valor study

Study contacts

_____

_____

_____

Inclusion Criteria

An individual will be eligible for participation in this study only if all of the following inclusion criteria are met:

Age and Sex

1. Male or female, and the participant must be ≥ 18 to ≤ 75 years of age at the time of signing the informed consent form (ICF).

Type of Participant and Disease Characteristics

2. Participants with a diagnosis of dermatomyositis according to 2017 EULAR/ACR Classification Criteria for Idiopathic Inflammatory Myopathies (see Appendix 1) [Lundberg, 2017].
   Note: Participants with possible IIM are not eligible. For patients with probable IIM, diagnosis confirmation from the Independent Eligibility Adjudication Committee will be required prior to randomization.
   Note: The classification criteria can be met with past signs, symptoms, and diagnostic findings (e.g., the muscle biopsy findings can be from a past procedure).
3. Participants meeting both of the following disease severity criteria (at screening and randomization):
   - MMT-8 score ≥ 80 and ≤ 142 (out of 150 total possible)
     and
   - Active cutaneous manifestation of dermatomyositis documented as CDASI Activity Score ≥ 6.

   Note: For MMT-8, if a non-assessable muscle is present, the score will be adjusted and a total score out of 150 will be provided.
4. For participants with onset of dermatomyositis symptoms within 3 years of screening, have a documented computed tomography (CT) (or positron emission tomography-computed tomography [PET-CT]) scan with contrast of the chest, abdomen, and pelvis, taken after the onset of symptoms and within 1 year of screening, without findings suggestive of malignancy.
   Note: For participants without available CT (or PET-CT) scan results, a CT (or PET-CT) scan may be performed during the Screening Period.
5. Current therapy consisting of corticosteroid ≤ 20 mg/day (including a dose of 0 mg [i.e., not taking corticosteroid]) of prednisone or equivalent (see Appendix 2 for commonly-used corticosteroid equivalents). The dose must be stable for at least 4 weeks, and total duration of therapy at least 12 weeks, prior to randomization.
6. At most, one non-steroid immunomodulatory/immunosuppressive therapy (see Table 5 for eligible therapies and maximally allowed dose), with a stable dose for at least 12 weeks prior to randomization.
   Note: Hydroxychloroquine is allowed in addition to a non-steroid immunomodulatory/ immunosuppressant therapy, and the hydroxychloroquine dose (maximally allowed dose is 400 mg daily) must be stable for at least 12 week prior to randomization.
   Note: Participants not receiving either corticosteroids or non-steroid immunomodulatory/ immunosuppressive therapy for the treatment of dermatomyositis require documented failure of response (which may include medical history by participant report) or intolerance to at least 1 prior dermatomyositis-related corticosteroid and/or non-steroid immunomodulatory/ immunosuppressive therapy (hydroxychloroquine alone is not sufficient to meet this criterion) and must have been discontinued per the timelines specified in Table 8 or Table 17 prior to randomization.

Inclusion Criteria (continued)

Table 5: Allowed Non-Steroid Immunomodulatory/Immunosuppressive Therapy

Drug	Maximally allowed stable dose as concomitant therapy:
Azathioprine	2.5 mg/kg daily
Cyclosporine	5 mg/kg daily
Hydroxychloroquine	400 mg daily
Leflunomide	20 mg daily
Methotrexate	25 mg weekly
Mycophenolate mofetil (MMF)	3000 mg daily
Mycophenolic acid (MPA)	2160 mg daily
Sulfasalazine	3000 mg daily
Tacrolimus	0.2 mg/kg daily

7. Participants with disease activity that includes abnormalities in at least 2 of the 5 following International Myositis Assessment and Clinical Studies Group (IMACS) Disease Activity CSMs (at least 2 must be present at both screening and randomization, however the 2 CSMs do not need to be the same ones at both timepoints):
   i. PhGA-VAS ≥ 2 cm,
   ii. PtGA-VAS of ≥ 2 cm,
   iii. HAQ Disability Index ≥ 0.25,
   iv. At least one muscle enzyme (creatine kinase [CK], aldolase, alanine aminotransferase [ALT], aspartate aminotransferase [AST], and lactate dehydrogenase [LDH]) > 1.5 times upper limit of normal (ULN),
   v. Extramuscular Global Assessment-VAS ≥ 2 cm.

Weight

8. Participants weighing > 40 kg to < 130 kg, and with a body mass index (BMI) < 40 kg/m^2.

Informed Consent

9. Participants who are able and willing to understand and comply with the study requirements.
10. Capable of giving signed informed consent, which includes compliance with the requirements and restrictions listed in the ICF and in this protocol.

Exclusion Criteria

An individual will be excluded from participation in this study if any of the following exclusion criteria apply:

Medical Conditions

1. In the opinion of the investigator, dermatomyositis with end-stage organ involvement that will pose additional risk to the participant or confound the assessment of the participant in the study. This may include advanced symptomatic ILD (for example, abnormal forced vital capacity [FVC] and/or requiring oxygen therapy), severe dysphagia impacting compliance with oral therapies, etc.
2. In the opinion of the investigator, dermatomyositis with irreversible muscle involvement and/or severe atrophy that will pose any additional risk to the participant or confound the assessment of the participant in the study. This may include Muscle Damage-VAS ≥ 5 cm, documented history of severe atrophy (based on MRI), and/or wheelchair bound.
3. Calcinosis that is motion-limiting and would prevent accurate assessment of disease activity (e.g., unable to properly perform MMT-8).

Exclusion Criteria (continued)

4. History of any lymphoproliferative disorder (such as Epstein-Barr virus [EBV]-related lymphoproliferative disorder, lymphoma, leukemia).
5. Cancer-associated condition, cancer, or history meeting any of the following conditions:
   - Active malignancy;
   - History of cancer within 5 years prior to screening, with the exception of the following cancers with documentation of complete resection and no evidence of recurrence for ≥ 1 year: basal cell carcinoma, squamous cell carcinoma, ductal carcinoma in situ of the breast, carcinoma in situ of the uterine cervix, or thyroid carcinoma.
     Note: Potential participants who have an unacceptably high risk of recurrence may be rejected by the sponsor or their delegate. Additionally, the participant is required to comply with recommended follow-up testing with their treating healthcare provider of record while participating in the study.
   - Cancer-associated dermatomyositis, defined as the diagnosis of myositis or the onset of myositis symptoms within 2 years (before or after) of the diagnosis of cancer (with the exception of basal cell carcinoma or squamous cell carcinoma, ductal carcinoma in situ of the breast, carcinoma in situ of the cervix, or thyroid carcinoma that has undergone complete resection and no evidence of recurrence).
6. Participants with overlap myositis/connective tissue disease associated dermatomyositis, inclusion body myositis, polymyositis, immune-mediated necrotizing myopathy, juvenile dermatomyositis, or drug-induced myopathy.
   Note: Secondary Sjögren's syndrome is allowed.
7. Participants with generalized, symptomatic musculoskeletal or neuro-muscular conditions other than dermatomyositis that prevent a sufficient assessment of the participant by the investigator.
8. Severe liver disease, indicated by a Child-Pugh class B or class C designation (see Appendix 3 for Child-Pugh scoring).
9. History of any of the following:
   - Thrombosis or cerebrovascular ischemic event within the last 12 months, or history of recurrent (≥2) venous thrombosis or arterial thromboembolism;
   - Known hypercoagulable state (for example, protein C deficiency, protein S deficiency, Factor V Leiden mutation, etc.), which in the opinion of the investigator places the participant at high risk for thrombosis.
10. Any of the following cardiovascular risk factors:
    - A history of cardiac insufficiency defined as meeting either New York Heart Association (NYHA) Class III or Class IV criteria:
      - NYHA Class III: Marked limitation of physical activity; comfortable at rest; less than ordinary activity causes fatigue, palpitation, or dyspnea;
      - NYHA Class IV: Unable to carry on any physical activity without discomfort; symptoms of heart failure at rest; if any physical activity is undertaken, discomfort increases;
    - Clinically significant cardiac dysrhythmia;
    - Fridericia corrected QT interval (QTcF) > 450 msec;
    - Unstable angina within 3 months of screening;
    - Myocardial infarction (MI) within 1 year prior to screening (if an MI of indeterminate age is recorded on ECG and there is no known cardiac history, a cardiology consultation is required prior to entry);
    - Coronary artery bypass graft surgery within 1 year prior to screening.
11. Recipient of a solid organ transplant who is currently receiving systemic immunosuppressive therapy.
12. Any condition possibly affecting oral drug absorption (e.g., gastrectomy, clinically significant diabetic gastroenteropathy, or certain types of bariatric surgery such as gastric bypass).
    Note: Procedures that simply divide the stomach into separate chambers (e.g., gastric banding, gastric sleeve) are not exclusionary.
13. Any other acute or chronic medical condition, psychiatric condition, or laboratory abnormality, that in the judgment of the investigator or sponsor, may increase the risk associated with study participation or study drug administration, or may interfere with the interpretation of study results, and would make the participant inappropriate for entry into this study (including active suicidal ideation or behavior within the past 1 year).

Exclusion Criteria (continued)

Prior/Concomitant Therapy

14. Treatment-naïve (i.e., no prior dermatomyositis therapy with corticosteroids or other immunosuppressive agents).
15. Current or planned treatment with prohibited concomitant medications, including investigational agents (see Section 6.7.3 and Appendix 5) and new and/or changes in physical therapy during the Blinded Treatment Period. Prior treatment is permitted provided the specified discontinuation period is met prior to randomization (see Section 6.7.1 and Appendix 5).
16. Prior exposure to brepocitinib, or participation in a brepocitinib clinical trial.
17. History of hypersensitivity to any constituents of the study drug formulation or other JAK inhibitors.

Vaccinations

18. Has been exposed to a live vaccine within 6 weeks of randomization or is expected to need/receive a live vaccine during the course of the study. Participants must not have received a Bacillus Calmette-Guerin (BCG) vaccination within 52 weeks of randomization.
    Note: Although not mandated by the protocol, vaccines recommended by local guidelines should be considered. Administration of inactivated or RNA-based (non-live) vaccines is permitted prior to or during the study; however, it should not be administered in the 2 weeks prior to any scheduled study visit.

Infection

19. Active bacterial (with the exception of uncomplicated urinary tract infection), viral, fungal (with the exception of infections that only require topical antifungal therapy), mycobacterial, or other infections (including but not limited to tuberculosis [TB; see Exclusion Criterion #23] and atypical mycobacterial disease, allergic aspergillosis, or cavitary lung lesions or granulomatous disease on chest x-ray).
20. History of recurrent bacterial (with the exception of uncomplicated urinary tract infection), viral, fungal (with the exception of infections that only required topical antifungal therapy), mycobacterial, or other infections (including but not limited to pyelonephritis, TB and atypical mycobacterial disease, and granulomatous disease on chest x-ray) that would substantially increase the risk to the participant if they participate in the study.
21. Have required management of acute or chronic infections as follows:
    - Currently on suppressive therapy for any chronic infection (e.g., pneumocystis, cytomegalovirus [CMV], and atypical mycobacteria) that, in the opinion of the investigator and sponsor, would place the participant at risk for reactivation and/or infection.
      Note: Participants receiving stable suppressive therapy for herpes simplex virus may be enrolled with the expectation that this treatment will continue for the duration of the study.
    - Hospitalization for infection within 60 days of randomization (Day 1/Visit 2).
    - Use of intravenous (IV) or intramuscular (IM) antibacterials, antivirals, antifungals, or anti-parasitic agents within 60 days of randomization (Day 1/Visit 2).
    - Use of oral antibiotics to treat an active infection within 14 days of randomization (Day 1/Visit 2).
22. History (≥ 1 episode) of disseminated herpes zoster, disseminated herpes simplex, or recurrent (≥ 2 episodes within last 5 years) localized, single unilateral dermatomal herpes zoster.
23. Infection with *Mycobacterium tuberculosis* (TB) as defined by <u>any</u> of the following:
    - A positive interferon gamma release assay (IGRA) test performed at screening or within the 12 weeks prior to screening.
      - If the results of the IGRA are indeterminate, the test may be repeated once, and if a negative result is obtained, enrollment may proceed. A positive test on repeat is exclusionary.
      - Participants with repeat indeterminate IGRA results should have a different IGRA performed (e.g., T spot) and may be enrolled after consultation with an infectious disease and/or pulmonary specialist and sponsor agreement.
      - Participants who have previously completed an adequate course of therapy (in the opinion of an infectious disease and/or pulmonary specialist) for latent TB infection within 6 months prior to screening may be enrolled regardless of screening IGRA results provided that 1) there are no current signs or symptoms of active TB and 2) the treatment is well documented in the participant's medical records and/or provided as a source documentation prior to enrollment in the study.

Exclusion Criteria (continued)

- Participants who have been diagnosed with latent TB prior to screening and are currently receiving treatment for latent TB during the screening period may be eligible for the study only if the participant is seen by an infectious disease and/or pulmonary specialist and confirmed to have no findings of active TB and if the consultant agrees that the participant's latent TB can be adequately treated with isoniazid (INH) plus vitamin B6. The participant must agree to complete the course of INH and B6 during the study.

- Chest x-ray taken at screening with changes suggestive of active TB infection; a chest x-ray previously performed and documented within 12 weeks prior to screening does not require repeat.

Diagnostic Assessments

24. Positive screening result for hepatitis B (HBsAg positive; HBsAg negative, HBcAb positive, and HBsAb negative; HBsAg negative, HBcAb negative, and HBsAb positive [unless documentation of prior vaccination]; HBsAg negative, HBcAb positive, and HBsAb positive; or HBV DNA positive on reflex testing), hepatitis C (HCVAb positive and HCV RNA positive on reflex testing), or HIV infection.
25. Impaired kidney function, defined as any of the following and confirmed by a single repeat, if deemed necessary:
    - Serum cystatin C-based estimated glomerular filtration rate (eGFR) < 30 mL/min/1.73 m^2
    - Proteinuria, defined as urine protein/creatinine ratio > 1 g/g
    - Symptomatic nephrolithiasis within 6 months of screening.
26. Any of the following abnormalities in clinical laboratory tests at screening, as assessed by the central laboratory and confirmed by a single repeat, if deemed necessary:
    - Hemoglobin < 10 g/dL (100 g/L)
    - Platelet count < 100 x 10^9/L (< 100,000/mm^3)
    - Absolute neutrophil count (ANC) < 1.5 x 10^9/L (< 1500/mm^3)
    - Absolute lymphocyte count (ALC) < 0.75 x 10^9/L (< 750/mm^3)
    - AST or ALT values ≥ 3 × ULN (unless deemed due to myositis disease activity); for individuals with myositis disease activity-related elevations in AST or ALT, values ≥ 5 × ULN are exclusionary.
      Note: In order for AST or ALT elevations to be deemed related to myositis disease activity, there must be a concomitant CK elevation of ≥ 3 × ULN.
    - Total bilirubin ≥ 1.5 × ULN; participants with a history of Gilbert's syndrome may have a direct bilirubin measured and would be eligible for this study provided the direct bilirubin is < ULN.

Other Exclusions

27. Recently started (< 4 weeks prior to randomization) or planning to start a physical therapy-directed or other scheduled/planned/supervised exercise regimen during the study.
    Note: If the participant is currently on a stable scheduled and supervised exercise regimen that was started ≥ 4 weeks prior to randomization, then the participant should continue the same regimen until the end of the study.
28. Have had significant trauma or major surgery or blood transfusion within 4 weeks of screening or scheduled to occur during the study.
29. History of alcohol or drug abuse, in the investigator's opinion, unless in full remission for greater than 12 months prior to randomization.
30. Women who are breastfeeding, pregnant, or planning to become pregnant, or women of childbearing potential who are unwilling to apply a highly effective birth control method for the time periods specified in Appendix 4 prior to randomization (Visit 2) (see Contraception Guidance for WOCBP), during the study, and up to 28 days after the last dose of study drug.
    Note: Postmenopausal women must be amenorrheic for ≥ 1 year prior to screening AND require confirmation of elevated FSH levels in the postmenopausal range in order to be considered as not having childbearing potential.
31. Investigator site staff members directly involved in the conduct of the study and their family members, site staff members otherwise supervised by the investigator, or Priovant Therapeutics, Inc. or affiliate employees, including their family members, directly involved in the conduct of the study.

Table 1: Study PVT-2201-301 Schedule of Activities (Screening Period and Blinded Treatment Period)

Study Period	Screening		Blinded Treatment						Off-Drug Follow-Up
Visit Name*/Number	Screening/ V1a†[a] (symptoms < 3 years)	Screening/ V1b†[a] (symptoms ≥ 3 years)	Baseline/ Randomization/ V2	V3	V4, V5, V6	V7	V8, V9, V10, V11	V12 (or EoT1)	Follow-Up[b]
Visit Day			D1	D29	D57, 85, 127	D169	D211, 253, 295, 337	D365	(28 days post dose*)
Visit Week	Wk -8 to 0*	Wk -4 to 0*	Wk 0	Wk 4	Wk 8, 12, 18	Wk 24	Wk 30, 36, 42, 48	Wk 52 (or EoT1)	Wk 56 (or Wk 108[b])
Scheduling Window Permitted*				±3 days	±3 days	±5 days	±5 days	±5 days	±5 days
Administrative Procedures									
Informed consent	X	X							
Eligibility criteria review	X	X	X					X*	
Demographic and baseline characteristics	X	X							
Medical history/prior medications*	X	X	X						
Medical Procedures*									
Vital signs (BP, HR, respirations, temperature)	X	X	X	X	X	X	X	X	X
Height	X	X							
Body weight	X	X	X			X		X	
Physical examination	X	X				X		X	
Standard 12-lead ECG	X	X	X	X		X		X	X
Chest x-ray[c]	X	X							
Clinical Assessments*									
5 Disease Activity Core Set Measures*[d]	X	X	X	X	X	X	X	X	
MDAAT	X	X	X	X	X	X	X	X	
Muscle Damage-VAS	X	X				X		X	
CDASI	X	X	X	X	X (Wk 12 only)	X	X (Wks 36 and 48 only)	X	
CDA-IGA	X	X	X	X	X (Wk 12 only)	X	X (Wks 36 and 48 only)	X	
PhGI-S	X	X	X	X	X	X	X	X	
PhGI-C				X	X	X	X	X	
FACIT-Fatigue			X			X		X	

Table 1: Study PVT-2201-301 Schedule of Activities (Screening Period and Blinded Treatment Period) (continued)

Study Period	Screening		Blinded Treatment						Off-Drug Follow-Up
Visit Name*/Number	Screening/ V1a†[a] (symptoms < 3 years)	Screening/ V1b†[a] (symptoms ≥ 3 years)	Baseline/ Randomization/ V2	V3	V4, V5, V6	V7	V8, V9, V10, V11	V12 (or EoT1)	Follow-Up[b]
Visit Day			D1	D29	D57, 85, 127	D169	D211, 253, 295, 337	D365	(28 days post dose*)
Visit Week	Wk -8 to 0*	Wk -4 to 0*	Wk 0	Wk 4	Wk 8, 12, 18	Wk 24	Wk 30, 36, 42, 48	Wk 52 (or EoT1)	Wk 56 (or Wk 108[b])
Scheduling Window Permitted*				±3 days	±3 days	±5 days	±5 days	±5 days	±5 days
PP-NRS			X	X		X		X	
Skindex-16			X	X		X		X	
PtGA-Skin	X	X	X	X	X	X	X	X	
PtGA-Muscle	X	X	X	X	X	X	X	X	
PtGA-Pain	X	X	X	X	X	X	X	X	
PtGA-Swallow	X	X	X	X	X	X	X	X	
PtGA-Flexibility	X	X	X	X	X	X	X	X	
PtGI-S	X	X	X	X	X	X	X	X	
PtGI-C				X	X	X	X	X	
SF-36v2			X			X		X	
PROMIS v2.0 – Physical Function – Short Form 8b*			X			X		X	
PROMIS v1.0 – Fatigue – Short Form 7a*			X			X		X	
PROMIS v1.1 – Pain Interference – Short Form 6a*			X			X		X	
Safety Assessments*									
Adverse events monitoring	X	X	X (Throughout the study, including all events occurring between visits)						
Concomitant medication	X	X	X (Throughout the study, including all rescue or other medications taken between visits)						

Table 1: Study PVT-2201-301 Schedule of Activities (Screening Period and Blinded Treatment Period) (continued)

Study Period	Screening		Blinded Treatment						Off-Drug Follow-Up
Visit Name*/Number	**Screening/ V1a†[a]** (symptoms < 3 years)	**Screening/ V1b†[a]** (symptoms ≥ 3 years)	**Baseline/ Randomization/ V2**	**V3**	**V4, V5, V6**	**V7**	**V8, V9, V10, V11**	**V12 (or EoT1)**	**Follow-Up[b]**
Visit Day			**D1**	**D29**	**D57, 85, 127**	**D169**	**D211, 253, 295, 337**	**D365**	**(28 days post dose*)**
Visit Week	**Wk -8 to 0***	**Wk -4 to 0***	**Wk 0**	**Wk 4**	**Wk 8, 12, 18**	**Wk 24**	**Wk 30, 36, 42, 48**	**Wk 52 (or EoT1)**	**Wk 56 (or Wk 108[b])**
Scheduling Window Permitted*				**±3 days**	**±3 days**	**±5 days**	**±5 days**	**±5 days**	**±5 days**
Contraception check (only women of childbearing potential)	X	X	X (Throughout the study)						
Laboratory Assessments*									
Pregnancy test (only women of childbearing potential)*	X†	X†	X‡	X‡	X‡	X‡	X‡	X‡	X‡
Serum FSH (only women of non-childbearing potential)	X*	X*							
Blood sample for chemistry* and hematology†	X	X	X	X	X	X	X	X	X
Blood sample for lipid profile panel*			X	X	X (Wk 8 only)	X	X (Wk 36 only)	X	X
Urine sample for urinalysis and protein/ creatinine ratio*	X	X	X	X	X	X	X	X	X
Blood sample for HIV, Hep B, Hep C serology[e]	X	X							
HBV DNA*	X†	X†	X	X	X	X	X	X	X
Tuberculosis testing (IGRA)	X	X							
Pharmacokinetic Assessments*									
Blood sample for PK			X[f]	X[g]	X[h] (Wk 12 only)	X[i]			
Biomarker Assessments*									
Blood sample for exploratory biomarkers			X		X (Wk 12 only)	X		X	

Table 1: Study PVT-2201-301 Schedule of Activities (Screening Period and Blinded Treatment Period) (continued)

Study Period	Screening		Blinded Treatment						Off-Drug Follow-Up
Visit Name*/Number	Screening/ V1a†[a] (symptoms < 3 years)	Screening/ V1b†[a] (symptoms ≥ 3 years)	Baseline/ Randomization/ V2	V3	V4, V5, V6	V7	V8, V9, V10, V11	V12 (or EoT1)	Follow-Up[b]
Visit Day			D1	D29	D57, 85, 127	D169	D211, 253, 295, 337	D365	(28 days post dose*)
Visit Week	Wk -8 to 0*	Wk -4 to 0*	Wk 0	Wk 4	Wk 8, 12, 18	Wk 24	Wk 30, 36, 42, 48	Wk 52 (or EoT1)	Wk 56 (or Wk 108[b])
Scheduling Window Permitted*				±3 days	±3 days	±5 days	±5 days	±5 days	±5 days
Study Drug Procedures*									
Randomization			X*						
Dispense study drug			X	X	X	X	X		
Dose of study drug taken in clinic			X	X		X		X*	
Dose of study drug taken at home*			X (From Day 2 until the day before Week 52; study drug is self-administered at home once daily)						
Return of study drug by participant/ compliance review				X	X	X	X	X	
Protocol-defined steroid taper (if applicable)					X (Continuous, starting at Wk 12 through Wk 36)				
Additional Procedures*									
CT (or PET-CT) scan with contrast (chest, abdomen, pelvis)*	X†								
Spirometry*	X	X				X		X	
Photography*	X	X	X	X	X	X	X	X	X

a. **Screening (Visit 1a or Visit 1b)**: VVisit 1a is applicable only to participants with dermatomyositis symptom onset < 3 years or if timing of onset is unknown, whereas Visit 1b is applicable only to participants with dermatomyositis symptom onset ≥ 3 years.

b. **Follow-Up Visit (Week 56 or Week 108)**: A single Follow-Up Visit will be conducted during the study, either at Week 56 or Week 108 (or 28 days after the last dose of study drug for participants who withdraw early from the study). The Follow-Up Visit shown in this table is identical to the Follow-Up Visit shown in Table 2. The Follow-Up Visit will be conducted approximately 4 weeks after Week 52/Visit 12 (or EoT1) for participants who **do not** continue into the OLE Period or approximately 4 weeks after Week 104/Visit 19 (or EoT2) for participants who **do** enter the OLE Period.

c. **Chest x-ray**: Historical results from ≤ 12 weeks prior to screening are acceptable; however, if the participant has a CT (or PET-CT) scan result within 12 weeks of screening showing no abnormalities suggestive of TB or ILD, the chest x-ray is not required. The official reading must be included in the source documentation and recorded in the eCRF.

Table 1: Study PVT-2201-301 Schedule of Activities (Screening Period and Blinded Treatment Period) (continued)

d. **5 Disease Activity Core Set Measures**: The IMACS Disease Activity CSMs (or components of them) to be completed are:
   - PhGA-VAS (see Section 8.2.2.1);
   - PtGA-VAS (see Section 8.2.2.2);
   - MMT-8 (see Section 8.2.2.3);
   - HAQ (see Section 8.2.2.4);
   - Extramuscular Global Assessment-VAS (see Section 8.2.2.6)

   Physician completed assessments should be evaluated by a qualified rater (see Section 8.2.1), and the same rater should be used across all study visits for a given participant. The sixth Disease Activity CSM (muscle enzyme assessment, see Section 8.2.2.5) is determined from laboratory analysis results.

e. **Hep B, Hep C serology**: Hep B and Hep C testing includes HBsAg, HBcAb, HBsAb, and HCVAb (HBV DNA and/or HCV RNA reflex testing if necessary).

f. **Day 1 PK sampling**: Collect pre-dose.

g. **Week 4 PK sampling**: Collect pre-dose and at 0.5 hours (± 10 min), 1 hour (± 10 min), 2 hours (± 20 min), and 4 hours (± 20 min) post-dose. On the day of the visit, the participant will refrain from dosing at home and will dose study drug in the clinic. The date and time of the prior dose, dose taken at the clinic, and each PK sample will be recorded.

h. **Week 12 PK sampling**: Collect post-dose during the clinic visit (with the routine blood draw for laboratory testing). On the day of the visit, the participant should dose at home prior to the visit. The date and time of the prior dose and PK sample will be recorded.

i. **Week 24 PK sampling**: Collect pre-dose. On the day of the visit, the participant will refrain from dosing at home and will dose study drug in the clinic. The date and time of the prior dose, dose taken at the clinic, and the PK sample will be recorded.

Abbreviations: BP = blood pressure; CDA-IGA = Cutaneous Dermatomyositis Activity Physician's Global Assessment; CDASI = Cutaneous Dermatomyositis Disease Area and Severity Index; CSM = Core Set Measure; CT = computed tomography; D = day; DNA = deoxyribonucleic acid; ECG = electrocardiogram; eCRF = electronic case report form; EoT = End of Treatment; Extramuscular Global Assessment-VAS = extramuscular global assessment visual analog scale component of the International Myositis Assessment and Clinical Studies Group Myositis Disease Activity Assessment Tool; FACIT-Fatigue = Functional Assessment of Chronic Illness Therapy-Fatigue Scale; FSH = follicle stimulating hormone; HAQ = Health Assessment Questionnaire; HBcAb = hepatitis B core antibody; HBsAb = hepatitis B surface antibody; HBsAg = hepatitis B surface antigen; HBV = hepatitis B virus; HCV = hepatitis C virus; HCVAb = hepatitis C virus antibody; Hep B = hepatitis B; Hep C = hepatitis C; HIV = human immunodeficiency virus; HR = heart rate; IGRA = interferon gamma release assay; ILD = interstitial lung disease; IMACS =International Myositis Assessment and Clinical Studies Group; INR = international normalized ratio; MDAAT = Myositis Disease Activity Assessment Tool; MMT-8 = abbreviated group of 8 proximal, distal, and axial muscles from the International Myositis Assessment and Clinical Studies Group Manual Muscle Testing Core Set Measure; Muscle Damage-VAS = visual analog scale component of the muscle damage subscore from the International Myositis Assessment and Clinical Studies Group Muscle Damage Index; OLE = Open-Label Extension; PET = positron emission tomography; PhGA-VAS = Physician Global Activity Visual Analogue Scale; PhGI-C = Physician Global Impression of Change; PhGI-S = Physician Global Impression of Severity; PK = pharmacokinetic; PP-NRS = Peak Pruritus-Numerical Rating Scale; PROMIS = Patient-Reported Outcomes Measurement Information System; PtGA-Flexibility = Patient Global Assessment of Flexibility; PtGA-Muscle = Patient Global Assessment of Muscle; PtGA-Pain = Patient Global Assessment of Pain; PtGA-Skin = Patient Global Assessment of Skin; PtGA-Swallow = Patient Global Assessment of Swallowing; PtGA-VAS = Patient Global Activity-Visual Analogue Scale; PtGI-C = Patient Global Impression of Change; PtGI-S = Patient Global Impression of Severity; RNA = ribonucleic acid; SF 36v2 = Short Form (36) Health Survey, Version 2, Standard; TB = tuberculosis; V = visit; VAS = visual analogue scale; Wk = week

Table 8: Discontinuation Periods (if Applicable) to be Fulfilled Prior to Screening or Dose Limitations for Prior/Permitted Concomitant Dermatomyositis-Related Therapies

Drug	If drug was discontinued prior to randomization (Day 1/ Visit 2): Minimum Period since Discontinuation	If drug is to be continued as concomitant therapy: Maximally-allowed Stable Dose
Azathioprine	12 weeks	2.5 mg/kg daily
Corticosteroids	4 weeks	20 mg daily prednisone equivalent
Cyclosporine	12 weeks	5 mg/kg daily
Hydroxychloroquine	12 weeks	400 mg daily
Leflunomide	12 weeks	20 mg daily
Methotrexate	12 weeks	25 mg weekly
Mycophenolate mofetil (MMF)	12 weeks	3000 mg daily
Mycophenolic acid (MPA)	12 weeks	2160 mg daily
Sulfasalazine	12 weeks	3000 mg daily
Tacrolimus	12 weeks	0.2 mg/kg daily

Note: Therapeutic drug monitoring and careful monitoring of renal function are recommended for calcineurin inhibitors

Table 17: Prohibited Concomitant Medications/Therapies

Medications	Minimum Discontinuation Period (prior to randomization [i.e., baseline])
Note: Contact the medical monitor for confirmation for any immunosuppressants not listed.	
Abatacept (CTLA4Ig)	12 weeks
Acthar® gel (repository corticotropin injection)	6 weeks
Adalimumab	12 weeks
Anakinra	8 weeks
Apremilast	4 weeks
Brodalumab	8 weeks
Canukinumab	8 weeks
Certolizumab pegol	24 weeks
Cyclophosphamide	24 weeks
Dapsone	4 weeks
Etanercept	4 weeks
Everolimus	12 weeks
Golimumab	12 weeks
Guselkumab	12 weeks
Infliximab	12 weeks
Ixekizumab	12 weeks

Table 17: Prohibited Concomitant Medications/Therapies (continued)

Medications	Minimum Discontinuation Period (prior to randomization [i.e., baseline])
Note: Contact the medical monitor for confirmation for any immunosuppressants not listed.	
Lenalidomide with cholestyramine	24 weeks
Memantine	4 weeks
Obinutuzumab	26 weeks
Retinoids (oral isotretinoin and acitretin; topical retinoids are allowed)	4 weeks
Rilonacept	8 weeks
Rituximab	52 weeks or 24 weeks with normal CD19 count
Risankizumab	12 weeks
Secukinumab	12 weeks
Sirolimus	12 weeks
Thalidomide	4 weeks
Tidrakizumab	12 weeks
Tocilizumab	12 weeks
Ustekinumab	12 weeks
Topical steroids *Note: Allowed use on scalp at stable dose or short-term 1% hydrocortisone for non-dermatomyositis event (Section 6.7.1)*	2 weeks
Other experimental or investigational agents	12 weeks or 5-half-lives, whichever is longer; confirm with medical monitor
Calcineurin inhibitors – topical creams/ointments (e.g., pimecrolimus, tacrolimus) *(Note: ocular cyclosporine permitted)*	8 weeks
Oral or topical JAK inhibitors (e.g., ruxolitinib, tofacitinib, baricitinib, filgotinib, upadacitinib)	12 weeks
Narrow therapeutic index P-gp/BCRP substrates: Colchicine Digoxin Fentanyl Quinidine	2 weeks
Narrow therapeutic index OCT1/OCT2 substrates: Dofetilide Procainamide	2 weeks
Moderate and strong CYP3A inducers: Bosentan Carbamazepine Primidone Rifampin Rifabutin Rifapentine Phenytoin Pioglitazone Troglitazone St. John's Wort	2 weeks

Abbreviations: BCRP = breast cancer resistance protein; CYP = cytochrome P450; JAK = Janus kinase; OCT = organic cation transporter; P-gp = permeability glycoprotein