, the active collection period ends when consent is withdrawn.

If a participant permanently discontinues or temporarily discontinues study intervention because of an AE or SAE, the AE or SAE must be recorded on the CRF and the SAE reported using the CT SAE Report Form.

Investigators are not obligated to actively seek information on AEs or SAEs after the participant has concluded study participation. However, if the investigator learns of any SAE, including a death, at any time after a participant has completed the study, and they consider the event to be reasonably related to the study intervention, the investigator must promptly report the SAE to Pfizer using the CT SAE Report Form. In addition, if the investigator learns of any second primary malignancy, irrespective of causality or time of diagnosis, the investigator must promptly report the SAE to Pfizer.

8.4.1.1. Reporting SAEs to Pfizer Safety

All SAEs occurring in a participant during the active collection period as described in Section 8.4.1 are reported to Pfizer Safety on the CT SAE Report Form immediately upon awareness and under no circumstance should this exceed 24 hours, as indicated in [Appendix 3](#). The investigator will submit any updated SAE data to the sponsor within 24 hours of its being available.

If a participant begins a new anticancer therapy, SAEs occurring during the above-indicated active collection period must still be reported to Pfizer Safety irrespective of any intervening treatment. Note that a switch to a commercially available version of the study intervention is considered as a new anticancer therapy for purposes of SAE reporting.

8.4.1.2. Recording Nonserious AEs and SAEs on the CRF

All nonserious AEs and SAEs occurring in a participant during the active collection period which begins after obtaining informed consent as described in [Section 8.4.1](#), will be recorded on the AE section of the CRF.

The investigator is to record on the CRF all directly observed and all spontaneously reported AEs and SAEs reported by the participant.

As part of ongoing safety reviews conducted by the sponsor, any nonserious AE that is determined by the sponsor to be serious will be reported by the sponsor as an SAE. To assist in the determination of case seriousness, further information may be requested from the investigator to provide clarity and understanding of the event in the context of the clinical study.

If a participant begins a new anticancer therapy, the recording period for nonserious AEs ends at the time the new treatment is started; however, SAEs must continue to be recorded on the CRF during the above-indicated active collection period. Note that a switch to a commercially available version of the study intervention is considered as a new anticancer therapy for the purposes of SAE reporting.

8.4.2. Method of Detecting AEs and SAEs

The method of recording, evaluating, and assessing causality of AEs and SAEs and the procedures for completing and transmitting SAE reports are provided in [Appendix 3](#).

Care will be taken not to introduce bias when detecting AEs and/or SAEs. Open-ended and nonleading verbal questioning of the participant is the preferred method to inquire about AE occurrences.

8.4.3. Follow-Up of AEs and SAEs

After the initial AE or SAE report, the investigator is required to proactively follow each participant at subsequent visits/contacts. For each event, the investigator must pursue and obtain adequate information until resolution, stabilization, the event is otherwise explained, or the participant is lost to follow-up (as defined in [Section 7.3](#)).

In general, follow-up information will include a description of the event in sufficient detail to allow for a complete medical assessment of the case and independent determination of possible causality. Any information relevant to the event, such as concomitant medications and illnesses, must be provided. In the case of a participant death, a summary of available autopsy findings must be submitted as soon as possible to Pfizer Safety.

Further information on follow-up procedures is provided in [Appendix 3](#).

8.4.4. Regulatory Reporting Requirements for SAEs

Prompt notification by the investigator to the sponsor of an SAE is essential so that legal obligations and ethical responsibilities toward the safety of participants and the safety of a study intervention under clinical investigation are met.

The sponsor has a legal responsibility to notify both the local regulatory authority and other regulatory agencies about the safety of a study intervention under clinical investigation. The sponsor will comply with country-specific regulatory requirements relating to safety reporting to the regulatory authority, IRBs/ECs, and investigators.

Investigator safety reports must be prepared for SUSARs according to local regulatory requirements and sponsor policy and forwarded to investigators as necessary.

An investigator who receives SUSARs or other specific safety information (eg, summary or listing of SAEs) from the sponsor will review and then file it along with the SRSD(s) for the study and will notify the IRB/EC, if appropriate according to local requirements.

8.4.5. Environmental Exposure, Exposure During Pregnancy or Breastfeeding, and Occupational Exposure

Environmental exposure occurs when a person not enrolled in the study as a participant receives unplanned direct contact with or exposure to the study intervention. Such exposure may or may not lead to the occurrence of an AE or SAE. Persons at risk for environmental exposure include healthcare providers, family members, and others who may be exposed. An environmental exposure may include EDP, EDB, and occupational exposure.

Any such exposure to the study intervention under study are reportable to Pfizer Safety within 24 hours of investigator awareness.

8.4.5.1. Exposure During Pregnancy

An EDP occurs if:

- A female participant is found to be pregnant while receiving or after discontinuing study intervention.
- A male participant who is receiving or has discontinued study intervention inseminates a female partner prior to or around the time of conception.

- A female nonparticipant is found to be pregnant while being exposed or having been exposed to study intervention because of environmental exposure. Below are examples of environmental EDP:
 - A female family member or healthcare provider reports that she is pregnant after having been exposed to the study intervention by ingestion, inhalation, or skin contact.
 - A male family member or healthcare provider who has been exposed to the study intervention by ingestion, inhalation, or skin contact then inseminates his female partner prior to or around the time of conception.

The investigator must report EDP to Pfizer Safety within 24 hours of the investigator's awareness, irrespective of whether an SAE has occurred. The initial information submitted should include the anticipated date of delivery (see below for information related to termination of pregnancy).

- If EDP occurs in a participant/participant's partner, the investigator must report this information to Pfizer Safety on the CT SAE Report Form and an EDP Supplemental Form, regardless of whether an SAE has occurred. Details of the pregnancy will be collected after the start of study intervention and until 45 days after the last dose of PF-07901801 and 90 days after the last dose of tafasitamab or 28 days after the last dose of lenalidomide.
- If EDP occurs in the setting of environmental exposure, the investigator must report information to Pfizer Safety using the CT SAE Report Form and EDP Supplemental Form. Since the exposure information does not pertain to the participant enrolled in the study, the information is not recorded on a CRF; however, a copy of the completed CT SAE Report Form is maintained in the investigator site file.

Follow-up is conducted to obtain general information on the pregnancy and its outcome for all EDP reports with an unknown outcome. The investigator will follow the pregnancy until completion (or until pregnancy termination) and notify Pfizer Safety of the outcome as a follow-up to the initial EDP Supplemental Form. In the case of a live birth, the structural integrity of the neonate can be assessed at the time of birth. In the event of a termination, the reason(s) for termination should be specified and, if clinically possible, the structural integrity of the terminated fetus should be assessed by gross visual inspection (unless pre-procedure test findings are conclusive for a congenital anomaly and the findings are reported).

Abnormal pregnancy outcomes are considered SAEs. If the outcome of the pregnancy meets the criteria for an SAE (ie, ectopic pregnancy, spontaneous abortion, intrauterine fetal demise, neonatal death, or congenital anomaly in a live-born baby, a terminated fetus, or an intrauterine fetal demise, or a neonatal death), the investigator should follow the procedures

for reporting SAEs. Additional information about pregnancy outcomes that are reported to Pfizer Safety as SAEs follows:

- Spontaneous abortion including miscarriage and missed abortion should be reported as an SAE;
- Neonatal deaths that occur within 1 month of birth should be reported, without regard to causality, as SAEs. In addition, infant deaths after 1 month should be reported as SAEs when the investigator assesses the infant death as related or possibly related to exposure to the study intervention.

Additional information regarding the EDP may be requested by the sponsor. Further follow-up of birth outcomes will be handled on a case-by-case basis (eg, follow-up on preterm infants to identify developmental delays). In the case of paternal exposure, the investigator will provide the participant with the Pregnant Partner Release of Information Form to deliver to his partner. The investigator must document in the source documents that the participant was given the Pregnant Partner Release of Information Form to provide to his partner.

8.4.5.2. Exposure During Breastfeeding

An EDB occurs if:

- A female participant is found to be breastfeeding while receiving or after discontinuing study intervention.
- A female nonparticipant is found to be breastfeeding while being exposed or having been exposed to study intervention (ie, environmental exposure). An example of environmental EDB is a female family member or healthcare provider who reports that she is breastfeeding after having been exposed to the study intervention by ingestion, inhalation, or skin contact.

The investigator must report EDB to Pfizer Safety within 24 hours of the investigator's awareness, irrespective of whether an SAE has occurred. The information must be reported using the CT SAE Report Form. When EDB occurs in the setting of environmental exposure, the exposure information does not pertain to the participant enrolled in the study, so the information is not recorded on a CRF. However, a copy of the completed CT SAE Report Form is maintained in the investigator site file.

An EDB report is not created when a Pfizer drug specifically approved for use in breastfeeding women (eg, vitamins) is administered in accordance with authorized use. However, if the infant experiences an SAE associated with such a drug, the SAE is reported together with the EDB.

8.4.5.3. Occupational Exposure

The investigator must report any instance of occupational exposure to Pfizer Safety within 24 hours of the investigator's awareness using the CT SAE Report Form regardless of

whether there is an associated SAE. Since the information about the occupational exposure does not pertain to a participant enrolled in the study, the information is not recorded on a CRF; however, a copy of the completed CT SAE Report Form must be maintained in the investigator site file.

8.4.6. Cardiovascular and Death Events

Not applicable.

8.4.7. Disease-Related Events and/or Disease-Related Outcomes Not Qualifying as AEs or SAEs

Not applicable.

8.4.8. Adverse Events of Special Interest

Not applicable.

8.4.8.1. Lack of Efficacy

The investigator must report signs, symptoms, and/or clinical sequelae resulting from lack of efficacy. Lack of efficacy or failure of expected pharmacological action is reportable to Pfizer Safety **only if associated with an SAE**.

8.4.9. Medical Device Deficiencies

Not applicable.

8.4.10. Medication Errors

Medication errors may result from the administration or consumption of the study intervention(s) by the wrong participant, or at the wrong time, or at the wrong dosage strength.

Medication errors are recorded and reported as follows:

Recorded on the Medication Error Page of the CRF	Recorded on the AE Page of the CRF	Reported on the CT SAE Report Form to Pfizer Safety Within 24 Hours of Awareness
All (regardless of whether associated with an AE)	Any AE or SAE associated with the medication error	Only if associated with an SAE

Medication errors include:

- Medication errors involving participant exposure to the study intervention;

- Potential medication errors or uses outside of what is foreseen in the protocol that do or do not involve the study participant;
- The administration of expired study intervention;
- The administration of an incorrect study intervention;
- The administration of an incorrect dosage ($\pm 20\%$);
- Failure to modify dose as required per protocol for toxicity management (interruption or dose reduction or discontinuation);
- The administration of study intervention that has undergone temperature excursion from the specified storage range, unless it is determined by the sponsor that the study intervention under question is acceptable for use.

Such medication errors occurring to a study participant are to be captured on the medication error page of the CRF, which is a specific version of the AE page.

Whether or not the medication error is accompanied by an AE, as determined by the investigator, the medication error is recorded on the medication error page of the CRF and, if applicable, any associated AE(s), serious and nonserious, are recorded on the AE page of the CRF.

In the event of a medication dosing error, the sponsor should be notified within 24 hours.

Medication errors should be reported to Pfizer Safety within 24 hours on a CT SAE Report Form **only when associated with an SAE**.

8.5. Pharmacokinetics

Blood samples for the PK analysis of PF-07901801, tafasitamab and lenalidomide concentrations will be collected into appropriately labeled tubes at the times specified in the [SoA](#). For each time point, blood samples will be collected for measurement of concentrations of PF-07901801, tafasitamab and lenalidomide, respectively. Instructions for the collection and handling of biological samples are provided in the Laboratory Manual or by the sponsor.

All efforts will be made to obtain the samples at the exact nominal time relative to dosing. Collection of samples within the sampling time window specified in the [SoA](#) will not be captured as a protocol deviation. The actual date and time (24 hour clock time) of PK sample collection as well as the date and time of the last dose prior to PK sample collection for each sample will be recorded in the CRF.

If possible, blood for PK should be drawn from a peripheral vein or from the lumen of a central venous catheter that is not used for infusion of PF-07901801 or tafasitamab.

Samples collected for measurement of study intervention concentrations will be analyzed using validated analytical methods in compliance with applicable SOPs.

Samples collected for analyses of study intervention concentration may also be used to evaluate safety or efficacy aspects related to concerns arising during or after the study or evaluation of the bioanalytical method. These data will be used for internal exploratory purposes and not reported in the CSR.

The PK samples must be processed and shipped as indicated in the instructions provided to the investigator site to maintain sample integrity. Any deviations from the PK sample handling procedure (eg, sample collection and processing steps, interim storage or shipping conditions), including any actions taken, must be documented and reported to the sponsor. On a case by case basis, the sponsor may make a determination as to whether sample integrity has been compromised.

8.6. Genetics

8.6.1. Specified Genetics

Specified genetic analyses (germline DNA sequencing) may be performed to evaluate the relationship between patient outcomes or AEs, and variations at specific genetic loci (such as FCGR genes). However, analysis of genetic predisposition to disease will not be performed in this study and the sequencing methods will not have been validated for diagnostic use.

Please refer to [Section 8.7.5](#) and [Section 8.7.6](#).

8.6.2. Retained Research Samples for Genetics

A 4-mL blood sample optimized for DNA isolation Prep D1 will be collected according to the [SoA](#), as local regulations and IRBs/ECs allow.

Retained Research Samples may be used for research related to the study intervention(s) and DLBCL. Genes and other analytes (eg, proteins, RNA, nondrug metabolites) may be studied using the banked samples.

See [Appendix 5](#) for information regarding genetic research. Details on processes for collection and shipment of these samples can be found in the Laboratory Manual.

8.7. Biomarkers

Unless prohibited by local regulations or ethics committee decision, biospecimens will be collected to analyze DNA, RNA, protein or metabolic biomarkers for achieving study objectives. Specific analyses may not be performed if emerging data indicate that they would no longer support study objectives. Details regarding the types of biospecimen and purposes of collection are listed below. Refer to the [SoA](#) for sample collection time points (note: pre-dose samples are to be collected before any pre-medication or study intervention on indicated visits) and Laboratory Manual for sample collection, processing and shipping.

The following samples for biomarker research are required and will be collected from all participants in this study as specified in the [SoA](#):

- Blood samples at designated timepoints to be processed into serum for circulating biomarker analysis;
- Whole blood samples at designated timepoints for measurement of CD47 receptor occupancy, TCR sequencing, immune cell profiling and specified genetic research;
- Saliva samples at C1D1 as matched control for filtering somatic mutation data and for specified genetic research;
- Blood samples at designated timepoints to be processed into plasma for assessment of cfDNA;
- Baseline pre-treatment tumor tissue samples to enable genetic and biomarker analyses.

Optional samples for biomarker research that should be collected from participants in the study as appropriate are the following:

- Tumor tissue samples collected at relapse/PD or EOT are strongly recommended; tumor tissue samples collected at other disease assessments if clinically indicated. These samples will be used to enable genetic and biomarker analyses.

8.7.1. Blood Sample for Circulating Biomarker Analysis

A blood sample will be collected at time points and processed into serum sample specified in the [SoA](#). This sample may be used for circulating biomarker analysis, which may include protein analysis, nuclei acid analysis and/or other metabolomic analysis.

8.7.2. Blood Sample for CD47 Receptor Occupancy Analysis

A whole blood sample will be collected at time points specified in the [SoA](#). This sample may be used to assess peripheral CD47 receptor occupancy and distribution of various blood cell populations by flow cytometry.

8.7.3. Blood Sample for T-cell Receptor Sequencing

A whole blood sample will be collected at time points specified in the [SoA](#). This sample may be used to assess the clonality, diversity and pharmacodynamics of the peripheral blood TCR repertoire.

8.7.4. Blood Sample for Immune Cell Profiling

A whole blood sample will be collected at time points specified in the [SoA](#). This sample may be used to examine the gene expression and distribution of blood cell populations by molecular sequencing (RNA sequencing analysis and/or DNA sequencing and/or specialized epigenetic phenotyping approaches).

8.7.5. Blood Sample for Specified Genetic Research

A whole blood sample will be collected from all participants on C1D1 at pre-dose. This sample may be used to confirm somatic vs germline origin of alternations in tumor DNA or cfDNA. The sample may also be used to evaluate the relationship between patient outcomes or AEs, and variations at specific loci (such as FCGR genes), or epigenetic modifications of DNA.

8.7.6. Saliva Sample for Matched Control and Specified Genetic Research

Saliva samples will be collected from all participants on C1D1 at predose. This sample may be used to confirm somatic vs germline origin of DNA alterations in tumor DNA or cell-free DNA. The sample may also be used to evaluate the relationship between clinical outcomes or AEs, and variations at specific loci (such as FCGR genes), or epigenetic modifications of DNA.

8.7.7. Blood Sample for Cell-Free DNA (cfDNA) Analysis

A blood sample for cfDNA analyses will be collected at time points and processed into plasma specified in the [SoA](#). This sample may be used to assess genetic changes in cfDNA to evaluate ctDNA burden (as assessed by variant allele fraction) with response to study treatment, potentially explore correlations with tumor molecular profiling and to understand potential mechanisms of acquired resistance to study treatment. A targeted sequencing panel may be used for these analyses. Exploratory whole exome/genome sequencing and/or epigenetic analyses may be performed.

8.7.8. Tumor Tissue for Genetic/Biomarker Analysis

Tumor biospecimens from archival and/or de novo biopsies collected at Screening and/or on-treatment timepoints may be used to analyze candidate nucleic acid and protein biomarkers, or relevant signature of markers, for their ability to identify those participants who are most likely to benefit from treatment with the study drugs. Biomarkers may include, but are not limited to target expression, nucleic acid analyses, as well as cell types and constituents of the tumor microenvironment. RNA and/or DNA sequencing analysis, which may include targeted and/or whole exome/genome sequencing and/or transcriptome and/or epigenetic analyses, may be performed to examine genomic landscape, cell of origin subtyping, correlations between gene mutation status or gene expression signatures and clinical outcome. As samples may be collected while participants are on treatment, these analyses may also define the pharmacodynamics of PF-07901801 and/or combination molecules(s) or identify biomarkers that correlate with and potentially define mechanisms of resistance and relapse.

Tumor biospecimens collected during Screening may be used for evaluation of CD19 expression for the participants with prior CAR-T treatment. In addition, samples from all tested participants may be used to help support development of a potential tumor tissue diagnostic test.

Newly acquired FFPE/NBF tumor tissue obtained at Screening Visit (preferably tumor block; if not, unstained slides are also acceptable) will be submitted for genetic/biomarker analysis.

Archival tissue is acceptable only if tissue at Screening Visit is not available, and the baseline tissue chosen should be the most recently collected specimen before the start of the study therapy and after the most recent systemic therapy.

For central CD19 positivity testing (for participants exposed to prior CD19 CAR-T, see inclusion criterion #4), a tumor block is sufficient for both CD19 test and genetic/biomarker analysis. If slides are provided, additional tumor tissue slides will be required for CD19 expression assessment in addition to what is needed for genetic/biomarker analysis (see laboratory manual for details).

Furthermore, if the participant undergoes tumor biopsy or resection as part of clinical care at any time during the treatment period, every effort should be taken to submit a portion of the tumor tissue for study purposes. Every effort should be made to obtain tumor tissue at relapse/PD/EOT except in instances where the procedure, as performed in the clinical research setting, poses an unacceptable risk to the participant. To limit interference with disease assessments, for on-treatment tumor biopsies that are taken after baseline and prior to EOT, new lesions are to be selected when feasible (providing there is no impact on clinical care).

Only core needle biopsies, excisional biopsies, or resection specimens are suitable. Cytologic preparations, such as fine needle aspirate biopsies, are not acceptable. Tumor biospecimens should be submitted in the form of a FFPE tumor block. If FFPE tissue blocks cannot be provided, the tissue should be submitted as FFPE tissue sections that are freshly cut (preferred to be cut no more than 30 days prior to shipment to the central lab). Additional information on tissue collection procedures and sample requirements can be found in the Laboratory Manual.

8.8. Immunogenicity Assessments

8.8.1. Anti-PF-07901801 Antibody (ADA) and Neutralizing Anti-PF-07901801 Antibody (NAb)

Blood samples will be collected for determination of ADA and NAb for PF-07901801 into appropriately labeled tubes at times specified in the [SoA](#). Instructions for the collection and handling of biological samples will be provided in the Laboratory Manual. The actual date and time (24-hour clock time) of each sample will be recorded.

Samples collected for determination of ADA and NAb will be analyzed using a validated analytical method in compliance with applicable SOPs. Samples determined to be positive for ADA may be further characterized for NAb.

Samples may also be used for additional characterization of the immune response and/or evaluation of the bioanalytical method, or for other internal exploratory purposes. These data will be used for internal exploratory purposes and not reported in the CSR.

The immunogenicity samples must be processed and shipped as indicated in the instructions provided to the investigator site to maintain sample integrity. Any deviations from the immunogenicity sample handling procedure (eg, sample collection and processing steps,

interim storage, or shipping conditions), including any actions taken, must be documented and reported to the sponsor. On a case by case basis, the sponsor may make a determination as to whether sample integrity has been compromised.

8.8.2. Anti-Tafasitamab Antibody (ADA) and Neutralizing Anti-Tafasitamab Antibody (NAb)

Blood samples will be collected for determination of ADA and NAb for tafasitamab into appropriately labeled tubes at times specified in the [SoA](#). Instructions for the collection and handling of biological samples will be provided in the Laboratory Manual. The actual date and time (24-hour clock time) of each sample will be recorded.

Samples collected for determination of ADA and NAb will be analyzed using a validated analytical method in compliance with applicable SOPs. Samples determined to be positive for ADA may be further characterized for NAb.

Samples may also be used for additional characterization of the immune response and/or evaluation of the bioanalytical method, or for other internal exploratory purposes. These data will be used for internal exploratory purposes and not reported in the CSR.

The immunogenicity samples must be processed and shipped as indicated in the instructions provided to the investigator site to maintain sample integrity. Any deviations from the immunogenicity sample handling procedure (eg, sample collection and processing steps, interim storage, or shipping conditions), including any actions taken, must be documented and reported to the Sponsor. On a case by case basis, the Sponsor may make a determination as to whether sample integrity has been compromised.

8.9. Pharmacodynamics

Biomarker samples may be used for exploratory pharmacodynamics analyses (see [Section 8.7](#)).

As part of understanding the pharmacodynamics of the investigational products, samples may be used for evaluation of the bioanalytical method, as well as for other internal exploratory purposes. These data may not be included in the CSR.

The pharmacodynamic samples must be processed and shipped as indicated in the instructions provided to the investigator site to maintain sample integrity. Any deviations from the pharmacodynamic sample handling procedures (eg, sample collection and processing steps, interim storage or shipping conditions), including any actions taken, must be documented and reported to the sponsor. On a case-by-case basis, the sponsor may decide whether sample integrity has been compromised.

9. STATISTICAL CONSIDERATIONS

Detailed methodology for summary and statistical analyses of the data collected in this study is outlined here and further detailed in the SAP, which will be maintained by the sponsor. The SAP may modify what is outlined in the protocol where appropriate; however, any major

modifications of the primary endpoint definitions or their analyses will also be reflected in a protocol amendment.

Per protocol amendment, Phase 2 of the study will not be initiated therefore the Phase 2 endpoints will not be analyzed (protocol amendment 2).

9.1. Health Economics

Health economics/medical resource utilization and health economics parameters are not evaluated in this study.

9.2. Statistical Hypothesis

There is no formal hypothesis testing for the study.

9.2.1. Primary Estimands

9.2.1.1. Phase 1b Primary Estimand

Primary Estimand: DLT rate estimated based on data from DLT-evaluable participants during the DLT observation period (28 days following C1D1). The estimand has the following attributes:

- Population: DLT-evaluable participants with R/R DLBCL, as defined by the inclusion and exclusion criteria to reflect the targeted population of the treatment, who receive at least 1 dose of the study intervention in the Phase 1b of the study and either experience DLT(s) during the DLT observation period or complete the DLT observation period without DLT. Participants without DLTs who receive less than 80% of the planned dose of PF-07901801 or less than 75% of the planned dose of any component of the tafasitamab and lenalidomide regimen in the DLT observation period are not evaluable for DLTs.
- Variable: Occurrence of DLTs during the DLT observation period.
- Intercurrent event: The data from participants who are not DLT-evaluable will be excluded. Participants without DLTs who stopped treatment before receiving at least 80% of the planned dose of PF-07901801 and at least 75% of the planned dose of any component of the tafasitamab and lenalidomide regimen will be excluded.
- Population-level summary measure: DLT rate defined as the number of DLT-evaluable participants with DLTs in the DLT observation period divided by the number of DLT-evaluable participants.

9.2.1.2. Phase 2 Primary Estimand

Primary Estimand: The treatment effect of PF-07901801 in combination with tafasitamab and lenalidomide on OR per the Lugano 2014 response criteria as determined by investigator assessment. The estimand has the following attributes:

- Population: R/R DLBCL participants, as defined by the inclusion and exclusion criteria to reflect the targeted population of the treatment, who received at least 1 dose of study intervention.
- Variable: Objective response defined as CR or PR per Lugano 2014 response criteria as determined by investigator, from the date of first dose until the first documentation of PD, death, or start of new anticancer therapy.
- Intercurrent events: All data collected after an intercurrent event of subsequent anticancer therapy will be excluded. All response assessments regardless of gaps in disease assessments will be considered. Participants who do not have a post-baseline disease assessment due to early PD, who receive anticancer therapies other than the study intervention prior to achieving an objective response, or who die, experience PD, or stop disease assessments for any reason prior to achieving an objective response will be counted as non-responders.
- Population-level summary measure: ORR defined as the proportion of participants in the analysis population with an objective response, and 2-sided 95% CI for ORR using the Wilson method. Results will be displayed by treatment group.

9.3. Analysis Sets

For purposes of analysis, the following analysis sets are defined.

Participant Analysis Set	Description
DLT Evaluable Set	All enrolled participants who receive at least 1 dose of the study intervention in the Phase 1b of the study and either experience DLT(s) or complete the DLT observation period without DLT. Participants without DLTs who receive less than 80% of the planned dose of PF-07901801 or less than 75% of the planned dose of any component of the tafasitamab and lenalidomide regimen in the DLT observation period are not evaluable for DLTs. The DLT observation period is 28 days following C1D1.
Safety Analysis Set	All enrolled participants who received at least 1 dose of study intervention.
PK Analysis Set	The PK analysis set will include all participants in the safety analysis set who have at least 1 post-dose concentration measurement. The PK parameter analysis set will include all participants in the safety analysis set who have at least one of the PK parameters of interest for PF-07901801.

Participant Analysis Set	Description
Immunogenicity Analysis Set	All participants in the safety analysis set who have at least 1 sample tested for ADA.
Biomarker Analysis Set	All participants in the safety analysis set who have at least 1 baseline biomarker assessment. Analysis sets will be defined separately for biomarkers based on blood, saliva, and tumor tissue samples.

“Enrolled” means a participant's, or their legally authorized representative's, agreement to participate in a clinical study following completion of the informed consent process and assignment to study intervention.

9.4. Statistical Analyses

The SAP will be developed and finalized before any analyses are performed and will describe the analyses and procedures for accounting for missing, unused, and spurious data. This section is a summary of the planned statistical analyses of the primary and secondary endpoints.

9.4.1. General Considerations

All analyses will be performed for the Phase 1b and Phase 2 of the study separately. All efficacy analyses and safety analyses will be performed using the Safety Analysis Set (if not otherwise specified).

In general, descriptive summaries will be presented for the efficacy and safety variables collected. Continuous variables will be summarized using mean, SD, minimum, median, and maximum. Categorical variables will be summarized using frequency counts and percentages.

Unless otherwise specified, the calculation of proportions will be based on the sample size of the population of interest. Counts of missing observations will be included in the denominator and presented as a separate category if not otherwise specified in the SAP.

9.4.2. Primary Endpoints/Analysis

9.4.2.1. Phase 1b

The primary endpoint of the Phase 1b of the study is the DLTs during the DLT observation period. The number and proportion of participants experiencing DLTs during the DLT observation period will be summarized and listed by dose level. Analyses of DLTs will be performed on DLT Evaluable Set (as defined in [Section 9.3](#)).

9.4.2.2. Phase 2

The primary endpoint in the Phase 2 of the study is OR per Lugano Response Classification Criteria 2014 as assessed by the investigator.

OR is defined as a BOR of CR or PR according to Lugano Response Classification Criteria 2014.

Treated participants who do not have a post-baseline tumor assessment due to early clinical progression of disease, who receive anti-cancer therapies other than the study interventions prior to reaching a CR or PR, or who die, have documented PD, or stop tumor assessments for any reason prior to reaching a CR or PR will be counted as non-responders in the assessment of OR. OR rate is the proportion of participants with OR in the safety analysis set. ORR will be calculated along with the 2-sided 95% CI using the Wilson method.

9.4.3. Secondary Endpoints/Analysis

9.4.3.1. Efficacy Analyses

Complete Response

CR rate is defined as the proportion of participants in the Safety Analysis Set with a CR per Lugano Response Classification Criteria 2014 as assessed by the investigator.

Point estimates of CRR will be calculated along with the 2-sided exact 95% CIs using the Wilson method.

CRR will be summarized by dose levels for Phase 1b and Phase 2 of the study separately.

Duration of Response

DoR is defined, for participants with an objective response per Lugano Response Classification Criteria 2014, as the time from the first documentation of objective response until PD, or death due to any cause, whichever occurs first.

DoR will be censored on the date of the last adequate disease assessment for participants who do not have an event (PD or death due to any cause), on the date of the last adequate disease assessment before the new anti-cancer therapy for participants who start a new anti-cancer therapy prior to an event, or on the date of the last adequate disease assessment before the 2 or more missing disease assessments for participants with an event after 2 or more missing disease assessments.

DoR will be summarized using Kaplan Meier method and displayed graphically. Median DoR and 2-sided 95% CI (based on the Brookmeyer-Crowley method) will be provided.

DoR will be summarized by dose levels for Phase 1b and Phase 2 of the study separately.

Duration of Complete Response

DoCR is defined, for participants with a CR per Lugano Response Classification Criteria 2014, as the time from the first documentation of a CR until PD, or death due to any cause, whichever occurs first.

DoCR will be censored on the date of the last adequate disease assessment for participants who do not have an event (PD or death due to any cause), on the date of the last adequate disease assessment before the new anti-cancer therapy for participants who start a new

anti-cancer therapy prior to an event, or on the date of the last adequate disease assessment before the 2 or more missing disease assessments for participants with an event after 2 or more missing disease assessments.

DoCR will be summarized using Kaplan Meier method and displayed graphically. Median DoCR and 2-sided 95% CI will be provided.

DoCR will be summarized by dose levels for Phase 1b and Phase 2 of the study separately.

Progression Free Survival

PFS is defined as the time from the date of first dose until PD per Lugano Response Classification Criteria 2014, or death due to any cause, whichever occurs first.

PFS will be censored as follows:

- For participants who do not have an event (PD per Lugano Response Classification Criteria 2014 or death due to any cause), censoring will occur on the date of the last adequate disease assessment;
- For participants who start a new anticancer therapy prior to an event, censoring will occur on the date of the last adequate disease assessment before the new anticancer therapy;
- For participants with an event after a gap of 2 or more missing disease assessments, censoring will occur on the date of the last adequate disease assessment before the gap;
- Participants who do not have an adequate post-baseline disease assessment will be censored on the date of first dose of study intervention unless death occurs on or before the time of the second planned disease assessment (ie, ≤ 24 weeks after the date of first dose) in which case the death will be considered an event.

PFS will be summarized using Kaplan Meier method and displayed graphically. Median PFS and 2-sided 95% CI will be provided.

PFS will be summarized by dose levels for Phase 1b and Phase 2 of the study separately.

9.4.3.2. Safety Analyses

9.4.3.2.1. Adverse Events

AEs will be graded by the investigator according to the CTCAE v5.0 and coded using MedDRA. AE data will be reported in tables and listings. Summaries of AE by appropriate MedDRA terms, toxicity grade, and seriousness and relationship to study treatment will be presented by dose levels, as well as summaries of AEs leading to death and premature withdrawal from study treatment. The number and percentage of participants who experienced any AE, SAE, treatment related AE, and treatment related SAE will be

summarized according to worst toxicity grades. The summaries will present AEs on the entire study period.

9.4.3.2.2. Laboratory Test Abnormalities

The laboratory results will be graded according to the NCI CTCAE v5.0 severity grade and will be analyzed using summary statistics. The worst on-treatment grades during the treatment period will be summarized. Shifts in toxicity grading from baseline to highest grade during the on-treatment period will be displayed for each laboratory test. The analyses will summarize laboratory tests on the entire study period.

For laboratory tests without NCI CTCAE grade definitions, results will be categorized as normal, abnormal, or not done. Only participants with post-baseline laboratory values will be included in these analyses. Further details of analyses for all the laboratory parameters will be provided in the SAP.

9.4.3.3. Pharmacokinetic Analyses for PF-07901801

PK data analyses will include descriptive summary statistics of the pre-dose and EOI PF-07901801 concentrations by study visit, time points, and dose levels. In addition, the PK data from this study may be used to develop a population PK model and may also be pooled with other studies for population PK model development. The correlations between PF-07901801 exposure parameters and pharmacodynamic biomarker, efficacy and/or safety outcomes will be explored if data allows. The results of these modeling analyses will be reported separately from the clinical study report.

The potential DDI between PF-07901801, tafasitamab, and/or lenalidomide may also be evaluated if data allows.

9.4.3.4. Immunogenicity Analyses for PF-07901801

For immunogenicity data, the percentage of participants with positive ADA will be summarized. Listings and summary tabulations of the ADA data at baseline and post-first dose will be generated. Samples may also be analyzed for the presence of NAb, and any data will be similarly summarized. For participants with positive ADA or NAb, the magnitude (titer), time of onset, and duration of ADA or NAb response will also be described, if data permit. The potential impact of immunogenicity on PK and clinical response including pharmacodynamic markers, safety/tolerability and efficacy may be explored, if warranted by the data.

9.4.4. Tertiary/Exploratory Endpoint(s) Analysis

Results of exploratory endpoint analyses may be described in the CSR to the extent possible. Due to the exploratory nature of the endpoints, the associated data analyses may not be completed at the time of the CSR preparation. If results of exploratory endpoint analyses cannot be included in the CSR, they may be disseminated to the scientific community to the extent possible through presentation at scientific meetings and/or publication in peer-reviewed scientific journals.

9.4.5. Other Safety Analyses

The Safety Analysis Set will be the primary population for safety evaluation.

AEs, ECGs, and safety laboratory data will be reviewed and summarized by the sponsor on an ongoing basis during the study to evaluate the safety of participants. Any clinical laboratory, ECG, BP, and PR abnormalities of potential clinical concern will be described. Safety data will be presented in tabular and/or graphical format and summarized descriptively, where appropriate.

Medical history and physical examination collected during the course of the study will be considered source data and will not be required to be reported, unless otherwise noted. However, any untoward findings identified on physical and/or neurological examinations conducted during the active collection period will be captured as AEs, if those findings meet the definition of an AE. Data collected at Screening that are used for inclusion/exclusion criteria, such as ECGs, and vital signs, will be considered source data, and will not be required to be reported, unless otherwise noted. Demographic data collected at Screening will be reported.

9.4.5.1. Electrocardiogram Analyses

Changes from baseline for the ECG parameters QT interval, heart rate, QTcF interval, PR interval, and QRS complex will be summarized by dose level and time.

The number (%) of participants with maximum post-dose QTcF values and maximum increases from baseline in the following categories will be tabulated by treatment:

Safety QTcF Assessment

Degree of Prolongation	Mild (ms)	Moderate (ms)	Severe (ms)
Absolute value	>450-480	>480-500	>500
Increase from baseline		30-60	>60

9.4.6. Other Analyses

Pharmacogenomic or biomarker data from Retained Research Samples may be collected during or after the trial and retained for future analyses; the results of such analyses are not planned to be included in the CSR.

9.5. Interim Analyses

No formal interim analysis will be conducted for this study. As this is an open-label study, the sponsor may conduct unblinded reviews of the data during the course of the study for the purpose of safety assessment, and/or supporting clinical development.

9.6. Sample Size Determination

Phase 2 of the study will not be initiated per business decision made by Pfizer (protocol amendment 2).

Phase 1b:

The primary objective in the Phase 1b of the study is to assess DLTs, safety and tolerability of PF-07901801 in combination with tafasitamab and lenalidomide in order to select up to 2 fixed doses of PF-07901801 to explore in Phase 2. The target number of participants per cohort is 2-4, and a minimum of 2-4 DLT-evaluable participants is required at each tested dose level of PF-07901801. Approximately 6 to 9 DLT-evaluable participants will be treated at the MTD or highest safe tested dose level for PF-07901801 before proceeding to Phase 2. The actual number of participants to be enrolled will depend on the number of dose levels evaluated and the number of participants treated at each dose level. It is estimated that approximately 20 participants will be enrolled in Phase 1b.

If any participant is deemed non-evaluable for DLT, additional participants may be enrolled to ensure there are a sufficient number of evaluable participants in the Phase 1b.

Phase 2:

Up to 2 fixed doses will be selected based on Phase 1b data for further evaluation in Phase 2 of the study. Approximately 25 participants will be treated for each selected dose. The sample size is not determined based on statistical hypothesis testing considerations; rather, it is based on clinical considerations that the stated sample size will provide sufficient evidence of preliminary antitumor activity of PF-07901801 in combination with tafasitamab and lenalidomide, and for dose selection based on exposure-response analyses.

ORR can be estimated with a maximum standard error of 10% with 25 participants per arm.

[Table 11](#) provides the 95% CIs for ORR based on Wilson method for different observed responses.

Table 11. Sample Size and 95% CI for ORR based on Wilson Method (with Continuity Correction)

N = 25	Number of responses	Observed ORR	95% CI for ORR
	1	0.04	0.002, 0.223
	2	0.08	0.014, 0.275
	3	0.12	0.032, 0.323
	4	0.16	0.053, 0.369
	5	0.2	0.076, 0.413
	6	0.24	0.102, 0.455
	7	0.28	0.129, 0.496
	8	0.32	0.157, 0.536
	9	0.36	0.187, 0.574
	10	0.4	0.218, 0.611
	11	0.44	0.250, 0.647
	12	0.48	0.283, 0.682
	13	0.52	0.318, 0.717
	14	0.56	0.353, 0.750
	15	0.6	0.389, 0.782
	16	0.64	0.426, 0.813
	18	0.72	0.504, 0.871
	20	0.8	0.587, 0.924
	22	0.88	0.677, 0.968

9.7. Statistical Methods and Decision Criteria

The mTPI-2 design (with target $p_T=0.3$, $e_1=0.05$, $e_2=0.05$) will be utilized for dose finding of the combination therapy, with the dose level of tafasitamab and lenalidomide fixed. The mTPI-2 design uses a Bayesian statistics framework and a beta binomial hierarchical model to compute the UPM of dosing intervals. The dose interval that has the largest UPM is selected as the winning model. The dose de-escalation/escalation recommendation is as shown below:

- If intervals $\{(0.15, 0.25), (0.05, 0.15), (0, 0.05)\}$ exhibit the largest UPM: escalate to next higher dose;
- If interval $(0.25, 0.35)$ exhibits the largest UPM: stay at current dose;
- If intervals $\{(0.35, 0.45), (0.45, 0.55), (0.55, 0.65), (0.65, 0.75), (0.75, 0.85), (0.85, 0.95), (0.95, 1)\}$ exhibit the largest UPM: de-escalate to a lower dose.

The decision rules for mTPI-2 design (target $p_T=0.3$, $e_1=0.05$, $e_2=0.05$) are listed in [Table 12](#).

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Table 12. mTPI-2 Decision Rules (pT=0.3, e1=0.05, e2=0.05)

		Number of Patients														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Number of Patients with DLTs	0	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E
	1	D	D	S	S	E	E	E	E	E	E	E	E	E	E	E
	2		DU	D	D	D	S	S	S	E	E	E	E	E	E	E
	3			DU	DU	D	D	D	D	S	S	S	S	E	E	E
	4				DU	DU	DU	D	D	D	D	D	S	S	S	S
	5					DU	DU	DU	DU	DU	D	D	D	D	D	S
	6						DU	DU	DU	DU	DU	DU	D	D	D	D
	7							DU	DU	DU	DU	DU	DU	DU	D	D
	8								DU	DU	DU	DU	DU	DU	DU	DU
	9									DU	DU	DU	DU	DU	DU	DU
	10										DU	DU	DU	DU	DU	DU
	11											DU	DU	DU	DU	DU
	12												DU	DU	DU	DU
	13													DU	DU	DU
	14														DU	DU
	15															DU

E = Escalate to the next higher dose level
 S = Stay at the current dose level
 D = De-escalate to the next lower dose level
 DU = The current dose level is unacceptably toxic and should be eliminated from further dose finding

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10. SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1. Appendix 1: Regulatory, Ethical, and Study Oversight Considerations

10.1.1. Regulatory and Ethical Considerations

This study will be conducted in accordance with the protocol and with the following:

- Consensus ethical principles derived from international guidelines, including the Declaration of Helsinki and CIOMS International Ethical Guidelines;
- Applicable ICH GCP guidelines;
- Applicable laws and regulations, including applicable privacy laws.

The protocol, protocol amendments, ICD, SRSD(s), and other relevant documents (eg, advertisements) must be reviewed and approved by the sponsor, submitted to an IRB/EC by the investigator, and reviewed and approved by the IRB/EC before the study is initiated.

Any amendments to the protocol will require IRB/EC approval before implementation of changes made to the study design, except for changes necessary to eliminate an immediate hazard to study participants.

Protocols and any substantial amendments to the protocol will require health authority approval prior to initiation except for changes necessary to eliminate an immediate hazard to study participants.

The investigator will be responsible for the following:

- Providing written summaries of the status of the study to the IRB/EC annually or more frequently in accordance with the requirements, policies, and procedures established by the IRB/EC.
- Notifying the IRB/EC of SAEs or other significant safety findings as required by IRB/EC procedures.
- Providing oversight of the conduct of the study at the site and adherence to requirements of 21 CFR, ICH GCP guidelines, the IRB/EC, European regulation 536/2014 for clinical studies, European MDR 2017/745 for clinical device research, and all other applicable local regulations.

10.1.1.1. Reporting of Safety Issues and Serious Breaches of the Protocol or ICH GCP

In the event of any prohibition or restriction imposed (ie, clinical hold) by an applicable regulatory authority in any area of the world, or if the investigator is aware of any new information that might influence the evaluation of the benefits and risks of the study intervention, Pfizer should be informed immediately.

In addition, the investigator will inform Pfizer immediately of any urgent safety measures taken by the investigator to protect the study participants against any immediate hazard, and of any serious breaches of this protocol or of the ICH GCP that the investigator becomes aware of.

10.1.2. Financial Disclosure

Investigators and sub-investigators will provide the sponsor with sufficient, accurate financial information as requested to allow the sponsor to submit complete and accurate financial certification or disclosure statements to the appropriate regulatory authorities. Investigators are responsible for providing information on financial interests during the course of the study and for 1 year after completion of the study.

10.1.3. Informed Consent/Assent Process

The investigator or the investigator's representative will explain the nature of the study, including the risks and benefits, to the participant or their legally authorized representative and answer all questions regarding the study. The participant or their legally authorized representative should be given sufficient time and opportunity to ask questions and to decide whether or not to participate in the trial.

Participants must be informed that their participation is voluntary. Participants or their legally authorized representative (if allowed by local regulations) will be required to sign a statement of informed consent that meets the requirements of 21 CFR 50, local regulations, ICH GCP guidelines, privacy and data protection requirements, where applicable, and the IRB/EC or study center.

The investigator must ensure that each study participant or their legally authorized representative is fully informed about the nature and objectives of the study, the sharing of data related to the study, and possible risks associated with participation, including the risks associated with the processing of the participant's personal data.

The participant or their legally authorized representative must be informed that their personal study-related data will be used by the sponsor in accordance with local data protection law. The level of disclosure must also be explained to the participant or their legally authorized representative.

The participant or their legally authorized representative must be informed that their medical records may be examined by Clinical Quality Assurance auditors or other authorized personnel appointed by the sponsor, by appropriate IRB/EC members, and by inspectors from regulatory authorities.

The investigator further must ensure that each study participant or their legally authorized representative is fully informed about his or her right to access and correct their personal data and to withdraw consent for the processing of his or her personal data.

The medical record must include a statement that written informed consent was obtained before the participant was enrolled in the study and the date on which the written consent was obtained. The authorized person obtaining the informed consent must also sign the ICD.

Participants or their legally authorized representative must be re-consented to the most current IRB/EC version of the IRB/EC-approved ICD(s) during their participation in the study as required per local regulations.

A copy of the ICD(s) must be provided to the participant or their legally authorized representative (if allowed by local regulations).

A participant who is rescreened is not required to sign another ICD if the rescreening occurs within 28 days from the previous ICD signature date.

10.1.4. Data Protection

All parties will comply with all applicable laws, including laws regarding the implementation of organizational and technical measures to ensure protection of participant data.

Participants' personal data will be stored at the study site in encrypted electronic and/or paper form and will be password-protected or secured in a locked room to ensure that only authorized study staff have access. The study site will implement appropriate technical and organizational measures to ensure that the personal data can be recovered in the event of disaster. In the event of a potential personal data breach, the study site will be responsible for determining whether a personal data breach has in fact occurred and, if so, providing breach notifications as required by law.

To protect the rights and freedoms of participants with regard to the processing of personal data, participants will be assigned a single, participant-specific numerical code. Any participant records or data sets that are transferred to the sponsor will contain the numerical code; participant names will not be transferred. All other identifiable data transferred to the sponsor will be identified by this single, participant-specific code. The study site will maintain a confidential list of participants who participated in the study, linking each participant's numerical code to their actual identity and medical record ID. In case of data transfer, the sponsor will protect the confidentiality of participants' personal data consistent with the clinical study agreement and applicable privacy laws.

Information technology systems used to collect, process, and store study-related data are secured by technical and organizational security measures designed to protect such data against accidental or unlawful loss, alteration, or unauthorized disclosure or access.

The sponsor maintains SOPs on how to respond in the event of unauthorized access, use, or disclosure of sponsor information or systems.

10.1.5. Committees Structure

This study will not use an E-DMC.

10.1.6. Dissemination of Clinical Study Data

Pfizer fulfills its commitment to publicly disclose clinical study results through posting the results of studies on www.clinicaltrials.gov (ClinicalTrials.gov), the EudraCT/CTIS, and/or www.pfizer.com, and other public registries and websites in accordance with applicable local laws/regulations. In addition, Pfizer reports study results outside of the requirements of local laws/regulations pursuant to its SOPs.

In all cases, study results are reported by Pfizer in an objective, accurate, balanced, and complete manner and are reported regardless of the outcome of the study or the country in which the study was conducted.

www.clinicaltrials.gov

Pfizer posts clinical trial results on www.clinicaltrials.gov for Pfizer-sponsored interventional studies (conducted in patients) that evaluate the safety and/or efficacy of a product, regardless of the geographical location in which the study is conducted. These results are submitted for posting in accordance with the format and timelines set forth by US law.

EudraCT/CTIS

Pfizer posts clinical trial results on EudraCT/CTIS for Pfizer-sponsored interventional studies in accordance with the format and timelines set forth by EU requirements.

www.pfizer.com

Pfizer posts CSR synopses and plain-language study results summaries on www.pfizer.com for Pfizer-sponsored interventional studies at the same time the corresponding study results are posted to www.clinicaltrials.gov. CSR synopses will have personally identifiable information anonymized.

Documents within marketing applications

Pfizer complies with applicable local laws/regulations to publish clinical documents included in marketing applications. Clinical documents include summary documents and CSRs including the protocol and protocol amendments, sample CRFs, and SAPs. Clinical documents will have personally identifiable information anonymized.

Data sharing

Pfizer provides researchers secure access to participant-level data or full CSRs for the purposes of “bona-fide scientific research” that contributes to the scientific understanding of the disease, target, or compound class. Pfizer will make data from these trials available 18 months after study completion. Participant-level data will be anonymized in accordance with applicable privacy laws and regulations. CSRs will have personally identifiable information anonymized.

Data requests are considered from qualified researchers with the appropriate competencies to perform the proposed analyses. Research teams must include a biostatistician. Data will not be provided to applicants with significant conflicts of interest, including individuals requesting access for commercial/competitive or legal purposes.

10.1.7. Data Quality Assurance

All participant data relating to the study will be recorded on printed or electronic CRF unless transmitted to the sponsor or designee electronically (eg, laboratory data). The investigator is responsible for verifying that data entries are accurate and correct by physically or electronically signing the CRF.

Guidance on completion of CRFs will be provided in the CRF Completion Requirements document.

The investigator must ensure that the CRFs are securely stored at the study site in encrypted electronic and/or paper form and are password-protected or secured in a locked room to prevent access by unauthorized third parties.

QTLs are predefined parameters that are monitored during the study. Important deviations from the QTLs and any remedial actions taken will be summarized in the CSR.

The investigator must permit study-related monitoring, audits, IRB/EC review, and regulatory agency inspections and provide direct access to source records and documents. This verification may also occur after study completion. It is important that the investigator(s) and their relevant personnel are available during the monitoring visits and possible audits or inspections and that sufficient time is devoted to the process.

Monitoring details describing strategy, including definition of study-critical data items and processes (eg, risk-based initiatives in operations and quality, such as risk management and mitigation strategies and analytical risk-based monitoring), methods, responsibilities, and requirements, including handling of noncompliance issues and monitoring techniques (central, virtual, or on-site monitoring), are provided in the Data Management Plan and monitoring plan maintained and utilized by the sponsor or designee.

The sponsor or designee is responsible for the data management of this study, including quality checking of the data.

Records and documents, including signed ICDs, pertaining to the conduct of this study must be retained by the investigator for 15 years after study completion unless local regulations or institutional policies require a longer retention period. No records may be destroyed during the retention period without the written approval of the sponsor. No records may be transferred to another location or party without written notification to the sponsor. The investigator must ensure that the records continue to be stored securely for as long as they are maintained.

When participant data are to be deleted, the investigator will ensure that all copies of such data are promptly and irrevocably deleted from all systems.

The investigator(s) will notify the sponsor or its agents immediately of any regulatory inspection notification in relation to the study. Furthermore, the investigator will cooperate with the sponsor or its agents to prepare the investigator site for the inspection and will allow the sponsor or its agent, whenever feasible, to be present during the inspection. The investigator site and investigator will promptly resolve any discrepancies that are identified between the study data and the participant's medical records. The investigator will promptly provide copies of the inspection findings to the sponsor or its agent. Before response submission to the regulatory authorities, the investigator will provide the sponsor or its agents with an opportunity to review and comment on responses to any such findings.

10.1.8. Source Documents

Source documents provide evidence for the existence of the participant and substantiate the integrity of the data collected. Source documents are filed at the investigator site.

Data reported on the CRF or entered in the eCRF that are from source documents must be consistent with the source documents or the discrepancies must be explained. The investigator may need to request previous medical records or transfer records, depending on the study. Also, current medical records must be available.

Definition of what constitutes source data and its origin can be found in the Source Document Locator, which is maintained by the sponsor.

Description of the use of the computerized system is documented in the Data Management Plan, which is maintained by the sponsor.

The investigator must maintain accurate documentation (source data) that supports the information entered in the CRF.

The sponsor or designee will perform monitoring to confirm that data entered into the CRF by authorized site personnel are accurate, complete, and verifiable from source documents; that the safety and rights of participants are being protected; and that the study is being conducted in accordance with the currently approved protocol and any other study agreements, the ICH GCP guidelines, and all applicable regulatory requirements.

10.1.9. Use of Medical Records

In certain situations, sponsor review of redacted copies of participant medical records may be performed (e.g., potential review of radiographic images by an independent third party imaging laboratory), where ethically and scientifically justified and permitted by local regulations, to ensure participant safety.

Due to the potential for a participant to be re-identified from their medical records, the following actions must be taken when medical records are sent to the sponsor or sponsor designee:

- The investigator or site staff must redact personal information from the medical record. The personal information includes, but is not limited to, the following: participant names or initials, participant dates (eg, birth date, date of hospital admission/discharge, date of death), participant identification numbers (eg, Social Security number, health insurance number, medical record number, hospital/institution identifier), participant location information (eg, street address, city, country, postal code, IP address), participant contact information (eg, telephone/fax number, email address).
- Each medical record must be transmitted to the sponsor or sponsor designee using systems with technical and organizational security measures to ensure the protection of personal data (eg, Florence is the preferred system if available).
- There may be unplanned situations where the sponsor may request medical records (eg, sharing medical records so that the sponsor can provide study-related advice to the investigator). The medical records should be submitted according to the procedure described above.

10.1.10. Study and Site Start and Closure

The study start date is the date of the first participant's first visit.

The sponsor designee reserves the right to close the study site or terminate the study at any time for any reason at the sole discretion of the sponsor, including (but not limited to) regulatory authority decision, change in opinion of the IRB/EC, or change in benefit-risk assessment. Study sites will be closed upon study completion. A study site is considered closed when all required documents and study supplies have been collected and a study-site closure visit has been performed.

The investigator may initiate study-site closure at any time upon notification to the sponsor or designee/CRO if requested to do so by the responsible IRB/EC or if such termination is required to protect the health of study participants.

Reasons for the early closure of a study site by the sponsor may include but are not limited to:

- Failure of the investigator to comply with the protocol, the requirements of the IRB/EC or local health authorities, the sponsor's procedures, or the ICH GCP guidelines;
- Inadequate recruitment of participants by the investigator;
- Discontinuation of further study intervention development.

If the study is prematurely terminated or suspended, the sponsor shall promptly inform the investigators, the ECs/IRBs, the regulatory authorities, and any CRO(s) used in the study of the reason for termination or suspension, as specified by the applicable regulatory requirements. The investigator shall promptly inform the participant and should assure appropriate participant therapy and/or follow-up.

If the sponsor decides to terminate the study for a reason unrelated to the safety of study intervention(s), participants may continue to receive study intervention(s) per the investigator's judgment and protocol-specified safety assessments will continue to be performed for these participants until the end of the study as defined in [Section 4.4](#). Any non-safety-related study procedures and assessments may be stopped upon written notification from the sponsor.

Study termination is also provided for in the clinical study agreement. If there is any conflict between the contract and this protocol, the contract will control as to termination rights.

10.1.11. Publication Policy

For multicenter trials, the primary publication will be a joint publication developed by the investigator and Pfizer reporting the primary endpoint(s) of the study covering all study sites. The investigator agrees to refer to the primary publication in any subsequent publications. Pfizer will not provide any financial compensation for the investigator's participation in the preparation of the primary congress abstract, poster, presentation, or primary manuscript for the study.

Investigators are free to publish individual center results that they deem to be clinically meaningful after publication of the overall results of the study or 12 months after primary completion date or study completion at all sites, whichever occurs first, subject to the other requirements described in this section.

The investigator will provide Pfizer an opportunity to review any proposed publication or any other type of disclosure of the study results (collectively, "publication") before it is submitted or otherwise disclosed and will submit all publications to Pfizer 30 days before submission. If any patent action is required to protect intellectual property rights, the investigator agrees to delay the disclosure for a period not to exceed an additional 60 days upon request from Pfizer. This allows Pfizer to protect proprietary information and to provide comments, and the investigator will, on request, remove any previously undisclosed confidential information before disclosure, except for any study-intervention or Pfizer-related information necessary for the appropriate scientific presentation or understanding of the study results. For joint publications, should there be disagreement regarding interpretation and/or presentation of specific analysis results, resolution of, and responsibility for, such disagreements will be the collective responsibility of all authors of the publication.

For all publications relating to the study, the investigator and Pfizer will comply with recognized ethical standards concerning publications and authorship, including those established by the International Committee of Medical Journal Editors. The investigator will disclose any relationship with Pfizer and any relevant potential conflicts of interest, including

any financial or personal relationship with Pfizer, in any publications. When applicable, editorial or technical support provided by a third party and paid for by Pfizer, or provided by a Pfizer employee, may be a reportable transfer of value under the Sunshine Act for US licensed physicians or other healthcare professionals. All authors will have access to the relevant statistical tables, figures, and reports (in their original format) required to develop the publication. The results of this study may be published or presented at scientific meetings by the investigator after publication of the overall study results or 1 year after the end of the study (or study termination), whichever comes first.

10.1.12. Sponsor’s Medically Qualified Individual

The sponsor will designate a medically qualified individual (MQI, also known as the medical monitor) to advise the investigator on study-related medical questions. The contact information for the study medical monitor is documented in the Study Team Contact List located in the Investigator Site File.

Participants are provided with a Pfizer study information card at the time of informed consent, which includes contact information for their investigator in case of study-related medical questions. The study information card contains, at a minimum, (a) study number, (b) participant’s study identification number, and (c) principal investigator contact information.

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10.2. Appendix 2: Clinical Laboratory Assessments

The following safety laboratory tests will be performed at times defined in the [SoA](#) section of this protocol. Additional laboratory results may be reported on these samples as a result of the method of analysis or the type of analyzer used by the clinical laboratory, or as derived from calculated values. These additional tests would not require additional collection of blood. Unscheduled clinical laboratory measurements may be obtained at any time during the study to assess any perceived safety issues.

Table 13. Study-Specific Clinical Laboratory Assessments

Test	Notes
Hematology	
Hemoglobin	
Platelets	
WBC	
Absolute Neutrophils	Results will be reported as absolute values after conversion and graded according to CTCAE v5.0 criteria.
Absolute Lymphocytes	
Absolute Monocytes	
Absolute Eosinophils	
Absolute Basophils	
<ul style="list-style-type: none"> Reticulocytes 	<ul style="list-style-type: none"> At C1 (to be entered in the CRF for anemia \geq Grade 2 at baseline). As clinically indicated (when \geq Grade 2 anemia).
Chemistry	
ALT	
AST	
ALP	
Sodium	
Potassium	
Magnesium	
Chloride	
Total Calcium	
Total Bilirubin***	***For Hy's law potential cases, in addition to repeating AST and ALT, laboratory tests include albumin, creatine kinase, total bilirubin, direct and indirect bilirubin, gamma-glutamyl transferase, PT/INR, and alkaline phosphatase
Urea	
Creatinine	
Uric Acid	
Glucose (non-fasted)	
Albumin	
Phosphorus or Phosphate	
LDH	Screening, C1 visits and as clinically indicated.
Coagulation	
PT or INR	
PTT or aPTT	
Urinalysis (dipstick is acceptable)	

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Table 13. Study-Specific Clinical Laboratory Assessments

Test	Notes
Urine dipstick for urine protein, blood, leukocytes. If positive, collect a microscopic (reflex testing).	
Immunoglobulin	
IgG, IgM, IgA	
Hepatitis panel for screening	
HBV tests (HBsAg, HBcAb, HBsAb), and HCV Ab	To be performed at Screening and as clinically indicated per PI assessment throughout study period. In the case of apparent ongoing HBV or HCV infection, reflex serum DNA or RNA viral load testing, respectively, will be performed if required by local regulation. Participants previously infected with HBV but without active infection should be monitored for signs and symptoms of HBV reactivation while receiving lenalidomide. For participants with active HBV at any time during the study, administration of study interventions should be interrupted and starting HBV treatment should be considered in parallel with consultation with a hepatologist. See also REVLIMID SmPC and Section 10.10.2 requirements in Japan.
HIV at screening	
CD4 count and HIV viral load	<ul style="list-style-type: none"> • For participants with history of HIV • CD4 and HIV viral load results are to be documented in source documents (are not required in the CRF).
Pregnancy Test	
For female participants of childbearing potential, on serum or urine	Test sensitivity must be at least 25 mIU/mL.
FSH	Screening only; for confirmation of postmenopausal status.

The investigator must review the laboratory report, document this review, and record any clinically relevant changes occurring during the study in the AE section of the CRF.

10.3. Appendix 3: Adverse Events: Definitions and Procedures for Recording, Evaluating, Follow-Up, and Reporting

10.3.1. Definition of AE

AE Definition
<ul style="list-style-type: none">• An AE is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention.• Note: An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of study intervention.

Events Meeting the AE Definition
<ul style="list-style-type: none">• Any abnormal laboratory test results (hematology, clinical chemistry, or urinalysis) or other safety assessments (eg, ECG, radiological scans, vital sign measurements), including those that worsen from baseline, considered clinically significant in the medical and scientific judgment of the investigator. Any abnormal laboratory test results that meet any of the conditions below must be recorded as an AE:<ul style="list-style-type: none">○ Is associated with accompanying symptoms;○ Requires additional diagnostic testing or medical/surgical intervention;○ Leads to a change in study dosing (outside of any protocol-specified dose adjustments) or discontinuation from the study, significant additional concomitant drug treatment, or other therapy.• Exacerbation of a chronic or intermittent preexisting condition, including an increase in either frequency and/or intensity of the condition.• New condition detected or diagnosed after study intervention administration, even though it may have been present before the start of the study.• Signs, symptoms, or the clinical sequelae of a suspected drug-drug interaction.• Signs, symptoms, or the clinical sequelae of a suspected overdose of either study intervention or a concomitant medication. Overdose per se will not be reported as an AE or SAE unless it is an intentional overdose taken with possible suicidal/self-harming intent. Such overdoses should be reported regardless of sequelae.

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Events NOT Meeting the AE Definition

- Any clinically significant abnormal laboratory findings or other abnormal safety assessments that are associated with the underlying disease, unless judged by the investigator to be more severe than expected for the participant’s condition.
- The disease/disorder being studied or expected progression, signs, or symptoms of the disease/disorder being studied, unless more severe than expected for the participant’s condition.
- Worsening of signs and symptoms of the malignancy under study should be recorded as AEs in the appropriate section of the CRF. Disease progression assessed by measurement of malignant lesions on radiographs or other methods should not be reported as AEs
- Medical or surgical procedure (eg, endoscopy, appendectomy): the condition that leads to the procedure is the AE.
- Situations in which an untoward medical occurrence did not occur (social and/or convenience admission to a hospital).
- Anticipated day-to-day fluctuations of preexisting disease(s) or condition(s) present or detected at the start of the study that do not worsen.

10.3.2. Definition of an SAE

An SAE is defined as any untoward medical occurrence that, at any dose, meets 1 or more of the criteria listed below:

a. Results in death

b. Is life-threatening

The term “life-threatening” in the definition of “serious” refers to an event in which the participant was at risk of death at the time of the event. It does not refer to an event that hypothetically might have caused death if it were more severe.

c. Requires inpatient hospitalization or prolongation of existing hospitalization

In general, hospitalization signifies that the participant has been detained (usually involving at least an overnight stay) at the hospital or emergency ward for observation and/or treatment that would not have been appropriate in the physician’s office or outpatient setting. Complications that occur during hospitalization are AEs. If a complication prolongs hospitalization or fulfills any other serious criteria, the event is serious. When in doubt as to whether “hospitalization” occurred or was necessary, the AE should be considered serious.

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Hospitalization for elective treatment of a preexisting condition that did not worsen from baseline is not considered an AE.

d. Results in persistent or significant disability/incapacity

- The term disability means a substantial disruption of a person’s ability to conduct normal life functions.
- This definition is not intended to include experiences of relatively minor medical significance, such as uncomplicated headache, nausea, vomiting, diarrhea, influenza, and accidental trauma (eg, sprained ankle), that may interfere with or prevent everyday life functions but do not constitute a substantial disruption.

e. Is a congenital anomaly/birth defect.

f. Is a suspected transmission via a Pfizer product of an infectious agent, pathogenic or non-pathogenic.

The event may be suspected from clinical symptoms or laboratory findings indicating an infection in a participant exposed to a Pfizer product. The terms “suspected transmission” and “transmission” are considered synonymous. These cases are considered unexpected and handled as serious expedited cases by pharmacovigilance personnel. Such cases are also considered for reporting as product defects, if appropriate.

g. Other situations:

- Medical or scientific judgment should be exercised by the investigator in deciding whether SAE reporting is appropriate in other situations, such as significant medical events that but may jeopardize the participant or may require medical or surgical intervention to prevent one of the other outcomes listed in the above definition. These events should usually be considered serious.
- Examples of such events include invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalization, or development of drug dependency or drug abuse.
- Progression of the malignancy under study (including signs and symptoms of progression) should not be reported as an SAE unless the outcome is fatal within the active collection period. Hospitalization due to signs and symptoms of disease progression should not be reported as an SAE. If the malignancy has a fatal outcome during the study, the event leading to death must be recorded as an AE on the CRF, and as an SAE with CTCAE Grade 5 (see the [Assessment of Severity](#) section) if it occurs during the active collection period.

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10.3.3. Recording/Reporting and Follow-Up of AEs and/or SAEs During the Active Collection Period

AE and SAE Recording/Reporting		
<p>The table below summarizes the requirements for recording AEs on the CRF and for reporting SAEs on the CT SAE Report Form to Pfizer Safety throughout the active collection period. These requirements are delineated for 3 types of events: (1) SAEs; (2) nonserious AEs; and (3) exposure to the study intervention under study during pregnancy or breastfeeding, and occupational exposure.</p> <p>It should be noted that the CT SAE Report Form for reporting of SAE information is not the same as the AE page of the CRF. When the same data are collected, the forms must be completed in a consistent manner. AEs should be recorded using concise medical terminology and the same AE term should be used on both the CRF and the CT SAE Report Form for reporting of SAE information.</p>		
Safety Event	Recorded on the CRF	Reported on the CT SAE Report Form to Pfizer Safety Within 24 Hours of Awareness
SAE	All	All
Nonserious AE	All	None
Exposure to the study intervention under study during pregnancy or breastfeeding	All AEs/SAEs associated with EDP or EDB Note: Instances of EDP or EDB not associated with an AE or SAE are not captured in the CRF	All instances of EDP are reported (whether or not there is an associated SAE)* All instances of EDB are reported (whether or not there is an associated SAE)**
Environmental or occupational exposure to the product under study to a non-participant (not involving EDP or EDB)	None. Exposure to a study non-participant is not collected on the CRF	The exposure (whether or not there is an associated AE or SAE) must be reported***
<p>* EDP (with or without an associated AE or SAE): any pregnancy information is reported to Pfizer Safety using the CT SAE Report Form and EDP Supplemental Form; if the EDP is associated with an SAE, then the SAE is reported to Pfizer Safety using the CT SAE Report Form.</p> <p>**EDB is reported to Pfizer Safety using the CT SAE Report Form, which would also include details of any SAE that might be associated with the EDB.</p> <p>*** Environmental or occupational exposure: AEs or SAEs associated with occupational exposure are reported to Pfizer Safety using the CT SAE Report Form.</p>		

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- When an AE or SAE occurs, it is the responsibility of the investigator to review all documentation (eg, hospital progress notes, laboratory reports, and diagnostic reports) related to the event.
- The investigator will then record all relevant AE or SAE information in the CRF.
- It is **not** acceptable for the investigator to send photocopies of the participant’s medical records to Pfizer Safety in lieu of completion of the CT SAE Report Form/AE or SAE CRF page.
- There may be instances when copies of medical records for certain cases are requested by Pfizer Safety. In this case, all participant identifiers, with the exception of the participant number, will be redacted on the copies of the medical records before submission to Pfizer Safety.
- The investigator will attempt to establish a diagnosis of the event based on signs, symptoms, and/or other clinical information. Whenever possible, the diagnosis (not the individual signs/symptoms) will be documented as the AE or SAE.

Assessment of Intensity

The investigator will make an assessment of intensity for each AE and SAE reported during the study and assign it to 1 of the categories listed below (as defined by the NCI CTCAE v5.0 system).

GRADE	Clinical Description of Intensity
1	MILD AE
2	MODERATE AE
3	SEVERE AE
4	LIFE-THREATENING; urgent intervention indicated
5	DEATH RELATED TO AE

Assessment of Causality

- The investigator is obligated to assess the relationship between study intervention and each occurrence of each AE or SAE. The investigator will use clinical judgment to determine the relationship.
- A “reasonable possibility” of a relationship conveys that there are facts, evidence, and/or arguments to suggest a causal relationship, rather than a relationship cannot be ruled out.
- Alternative causes, such as underlying disease(s), concomitant therapy, and other risk factors, as well as the temporal relationship of the event to study intervention administration, will be considered and investigated.

- The investigator will also consult the IB and/or product information, for marketed products, in their assessment.
- For each AE or SAE, the investigator **must** document in the medical notes that they have reviewed the AE or SAE and have provided an assessment of causality.
- There may be situations in which an SAE has occurred and the investigator has minimal information to include in the initial report to the sponsor. However, **it is very important that the investigator always make an assessment of causality for every event before the initial transmission of the SAE data to the sponsor.**
- The investigator may change his/her opinion of causality in light of follow-up information and send an SAE follow-up report with the updated causality assessment.
- The causality assessment is one of the criteria used when determining regulatory reporting requirements.
- If the investigator does not know whether or not the study intervention caused the event, then the event will be handled as “related to study intervention” for reporting purposes, as defined by the sponsor. In addition, if the investigator determines that an SAE is associated with study procedures, the investigator must record this causal relationship in the source documents and CRF, and report such an assessment in the dedicated section of the CT SAE Report Form and in accordance with the SAE reporting requirements.

Follow-Up of AEs and SAEs

- The investigator is obligated to perform or arrange for the conduct of supplemental measurements and/or evaluations, as medically indicated or as requested by the sponsor, to elucidate the nature and/or causality of the AE or SAE as fully as possible. This may include additional laboratory tests or investigations, histopathological examinations, or consultation with other healthcare providers.
- New or updated information will be recorded in the originally submitted documents.
- The investigator will submit any updated SAE data to the sponsor within 24 hours of receipt of the information.

10.3.4. Reporting of SAEs

SAE Reporting to Pfizer Safety via an Electronic DCT
<ul style="list-style-type: none">• The primary mechanism for reporting an SAE to Pfizer Safety will be the electronic DCT.• If the electronic system is unavailable, then the site will use the paper SAE DCT (see next section) to report the event within 24 hours.• The site will enter the SAE data into the electronic DCT (eg, eSAE or PSSA) or paper form (as applicable) as soon as the data become available.• After the study is completed at a given site, the electronic DCT will be taken off-line to prevent the entry of new data or changes to existing data.• If a site receives a report of a new SAE from a study participant or receives updated data on a previously reported SAE after the electronic DCT has been taken off-line, then the site can report this information on a paper SAE form (see next section) or to Pfizer Safety by telephone.

SAE Reporting to Pfizer Safety via the CT SAE Report Form
<ul style="list-style-type: none">• Facsimile transmission of the CT SAE Report Form is the preferred method to transmit this information to Pfizer Safety.• In circumstances when the facsimile is not working, an alternative method should be used, eg, secured (Transport Layer Security) or password-protected email. If none of these methods can be used, notification by telephone is acceptable with a copy of the CT SAE Report Form sent by overnight mail or courier service.• Initial notification via telephone does not replace the need for the investigator to complete and sign the CT SAE Report Form pages within the designated reporting time frames.

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10.4. Appendix 4: Contraceptive and Barrier Guidance

For contraception guidelines for tafasitamab and lenalidomide, refer to the local prescribing information. In addition, any PPP or other applicable program required per local regulations for lenalidomide must be followed; details of the PPP for lenalidomide are included in Section 10.4.2.

10.4.1. Male Participant Reproductive Inclusion Criteria

Male participants are eligible to participate if they agree to the following requirements during the intervention period and for at least 4 weeks after the last dose of lenalidomide, which corresponds to the time needed to eliminate reproductive safety risk of the study intervention(s):

- Refrain from donating sperm.

PLUS either:

- Be abstinent from heterosexual or homosexual intercourse as their preferred and usual lifestyle (abstinent on a long-term and persistent basis) and agree to remain abstinent.

OR

- Must agree to use a male condom when engaging in any activity that allows for passage of ejaculate to another person even after vasectomy.
- The male participants should be advised of the benefit for a WOCBP partner using a highly effective method of contraception with a failure rate of <1% per year, as described in Section 10.4.4.

In the event that a male participant has discontinued two of the 3 combination therapies and remains on monotherapy: requirements are to be continued for at least 4 weeks after the last dose of lenalidomide monotherapy. No contraception or barrier measures are required for male participants on PF-07901801 or tafasitamab.

10.4.2. Female Participant Reproductive Inclusion Criteria

The criteria below are part of Inclusion Criterion No. 1 (Age and Sex; [Section 5.1](#)) and specify the reproductive requirements for including female participants. Refer to [Section 10.4.4](#) for a complete list of contraceptive methods permitted in the study.

A female participant is eligible to participate if she (a) is not pregnant or breastfeeding; and (b) agrees not to donate eggs (ova, oocytes) for the purpose of reproduction from the time of screening through 90 days after the last dose of study intervention; and (c) at least 1 of the following conditions applies:

- Is not a WOCBP (see definition in [Section 10.4.3](#)).

OR

- Is a WOCBP and agrees to use a contraceptive method that is highly effective (failure rate of <1% per year) with low user dependency during the intervention period and agrees to use it for at least 90 days after the last dose of study intervention, which corresponds to the time needed to eliminate any reproductive safety risk of the study intervention(s). The investigator should evaluate the effectiveness of the contraceptive method in relationship to the first dose of study intervention.

OR

- Is a WOCBP and agrees to use a highly effective (failure rate of <1% per year) user-dependent method of contraception during the intervention period and for at least 90 days after the last dose of study intervention, which corresponds to the time needed to eliminate any reproductive safety risk of the study intervention(s). In addition to her use of the highly effective method above, she agrees to concurrently use an effective barrier method. The investigator should evaluate the effectiveness of the contraceptive method in relationship to the first dose of study intervention.

In the event that a WOCBP participant has discontinued 2 of the 3 combination therapies and remains on monotherapy: the contraceptive method must be used for at least 45 days after the last dose of PF-07901801 monotherapy, for at least 28 days after the last dose of lenalidomide monotherapy and/or for at least 90 days after the last dose of tafasitamab.

The investigator is responsible for review of medical history, menstrual history, and recent sexual activity to decrease the risk for inclusion of a woman with an early undetected pregnancy. This is to be documented in the source documentation.

10.4.3. Woman of Childbearing and Non-Childbearing Potential

A woman is considered fertile following menarche and until becoming postmenopausal unless permanently sterile (see below).

If fertility is unclear (eg, amenorrhea in adolescents or athletes) and a menstrual cycle cannot be confirmed before the first dose of study intervention, additional evaluation should be considered.

Women in the following categories are not considered WOCBP:

1. Premenopausal female with 1 of the following:
 - Documented hysterectomy;
 - Documented bilateral salpingectomy;
 - Documented bilateral oophorectomy.

For individuals with permanent infertility due to a medical cause other than the above (eg, mullerian agenesis, androgen insensitivity), investigator discretion should be applied to determining study entry.

Note: Documentation for any of the above categories can come from the site personnel's review of the participant's medical records, medical examination, or medical history interview. The method of documentation should be recorded in the participant's medical record for the study.

2. Postmenopausal female:

- A postmenopausal state is defined as no menses for 12 months without an alternative medical cause. In addition,
 - A high FSH level in the postmenopausal range must be used to confirm a postmenopausal state in women under 60 years of age and not using hormonal contraception or HRT.
 - A female on HRT and whose menopausal status is in doubt will be required to use one of the highly effective non-estrogen hormonal contraception methods if she wishes to continue her HRT during the study. Otherwise, she must discontinue HRT to allow confirmation of postmenopausal status before study enrollment.

10.4.4. Contraception Methods

Contraceptive use by men or women should be consistent with local availability/regulations regarding the use of contraceptive methods for those participating in clinical trials.

In addition, for Lenalidomide, the PPP and any other applicable program-required contraceptive methods must be followed (whichever is most stringent). The PPP will be detailed with the Healthcare Professional/Prescriber PPP educational materials provided to the sites.

The following contraceptive methods are appropriate for this study:

Highly Effective Methods That Have Low User Dependency

1. Implantable progestogen-only hormone contraception associated with inhibition of ovulation.
2. Intrauterine device.
3. Intrauterine hormone-releasing system.
4. Bilateral tubal occlusion.

5. Vasectomized partner.

- Vasectomized partner is a highly effective contraceptive method provided that the partner is the sole sexual partner of the WOCBP and the absence of sperm has been confirmed. If not, an additional highly effective method of contraception should be used. The spermatogenesis cycle is approximately 90 days.

Highly Effective Methods That Are User-Dependent

6. Combined (estrogen- and progestogen-containing) hormonal contraception associated with inhibition of ovulation:

- Oral + barrier*
- Intravaginal + barrier*
- Transdermal + barrier*

7. Progestogen-only hormone contraception associated with inhibition of ovulation:

- Oral + barrier*
- Injectable + barrier*

Sexual Abstinence

8. Sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the study intervention. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the study and the preferred and usual lifestyle of the participant.

* Acceptable barrier methods to be used concomitantly with options 6 or 7 for the study include any of the following:

- Male or female condom with or without spermicide;
- Cervical cap, diaphragm, or sponge with spermicide;
- A combination of male condom with either cervical cap, diaphragm or sponge with spermicide (double-barrier methods).

10.4.5. Lenalidomide Pregnancy Prevention Program

This section contains the general requirements of post-marketing lenalidomide use that must be followed in this study in addition to any protocol specific requirements. The requirements may slightly differ from country to country, as agreed with each National Competent

Authority or other Regulatory Agency. A PPP is a set of measures meant to reduce to a minimum the risk of lenalidomide exposure during pregnancy. To avoid embryo-fetal exposure, the PPP must be implemented.

Steps the Healthcare Professional must follow for this protocol:

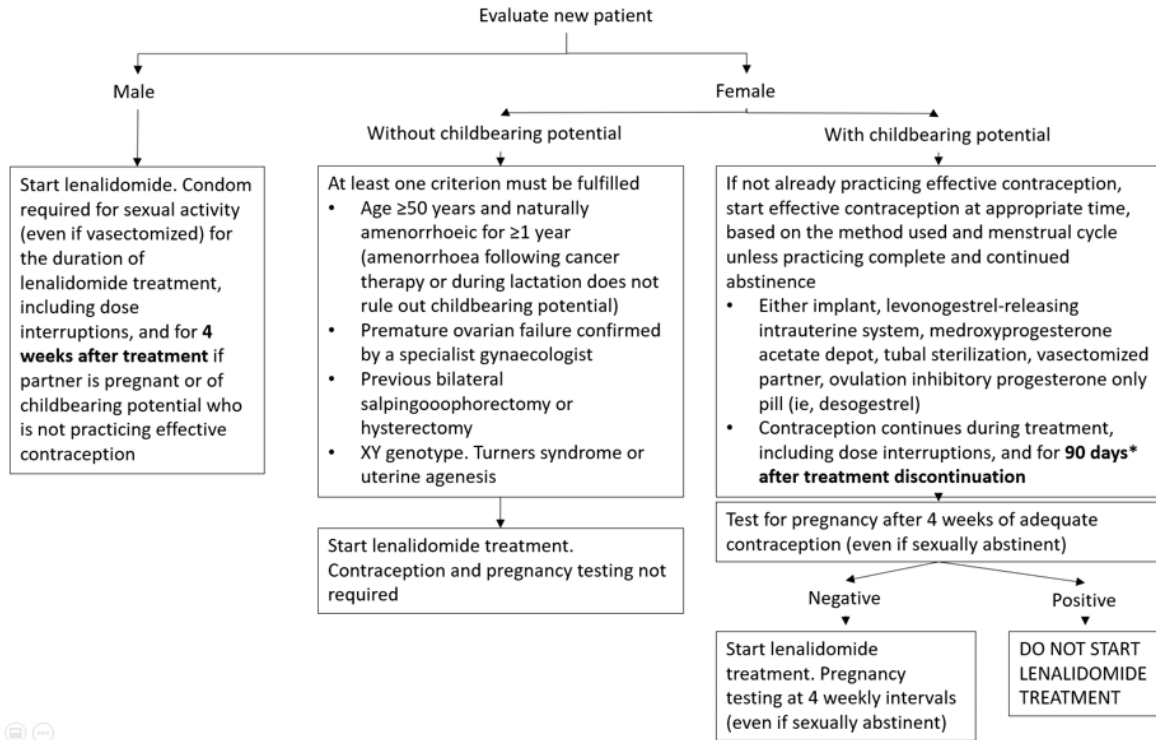
1. Receive Healthcare Professional/Prescriber PPP educational materials (as supplied by the Sponsor and specific by region);
2. Inform the participant regarding the benefits and risks of treatment with lenalidomide, not sharing lenalidomide, not donating blood, risks associated with fetal exposure, and the necessity to take adequate measures to avoid fetal exposure to lenalidomide;
3. Give the participant the appropriate corresponding educational brochure (for participants of childbearing potential, for participants not of childbearing potential, or for male participants) and counsel the participant on contraception requirements and emergency contraception use (in countries where available);
4. Apply steps from the PPP algorithm (see [Figure 4](#)). The Healthcare Professional must evaluate the participant from a reproductive potential point of view prior to the start of the study and every 4 weeks prior to dispensing lenalidomide, to ensure that:
 - Male participants are informed that they must use condoms if engaging in sexual intercourse with pregnant women or women of childbearing potential (even if the participant had a vasectomy) and must not donate sperm during lenalidomide treatment and for **4 weeks after cessation of lenalidomide**.
 - Female participants must meet one of the following conditions to be considered of non-childbearing potential:
 - Aged 50+ and naturally occurring amenorrhea of over 1 year (amenorrhea that occurred as a result of cytostatic therapy or during breastfeeding period does not exclude the possibility that the participant is fertile);
 - Premature ovarian failure that was confirmed by a gynecologist;
 - Bilateral salpingo-oophorectomy or hysterectomy as part of medical history;
 - XY genotype, Turner syndrome, uterine agenesis.
 - Female participants of childbearing potential must be informed of the necessity to:
 - Utilize highly effective contraceptive method(s) as per the PPP or other applicable program for 4 weeks before treatment, during treatment, and for 90 days after complete cessation of treatment [4 weeks after cessation is the standard timing for lenalidomide but note that a longer duration is required per

SmPC for MINJUVI (tafasitamab)], including during temporary discontinuation of treatment; or

- To maintain total and continuous abstinence; and
- To take, under medical supervision, pregnancy tests with a sensitivity of at least 25 mIU/mL, after utilizing an efficient contraceptive measure for at least 4 weeks, every 4 weeks (including during temporary discontinuation of treatment), at EOT, and 4 weeks after lenalidomide discontinuation. This also includes women of childbearing potential who practice total and continuous abstinence.
- During treatment before lenalidomide is dispensed:
 - For female participants of childbearing potential, counsel the participant on contraception requirements and emergency contraception use (in countries where available) and ensure that the required pregnancy test is negative.
 - For male participants, counsel the participant on the barrier contraception requirements and emergency contraception use (in countries where available).
- Do not dispense more than a 28-day supply of lenalidomide.

Follow instructions in the PPP educational materials if a pregnancy occurs.

Figure 4. Pregnancy Prevention Plan Algorithm



*4 weeks is the standard timing for the PPP for lenalidomide but note that a longer duration is required per protocol for tafasitamab; see [Section 10.4.5](#) for details regarding monotherapies.

For contraception methods, refer also to the region-specific PPP educational materials as supplied by the Sponsor.

10.5. Appendix 5: Genetics

Use/Analysis of DNA

- Genetic variation may impact a participant's response to study intervention, susceptibility to, and severity and progression of disease. Therefore, where local regulations and IRBs/ECs allow, a blood sample will be collected for DNA analysis.
- The scope of the genetic research may be narrow (eg, 1 or more candidate genes) or broad (eg, the entire genome), as appropriate to the scientific question under investigation.
- The samples may be analyzed as part of a multi-study assessment of genetic factors involved in the response to PF-07901801, tafasitamab or lenalidomide or study interventions of this class to understand treatments for the disease(s) under study or the disease(s) themselves.
- The results of genetic analyses may be reported in the CSR or in a separate study summary or may be used for internal decision making without being included in a study report.
- The sponsor will store the DNA samples in a secure storage space with adequate measures to protect confidentiality.
- The samples will be retained as indicated:
 - Samples for specified genetic analysis (see [Section 8.6.1](#)) will be stored for up to 15 years or other period as per local requirements beyond the completion of this study (eg, CSR finalization).
 - Retained samples will be stored indefinitely or for another period as per local requirements.
- Participants may withdraw their consent for the storage and/or use of their Retained Research Samples at any time by making a request to the investigator; in this case, any remaining material will be destroyed. Data already generated from the samples will be retained to protect the integrity of existing analyses.
- Samples for genetic research will be labeled with a code. The key between the code and the participant's personally identifying information (eg, name, address) will be held securely at the study site.

10.6. Appendix 6: Liver Safety: Suggested Actions and Follow-Up Assessments

Potential Cases of Drug-Induced Liver Injury

Humans exposed to a drug who show no sign of liver injury (as determined by elevations in transaminases) are termed “tolerators,” while those who show transient liver injury but adapt are termed “adaptors.” In some participants, transaminase elevations are a harbinger of a more serious potential outcome. These participants fail to adapt and therefore are “susceptible” to progressive and serious liver injury, commonly referred to as DILI. Participants who experience a transaminase elevation above $3 \times \text{ULN}$ should be monitored more frequently to determine if they are “adaptors” or are “susceptible.”

In the majority of DILI cases, elevations in AST and/or ALT precede T bili elevations ($>2 \times \text{ULN}$) by several days or weeks. The increase in T bili typically occurs while AST/ALT is/are still elevated above $3 \times \text{ULN}$ (ie, AST/ALT and T bili values will be elevated within the same laboratory sample). In rare instances, by the time T bili elevations are detected, AST/ALT values might have decreased. This occurrence is still regarded as a potential DILI. Therefore, abnormal elevations in either AST OR ALT in addition to T bili that meet the criteria outlined below are considered potential DILI (assessed per Hy’s law criteria) cases and should always be considered important medical events, even before all other possible causes of liver injury have been excluded.

The threshold of laboratory abnormalities for a potential DILI case depends on the participant’s individual baseline values and underlying conditions. Participants who present with the following laboratory abnormalities should be evaluated further as potential DILI (Hy’s law) cases to definitively determine the etiology of the abnormal laboratory values:

- Participants with AST/ALT and T bili baseline values within the normal range who subsequently present with AST OR ALT values $\geq 3 \times \text{ULN}$ AND a T bili value $\geq 2 \times \text{ULN}$ with no evidence of hemolysis and an alkaline phosphatase value $< 2 \times \text{ULN}$ or not available.

For participants with baseline AST **OR** ALT **OR** T bili values above the ULN, the following threshold values are used in the definition mentioned above, as needed, depending on which values are above the ULN at baseline:

- Preexisting AST or ALT baseline values above the normal range: AST or ALT values ≥ 2 times the baseline values AND $\geq 3 \times \text{ULN}$; or $\geq 8 \times \text{ULN}$ (whichever is smaller).
- Preexisting values of T bili above the normal range: T bili level increased from baseline value by an amount of $\geq 1 \times \text{ULN}$ **or** if the value reaches $\geq 3 \times \text{ULN}$ (whichever is smaller).

Rises in AST/ALT and T bili separated by more than a few weeks should be assessed individually based on clinical judgment; any case where uncertainty remains as to whether it represents a potential Hy’s law case should be reviewed with the sponsor.

The participant should return to the investigator site and be evaluated as soon as possible, preferably within 48 hours from awareness of the abnormal results. This evaluation should include laboratory tests, detailed history, and physical assessment.

In addition to repeating measurements of AST and ALT and T bili for suspected Hy's law cases, additional laboratory tests should include albumin, CK, direct and indirect bilirubin, GGT, PT/INR, total bile acids, and alkaline phosphatase. Consideration should also be given to drawing a separate tube of clotted blood and an anticoagulated tube of blood for further testing, as needed, for further contemporaneous analyses at the time of the recognized initial abnormalities to determine etiology. A detailed history, including relevant information, such as review of ethanol, acetaminophen/paracetamol (either by itself or as a co-formulated product in prescription or over-the-counter medications), recreational drug, or supplement (herbal) use and consumption, family history, sexual history, travel history, history of contact with a jaundiced person, surgery, blood transfusion, history of liver or allergic disease, and potential occupational exposure to chemicals, should be collected. Further testing for acute hepatitis A, B, C, D, and E infection, liver imaging (eg, biliary tract), and collection of serum samples for acetaminophen/paracetamol drug and/or protein adduct levels may be warranted.

All cases demonstrated on repeat testing as meeting the laboratory criteria of AST/ALT and T bili elevation defined above should be considered potential DILI (Hy's law) cases if no other reason for the LFT abnormalities has yet been found. **Such potential DILI (Hy's law) cases are to be reported as SAEs, irrespective of availability of all the results of the investigations performed to determine etiology of the LFT abnormalities.**

A potential DILI (Hy's law) case becomes a confirmed case only after all results of reasonable investigations have been received and have excluded an alternative etiology.

10.7. Appendix 7: Kidney Safety: Monitoring Guidelines

10.7.1. Laboratory Assessment of Change in Kidney Function and Detection of Kidney Injury

Standard kidney safety monitoring requires assessment of baseline and postbaseline (Scr measurement to eGFR [Scr-based eGFR]) or eCrCl. Baseline and post baseline Scys makes it feasible to distinguish AKI from other causes of Scr increase. If Scr increase is confirmed after baseline, then reflex measurement of Scys is indicated to estimate the combined Scr-Scys eGFR calculation (for adults only).

Regardless of whether kidney function monitoring tests are required as a routine safety monitoring procedure in the study, if the investigator or sponsor deems it necessary to further assess kidney safety and quantify kidney function, then these test results should be managed and followed per standard of care.

10.7.2. Age-Specific Kidney Function Calculation Recommendations

10.7.2.1. Adults (18 Years and Above)—2021 CKD-EPI Equations³⁴

2021 CKD-EPI Scr only	Scr <i>(mg/dL)</i>	Scys <i>(mg/L)</i>	Recommended eGFR Equation
Female	if ≤ 0.7	N/A	$eGFR = 143 \times (Scr/0.7)^{-0.241} \times (0.9938)^{Age}$
Female	if > 0.7	N/A	$eGFR = 143 \times (Scr/0.7)^{-1.200} \times (0.9938)^{Age}$
Male	if ≤ 0.9	N/A	$eGFR = 142 \times (Scr/0.9)^{-0.302} \times (0.9938)^{Age}$
Male	if > 0.9	N/A	$eGFR = 142 \times (Scr/0.9)^{-1.200} \times (0.9938)^{Age}$
2021 CKD-EPI Scr-Scys Combined	Scr <i>(mg/dL)</i>	Scys <i>(mg/L)</i>	Recommended eGFR Equation
Female	if ≤ 0.7	if ≤ 0.8	$eGFR = 130 \times (Scr/0.7)^{-0.219} \times (Scys/0.8)^{-0.323} \times (0.9961)^{Age}$
Female	if ≤ 0.7	if > 0.8	$eGFR = 130 \times (Scr/0.7)^{-0.219} \times (Scys/0.8)^{-0.778} \times (0.9961)^{Age}$
Female	if > 0.7	if ≤ 0.8	$eGFR = 130 \times (Scr/0.7)^{-0.544} \times (Scys/0.8)^{-0.323} \times (0.9961)^{Age}$
Female	if > 0.7	if > 0.8	$eGFR = 130 \times (Scr/0.7)^{-0.544} \times (Scys/0.8)^{-0.778} \times (0.9961)^{Age}$
Male	if ≤ 0.9	if ≤ 0.8	$eGFR = 135 \times (Scr/0.9)^{-0.144} \times (Scys/0.8)^{-0.323} \times (0.9961)^{Age}$
Male	if ≤ 0.9	if > 0.8	$eGFR = 135 \times (Scr/0.9)^{-0.144} \times (Scys/0.8)^{-0.778} \times (0.9961)^{Age}$
Male	if > 0.9	if ≤ 0.8	$eGFR = 135 \times (Scr/0.9)^{-0.544} \times (Scys/0.8)^{-0.323} \times (0.9961)^{Age}$
Male	if > 0.9	if > 0.8	$eGFR = 135 \times (Scr/0.9)^{-0.544} \times (Scys/0.8)^{-0.778} \times (0.9961)^{Age}$

10.7.3. Adverse Event Grading for Kidney Safety Laboratory Abnormalities

AE grading for decline in kidney function (ie, eGFR or eCrCl) will be according to CTCAE criteria.

10.8. Appendix 8: ECG Findings of Potential Clinical Concern

ECG Findings That <u>May</u> Qualify as AEs
<ul style="list-style-type: none">• Marked sinus bradycardia (rate <40 bpm) lasting minutes.• New PR interval prolongation >280 ms.• New prolongation of QTcF to >480 ms (absolute) or by ≥ 60 ms from baseline.• New-onset atrial flutter or fibrillation, with controlled ventricular response rate: ie, rate <120 bpm.• New-onset type I second degree (Wenckebach) AV block of >30 seconds' duration.• Frequent PVCs, triplets, or short intervals (<30 seconds) of consecutive ventricular complexes.
ECG Findings That <u>May</u> Qualify as SAEs
<ul style="list-style-type: none">• QTcF prolongation >500 ms.• New STT changes suggestive of myocardial ischemia.• New onset LBBB (QRS complex >120 ms).• New-onset right bundle branch block (QRS complex >120 ms).• Symptomatic bradycardia.• Asystole:<ul style="list-style-type: none">○ In awake, symptom-free participants in sinus rhythm, with documented periods of asystole ≥ 3.0 seconds or any escape rate <40 bpm, or with an escape rhythm that is below the AV node.○ In awake, symptom-free participants with atrial fibrillation and bradycardia with 1 or more pauses of at least 5 seconds or longer.○ Atrial flutter or fibrillation, with rapid ventricular response rate: rapid = rate >120 bpm.• Sustained supraventricular tachycardia (rate >120 bpm) ("sustained" = short duration with relevant symptoms or lasting >1 minute).• Ventricular rhythms >30 seconds' duration, including idioventricular rhythm (heart rate <40 bpm), accelerated idioventricular rhythm (HR >40 bpm to <100 bpm), and

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<p>monomorphic/polymorphic ventricular tachycardia (HR >100 bpm [such as torsades de pointes]).</p> <ul style="list-style-type: none">• Type II second degree (Mobitz II) AV block.• Complete (third degree) heart block.
<p>ECG Findings That Qualify as SAEs</p> <ul style="list-style-type: none">• Change in pattern suggestive of new myocardial infarction.• Sustained ventricular tachyarrhythmias (>30 seconds' duration).• Second or third degree AV block requiring pacemaker placement.• Asystolic pauses requiring pacemaker placement.• Atrial flutter or fibrillation with rapid ventricular response requiring cardioversion.• Ventricular fibrillation/flutter.• At the discretion of the investigator, any arrhythmia classified as an adverse experience.

The enumerated list of major events of potential clinical concern are recommended as “alerts” or notifications from the core ECG laboratory to the investigator and Pfizer study team, and not to be considered as all-inclusive of what to be reported as AEs/SAEs.

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10.9. Appendix 9: Prohibited Concomitant Medications That May Result in DDI

There are currently no drugs identified to have potential DDI concerns with PF-07901801.

Investigators should consult the SmPCs for tafasitamab and lenalidomide as well as any non-IMP medication used during the study for information regarding medication that is prohibited for concomitant use.

The Pfizer study team is to be notified of any prohibited medications taken during the study. After consulting with the sponsor, the investigator will make a judgment on the ongoing participation of any participant with prohibited medication use during the study.

10.10. Appendix 10: Country-Specific Requirements

10.10.1. France

Contrat Unique

1. GCP Training

Before enrolling any participants, the investigator and any sub-investigators will complete the Pfizer-provided Good Clinical Practice training course (“Pfizer GCP Training”) or training deemed equivalent by Pfizer. Any investigators who later join the study will do the same before performing study-related duties. For studies of applicable duration, the investigator and sub-investigators will complete Pfizer GCP Training or equivalent every 3 years during the term of the study, or more often if there are significant changes to the ICH GCP guidelines or course materials.

2. Study Intervention

No participants or third-party payers will be charged for study intervention.

3. Urgent Safety Measures

In addition, the investigator will inform Pfizer immediately of any urgent safety measures taken by the investigator to protect the study participants against any immediate hazard, and of any serious breaches of this protocol or of ICH GCP that the investigator becomes aware of.

4. Termination Rights

Pfizer retains the right to discontinue development of PF-07901801 at any time.

The investigator agrees to abide by the ethical principles set forth in the World Health Organization’s *Guiding Principles for Human Cell, Tissue and Organ Transplantation* (WHA63.22) with regard to the study.
(https://www.who.int/transplantation/Guiding_PrinciplesTransplantation_WHA63.22en.pdf)

10.10.2. Japan

Japan will participate in Phase 1b and Phase 2 after the confirmation of tolerability of PF-07901801 monotherapy in Japanese participants.

For all Japanese participants, the Japan-specific PPP must be followed for the use of lenalidomide. In addition to the protocol requirements ([Appendix 4](#)), the following criteria and procedures related to the Japan-specific PPP are applied for Japanese participants.

Phase 2 of the study will not be initiated per business decision made by Pfizer (protocol amendment 2).

Definition of Woman of Childbearing and Non-Childbearing Potential

A woman is considered fertile following menarche and until becoming postmenopausal unless permanently sterile (see below).

If fertility is unclear (eg, amenorrhea in adolescents or athletes) and a menstrual cycle cannot be confirmed before the first dose of study intervention, additional evaluation should be considered.

- Women in the following categories are not considered WOCBP:

1. Premenopausal female with 1 of the following:

- Documented hysterectomy;
- Documented bilateral oophorectomy.

Note: Documentation for any of the above categories can come from the site personnel's review of the participant's medical records, medical examination, or medical history interview. The method of documentation should be recorded in the participant's medical record for the study.

2. Postmenopausal status is defined as no menses for 24 months without an alternative medical cause (eg, anti-tumor therapy). In addition,

- A high FSH level in the postmenopausal range must be used to confirm a postmenopausal state in women under 60 years of age and not using hormonal contraception or HRT.
- A female on HRT and whose menopausal status is in doubt will be required to use one of the non-estrogen hormonal highly effective contraception methods if they wish to continue their HRT during the study. Otherwise, they must discontinue HRT to allow confirmation of postmenopausal status before study enrollment.

Required Contraceptive Method for Male Participants and Female Participants with Childbearing Potential

Japanese male participants must agree to continue abstinence or use condoms regardless if vasectomized during the required contraception period. To mitigate risk of exposure to fetus during pregnancy, male participants who have a pregnant partner are not eligible for this study.

For Japanese female participants, female participant with childbearing potential must agree to continue abstinence or use 2 methods to ensure contraception during the required

contraception period. One should be chosen from primary method and another should be chosen from secondary method shown below.

- Primary method
 - Intrauterine device
 - Hormonal contraception (oral, injectable, implant, intrauterine hormone releasing system, DMPA [depot medroxyprogesterone acetate] injection, progestogen-only pill [eg, desogestrel])
 - Bilateral tubal occlusion (eg, bilateral tubal ligation)
 - Vasectomized partner
- Secondary method
 - Condom
 - Diaphragm

Required Contraception Period

Japanese participants must initiate use of contraceptive method at least 28 days prior to the first dose of the study drug.

Schedule Of Pregnancy Test

For Japanese female participants with irregular menstrual cycle, pregnancy test should also be performed at Day 15 of every cycle and 14 days after the last dose of lenalidomide in addition to the timing designated in the [SoA](#).

Condition to be discharged

When a participant is discharged from the hospital during the DLT evaluation period, the following conditions (tests, medical examination, etc.) should be performed on the day of the scheduled discharge by the investigators, and the propriety of discharge should be determined. The tests/medical examinations which are needed to confirm the participant's status will be conducted per clinical practice in the study site as appropriate.

- There is no current clinically significant adverse or side effects, including cytokine release syndrome, or medical reasons that requires monitoring in a hospital setting.
- If a clinically significant adverse or side effect has occurred or continues to be present, the investigator has determined that the event is manageable by appropriate treatment or prophylaxis in an out of the hospital setting.
- Overall physical condition is stable and acceptable.

- In case of emergency, the participant may return to the clinical study site or other medical institution. If participants go to a medical institution other than the clinical study site, the clinical study site asks that the participants contact the study site contact information and study investigator and the doctor at the medical institution will communicate to discuss appropriate treatments. A study site keeps framework to ready for emergency situations that is available even during nights and holidays, and the sponsor will ensure that the selected study site will thoroughly follow all participants according to study procedures.

HBV Monitoring

For the [SoA](#) and [Section 8.3.4](#) Clinical Safety Laboratory Assessments, the following additional laboratory HBV monitoring during study intervention should be followed as a precaution:

- For participants with a positive HBsAb and positive HBcAb test but with a negative HBV DNA test at Screening, HB viral load should be monitored for re-activation every 12 weeks. If HBV relapse is observed, the event should be collected in the AE section of the CRF, but the test data will not be required to be reported on the CRF. Participants with an HBsAb positive test who have been vaccinated with HBV are exempt from the testing of HB viral load.
- Administration of study intervention will be interrupted for a participant with an HBV viral load positive test at any time during the study. Starting nucleoside antagonist administration immediately should be considered in parallel with consultation with a hepatologist in accordance with the Japanese Society of Hematology management of hepatitis B virus infection.

10.11. Appendix 11: Lugano Modification of Ann Arbor Staging System (for Primary Nodal Lymphomas)²⁷

Stage	Involvement	Extranodal (E) Status
Limited		
I	One node or group of adjacent nodes	Single extranodal lesions without nodal involvement
II	Two or more nodal groups on the same side of the diaphragm	Stage I or II by nodal extent with limited contiguous extranodal involvement
II bulky*	II as above with “bulky” disease	Not applicable
Advanced		
III	Nodes on both sides of the diaphragm; nodes above the diaphragm with spleen involvement	Not applicable
IV	Additional noncontiguous extralymphatic involvement	Not applicable

NOTE. Extent of disease is determined by positron emission tomography-computed tomography for avid lymphomas and computed tomography for non-avid histologies. Tonsils, Waldeyer’s ring, and spleen are considered nodal tissue.

* Whether stage II bulky disease is treated as limited or advanced disease may be determined by histology and a number of prognostic factors.

10.12. Appendix 12: Lugano Criteria

Criteria	CR	PR	PD
Lugano ^{a,27,35,36,37}	PET-CT, score 1, 2, or 3* with or without a residual mass on 5PS [†] OR on CT, target nodes/nodal masses must regress to ≤1.5 cm in LDi	PET-CT score 4 or 5 with reduced uptake compared with baseline and residual mass(es) of any size. OR On CT ≥50% decrease in SPD of up to 6 target measurable nodes and extranodal sites	<p>PET-CT score 4 or 5 with an increase in intensity of uptake from baseline and/or new FDG-avid foci consistent with lymphoma at interim or end-of-treatment assessment. OR On CT, an individual node/lesion must be abnormal with: LDi >1.5 cm and increase by ≥50% from PPD nadir and an increase in LDi or SDi from nadir 0.5 cm for lesions ≤2 cm 1.0 cm for lesions >2 cm</p> <p>In the setting of splenomegaly, the splenic length must increase by >50% of the extent of its prior increase beyond baseline (eg, a 15 cm spleen must increase to >16 cm). If no prior splenomegaly, must increase by ≥2 cm from baseline. New or recurrent splenomegaly</p> <p>New or clear progression of pre-existing non-measured lesions</p> <p>Regrowth of previously resolved lesions</p> <p>A new node >1.5 cm in any axis or a new extranodal site >1.0 cm in any axis; if <1.0 cm in any axis, its presence must be unequivocal and must be attributable to lymphoma</p> <p>Assessable disease of any size unequivocally attributable to lymphoma</p> <p>AND/OR new or recurrent involvement of the bone marrow</p>
LYRIC	Same as Lugano	Same as Lugano	<p>As with Lugano with the following exceptions:</p> <p>IR IR(1): ≥50% increase in SPD in first 12 weeks IR(2): <50% increase in SPD with a. New lesion(s), or b. ≥50% increase in PPD of a lesion or set of lesions at any time during treatment IR(3): Increase in FDG uptake without a concomitant increase in lesion size meeting criteria for PD</p>

*A score of 3 in many patients indicates a good prognosis with standard treatment, especially if at the time of an interim scan. However, in trials involving PET where de-escalation is investigated, it may be preferable to consider a score of 3 as inadequate response (to avoid undertreatment).

† PET 5PS: 1, no uptake above background; 2, uptake ≤ mediastinum; 3, uptake > mediastinum but ≤ liver; 4, uptake greater than liver; 5, uptake markedly higher than liver (2-3 times SUVmax in normal liver) and/or new lesions; X, new areas of uptake unlikely to be related to lymphoma.

a Efficacy assessments will be made according to the PRoLoG Consensus Initiative for Clinical and Technical clarifications for the application of Lugano as reported by Cheson et al., 2014²⁷, supportive publications Ricard et al., 2023^{36,37}

10.13. Appendix 13: ECOG Performance Status³⁸

Grade	Performance status
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair
5	Dead

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10.14. Appendix 14: International Prognostic Index (IPI)

- age older than 60
- lactate dehydrogenase level higher than normal
- ECOG performance status score of 2 or greater (see [Appendix 13](#))
- stage III or IV disease
- more than one involved extranodal disease site

The IPI gives one point for each of the above characteristics, for a total score ranging from zero to five correlating with the following risk groups:

- low risk: 0–1 points
- low-intermediate risk: 2 points
- high-intermediate risk: 3 points
- high risk: 4–5 points

10.15. Appendix 15: Protocol Amendment History

The protocol amendment summary of changes table for the current amendment is located directly before the TOC. The protocol amendment summary of changes tables for past amendment(s) can be found below:

Amendment 1 (14 March 2023)

Overall Rationale for the Amendment: The primary purpose of this amendment is to change Phase 2 dosing of PF-07901801 from body weight-based to a fixed dosing approach. Substantial changes also implemented at this time include the inclusion of HIV+ participants for Phase 2, revisions to the contraception requirement and pregnancy prevention plan language, a revision to the dose of permitted corticosteroids, a reduction in ECG requirements, and added references to PRoLoG for the application of Lugano efficacy assessments.

Other corrections or revisions were made to clarify or more completely define processes.

Description of Change	Brief Rationale	Section # and Name
Substantial Modification(s)		
For Phase 2: HIV+; Participants with an undetectable viral load and a CD4 count \geq 400 μ L are eligible. For HIV participants, CD4 count and HIV viral load added to the SOA and lab assessments (CD4 and HIV viral load to be documented in the source documents, are not required in the CRF). Detail added under risk for infections in the Section: Risk Assessment.	To be inclusive of participants with controlled HIV.	Section 1.1 Synopsis; Section 1.3 Schedule of Activities; Section 2.3.1 Risk Assessment; Section 5.2 Exclusion Criteria; Table 13 Study-Specific Clinical Laboratory Assessments
ECG frequency of collection reduced.	To simplify protocol requirements. Tafasitamab is unlikely to cause QTc prolongation per USPI and SmPC and due to the nature of being a mAb. The ECG of PF- 07901801 is already sufficiently monitored at Tmax after the first dose and multiple doses at steady state, and a few pre-dose samples and as clinically indicated.	Section 1.3 Schedule of Activities
Pregnancy Prevention Plan language updated throughout to remove reference to REMS	To reconcile differing regional requirements; REMS is not specifically applicable for this study.	Section 2.3.1; Section 10.4

Description of Change	Brief Rationale	Section # and Name
(Risk Evaluation Mitigation Strategy).		
Modified Phase 2 dosing of PF-07901801 from body weight-based to a fixed dosing approach.	<p>To harmonize dosing of PF-0701801 across studies and indications</p> <ul style="list-style-type: none"> • Body weight was not a significant covariate on clearance in the Population PK model. • Fixed dosing provides a potential lower inter-patient variability in PK compared to BWT based dosing. 	Section 4.3.1 Dosing Regimens of PF-07901801
Permitted use of systemic corticosteroids has been reduced from ≤ 20 mg/day to ≤ 10 mg/day of prednisone or equivalent.	To minimize potential confounding effects of steroids on disease under study.	Section 5.2 Exclusion criteria; Section 6.9.5 Corticosteroids
<p>For the administration of PF-07901801, added detail to the sentence that premedications are not required for PF-07901801: 'but may be administered per institutional guidelines at the investigator's discretion and/or if a prior IRR has been experienced' and added detail regarding the observation period: 'For at least the first 4 infusions of PF-07901801, the participant is to remain in the clinic for observation for at least 1 hour after the infusion (and this 1 hour must complete prior to starting the subsequent tafasitamab infusion).'</p> <p>For the administration of tafasitamab, the sentence 'Approximately 60 minutes must elapse after the completion of PF-07901801 prior to the start of the infusion of tafasitamab' has been deleted.</p>	To clarify administration of premedications and observation period for PF-07901801.	Section 2.3.1; Section 6.1.1.1 PF-07901801; Section 6.1.1.2 Tafasitamab

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Description of Change	Brief Rationale	Section # and Name
A ‘user-dependent’ method (with barrier) was added to the currently more restrictive (highly effective, non-user dependent) language.	For greater inclusion of women of child-bearing potential, a ‘user-dependent’ method (with barrier) is added to the currently more restrictive (highly effective, non-user dependent) language. This better corresponds with potential region-specific lenalidomide pregnancy prevention programs and provides appropriate options for women after the completion of lenalidomide but continuing other study drugs.	Section 10.4.2 Female Participant Reproductive Inclusion Criteria
Added: In addition, for Lenalidomide the Pregnancy Prevention Plan (PPP) and any other applicable program required contraceptive methods must be followed (whichever is most stringent).	To clarify that the most stringent contraceptive method (relevant for the region) must be followed.	Section 10.4.4 Contraception Methods
Added language: For contraception methods, refer also to the region-specific PPP educational materials as supplied by the Sponsor.	To clarify that PPP educational materials will be supplied by the Sponsor and will be specific by region.	Section 10.4.5, Figure 4. Pregnancy Prevention Plan Algorithm
Utilization of ‘two effective contraceptive methods’ has been revised to ‘highly effective contraception method(s) as per the PPP or other applicable programs...’	To reconcile differing regional requirements.	Section 10.4.5 Lenalidomide Pregnancy Prevention Program
Notes updated for reticulocytes: to be performed at baseline; clinically indicated is now defined as when there is \geq Grade 2 anemia).	To provide a baseline for eventual later abnormal results.	Table 13 Study-Specific Clinical Laboratory Assessments
Added: ‘Efficacy assessments will be made according to the PRoLoG Consensus Initiative for Clinical and Technical clarifications for the application of Lugano as reported by Cheson et al., 2014 , <i>supportive publications Ricard et al., 2023</i> ’	To include reference to the PRoLoG guidance documents which provide guidance for consistent application of the Lugano classification.	Appendix 12: Lugano Criteria

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Description of Change	Brief Rationale	Section # and Name
Non-Substantial Modification(s)		
Protocol synopsis was shortened, the table ‘Study Interventions Classified as NIMPs/AxMPs’ and the section Ethical Considerations were also added to the synopsis.	To comply with regulatory requirements concerning length of protocol synopsis.	Section 1.1 Synopsis
Updated ‘EBV positive DLBCL of the elderly’ to ‘EBV positive DLBCL’, ‘double’ or ‘triple hit’ DLBCL updated to ‘High-grade lymphoma (formerly known as ‘double or ‘triple hit’ DLBCL)’ and the referenced (current) edition of the WHO classification added; CNS lymphoma clarified as ‘involvement – present or past medical history’	To be consistent with the most recent WHO Classification of Lymphoid Neoplasms.	Section 1.1 Synopsis; Section 5.1 Inclusion Criteria
Exclusion of active GVHD has been deleted	To simplify enrollment criteria; active GVHD is not expected to be relevant in this population (prior allogeneic transplant is excluded).	Section 1.1 Synopsis; Section 5.2 Exclusion Criteria
Diagnostic CT scan added to End of Treatment and in parenthesis at LTFU on the SOA	To correct previous omission; CT scan is also to be collected at end of treatment imaging together with PET, and is required during LTFU if/when a participant is discontinued prior to progression.	Section 1.3 Schedule of Activities; Section 8.1.2 Follow-up Visits and LTFU
Added detail regarding saliva sample and planned use, together with blood biomarker samples, for specified genetic research	To clarify that saliva biomarker samples may also be used for specified genetic research.	Section 1.3 Schedule of Activities, Sections 8.7 Biomarkers, 8.7.6 Saliva Sample for Matched Control and Specified Genetic Research
Added detail to the sentence that Infusion Related Reaction (IRR) has not been prevalent ‘when administered with premedications’	To clarify available data regarding infusion related reactions.	Section 2.3.1
Added to clinical pharmacology section details	To provide more comprehensive detail regarding anti-tafasitamab antibodies	Section 2.3.3.2

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Description of Change	Brief Rationale	Section # and Name
regarding anti-tafasitamab antibodies		
Added details to the cardiovascular exclusion criterion.	To better clarify cardiac/cardiovascular/thromboembolic exclusion language, including the non-exclusion of atrial fibrillation.	Section 5.2 Exclusion Criteria
Added language that equivalent premedications include variations to the stated due to the formulations available locally and or in accordance with institutional guidelines.	To clarify that equivalent premedications to those specified may be used.	Section 6.0, Table 5 Study Interventions Classified as NIMPs/AxMPs; Section 6.1.1.2 Tafasitamab
Added detail to instruction regarding missed doses of Lenalidomide.	To provide further clarification, as from the product SmPC.	Section 6.1.1.3 Lenalidomide
Added detail 'radiographic images utilized for efficacy assessments may be collected and stored by an independent third party imaging laboratory, (see Imaging Manual for details).'	To clarify that scans may be collected and stored by a third party imaging laboratory.	Section 8.2 Efficacy Assessments
Added detail regarding options for CT scan contrast: abdominal and pelvic CT scans should be performed with oral or IV contrast.	To clarify that IV contrast may also be used for abdominal or pelvic CT scans.	Section 8.2.1 Computed Tomography Scans
Symbol correction: fevers of >38.0°C, not ≥38.0°C.	To correct the definition of B-Symptoms.	Section 8.3.6 B-Symptoms
Deleted note for WBC differential: 'Percent to be collected only if absolute values are not available.'	To clarify that percent will not be an option in the CRF. Sites without absolute values will calculate the absolute values as per instructions in the CRF Completion Guidance document.	Table 13 Study-Specific Clinical Laboratory Assessments
Alternative lab aPTT has been added.	To provide more flexibility for sites.	
Minor updates and clarifications	Minor updates or clarifications were made for accuracy and consistency.	Throughout protocol

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10.16. Appendix 16: Abbreviations

The following is a list of abbreviations that may be used in the protocol.

Abbreviation	Term
~	approximately
%	percent or percentage
5PS	5-point scale
Ab	antibody
ADA	antidrug antibodies
ADCC	antibody-dependent cell-mediated cytotoxicity
ADCP	antibody-dependent cell-mediated phagocytosis
AE	adverse event
AIDS	acquired immunodeficiency syndrome
AKI	acute kidney injury
ALP	alkaline phosphatase
ALT	alanine aminotransferase
AML	acute myeloid leukemia
ANC	absolute neutrophil count
aPTT	activated partial thromboplastin
ASCO	American Society of Clinical Oncology
ASCT	autologous stem cell transplantation
AST	aspartate aminotransferase
ASTCT	The American Society for Transplantation and Cellular Therapy
AUC	area under the curve
AV	atrioventricular
AxMP	auxiliary medicinal product
BCL	B-cell lymphoma
BOR	best overall response
BP	blood pressure
bpm	beats per minute
BR	best response
BWT	body weight
C#	Cycle 1, 2, 3, etc.
CAR-T	chimeric antigen receptor T-cell
CBC	complete blood count
CDC	Center for Disease Control
cfDNA	cell-free DNA
CFR	Code of Federal Regulations
CI	confidence interval
CIOMS	Council for International Organizations of Medical Sciences
CK	creatinine kinase
CKD	chronic kidney disease
C _{max}	maximum observed concentration
CNS	central nervous system

090177e1a258b721\Approved\Approved On: 13-Dec-2024 05:57 (GMT)

Abbreviation	Term
CONSORT	Consolidated Standards of Reporting Trials
COVID-19	coronavirus disease 2019
CR	complete response
CrCl	creatinine clearance
CRF	case report form
CRO	contract research organization
CRS	cytokine release syndrome
CRR	complete response rate
CSR	Clinical Study Report
CT	computed tomography/clinical trial
CTCAE	Common Terminology Criteria for Adverse Events
CTCL	cutaneous T-cell lymphoma
ctDNA	circulating tumor DNA
CTIS	Clinical Trial Information System
CV	coefficient of variation
D#	Day 1, 2, 3, etc.
DCT	data collection tools
DDI	drug-drug interaction
DILI	drug-induced liver injury
DL	dose level
DLBCL	diffuse large B cell lymphoma
DLR	Dose Level Review
DLT	dose-limiting toxicity
DoCR	duration of complete response
DoR	duration of response
DRESS	drug reaction with eosinophilia and systemic symptoms
DU	dispensable unit
DVT	deep vein thrombosis
EBV	Epstein-Barr virus
EC	ethics committee
ECG	electrocardiogram
Echo	echocardiogram
ECOG	Eastern Cooperative Oncology Group
eCrCl	estimated creatinine clearance
eCRF	electronic case report form
EDB	exposure during breastfeeding
EDP	exposure during pregnancy
E-DMC	External Data Monitoring Committee
eGFR	estimated glomerular filtration rate
EI	Equivalence Interval
EOI	end of infusion
EOT	end of treatment
EPI	Epidemiology Collaboration

090177e1a258b721\Approved\Approved On: 13-Dec-2024 05:57 (GMT)

Abbreviation	Term
eSAE	electronic serious adverse event
EU	European Union
EU CT	European Union Clinical Trials
EudraCT	European Union Drug Regulating Authorities Clinical Trials (European Clinical Trials Database)
Fc	fragment of the immunoglobulin that is encoded by constant (c) genes
FCGR	Fc gamma receptor
FcR	Fc receptor
FcRn	neonatal Fc receptor
FDG	fluorodeoxyglucose
FFPE	formalin-fixed paraffin-embedded
FIH	first-in-human
FISH	Fluorescence in situ hybridization
FL	follicular lymphoma
FSH	follicle-stimulating hormone
FU	follow-up
G#	CTCAE Grade 1, 2, etc
GCP	Good Clinical Practice
G-CSF	granulocyte colony-stimulating factor,
GGT	gamma-glutamyl transferase
GVHD	graft-versus-host disease
HBcAb	hepatitis B core antibody
HBsAb	hepatitis B surface antibody
HBsAg	hepatitis B surface antigen
HBV	hepatitis B virus
HCV	hepatitis C virus
HIV	human immunodeficiency virus
HL	Hodgkin lymphoma
HR	hazard ratio, heart rate
HRT	hormone replacement therapy
IB	Investigator's Brochure
ICD	informed consent document
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
ID	identification
IgA	immunoglobulin A
IgG	immunoglobulin G
IgM	immunoglobulin M
IMiD	immunomodulatory imide drug
IMP	investigational medicinal product
IND	Investigational New Drug
INR	international normalized ratio
IP	investigational product

Abbreviation	Term
IPAL	Investigational Product Accountability Log
IPI	International Prognostic Index
IR	immune response
IRB	Institutional Review Board
IRR	infusion related reaction
IRT	Interactive Response Technology
IV	intravenous
LBBB	left bundle branch block
LDH	lactate dehydrogenase
LDi	longest diameter
LFT	liver function test
LTFU	Long-Term Follow-Up
LVEF	left ventricular ejection fraction
MedDRA	Medical Dictionary for Regulatory Activities
MDR	Medical Device Regulation
MM	multiple myeloma
MoA	mechanism of action
MQI	medically qualified individual
MRI	magnetic resonance imaging
MTD	maximum tolerated dose
mTPI	modified toxicity probability interval
MUGA	multigated acquisition scan
N, n	number
NA	not applicable
NAb	neutralizing antibodies
NBF	neutral-buffered formalin
NCI	National Cancer Institute
NHL	non-Hodgkin Lymphoma
NIMP	non-investigational medicinal product
NK	natural killer
NOS	not otherwise specified
OR	objective response
ORR	objective response rate
OS	overall survival
PACL	Protocol Administrative Change Letter
PD	pharmacodynamics(s), progressive disease
PE	physical examination
PET	positron emission tomography
PFS	progression-free survival
PI	Principal Investigator
PK	pharmacokinetic(s)
PO	by mouth
PR	partial response/pulse rate

090177e1a258b721\Approved\Approved On: 13-Dec-2024 05:57 (GMT)

Abbreviation	Term
PPD	product of the perpendicular diameters
PPP	pregnancy prevention plan
RP2D	recommended Phase 2 dose
RP3D	recommended Phase 3 dose
PSSA	Pfizer's Serious Adverse Event Submission Assistant
pT	target probability
PT	prothrombin time
PTCL	peripheral T-cell lymphoma
PTT	partial thromboplastin time
PVC	premature ventricular contraction
Q2W	once every two weeks
Q12W	once every 12 weeks
QD	once daily
QTc	corrected QT interval
QTcF	QTc (Fridericia method)
QTL	quality tolerance limit
QW	once weekly
R-CHOP	rituximab, cyclophosphamide, doxorubicin, vincristine, prednisolone
R-CHP	rituximab, cyclophosphamide, doxorubicin, prednisolone
RBC	red blood cell
R-DHAP	rituximab, dexamethasone, cytarabine, cisplatin
REMS	Risk Evaluation and Mitigation Strategy
R-GemOx	rituximab, gemcitabine and oxaliplatin
R-ICE	rituximab, ifosfamide, carboplatin, etoposide
RNA	ribonucleic acid
R/R	relapsed/refractory
SAE	serious adverse event
SAP	Statistical Analysis Plan
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
Scr	serum creatinine
Scys	serum cystatin C
SD	stable disease, standard deviation
SDi	short diameter
SJS	Stevens-Johnson syndrome
SmPC	Summary of Product Characteristics
SIRP	signal regulatory protein
SoA	schedule of activities
SOP	standard operating procedure
SPD	sum of the product of the diameters
SRSD	Single reference Safety Document
SSID	single subject identifier
SUSAR	Suspected Unexpected Serious Adverse Reaction
t _{1/2}	terminal elimination half-life

090177e1a258b721\Approved\Approved On: 13-Dec-2024 05:57 (GMT)

Abbreviation	Term
SUV _{max}	maximum standard unit value
T bili	total bilirubin
TCR	T-cell receptor
TEAE	treatment-emergent adverse event
TEN	toxic epidermal necrolysis
TLS	tumor lysis syndrome
T _{max}	time to maximum concentration
ToC	table of content
TX	treatment
ULN	upper limit of normal
UPM	unit probability mass
US	United States
USPI	United State Prescribing Information
UVB	ultraviolet B
VTE	venous thromboembolism
WBC	white blood cell
WHO	World Health Organization
WOCBP	woman/women of childbearing potential

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