Exclusion Criteria

Subjects who meet any of the following criteria will be disqualified from entering the study:

1. Stage IV (metastatic) breast cancer.
2. History of any prior (ipsi- or contralateral) breast cancer except lobular carcinoma in situ (LCIS).
3. Evidence of clinically evident gross residual or recurrent disease following neoadjuvant therapy and surgery (see Section 8.1.2.1).
4. An overall response of progressive disease according to the investigator at the conclusion of preoperative systemic therapy
5. Prior treatment with T-DXd, T-DM1 or other anti-HER2 ADC.
6. History of exposure to the following cumulative doses of anthracyclines:

✧ Doxorubicin > 240 mg/m2

✧ Epirubicin or Liposomal Doxorubicin-Hydrochloride > 480 mg/m2

✧ For other anthracyclines, exposure equivalent to doxorubicin > 240 mg/m2

7. History of other malignancy within the last 5 years except for appropriately treated carcinoma in situ (CIS) of the cervix, non-melanoma skin carcinoma, Stage I melanoma skin carcinoma, Stage I uterine cancer, or other appropriately treated non-breast malignancies.
8. History of (noninfectious) ILD/pneumonitis that required steroids or has ILD/pneumonitis noted on computed tomography (CT) scan of the chest at Screening (asymptomatic interstitial changes confined to recent radiation therapy fields are not excluded).
9. Known pulmonary compromise resulting from intercurrent pulmonary illnesses including, but not limited to, any underlying pulmonary disorder (eg, pulmonary emboli within three months prior to randomization, severe asthma, severe chronic obstructive pulmonary disease (COPD), restrictive lung disease, etc.).
10. Any autoimmune, connective tissue or inflammatory disorders with pulmonary involvement (eg, Rheumatoid arthritis, Sjogren's, sarcoidosis, etc.), or prior lobectomy or pneumonectomy.
11. Uncontrolled or significant cardiovascular disease, including: Medical history of myocardial infarction within 6 months before randomization, symptomatic congestive heart failure (CHF) (New York Heart Association Class II to IV), troponin levels consistent with myocardial infarction as defined according to the manufacturer 28 days prior to randomization.
12. Has a corrected QT interval per Fridericia’s formula (QTcF) prolongation to > 470 msec (females) or > 450 msec (males) based on screening 12-lead electrocardiogram (ECG).

13. History of severe hypersensitivity reactions to either the drug substances or inactive ingredients in the drug product.

14. History of severe hypersensitivity reactions to other monoclonal antibodies (MAb).

15. Inadequate washout period before Randomization/Cycle 1 Day 1, defined as:

a. Major surgery: < 4 weeks prior to Randomization

b. Systemic anticancer chemotherapy:

- ✧ Immunotherapy (non-antibody based therapy), retinoid therapy: < 3 weeks prior to Randomization
- ✧ Small-molecule targeted agents (eg, 5-fluorouracil-based agents, folinate agents, weekly paclitaxel): < 2 weeks or < 5 half-lives prior to Randomization, whichever is longer

c. Antibody-based anticancer therapy: < 4 weeks prior to Randomization

d. Chloroquine/Hydroxychloroquine: ≤ 14 days prior to Cycle 1 Day 1

16. Substance abuse or medical conditions such as clinically significant cardiac or psychological conditions, that may, in the opinion of the investigator, interfere with the subject's participation in the clinical study or evaluation of the clinical study results.

17. Social, familial, or geographical factors that would interfere with study participation or follow-up.

18. Uncontrolled infection requiring IV antibiotics, antivirals, or antifungals.

19. Known human immunodeficiency virus (HIV) infection or active hepatitis B or C infection. Patients positive for hepatitis C virus (HCV) antibody are eligible only if polymerase chain reaction is negative for HCV RNA. Subjects should be tested for HIV prior to randomization if required by local regulations or institutional review board (IRB)/independent ethics committee (IEC).

20. Unresolved toxicities from previous anticancer therapy, defined as toxicities (other than alopecia) not yet resolved to Grade ≤ 1 or baseline. Subjects with chronic Grade 2 toxicities may be eligible per the discretion of the investigator after consultation with the Sponsor Medical Monitor or designee.

21. Is pregnant or breastfeeding or planning to become pregnant.