5.0 ELIGIBILITY CRITERIA

Each of the criteria in the following section must be met in order for a participant to be considered eligible for registration in OPEN. Section 5 may be printed and used to by the site, but is not to be uploaded in RAVE (unless specially stated).For each criterion requiring test results and dates, please record this information on the Onstudy Form and submit via Medidata Rave® (see Section 14.0). Any potential eligibility issues should be addressed to the SWOG SDMC in Seattle at 206/652-2267 or breastquestion@crab.org prior to registration.

NCI policy does not allow for waiver of any eligibility criterion (http://ctep.cancer.gov/protocolDevelopment/policies_deviations.htm).

In calculating days of tests and measurements, the day a test or measurement is done is considered Day 0. Therefore, if a test is done on a Monday, the Monday 4 weeks later would be considered Day 28. This allows for efficient participant scheduling without exceeding the guidelines. **If Day 7, 14, 21, 28, or 42 falls on a weekend or holiday, the limit may be extended to the next working day.**

5.1 Disease Related Criteria

a. Participants must have histologically confirmed HER2-negative (per 2018 ASCO/CAP joint guideline) invasive breast cancer that has metastasized to the brain. *(10)* NOTE: Pathology report must confirm HER2-negative invasive breast cancer. Brain metastases must be confirmed by radiology report.

b. Participants must have an MRI of the brain within 28 days prior to registration and must have central nervous system metastases with at least one measurable brain metastasis ≥ 1.0 cm in size (per RANO-BM See Section 10.1) that has not been irradiated, or has progressed despite prior radiation therapy (in the opinion of the treating physician). In the rare case that a previously irradiated brain metastasis is the sole target lesion and if there is concern about possible radiation necrosis, patient is eligible only if there is clear progression in the previously radiated lesion. CT of the head cannot substitute for brain MRI. All CNS disease must be assessed and documented on the **S2007** Brain Metastases Baseline Tumor Assessment Form.

c. Participants may have measurable or non-measurable extracranial disease (see Section 10.3). All measurable disease must be assessed within 28 days prior to registration; all non-measurable disease must be assessed within 42 days prior to registration. Participants are NOT required to have extracranial disease, but must have scans done to document disease status at baseline. All extracranial disease must be assessed and documented on the Baseline Tumor Assessment Form (RECIST 1.1). NOTE: Brain lesions should not be included on the Baseline Tumor Assessment Form (RECIST 1.1) for this study.

d. Participants must have had CNS progression after previous CNS-directed therapy (radiation therapy, surgery, or any combination of therapy). See Section 10.1 for definition of CNS progression by RANO-BM.

e. Participants must not have had more than 2 seizures within 28 days prior to registration.

5.2 Prior/Concurrent Therapy Criteria

a. Participants must have resolution of adverse event(s) of the most recent prior systemic anti-cancer therapy to < Grade 2, with the exception of alopecia and ≤ Grade 2 neuropathy, which are allowed.

b. Participants must not have received systemic therapy (including small-molecule kinase inhibitors) or non-cytotoxic hormonal therapy (e.g., tamoxifen) within 7 days prior to registration.

c. Participants must not have received anti-cancer biologic agents (antibodies, immune modulators, vaccines, cytokines) within 21 days prior to registration.

d. Participants must not have received nitrosoureas or mitomycin C within 42 days, metronomic/protracted low-dose chemotherapy within 14 days, or other cytotoxic chemotherapy within 28 days prior to registration.

e. Participants with a prior or concurrent malignancy whose natural history or treatment (in the opinion of the treating physician) does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen are eligible for this trial.

f. Human immunodeficiency virus (HIV)-positive patients on combination antiretroviral agents that are strong CYP3A4 inhibitors or inducers and who are unwilling or unable to change to antiretroviral therapies without such interactions are ineligible because of the potential for pharmacokinetic interactions with sacituzumab govitecan (IMMU-132). See Section 7.1b.3 for prohibited concomitant medications.

g. Due to potential drug interactions of anti-retroviral drugs with sacituzumab govitecan (IMMU-132), participants must not have known active or chronic hepatitis B virus (HBV) infection, requiring suppressive therapy or known active hepatitis C virus (HCV) infection. Participants with a known history of HCV infection must have been treated and cured.

h. Participants must not have received enzyme-inducing anti-epileptic agents (e.g., carbamazepine, phenytoin, phenobarbital, primidone) within 7 days prior to registration or within 14 days of planned start of Cycle 1, Day 1 treatment, and participants must not be planning to receive enzyme-inducing anti-epileptic agents (e.g., carbamazepine, phenytoin, phenobarbital, primidone) for the duration of protocol treatment).

i. Participants must not be receiving warfarin (or other coumarin derivatives) at time of registration or be planning to receive warfarin (or other coumarin derivatives) for the duration of protocol treatment. Participants who are able to switch to low molecular weight heparin (LMWH) or direct oral anticoagulants (DOACs) prior to date of registration (and plan to remain off of warfarin or other coumarin derivatives) for the duration of protocol treatment) are eligible.

j. Patients must not be receiving or be planning to receive concomitantly any other anti-cancer therapy, including endocrine therapy. Note: Concomitant hormone replacement therapy is allowed, as specified in Section 7.1b.

k. Participants must not have a condition requiring ongoing systemic treatment with corticosteroids (>4 mg daily dexamethasone (or bioequivalent)) or other immunosuppressive medications within 7 days prior to the baseline MRI. Corticosteroids administration must be stable and planned to remain ≤ 4 mg daily for the duration of protocol treatment. However, use of corticosteroids for clinical symptoms is allowed based upon treating physician discretion.

5.3 Clinical/Laboratory Criteria

a. Participants must be ≥ 18 years of age.

b. Participants must have Zubrod Performance Status 0 or 1. See Section 10.6.

c. Participants must have history and physical exam obtained within 21 days prior to registration.

d. Participants must have adequate organ and marrow function as defined below within 21 days prior to registration:

– absolute neutrophil count (ANC)	≥1,500/mcL
– platelet count	≥100,000/mcL
– hemoglobin	≥ 9.0 g/dL
– total bilirubin	≤ 1.5 times institutional upper limit of normal (ULN)
– ALT and AST	≤3 × institutional ULN

e. Participants must have a serum creatinine ≤ 1.5 times the IULN OR measured OR calculated creatinine clearance ≥ 30 mL/min using the following Cockroft-Gault Formula. This specimen must have been drawn and processed within 21 days prior to registration:

Calculated Creatinine Clearance =

$$\frac{(140 - \text{age}) \times (\text{weight in kg})^{\dagger} \times 1.00 \text{ (male) OR } \times 0.85 \text{ (female)}}{72 \times \text{serum creatinine}^{*}}$$

† The kilogram weight is the participant weight with an upper limit of 140% of the IBW.
* Actual lab serum creatinine value with a minimum of 0.7 mg/dL.

The MAXIMUM CrCl that can be used based on the Cockcroft and Gault method estimation should be 125 ml/min

f. Participants must have adequate cardiac function. Participants with known history or current symptoms of cardiac disease, or history of treatment with cardiotoxic agents, must have a clinical risk assessment of cardiac function using the New York Heart Association Functional Classification (See Section 18.1), and must be class 2B or better.

g. Participants must not have uncontrolled diabetes in the opinion of the treating investigator 21 days prior to registration.

h. Participants must not be pregnant or nursing. Women of reproductive potential must have a negative serum or urine pregnancy test within 7 days prior to registration. Women and men of reproductive potential must have agreed to use an effective contraceptive method for the duration of protocol treatment and for at least 6 months after the last dose of sacituzumab govitecan (IMMU-132). A woman is considered to be of "reproductive potential" if she has had menses at any time in the preceding 12 consecutive months. In addition to routine contraceptive methods, "effective contraception" also includes heterosexual celibacy and surgery intended to prevent pregnancy (or with a side-effect of pregnancy prevention) defined as a hysterectomy, bilateral oophorectomy or bilateral tubal ligation. However, if at any point a previously celibate participant chooses to become heterosexually active during the time period for use of contraceptive measures outlined in the protocol, he/she is responsible for beginning contraceptive measures.

5.4 Specimen Submission Criteria

Participants must be offered the opportunity to participate in specimen banking as outlined in Section 15.1. With participant consent, specimens must be collected and submitted via the SWOG Specimen Tracking System as outlined in Section 15.1.

5.5 Regulatory Criteria

a. Participants ***must*** be informed of the investigational nature of this study and must sign and give informed consent in accordance with institutional and federal guidelines.

b. As a part of the OPEN registration process (see Section 13.3 for OPEN access instructions) the treating institution's identity is provided in order to ensure that the current (within 365 days) date of institutional review board approval for this study has been entered in the system.