Recommended Protocol Text and Guidance for Inclusion/Exclusion		
	Guidance	**Template Language**
Patients with treated/stable brain metastases		Template for inclusion: Patients with treated brain metastases are eligible if there is no evidence of progression for at least 4 weeks after CNS-directed treatment, as ascertained by clinical examination and brain imaging (MRI or CT) during the screening period.
Patients with new, active, or progressive brain metastases	Guidance for inclusion in early-phase trials: Patients with active brain metastases should be included early in clinical development when there is strong scientific rationale for likelihood of benefit, based on molecular pathways or histology and preclinical data. For drugs/modalities with less robust preclinical information on potential CNS activity, inclusion of patients with active brain metastases should still be considered, particularly if brain metastases are common in the intended use population. The inclusion of a CNS-specific cohort can provide valuable dosing and preliminary efficacy data to either support or refute inclusion in later phase trials. Guidance for inclusion in later phase trials: Ideally, data from earlier phase trials, in concert with the strength of the scientific rationale and preclinical data, can inform decisions on inclusion of patients with active brain metastases in later phase trials. When such data are not available, several potential trial designs could allow patients with active brain metastases to enroll, either as a parallel cohort or as a defined subset within the larger clinical trial.	

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Patients with LMD	Guidance for inclusion: See above considerations. Guidance for exclusion: For the purposes of exclusion, LMD is a clinical diagnosis, defined as positive CSF cytology and/or unequivocal radiologic or clinical evidence of leptomeningeal involvement. Patients with leptomeningeal symptoms in the setting of leptomeningeal enhancement by imaging (MRI) would be considered to have LMD even in the absence of positive CSF cytology, unless a parenchymal lesion can adequately explain the neurologic symptoms and/or signs. In contrast, an asymptomatic or minimally symptomatic patient with mild or nonspecific leptomeningeal enhancement (MRI) would not be considered to have LMD. In that patient, CSF sampling is not required to formally exclude LMD, but can be performed at the investigator's discretion based on level of clinical suspicion.	Template for exclusion: *(If patients with LMD are to be excluded, the following wording is suggested to avoid unnecessary exclusion of patients with imaging-only equivocal findings.)* No known LMD.
Patients younger than age 18 years	Guidance for inclusion in early-phase trials: Pediatric-specific cohorts should be included when there is strong scientific rationale for likelihood of benefit, based on molecular pathways or histology as well as preclinical data.	Template for inclusion in early-phase trials: A) Adolescent/pediatric patients age [*protocol author to insert age minimum and maximum specific to the study under consideration*] will be included after enrollment of adult patients after safety and toxicity in the adult population have been established. Participating sites will be notified when adolescent/pediatric patient enrollment may begin.

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Patients younger than age 18 years *(continued)*		B) Adolescent/pediatric patients age [*protocol author to insert age minimum and maximum specific to the study under consideration*] will be included starting one dose cohort behind the current adult cohort in which there are no dose-limiting toxicities identified. Participating sites will be notified when enrollment onto the adolescent/pediatric stratum may begin. C) Adolescent/pediatric patients age [*protocol author to insert age minimum and maximum specific to the study under consideration*] will be included in age-specific cohorts that will be staggered starting one dose cohort behind the current adult cohort in which there are no dose-limiting toxicities identified. Participating sites will be notified when each adolescent/pediatric cohort enrollment may begin. D) Adolescent/pediatric patients age [*protocol author to insert age minimum and maximum specific to the study under consideration*] are included in this trial in a separate cohort that will accrue simultaneous to the adult cohort [*specify age 18 and older or protocol-specific upper age limit*].

	Guidance	Template Language
Patients younger than age 18 years *(continued)*		Template for inclusion in later phase trials: Patients age 12 years and older should be included in trials for diseases that span pediatric and adult populations. Patients younger than age 12 years may also be included if clinically appropriate.

	Guidance	Template Language
Patients with HIV infection	Guidance for inclusion: HIV-related eligibility criteria should be straightforward and focus on appropriate CD4+ T-cell thresholds for a given study based on current and past counts, history (if any) of AIDS-defining opportunistic infections, and status of HIV treatment, including requirements (if any) for standard-of-care antiretroviral agents. Patients should generally be treated with antiretroviral therapy for HIV. If there is ADME data to predict drug-drug interactions between specific HIV medication(s) and the investigational agent(s), specific anti-HIV medication(s) should be listed as contraindicated in the protocol. Patients on contraindicated medications should be evaluated for alternate HIV therapy that would allow eligibility in the study.	Template for inclusion: HIV-infected patients who are healthy and have a low risk of AIDS-related outcomes are included in this trial.
Kidney function	Guidance for renal function criteria: Measure based on creatinine clearance, rather than serum creatinine levels.	Template for inclusion: Patients with creatinine clearance >30 mL/min (measured using Cockcroft-Gault equation or the estimated glomerular filtration rate from the Modification of Diet in Renal Disease Study) are included in the study. Established dose-modification strategies can allow safe and effective administration.
Liver function	Guidance for liver function criteria: Liver function tests used to determine eligibility should be assessed relative to institutional normal ranges, not a universal cutoff point.	

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Cardiac function	Guidance for cardiac function criteria: Measurement should include investigator assessment of a potential participant's risk for heart failure with a validated clinical classification system (e.g., the New York Heart Association Functional Classification).	
Prior or concurrent malignancies	Guidance for inclusion: Inclusion of patients with prior or concurrent malignancies is recommended, especially when the risk of the malignancy interfering with either safety or efficacy endpoints is very low.	Template for inclusion: Patients with a prior or concurrent malignancy whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen should be included.

Abbreviations: ADME, absorption, distribution, metabolism, and excretion; CT, computed tomography; LMD, leptomeningeal disease; MRI, magnetic resonance imaging.