EMENDAMENTO N. 1 AL CONTRATTO PER LA CONDUZIONE DELLA SPERIMENTAZIONE CLINICA SU MEDICINALI	AMENDMENT No. 1 TO CLINICAL INVESTIGATION AGREEMENT FOR THE DRUGS
Emendamento n. 1 al CONTRATTO PER LA CONDUZIONE DELLA SPERIMENTAZIONE CLINICA SU MEDICINALI ("**Emendamento 1**") stipulato tra **Karyopharm Therapeutics Inc**., con sede legale in 85 Wells Ave. Newton MA 02459 USA, C.F. e partita IVA n. 26 3931704, in persona del Legale Rappresentante Ran Frenkel, in qualità di EVP, Chief Development Officer (d'ora innanzi denominata "**Promotore**"),e **ASL LATINA - Azienda Sanitaria Locale Latina** (d'ora innanzi denominata "**Ente**"), con sede legale in Viale P.L. Nervi snc, C.D.C. "Latina Fiori" Torre 2, 04100 Latina- C.F. e P. IVA n. 01684950593, in persona del Legale Rappresentante Dott.ssa Silvia Cavalli che ha delegato alla sottoscrizione del presente atto il Dott. Massimo Fabio Marciano, Direttore ad interim della UOC Affari Generali e Controllo Interno Indicate individualmente come la "Parte" e congiuntamente come le "Parti". Ai soli fini della sottoscrizione del presente Emendamento N. 1, il Promotore è rappresentato da PPD Italy S.r.l. (d'ora innanzi denominata "PPD" o "CRO"), con sede in Segreen Business Park, Via San Bovio, 3 San Felice, 20054 Segrate (MI), Italia.	Amendment No. 1 to the CLINICAL INVESTIGATION AGREEMENT FOR THE DRUGS ("**Amendment 1**") by and between **Karyopharm Therapeutics Inc**., headquartered in 85 Wells Ave. Newton MA 02459 USA, tax code and VAT no. 26 3931704, through its Legal Representative Ran Frenkel, EVP, Chief Development Officer (hereinafter the "**Sponsor**"), and **ASL LATINA - Azienda Sanitaria Locale Latina** (hereinafter the "**Entity**"), headquartered in Viale P.L. Nervi snc, C.D.C. "Latina Fiori" Torre 2, 04100 Latina, Tax Code and VAT no. 01684950593 through its Legal Representative Dott.ssa Silvia Cavalli, who has delegated the signature of this Agreement to Dr. Massimo Fabio Marciano, Interim Director of the General Affairs and Internal Control Unit Each a "Party" and collectively the "Parties". For the only purposes of signing this Amendment No. 1, Sponsor is represented by PPD Italy S.r.l. (hereinafter "PPD" or "CRO"), with offices at Segreen Business Park, Via San Bovio, 3 San Felice, 20054 Segrate (MI), Italy.
PREMESSE	WITNESSETH
PREMESSO CHE in data 31 maggio 2022 il Promotore, l'Azienda hanno stipulato la convenzione relativa al Protocollo XPORT-MF-035, dal titolo: "STUDIO MULTICENTRICO DI FASE 2, RANDOMIZZATO, IN APERTO, PER VALUTARE LA SICUREZZA E L'EFFICACIA DI SELINEXOR COME SINGOLO AGENTE RISPETTO AL TRATTAMENTO SCELTO DAL MEDICO IN PAZIENTI CON MIELOFIBROSI PRECEDENTEMENTE TRATTATA", n. EudraCT.: 2020-003809-60 ("Contratto"); e PREMESSO CHE le Parti desiderano modificare le condizioni del Contratto al fin di : - modificare l'Allegato A1 "Condizioni relative ai compensi e ai pagamenti" del Contratto a causa dell'Emendamento al Protocollo	WHEREAS, Sponsor, Entity have entered into the Agreement effective May 31, 2022 to proceed with Protocol XPORT-MF-035, entitled:" A PHASE 2, RANDOMIZED, OPEN-LABEL, MULTICENTER STUDY TO EVALUATE SAFETY AND EFFICACY OF SINGLE AGENT SELINEXOR VERSUS TREATMENT OF PHYSICIAN'S CHOICE IN PATIENTS WITH PREVIOUSLY TREATED MYELOFIBROSIS" EudraCT-Nr.: 2020-003809-60 (the "Agreement"); and WHEREAS, the Parties desire to amend the terms of the Agreement to: - amend Exhibit A1 "Compensation and Payment Terms" of the Agreement due to Protocol amendment version 4.0 effective

versione 4.0 effettivo dal 20 Ottobre 2021	October 20, 2021
TUTTO CIÒ PREMESSO, le Parti stipulano e convengono quanto segue:	NOW, THEREFORE, the Parties agree as follows:
1. La tabella budget dovrà essere eliminata nella sua interezza e sostituita con la versione revisionata ivi allegata e incorporata per riferimento	1. Budget Table shall be deleted in its entirety and replaced with the revised one attached hereto and incorporated by reference herein.
2. Una volta sottoscritto, il presente Emendamento 1 formerà parte del Contratto.	2. Upon execution, this Amendment 1 shall be made a part of the Agreement.
3. Tutte le previsioni contenute nel Contratto e non modificate in virtù del presente Emendamento 1 continuano ad essere pienamente efficaci. In caso di conflitto tra i termini del Contratto e quanto previsto dal presente Emendamento 1, prevarranno i termini dell'Emendamento 1 esclusivamente in relazione alle parti de Contratto modificate dall'Emendamento 1 stesso.	3. All other terms and conditions of the Agreement, not redefined by this Amendment 1, shall remain in full force and effect. In the event of any conflict between the terms of the Agreement and this Amendment 1, the terms of this Amendment 1 shall govern and control exclusively for the parts of the Agreement modified by this Amendment 1.
4. Tutti i termini con iniziale maiuscola, ma non altrimenti definiti nel presente documento, avranno il significato loro attribuito nel Contratto.	4. All capitalized terms used, but not otherwise defined herein, shall have the meanings ascribed to them in the Agreement.
Il presente Emendamento 1 viene sottoscritto con firma autografa. Le imposte e tasse inerenti e conseguenti alla stipula del presente Emendamento 1, ivi comprese l'imposta di bollo sull'originale di cui all'art. 2 della Tabella Allegato A – tariffa parte I del DPR n. 642/1972 e l'imposta di registro devono essere versate, nel rispetto della normativa applicabile.	This Amendment 1 is signed in wet ink. All the taxes and duties relating to or resulting from the stipulation of this Amendment 1, including the revenue stamp on the original as referred to in Article 2 of the table in Annex A – tariff part I of Presidential Decree 642/1972, and the registration tax, must be paid in accordance with the applicable regulations.
A TESTIMONIANZA DI QUANTO SOPRA, le Parti hanno stipulato il presente Emendamento. 1 con validità dalla data dell'ultima firma.	IN WITNESS WHEREOF, the Parties have executed this Amendment 1 as of the last signature date.

Per il Promotore/For the Sponsor: PPD Italy

Il Procuratore/The Attorney

Dott.ssa/Dr. Marta De MitriFirma/Signature

Per/For ASL LATINA - Azienda Sanitaria Locale Latina

Il Direttore ad interim dell'UOC Affari Generali e Controllo interno/Interim Director of the General Affairs and Internal Control Unit

Dott. /Dr. Massimo Fabio Marciano

Study Details	
Institution	ASL Latina
PI Name	Prof. Giuseppe Cimino
Site Number	1206
Study Code:	XPORT-MF-035 PV 4.0
Short Name:	
Drug / Compound:	Selinexor
Title:	A phase 2, randomized, open-label, multicenter study to evaluate safety and efficacy of single agent selinexor versus treatment of physician's choice in patients with previously treated myelofibrosis
Phase:	II

ICD Code	Indication	Primary
D75.81 (ICD10)	Myelofibrosis	✔

Currency: Euro	
Site OH rate	19,00%

Visit Description	Italy Site Costs			
Code	**Site Costs**	**Budget**	**OH**	**Total Budget**
SC003	Study Start-Up Fee/Site Set-Up Fee	1.434		1.434
SC023	Study Close out: including all activities related to closing out the site	843		843
Supportive Care	Costs for Supportive Care will be reimbursed in accordance with the Compensation and Payment Terms	INVOICE		INVOICE
Unscheduled Visits	Reimbursement for unscheduled visits will be made based on the procedures performed as set forth in this Budget	INVOICE		INVOICE
Screen Failures	Sponsor will reimburse Institution up to three (3) Screen Failures at the Screening Visit rate for the duration of the Study as verified by data entered into the CRF and in accordance with the Compensation and Payment Terms.	up to		INVOICE
Code	**PHARMACY COSTS**	**Budget**	**OH**	**Total Budget**
SC008	Pharmacy: Set-Up Fee	602		602
Code	**Patient Travel Reimbursement**	**Budget**	**OH**	**Total Budget**
NP007	Patient Travel Reimbursement-Per Study related in office visits only	up to 24		up to 24
NP037	Lodging reimbursement amount per night, inclusive of tax is not to exceed €150. Receipts are required for reimbursement.	up to 150		up to 150

Study Details	
Institution	ASL Latina
PI Name	Prof. Giuseppe Cimino
Site Number	1206
Study Code:	XPORT-MF-035 PV 2.0
Short Name:	
Drug / Compound:	Selinexor
Title:	A phase 2, randomized, open-label, multicenter study to evaluate safety and efficacy of single agent selinexor versus treatment of physician's choice in patients with previously treated myelofibrosis
Phase:	II

ICD Code	Indication	Primary
D75.81 (ICD10)	Myelofibrosis	✔

Currency: Euro

Visit Schedule **Italy**

Cost Per Procedure View

Code	Procedure		OH	Budget	Screening D -28 to -1	C1D1	C1D3 ± 2 days	C1D15 ± 3 days	C2D1 ± 3 days	C2D2	C3D1 ± 3 days	C4D1 ± 3 days	C5D1 ± 3 days	C6D1 ± 3 days	C7D1 ± 3 days	EoT Visit ≤ 28 Days Post Treatment Discontinuation	Follow-Up Visit 30 days after EoT ± 7 days	Follow Up Visit Every 3 months until 12 months ± 14 days
INCON	Informed consent			✔ 35	35													
INCEX	Inclusion/Exclusion criteria			✔ 33	33													
T9210	Medical History with Demographics			✔ 63	63													
S0042	Eastern Cooperative Oncology Group (ECOG) Performance Status			✔ 17	17											17		
93000	12-lead ECG Includes tracing, interpretation and report			✔ 53	53													
BSA	BSA (Body Surface Area)			✔ 17	17													
CONMD	Concomitant medications			✔ 19		19	19	19	19	19	19	19	19	19	19	19		
84702	Serum pregnancy, gonadotropin chorionic (hCG) (BetahCG); quantitative			✔ 21	11				11		11	11	11	11	11	11		
99211	Vital Signs			✔ 11		11			11		11	11	11	11	11			
99211	Weight			✔ 11		11			11		11	11	11	11	11	11		
99205	Physical Exam - Full*			✔ 116	116											116		
99212	Physical Exam - Symptom Directed*			✔ 72		INV			INV		INV	INV	INV	INV	INV			
ADEVT	Serious Adverse Events/Adverse events			✔ 21			21	21	21	21	21	21	21	21	21	21	21	
85025	CBC with complete differential			✔ 22		INV		22	22		22	22	22	22	22	22		
80053	Complete Serum Chemistry: Includes Bilirubin, total, direct Calcium Carbon Dioxide (bicarbonate) Chloride Creatinine Glucose Magnesium Phosphate, alkaline Potassium Protein, total Sodium Transferase, alanine amino (ALT) (SGPT) Transferase, aspartate amino (AST) (SGOT) Urea Nitrogen (BUN)			✔ 45		INV		45	45		45	45	45	45	45	45		
83615	Lactate dehydrogenase (LD) (LDH)			✔ 12		INV		12	12		12	12	12	12	12	12		
38221	Bone Marrow Biopsy			✔ 394	394										394			
38220	Bone Marrow Aspirate			✔ 392	392										392			
81403	MPN Mutation Panel			✔ 236	236										236			
74182	Magnetic resonance imaging, abdomen, abdominal (MRI); with contrast material(s) (eg, proton)**			✔ 677	INV							INV			INV	INV		
R4182	Interpretation and Report; Magnetic resonance imaging, abdomen, abdominal (MRI)**			✔ 214	INV							INV			INV	INV		
NP030	ePRO Instruction			✔ 26	26													
NP031	ePRO Monitoring/Review (Includes MFSAF V4.0, PGIC, EQ-5D-5L)			✔ 19		19			19		19	19	19	19	19	19	19	19
T0299	PK Sampling***			✔ 20					80	20								
T0299	PDn Sampling****			✔ 20	20				20							20		
	Procedures Sub Total (€)				**€ 1.413**	**€ 60**	**€ 40**	**€ 119**	**€ 271**	**€ 60**	**€ 171**	**€ 171**	**€ 171**	**€ 171**	**€ 1.193**	**€ 313**	**€ 40**	**€ 19**

Code	Non Procedure		OH	Budget	Screening D -28 to -1	C1D1	C1D3 ± 2 days	C1D15 ± 3 days	C2D1 ± 3 days	C2D2	C3D1 ± 3 days	C4D1 ± 3 days	C5D1 ± 3 days	C6D1 ± 3 days	C7D1 ± 3 days	EoT Visit ≤ 28 Days Post Treatment Discontinuation	Follow-Up Visit 30 days after EoT ± 7 days	Follow Up Visit Every 3 months until 12 months ± 14 days
NP006	Pharmacy, Simple - dispense drug			✔ 25		25			25		25	25	25	25	25			
NP021	Study Coordinator - PER HOUR			✔ 48	120	96	24	96	96	48	96	96	96	96	96	120	24	24
NP025	Physician - PER HOUR			✔ 71	71	71		71	71		71	71	71	71	71	71		
NP012	Study Coordinator, Electronic Data Capture (EDC) - Per Hour			✔ 28	42	42	14	42	42	28	42	42	42	42	42	42	14	14
	Non Procedures Sub Total(€)				**€ 233**	**€ 234**	**€ 38**	**€ 209**	**€ 234**	**€ 76**	**€ 234**	**€ 234**	**€ 234**	**€ 234**	**€ 234**	**€ 233**	**€ 38**	**€ 38**
	Overhead (all costs)	19%			**€ 313**	**€ 56**	**€ 15**	**€ 62**	**€ 96**	**€ 26**	**€ 77**	**€ 77**	**€ 77**	**€ 77**	**€ 271**	**€ 104**	**€ 15**	**€ 11**
	Total Cost Per Visit with Overhead(€)				**€ 1.959**	**€ 350**	**€ 93**	**€ 390**	**€ 601**	**€ 162**	**€ 482**	**€ 482**	**€ 482**	**€ 482**	**€ 1.698**	**€ 650**	**€ 93**	**€ 68**
	Total Cost Per Patient (€)				**€ 7.992**													

Code	Conditional Procedure	Budget	OH	Total Budget
93000	12-lead ECG Includes tracing, interpretation and report	53		✔ 63
99212	Physical Exam - Symptom Directed*	72		✔ 86
85025	CBC with complete differential	22		✔ 26
80053	Complete Serum Chemistry: Includes Bilirubin, total, direct Calcium Carbon Dioxide (bicarbonate) Chloride Creatinine Glucose Magnesium Phosphate, alkaline Potassium Protein, total Sodium Transferase, alanine amino (ALT) (SGPT) Transferase, aspartate amino (AST) (SGOT) Urea Nitrogen (BUN)	45		✔ 54
83615	Lactate dehydrogenase (LD) (LDH)	12		✔ 14
84702	Serum pregnancy, gonadotropin chorionic (hCG) (BetahCG); quantitative	21		✔ 25
84703	Urine pregnancy, gonadotropin chorionic (hCG) (BetahCG); qualitative	17		✔ 20
74182	Magnetic resonance imaging, abdomen, abdominal (MRI); with contrast material(s) (eg, proton)**	677		✔ 806
R4182	Interpretation and Report; Magnetic resonance imaging, abdomen, abdominal (MRI)**	214		✔ 255
74160	Computerized axial tomography, abdomen, abdominal (Cat Scan) (CT Scan); with contrast material(s)**	588		✔ 700
R4160	Interpretation and Report; Computerized axial tomography, abdomen, abdominal (Cat Scan) (CT Scan)**	174		✔ 207
81403	MPN Mutation Panel	236		✔ 281
T0299	PK Sampling (Per Draw)***	20		✔ 24
T0299	PDn Sampling****	20		✔ 24
NP029	Dry Ice - Per Sample	13		✔ 15
99000	Lab handling and/or shipping of specimen(s)	13		✔ 15
Additional Cycles	For those Subjects receiving additional cycles beyond Cycle 7, Institution will be reimbursed in accordance with the rates set forth in the column labeled C6D1 above.			

*Full physical examinations (PE) will be performed prior to receiving first dose of study drug and at EOT Visit. All other PEs during the study should be limited, symptom-directed PEs, including body systems as appropriate. **Spleen volume will be measured locally by MRI at screening, and at 12 weeks ±7 days, 24 weeks ±7 days, 36 weeks ±7 days, and 48 weeks ±7 days (on or around C4D1, C7D1, C10D1, C13D1). Abdominal CT is acceptable if MRI is contraindicated or not available for estimation of spleen volume. MRI (or CT) at the EoT visit should be performed for patients who discontinue for reasons other than documented PD, if previous imaging was more than 6 weeks old. ***Blood PK samples of approximately 2.0 mL for selinexor will be collected at 1, 2, 4, and 6 hours post-selinexor dose on C2D1 and 24 hours (C2D2) post selinexor dose from a subset of selinexor treated patients (n=25). ****PDn blood samples will be collected at Screening, C2D1, and EoT. PDn blood samples should be collected within 2 hours prior to dosing.

Study Details																		
Institution	ASL Latina																	
PI Name	Prof. Giuseppe Cimino																	
Site Number	1206																	
Study Code:	XPORT-MF-035 PV 4.0																	
Short Name:																		
Drug / Compound:	Selinexor																	
Title:	A phase 2, randomized, open-label, multicenter study to evaluate safety and efficacy of single agent selinexor versus treatment of physician's choice in patients with previously treated myelofibrosis																	
Phase:	II																	
ICD Code	**Indication**	**Primary**																
D75.81 (ICD10)	Myelofibrosis	✔																
Currency: Euro																		
Visit Schedule	**Italy**																	
Cost Per Procedure View																		

Code	Procedure		OH	Budget	C1D1	C1D3 ± 2 days	C1D15 ± 3 days	C2D1 ± 3 days	C3D1 ± 3 days	C4D1 ± 3 days	C5D1 ± 3 days	C6D1 ± 3 days	C7D1 ± 3 days	EoT Visit ≤ 28 Days Post-Treatment Discontinuation	Follow-Up Visit 30 days after EoT ± 7 days	Follow Up Visit Every 3 months until 12 months ± 14 days
INCON	Informed consent		✔	35	35											
INCEX	Inclusion/Exclusion criteria		✔	33	33											
S0042	Eastern Cooperative Oncology Group (ECOG) Performance Status		✔	17	17											
CONMD	Concomitant medications		✔	19	19	19	19	19	19	19	19	19	19	19		
84702	Serum pregnancy, gonadotropin chorionic (hCG) (BetahCG); quantitative		✔	21	11			11	11	11	11	11	11	11		
99211	Vital Signs		✔	11	Removed			11	11	11	11	11	11			
99211	Weight		✔	11	11			11	11	11	11	11	11	11		
99205	Physical Exam - Full*		✔	116	116									116		
99212	Physical Exam - Symptom Directed*		✔	72	Removed			INV	INV	INV	INV	INV	INV			
ADEVT	Serious Adverse Events/Adverse events		✔	21	21	21	21	21	21	21	21	21	21	21	21	
85025	CBC with complete differential		✔	22	INV		22	22	22	22	22	22	22	22		
80053	Complete Serum Chemistry: Includes Bilirubin, total, direct Calcium Carbon Dioxide (bicarbonate) Chloride Creatinine Glucose Magnesium Phosphate, alkaline Potassium Protein, total Sodium Transferase, alanine amino (ALT) (SGPT) Transferase, aspartate amino (AST) (SGOT) Urea Nitrogen (BUN)		✔	45	INV		45	45	45	45	45	45	45	45		
83615	Lactate dehydrogenase (LD) (LDH)		✔	12	INV		12	12	12	12	12	12	12	12		
38221	Bone Marrow Biopsy		✔	394	394								394			
38220	Bone Marrow Aspirate		✔	392	392								392			
81403	MPN Mutation Panel		✔	236	236								236			
74182	Magnetic resonance imaging, abdomen, abdominal (MRI); with contrast material(s) (eg, proton)**		✔	677	INV					INV			INV	INV		
R4182	Interpretation and Report; Magnetic resonance imaging, abdomen, abdominal (MRI)**		✔	214	INV					INV			INV	INV		
NP031	ePRO Monitoring/Review (Includes MFSAF V4.0, PGIC, EQ-5D-5L)		✔	19	19			19	19	19	19	19	19	19	19	19
	Procedures Sub Total (€)				**€ 1.304**	**€ 40**	**€ 119**	**€ 171**	**€ 171**	**€ 171**	**€ 171**	**€ 171**	**€ 1.193**	**€ 276**	**€ 40**	**€ 19**

Crossover

Code	Non Procedure		OH	Budget	C1D1	C1D3 ± 2 days	C1D15 ± 3 days	C2D1 ± 3 days	C3D1 ± 3 days	C4D1 ± 3 days	C5D1 ± 3 days	C6D1 ± 3 days	C7D1 ± 3 days	EoT Visit ≤ 28 Days Post-Treatment Discontinuation	Follow-Up Visit 30 days after EoT ± 7 days	Follow Up Visit Every 3 months until 12 months ± 14 days
NP006	Pharmacy, Simple - dispense drug		✔	25	25			25	25	25	25	25	25			
NP021	Study Coordinator - PER HOUR		✔	48	96	24	96	96	96	96	96	96	96	120	24	24
NP025	Physician - PER HOUR		✔	71	71		71	71	71	71	71	71	71	71		
NP012	Study Coordinator, Electronic Data Capture (EDC) - Per Hour		✔	28	42	14	42	42	42	42	42	42	42	42	14	14
	Non Procedures Sub Total(€)				**€ 234**	**€ 38**	**€ 209**	**€ 234**	**€ 234**	**€ 234**	**€ 234**	**€ 234**	**€ 234**	**€ 233**	**€ 38**	**€ 38**
	Overhead (all costs)	19%			**€ 292**	**€ 15**	**€ 62**	**€ 77**	**€ 77**	**€ 77**	**€ 77**	**€ 77**	**€ 271**	**€ 97**	**€ 15**	**€ 11**
	Total Cost Per Visit with Overhead(€)				**€ 1.830**	**€ 93**	**€ 390**	**€ 482**	**€ 482**	**€ 482**	**€ 482**	**€ 482**	**€ 1.698**	**€ 606**	**€ 93**	**€ 68**
	Total Cost Per Patient (€)				**€ 7.188**											

Code	Conditional Procedure	Budget	OH	Total Budget
93000	12-lead ECG Includes tracing, interpretation and report	53	✔	63
99212	Physical Exam - Symptom Directed*	72	✔	86
85025	CBC with complete differential	22	✔	26
80053	Complete Serum Chemistry: Includes Bilirubin, total, direct Calcium Carbon Dioxide (bicarbonate) Chloride Creatinine Glucose Magnesium Phosphate, alkaline Potassium Protein, total Sodium Transferase, alanine amino (ALT) (SGPT) Transferase, aspartate amino (AST) (SGOT) Urea Nitrogen (BUN)	45	✔	54
83615	Lactate dehydrogenase (LD) (LDH)	12	✔	14
84702	Serum pregnancy, gonadotropin chorionic (hCG) (BetahCG); quantitative	21	✔	25
84703	Urine pregnancy, gonadotropin chorionic (hCG) (BetahCG); qualitative	17	✔	20
74182	Magnetic resonance imaging, abdomen, abdominal (MRI); with contrast material(s) (eg, proton)**	677	✔	806
R4182	Interpretation and Report; Magnetic resonance imaging, abdomen, abdominal (MRI)**	214	✔	255
74160	Computerized axial tomography, abdomen, abdominal (Cat Scan) (CT Scan); with contrast material(s)**	588	✔	700
R4160	Interpretation and Report; Computerized axial tomography, abdomen, abdominal (Cat Scan) (CT Scan)**	174	✔	207
81403	MPN Mutation Panel	236	✔	281
NP029	Dry Ice - Per Sample	13	✔	15
99000	Lab handling and/or shipping of specimen(s)	50	✔	60
Additional Cycles	For those Subjects receiving additional cycles beyond Cycle 7, Institution will be reimbursed in accordance with the rates set forth in the column labeled C6D1 above.			

*Full physical examinations (PE) will be performed prior to receiving first dose of study drug and at EOT Visit. All other PEs during the study should be limited, symptom-directed PEs, including body systems as appropriate. **Spleen volume will be measured locally by MRI at screening, and at 12 weeks ±7 days, 24 weeks ±7 days, 36 weeks ±7 days, and 48 weeks ±7 days (on or around C4D1, C7D1, C10D1, C13D1). Abdominal CT is acceptable if MRI is contraindicated or not available for estimation of spleen volume. MRI (or CT) at the EoT visit should be performed for patients who discontinue for reasons other than documented PD, if previous imaging was more than 6 weeks old.