Exclusion Criteria

Subjects who meet any of the following exclusion criteria will not be eligible to receive study treatment:

1. History of known antidrug antibodies or severe allergic, anaphylactic, or other infusion-related reaction to a previous biologic agent (for subjects to be treated with pembrolizumab). Related reaction to a previous biologic agent (for subjects to be treated with pembrolizumab).
2. History of severe hypersensitivity (≥ Grade 3) to pembrolizumab and/or any of its excipients (for subjects to be treated with pembrolizumab)
3. In subjects who received prior therapy with an anti-PD-1, anti-PD-L1, or anti PD-L2 agent or an agent directed to another stimulatory or co-inhibitory T-cell receptor (e.g., CTLA-4, OX-40, CD137), any history of discontinuing prior treatment due to Grade 3–4 immune-related adverse events (irAEs).
4. Has received prior systemic anticancer therapy including investigational agents within 4 weeks (or < 5 half-lives for investigational/noncytotoxic agents, whichever is shorter) prior to first dose of study treatment.
5. Any active autoimmune disease or documented history of serious autoimmune disease within the past 2 years requiring systemic therapy (i.e., with use of disease-modifying agents, corticosteroids, or immunosuppressive drugs). Replacement therapy (e.g., thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency) is not considered a form of systemic treatment and is allowed.
6. History of idiopathic pulmonary fibrosis, organizing pneumonia, drug-induced pneumonitis, idiopathic pneumonitis, (non-infectious) pneumonitis that required steroids, or clinical symptoms of active pneumonitis.
7. Known carcinomatous meningitis and/or active central nervous system (CNS) metastasis. Participants with previously treated brain metastases may participate provided they are radiologically stable, i.e., without evidence of progression for at least 4 weeks by repeat imaging (note that the repeat imaging should be performed during study screening), clinically stable, and without requirement of steroid treatment for at least 14 days prior to first dose of study treatment.
8. History of another malignancy that has progressed or has required active treatment within the past 2 years except for the following: adequately treated local basal cell or squamous cell carcinoma of the skin; in situ cervical carcinoma; adequately treated papillary, noninvasive bladder cancer; asymptomatic prostate cancer without known metastatic disease and not requiring therapy or requiring only hormonal therapy, and with normal prostate specific antigen for ≥ 1 year prior to start of study treatment; other adequately treated Stage 1 or 2 cancers currently in complete remission, or any other cancer that has been in complete remission for ≥ 2 years.
9. Significant cardiovascular disease, including myocardial infarction, arterial thromboembolism, or cerebrovascular thromboembolism within 6 months prior to start of study treatment, symptomatic dysrhythmias or unstable dysrhythmias requiring medical therapy, angina requiring therapy, symptomatic peripheral vascular disease, clinically significant history of syncope, New York Heart Association (NYHA) Class 3 or 4

congestive heart failure (Appendix 3), or chronic Grade 3 hypertension (diastolic blood pressure ≥ 100 mmHg or systolic blood pressure ≥ 160 mmHg).

10. Significant screening electrocardiogram (ECG) abnormalities including atrial fibrillation (unstable or newly diagnosed), double (left and right) bundle-branch block, second-degree atrioventricular block type II, third-degree atrioventricular block, Grade ≥ 2 bradycardia, QTcF interval ≥ 450 msec, PR interval > 220 msec, or unstable cardiac arrhythmia requiring medication. Chronic asymptomatic atrial fibrillation stably controlled with medications is permitted.
11. Known family history of sudden cardiac death.
12. Ongoing risk for bleeding due to active peptic ulcer disease or bleeding diathesis.
13. Significant active gastrointestinal disease (e.g., malabsorption syndrome, resection of the stomach or small bowel, symptomatic inflammatory bowel disease, gastrointestinal perforation, or partial or complete bowel obstruction) that might impair absorption of study treatment.
14. Evidence of an ongoing, uncontrolled systemic bacterial, fungal, or viral infection or an uncontrolled local infection requiring therapy at the time of start of study treatment.
    Note: Subjects with localized fungal infections of skin or nails are eligible.
15. Subjects with human immunodeficiency virus (HIV) infection who do not meet the following criteria are excluded: HIV-infected subjects must be on anti-retroviral therapy (ART) and have well-controlled HIV infection/disease defined as: (a) $CD4_+$ T cell count > 350 cells/mm_3 at time of screening, (b) achieved and maintained virologic suppression defined as confirmed HIV RNA level <50 copies/mL or the lower limit of qualification (below the limit of detection) using the locally available assay at the time of screening and for at least 12 weeks prior to screening, (c) must have been on a stable anti-retroviral regimen, without changes in drugs or dose modification, for at least 4 weeks prior to start of study treatment (C1D1), and (d) the combination ART regimen must not contain any retroviral medications OTHER THAN abacavir, dolutegravir, emtricitabine, lamivudine, raltegravir, or tenofovir (due to potential CYP interactions, exceptions permitted only with prior Sponsor clearance). Subjects with a history of Kaposi Sarcoma and/or Multicentric Castleman Disease are excluded.
16. Known history of Hepatitis B (defined as Hepatitis B surface antigen reactive) or known active Hepatitis C virus (defined as detection of HCV RNA [qualitative]) infection.
17. Diagnosis of immunodeficiency or is receiving chronic systemic steroid therapy (at doses exceeding 10 mg daily of prednisone equivalent) or any other form of immunosuppressive therapy within 14 days prior to the first dose of study treatment.
18. Prior allogeneic organ transplant.
19. Receipt of live vaccine within 30 days prior to study entry or within 30 days of receiving study treatment. Examples of live vaccines include, but are not limited to, measles, mumps, rubella, varicella/zoster (chicken pox), yellow fever, rabies, Bacillus Calmette-Guérin (BCG), and typhoid vaccine. Seasonal influenza vaccines for injection are generally killed virus vaccines and are allowed; however, intranasal influenza vaccines (e.g., FluMist®) are live attenuated vaccines and are not allowed.
20. Has undergone prior allogeneic hematopoietic stem cell transplantation within the last

5 years. (Subjects who have had a transplant more than 5 years before the start of study treatment are eligible as long as there are no symptoms of graft-versus-host-disease).

21. Females who are pregnant, breastfeeding, or expect to become pregnant within the projected duration of the study, starting with the screening visit through 120 days after the final dose of study treatment. Males who plan to father children within the projected duration of the study, starting with the screening visit through 120 days after the fina dose of study treatment.
22. Major surgery within 28 days (or inadequate recovery from the toxicity or complications of the intervention) before the start of study treatment.
23. Radiotherapy within 14 days of start of study treatment. Subjects must have recovered from all radiation-related toxicities, not require corticosteroids, and not have had radiation pneumonitis. A 7-day washout is permitted for palliative radiation (i.e., ≤ 14-day course of radiotherapy) to non-CNS lesions.
24. Subjects currently receiving treatment with any medications that have the potential to prolong the QT interval and that cannot be either discontinued or substituted with a different medication prior to starting study treatment.
    Note: See Appendix 8 for a list of proscribed drugs.
25. Subjects currently receiving treatment with strong cytochrome P450 (CYP)3A4 inhibitors or inducers should discontinue such treatment or be switched to a different medication prior to starting study treatment.
    Note: See Appendix 8 for a list of proscribed drugs.
26. Current participation in another study of an investigational agent or device.
27. Any illness, medical condition, organ system dysfunction, or social situation, including mental illness or substance abuse, deemed by the investigator to be likely to interfere with a subject's ability to sign informed consent, adversely affect the subject's ability to cooperate and participate in the study, or compromise the interpretation of study results.