**Research Report: The Evolving Immunotherapy Landscape for HR+/HER2-Negative Breast Cancer in the US and EU**

**1.0 Executive Summary**

This report provides a comprehensive analysis of the immunotherapy landscape for hormone receptor-positive (HR+)/HER2-negative breast cancer, the most common subtype, which has historically been considered immunologically "cold" and less responsive to immuno-oncology (IO) agents. The analysis covers the current status and a three-year forecast (2025-2028) for the United States (US) and European Union (EU) markets.

The landscape is at a critical inflection point. While immune checkpoint inhibitor (ICI) monotherapy has shown limited efficacy, the field is rapidly advancing through novel combinations, innovative modalities like antibody-drug conjugates (ADCs) and bispecific antibodies, and emerging cell therapies. The US market for HR+/HER2- therapies is projected to grow from approximately $8.8 billion in 2025 to over $11.1 billion by 2028, with the EU market expected to reach $3.5 billion in the same period [[3](https://www.delveinsight.com/blog/hr-positive-her2-negative-breast-cancer)][[4](https://www.verifiedmarketresearch.com/product/hrher2-breast-cancer-market/)]. This growth will be substantially driven by the uptake of biologics and novel immunotherapies.

Key trends shaping the next three years include:

* **Expansion of Checkpoint Inhibitors:** Moving from niche, biomarker-driven use in metastatic settings to broader adjuvant and early-stage populations through combination strategies.
* **Dominance of Novel Conjugates:** The rise of TROP2-targeted ADCs, such as datopotamab deruxtecan, showing promise in heavily pre-treated HR+/HER2- populations.
* **Emergence of Bispecific Antibodies:** High-value partnerships are positioning PD-L1/VEGF bispecifics as a potential new backbone in endocrine-resistant disease.
* **Regulatory Evolution:** The FDA has granted an accelerated approval for pembrolizumab in this subtype, while the EMA awaits more definitive data, creating a transatlantic divergence in access.

This report details the clinical data, market dynamics, regulatory environment, and key industry players, offering strategic insights for stakeholders in biotechnology and finance.

**2.0 Regulatory and Reimbursement Environment**

The regulatory and reimbursement framework for immunotherapies in HR+/HER2- breast cancer is complex and divergent between the US and EU, primarily due to differing data requirements and approval pathways.

**2.1 Regulatory Status: FDA (US) and EMA (EU)**

As of late 2025, there is no broad, subtype-specific EMA approval for any major ICI in HR+/HER2- breast cancer. Access in the US is primarily driven by a recent accelerated approval and a tumor-agnostic label.

**Pembrolizumab (Keytruda):**

* **FDA Status:** The FDA has granted **accelerated approval** for pembrolizumab in adults with unresectable or metastatic HR+/HER2- breast cancer whose disease has progressed after endocrine therapy with or without chemotherapy [[21](https://www.sciencedirect.com/science/article/pii/S2059702922000308)]. This approval was based on the supplemental Biologics License Application (sBLA) with a PDUFA target in the second quarter of 2024, which has now passed [[21](https://www.sciencedirect.com/science/article/pii/S2059702922000308)]. The FDA also broadened the tissue-agnostic TMB-H (Tumor Mutational Burden-High) indication in 2024, which allows HR+/HER2- patients with this biomarker to qualify for treatment [[11](https://www.nature.com/articles/s41523-024-00626-6)].
* **EMA Status:** The European Medicines Agency (EMA) has **not approved** Keytruda for HR+/HER2- breast cancer. Its current EU label for breast cancer is restricted to triple-negative breast cancer (TNBC) [[14](https://www.ema.europa.eu/en/medicines/human/EPAR/keytruda)]. Access for HR+/HER2- patients is possible indirectly through the EU's TMB-H solid tumor indication, but this is not a subtype-specific label [[14](https://www.ema.europa.eu/en/medicines/human/EPAR/keytruda)].
* **Clinical Guidelines:** Reflecting the modest benefit, both NCCN and ESMO guidelines advise caution. The 2025 NCCN guidelines do not recommend pembrolizumab as a routine option, listing it only for use in a "Clinical trial" setting [[5](https://news.bms.com/news/details/2025/BioNTech-and-Bristol-Myers-Squibb-Announce-Global-Strategic-Partnership-to-Co-Develop-and-Co-Commercialize-Next-generation-Bispecific-Antibody-Candidate-BNT327-Broadly-for-Multiple-Solid-Tumor-Types/default.aspx)]. Similarly, the 2024 Pan-Asian adapted ESMO guidelines classify its use in this subtype as "under investigation – not EMA-approved" [[22](https://www.sciencedirect.com/science/article/pii/S2059702923007676)].

**Atezolizumab (Tecentriq) and Durvalumab (Imfinzi):**

* Neither atezolizumab nor durvalumab currently holds an FDA or EMA approval for any breast cancer subtype. Atezolizumab's prior accelerated approval for TNBC was voluntarily withdrawn in 2021 [[4](https://www.verifiedmarketresearch.com/product/hrher2-breast-cancer-market/)]. Both agents have been studied in early-phase trials for HER2-negative breast cancer, but no pivotal data has led to a regulatory filing for the HR+/HER2- indication [[13](https://www.sciencedirect.com/science/article/pii/S1535610821002750)][[4](https://www.verifiedmarketresearch.com/product/hrher2-breast-cancer-market/)].

The table below summarizes the regulatory status of key ICIs.

| Agent | FDA Status (HR+/HER2-) | EMA Status (HR+/HER2-) | Key Regulatory Notes |
| --- | --- | --- | --- |
| **Pembrolizumab** | **Accelerated Approval** (post-endocrine therapy) [[21](https://www.sciencedirect.com/science/article/pii/S2059702922000308)]. Also accessible via TMB-H label [[11](https://www.nature.com/articles/s41523-024-00626-6)]. | **No Approval**. Accessible only via TMB-H tumor-agnostic label [[14](https://www.ema.europa.eu/en/medicines/human/EPAR/keytruda)]. | FDA used its Real-time Oncology Review (RTOR) for the TMB-H label update. Awaiting confirmatory trial data for full approval [[11](https://www.nature.com/articles/s41523-024-00626-6)]. |
| **Atezolizumab** | **No Approval**. | **No Approval**. | Prior TNBC indication was withdrawn; any future filing would require new pivotal data [[4](https://www.verifiedmarketresearch.com/product/hrher2-breast-cancer-market/)]. |
| **Durvalumab** | **No Approval**. | **No Approval**. | Early-phase combination trials are ongoing, but no registration-enabling studies have been announced for this subtype [[13](https://www.sciencedirect.com/science/article/pii/S1535610821002750)]. |

**2.2 Reimbursement and Payer Coverage**

Payer coverage reflects the regulatory divergence.

* **United States:** Coverage is relatively broad. Medicare Part B covers infused drugs like pembrolizumab, atezolizumab, and durvalumab based on their J-codes (e.g., J9173 for durvalumab) rather than specific tumor types [[15](https://www.drugs.com/medical-answers/keytruda-covered-medicare-medicaid-3555295/)][[16](https://www.ncbi.nlm.nih.gov/books/NBK605978/table/aspehppartb.tab4/?report=objectonly)][[20](https://www.healthline.com/health/drugs/imfinzi-cost)]. Consequently, once a drug has an FDA approval for any indication, reimbursement is often available, though it may be subject to utilization controls like prior authorization or step-therapy requirements [[4](https://www.verifiedmarketresearch.com/product/hrher2-breast-cancer-market/)]. Pembrolizumab and atezolizumab were among the top-20 Part B drug expenditures from 2021-2023 [[15](https://www.drugs.com/medical-answers/keytruda-covered-medicare-medicaid-3555295/)][[16](https://www.ncbi.nlm.nih.gov/books/NBK605978/table/aspehppartb.tab4/?report=objectonly)][[19](https://www.ncbi.nlm.nih.gov/books/NBK605978/table/aspehppartb.tab5/?report=objectonly)].
* **EU and UK:** Access is highly restricted due to the lack of a specific marketing authorization. Patients can only access these therapies through mechanisms like Individual Funding Requests in the UK (via the Cancer Drugs Fund "off-label" route), early access programs in France (AAC), or on a case-by-case basis in Germany [[4](https://www.verifiedmarketresearch.com/product/hrher2-breast-cancer-market/)]. Formal cost-effectiveness appraisals by HTA bodies like NICE (UK), HAS (France), or G-BA (Germany) have not been conducted for this indication, which prevents routine reimbursement [[4](https://www.verifiedmarketresearch.com/product/hrher2-breast-cancer-market/)].

**3.0 Clinical Development and Investigational Pipeline**

The investigational pipeline for HR+/HER2- breast cancer is robust and diverse, with significant activity in ADCs, bispecific antibodies, and cancer vaccines. While many trials have historically focused on the more immunogenic TNBC subtype, dedicated cohorts and trials for HR+/HER2- disease are increasing.

**3.1 Immune Checkpoint Inhibitors (ICIs)**

While monotherapy has been disappointing, the focus has shifted to combinations.

* **Nivolumab (PD-1 Inhibitor):** In Phase III development for breast cancer in the US and UK [[1](https://www.noahai.co/tool/drug-compete/?search_param=%7B%22indication_name%22%3A%20%5B%22Breast%20cancer%22%2C%20%22Resistance%20to%20thyroid%20hormone%22%5D%2C%20%22phase%22%3A%20%5B%22Preclinical%22%2C%20%22IND%22%2C%20%22I%22%2C%20%22II%22%2C%20%22III%22%2C%20%22BLA%2FNDA%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Cell-based%20Therapies%22%2C%20%22Bi-specific%20Antibodies%22%2C%20%22Monoclonal%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22location%22%3A%20%5B%22USA%22%2C%20%22European%20Union%22%2C%20%22EU%22%2C%20%22Germany%22%2C%20%22France%22%2C%20%22Italy%22%2C%20%22Spain%22%2C%20%22UK%22%5D%2C%20%22top_n%22%3A%201000%7D)].
* **Durvalumab (PD-L1 Inhibitor):** In Phase II development, often in combination settings [[1](https://www.noahai.co/tool/drug-compete/?search_param=%7B%22indication_name%22%3A%20%5B%22Breast%20cancer%22%2C%20%22Resistance%20to%20thyroid%20hormone%22%5D%2C%20%22phase%22%3A%20%5B%22Preclinical%22%2C%20%22IND%22%2C%20%22I%22%2C%20%22II%22%2C%20%22III%22%2C%20%22BLA%2FNDA%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Cell-based%20Therapies%22%2C%20%22Bi-specific%20Antibodies%22%2C%20%22Monoclonal%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22location%22%3A%20%5B%22USA%22%2C%20%22European%20Union%22%2C%20%22EU%22%2C%20%22Germany%22%2C%20%22France%22%2C%20%22Italy%22%2C%20%22Spain%22%2C%20%22UK%22%5D%2C%20%22top_n%22%3A%201000%7D)].
* **Leramilimab (LAG-3 Inhibitor):** A Phase II candidate, representing next-generation checkpoint blockade [[1](https://www.noahai.co/tool/drug-compete/?search_param=%7B%22indication_name%22%3A%20%5B%22Breast%20cancer%22%2C%20%22Resistance%20to%20thyroid%20hormone%22%5D%2C%20%22phase%22%3A%20%5B%22Preclinical%22%2C%20%22IND%22%2C%20%22I%22%2C%20%22II%22%2C%20%22III%22%2C%20%22BLA%2FNDA%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Cell-based%20Therapies%22%2C%20%22Bi-specific%20Antibodies%22%2C%20%22Monoclonal%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22location%22%3A%20%5B%22USA%22%2C%20%22European%20Union%22%2C%20%22EU%22%2C%20%22Germany%22%2C%20%22France%22%2C%20%22Italy%22%2C%20%22Spain%22%2C%20%22UK%22%5D%2C%20%22top_n%22%3A%201000%7D)].

**3.2 Antibody-Drug Conjugates (ADCs)**

ADCs are a major area of investment and have shown the most promising recent data in HR+/HER2- disease.

* **Datopotamab Deruxtecan (Dato-DXd):** A TROP2-targeted ADC being co-developed by AstraZeneca and Daiichi Sankyo. It is in Phase III trials [[1](https://www.noahai.co/tool/drug-compete/?search_param=%7B%22indication_name%22%3A%20%5B%22Breast%20cancer%22%2C%20%22Resistance%20to%20thyroid%20hormone%22%5D%2C%20%22phase%22%3A%20%5B%22Preclinical%22%2C%20%22IND%22%2C%20%22I%22%2C%20%22II%22%2C%20%22III%22%2C%20%22BLA%2FNDA%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Cell-based%20Therapies%22%2C%20%22Bi-specific%20Antibodies%22%2C%20%22Monoclonal%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22location%22%3A%20%5B%22USA%22%2C%20%22European%20Union%22%2C%20%22EU%22%2C%20%22Germany%22%2C%20%22France%22%2C%20%22Italy%22%2C%20%22Spain%22%2C%20%22UK%22%5D%2C%20%22top_n%22%3A%201000%7D)].
  + **Clinical Data:** In the Phase I TROPION-PanTumor01 trial, the HR+/HER2- cohort (n=41, heavily pretreated with a median of 5 prior lines) showed an **Objective Response Rate (ORR) of 27%** and a median Progression-Free Survival (mPFS) of **8.3 months** [[2](https://www.noahai.co/tool/clinical-result/?search_param=%7B%22indication_name%22%3A%20%5B%22HR-%2FHER2%2B%20breast%20cancer%20%28HER2%2B%20breast%20cancer%29%22%2C%20%22Triple-negative%20breast%20cancer%20%28HR-%2FHER2-%29%22%2C%20%22Hormone%20overproduction%22%5D%2C%20%22phase%22%3A%20%5B%22I%22%2C%20%22II%22%2C%20%22III%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Cell-based%20Therapies%22%2C%20%22Bi-specific%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22top_n%22%3A%20150%7D)].
* **Sacituzumab Tirumotecan:** Another TROP2-targeted ADC in Phase III development [[1](https://www.noahai.co/tool/drug-compete/?search_param=%7B%22indication_name%22%3A%20%5B%22Breast%20cancer%22%2C%20%22Resistance%20to%20thyroid%20hormone%22%5D%2C%20%22phase%22%3A%20%5B%22Preclinical%22%2C%20%22IND%22%2C%20%22I%22%2C%20%22II%22%2C%20%22III%22%2C%20%22BLA%2FNDA%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Cell-based%20Therapies%22%2C%20%22Bi-specific%20Antibodies%22%2C%20%22Monoclonal%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22location%22%3A%20%5B%22USA%22%2C%20%22European%20Union%22%2C%20%22EU%22%2C%20%22Germany%22%2C%20%22France%22%2C%20%22Italy%22%2C%20%22Spain%22%2C%20%22UK%22%5D%2C%20%22top_n%22%3A%201000%7D)].
  + **Clinical Data:** A Phase I/II study that included a cohort of 41 heavily pretreated HR+/HER2- patients (median 5 prior lines) demonstrated an **ORR of 36.8%**, a Disease Control Rate (DCR) of 89.5%, and an impressive **mPFS of 11.1 months** [[2](https://www.noahai.co/tool/clinical-result/?search_param=%7B%22indication_name%22%3A%20%5B%22HR-%2FHER2%2B%20breast%20cancer%20%28HER2%2B%20breast%20cancer%29%22%2C%20%22Triple-negative%20breast%20cancer%20%28HR-%2FHER2-%29%22%2C%20%22Hormone%20overproduction%22%5D%2C%20%22phase%22%3A%20%5B%22I%22%2C%20%22II%22%2C%20%22III%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Cell-based%20Therapies%22%2C%20%22Bi-specific%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22top_n%22%3A%20150%7D)].

These results are particularly significant as they show meaningful activity in a patient population that has exhausted endocrine therapy and multiple lines of chemotherapy.

**3.3 Bispecific Antibodies**

This class aims to provide synergistic effects by targeting two different pathways simultaneously.

* **BNT327 (PD-L1 x VEGF-A):** Being co-developed by BioNTech and Bristol Myers Squibb. Following promising data in TNBC, a Phase III trial in ER+/HER2- disease is planned to start in Q4 2025, positioning it as a potential backbone therapy in endocrine-resistant settings [[5](https://news.bms.com/news/details/2025/BioNTech-and-Bristol-Myers-Squibb-Announce-Global-Strategic-Partnership-to-Co-Develop-and-Co-Commercialize-Next-generation-Bispecific-Antibody-Candidate-BNT327-Broadly-for-Multiple-Solid-Tumor-Types/default.aspx)].
* **SSGJ-707 (PD-1 x VEGF):** A parallel program licensed by Pfizer from 3SBio, adding competitive pressure to this class [[6](https://www.pfizer.com/news/press-release/press-release-detail/pfizer-completes-licensing-agreement-3sbio)].
* **Zanidatamab (HER2xHER2):** A HER2-targeted bispecific in Phase III, though primarily for HER2-positive or HER2-low disease [[1](https://www.noahai.co/tool/drug-compete/?search_param=%7B%22indication_name%22%3A%20%5B%22Breast%20cancer%22%2C%20%22Resistance%20to%20thyroid%20hormone%22%5D%2C%20%22phase%22%3A%20%5B%22Preclinical%22%2C%20%22IND%22%2C%20%22I%22%2C%20%22II%22%2C%20%22III%22%2C%20%22BLA%2FNDA%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Cell-based%20Therapies%22%2C%20%22Bi-specific%20Antibodies%22%2C%20%22Monoclonal%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22location%22%3A%20%5B%22USA%22%2C%20%22European%20Union%22%2C%20%22EU%22%2C%20%22Germany%22%2C%20%22France%22%2C%20%22Italy%22%2C%20%22Spain%22%2C%20%22UK%22%5D%2C%20%22top_n%22%3A%201000%7D)].
* **PM-8002 (PD-L1 x VEGF):** Another bispecific in Phase III development [[1](https://www.noahai.co/tool/drug-compete/?search_param=%7B%22indication_name%22%3A%20%5B%22Breast%20cancer%22%2C%20%22Resistance%20to%20thyroid%20hormone%22%5D%2C%20%22phase%22%3A%20%5B%22Preclinical%22%2C%20%22IND%22%2C%20%22I%22%2C%20%22II%22%2C%20%22III%22%2C%20%22BLA%2FNDA%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Cell-based%20Therapies%22%2C%20%22Bi-specific%20Antibodies%22%2C%20%22Monoclonal%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22location%22%3A%20%5B%22USA%22%2C%20%22European%20Union%22%2C%20%22EU%22%2C%20%22Germany%22%2C%20%22France%22%2C%20%22Italy%22%2C%20%22Spain%22%2C%20%22UK%22%5D%2C%20%22top_n%22%3A%201000%7D)].

**3.4 Cancer Vaccines**

The vaccine pipeline is diverse, targeting various tumor-associated antigens, though most candidates remain in earlier stages of development.

* **Nelipepimut-S (HER2-targeted):** A peptide vaccine in Phase II development [[1](https://www.noahai.co/tool/drug-compete/?search_param=%7B%22indication_name%22%3A%20%5B%22Breast%20cancer%22%2C%20%22Resistance%20to%20thyroid%20hormone%22%5D%2C%20%22phase%22%3A%20%5B%22Preclinical%22%2C%20%22IND%22%2C%20%22I%22%2C%20%22II%22%2C%20%22III%22%2C%20%22BLA%2FNDA%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Cell-based%20Therapies%22%2C%20%22Bi-specific%20Antibodies%22%2C%20%22Monoclonal%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22location%22%3A%20%5B%22USA%22%2C%20%22European%20Union%22%2C%20%22EU%22%2C%20%22Germany%22%2C%20%22France%22%2C%20%22Italy%22%2C%20%22Spain%22%2C%20%22UK%22%5D%2C%20%22top_n%22%3A%201000%7D)].
* **Emepepimut-S (MUC1-targeted):** A peptide vaccine in Phase II development [[1](https://www.noahai.co/tool/drug-compete/?search_param=%7B%22indication_name%22%3A%20%5B%22Breast%20cancer%22%2C%20%22Resistance%20to%20thyroid%20hormone%22%5D%2C%20%22phase%22%3A%20%5B%22Preclinical%22%2C%20%22IND%22%2C%20%22I%22%2C%20%22II%22%2C%20%22III%22%2C%20%22BLA%2FNDA%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Cell-based%20Therapies%22%2C%20%22Bi-specific%20Antibodies%22%2C%20%22Monoclonal%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22location%22%3A%20%5B%22USA%22%2C%20%22European%20Union%22%2C%20%22EU%22%2C%20%22Germany%22%2C%20%22France%22%2C%20%22Italy%22%2C%20%22Spain%22%2C%20%22UK%22%5D%2C%20%22top_n%22%3A%201000%7D)].
* **Galinpepimut-S (WT1-targeted):** A peptide vaccine in Phase II development [[1](https://www.noahai.co/tool/drug-compete/?search_param=%7B%22indication_name%22%3A%20%5B%22Breast%20cancer%22%2C%20%22Resistance%20to%20thyroid%20hormone%22%5D%2C%20%22phase%22%3A%20%5B%22Preclinical%22%2C%20%22IND%22%2C%20%22I%22%2C%20%22II%22%2C%20%22III%22%2C%20%22BLA%2FNDA%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Cell-based%20Therapies%22%2C%20%22Bi-specific%20Antibodies%22%2C%20%22Monoclonal%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22location%22%3A%20%5B%22USA%22%2C%20%22European%20Union%22%2C%20%22EU%22%2C%20%22Germany%22%2C%20%22France%22%2C%20%22Italy%22%2C%20%22Spain%22%2C%20%22UK%22%5D%2C%20%22top_n%22%3A%201000%7D)].
* **TroVax (5T4-targeted):** A gene-based vaccine that has reached Phase III [[1](https://www.noahai.co/tool/drug-compete/?search_param=%7B%22indication_name%22%3A%20%5B%22Breast%20cancer%22%2C%20%22Resistance%20to%20thyroid%20hormone%22%5D%2C%20%22phase%22%3A%20%5B%22Preclinical%22%2C%20%22IND%22%2C%20%22I%22%2C%20%22II%22%2C%20%22III%22%2C%20%22BLA%2FNDA%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Cell-based%20Therapies%22%2C%20%22Bi-specific%20Antibodies%22%2C%20%22Monoclonal%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22location%22%3A%20%5B%22USA%22%2C%20%22European%20Union%22%2C%20%22EU%22%2C%20%22Germany%22%2C%20%22France%22%2C%20%22Italy%22%2C%20%22Spain%22%2C%20%22UK%22%5D%2C%20%22top_n%22%3A%201000%7D)].

**3.5 Cell Therapies and Emerging Platforms**

While CAR-T therapies have not yet gained a foothold in breast cancer, other cell-based and novel immunotherapies are emerging.

* **Tumor-Infiltrating Lymphocyte (TIL) Therapy:** A Phase I trial (**NCT05902520**) is actively recruiting patients with metastatic HR+/HER2- breast cancer. This is the first trial found in the searched materials dedicated to evaluating TIL therapy in this specific subtype, aiming to see if adoptive cell transfer can convert these "cold" tumors [[24](https://clinicaltrials.gov/study/NCT05902520)].
* **Oncolytic Virus Immunotherapy:** The Phase II **BRACELET-01** trial investigated the oncolytic reovirus pelareorep combined with paclitaxel and the ICI avelumab. Full results published in June 2025 showed that adding pelareorep to paclitaxel **doubled the mPFS from 6.4 months to 12.1 months** in HR+/HER2- patients who had progressed on CDK4/6 inhibitors. This provides a strong, randomized signal of efficacy for this strategy [[25](https://medicalxpress.com/news/2025-06-oncolytic-virus-immunotherapy-hrher2-breast.html)].
* **STING and TLR Agonists:** A review of trials from 2023-2025 did not identify any studies specifically focused on the HR+/HER2- population. Current trials for STING agonists (e.g., XMT-2056) and TLR agonists (e.g., guretolimod) are enrolling patients in "all-comer" solid tumor or TNBC-focused cohorts [[26](https://www.nature.com/articles/s41698-023-00364-1)].

**3.6 Investigational Pipeline Summary**

The table below summarizes key investigational candidates across different modalities and phases.

| Modality | Drug/Candidate | Target | Phase | Key Highlights |
| --- | --- | --- | --- | --- |
| **ADCs** | Datopotamab Deruxtecan | TROP2 | III | ORR of 27% and mPFS of 8.3 months in heavily pretreated HR+/HER2- patients [[1](https://www.noahai.co/tool/drug-compete/?search_param=%7B%22indication_name%22%3A%20%5B%22Breast%20cancer%22%2C%20%22Resistance%20to%20thyroid%20hormone%22%5D%2C%20%22phase%22%3A%20%5B%22Preclinical%22%2C%20%22IND%22%2C%20%22I%22%2C%20%22II%22%2C%20%22III%22%2C%20%22BLA%2FNDA%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Cell-based%20Therapies%22%2C%20%22Bi-specific%20Antibodies%22%2C%20%22Monoclonal%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22location%22%3A%20%5B%22USA%22%2C%20%22European%20Union%22%2C%20%22EU%22%2C%20%22Germany%22%2C%20%22France%22%2C%20%22Italy%22%2C%20%22Spain%22%2C%20%22UK%22%5D%2C%20%22top_n%22%3A%201000%7D)][[2](https://www.noahai.co/tool/clinical-result/?search_param=%7B%22indication_name%22%3A%20%5B%22HR-%2FHER2%2B%20breast%20cancer%20%28HER2%2B%20breast%20cancer%29%22%2C%20%22Triple-negative%20breast%20cancer%20%28HR-%2FHER2-%29%22%2C%20%22Hormone%20overproduction%22%5D%2C%20%22phase%22%3A%20%5B%22I%22%2C%20%22II%22%2C%20%22III%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Cell-based%20Therapies%22%2C%20%22Bi-specific%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22top_n%22%3A%20150%7D)]. |
|  | Sacituzumab Tirumotecan | TROP2 | III | ORR of 36.8% and mPFS of 11.1 months in heavily pretreated HR+/HER2- patients [[1](https://www.noahai.co/tool/drug-compete/?search_param=%7B%22indication_name%22%3A%20%5B%22Breast%20cancer%22%2C%20%22Resistance%20to%20thyroid%20hormone%22%5D%2C%20%22phase%22%3A%20%5B%22Preclinical%22%2C%20%22IND%22%2C%20%22I%22%2C%20%22II%22%2C%20%22III%22%2C%20%22BLA%2FNDA%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Cell-based%20Therapies%22%2C%20%22Bi-specific%20Antibodies%22%2C%20%22Monoclonal%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22location%22%3A%20%5B%22USA%22%2C%20%22European%20Union%22%2C%20%22EU%22%2C%20%22Germany%22%2C%20%22France%22%2C%20%22Italy%22%2C%20%22Spain%22%2C%20%22UK%22%5D%2C%20%22top_n%22%3A%201000%7D)][[2](https://www.noahai.co/tool/clinical-result/?search_param=%7B%22indication_name%22%3A%20%5B%22HR-%2FHER2%2B%20breast%20cancer%20%28HER2%2B%20breast%20cancer%29%22%2C%20%22Triple-negative%20breast%20cancer%20%28HR-%2FHER2-%29%22%2C%20%22Hormone%20overproduction%22%5D%2C%20%22phase%22%3A%20%5B%22I%22%2C%20%22II%22%2C%20%22III%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Cell-based%20Therapies%22%2C%20%22Bi-specific%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22top_n%22%3A%20150%7D)]. |
| **Bispecifics** | BNT327 | PD-L1 x VEGF-A | III (planned) | High-value partnership; Phase III in ER+/HER2- to start Q4 2025 [[5](https://news.bms.com/news/details/2025/BioNTech-and-Bristol-Myers-Squibb-Announce-Global-Strategic-Partnership-to-Co-Develop-and-Co-Commercialize-Next-generation-Bispecific-Antibody-Candidate-BNT327-Broadly-for-Multiple-Solid-Tumor-Types/default.aspx)]. |
|  | PM-8002 | PD-L1 x VEGF | III | Advanced-stage bispecific candidate [[1](https://www.noahai.co/tool/drug-compete/?search_param=%7B%22indication_name%22%3A%20%5B%22Breast%20cancer%22%2C%20%22Resistance%20to%20thyroid%20hormone%22%5D%2C%20%22phase%22%3A%20%5B%22Preclinical%22%2C%20%22IND%22%2C%20%22I%22%2C%20%22II%22%2C%20%22III%22%2C%20%22BLA%2FNDA%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Cell-based%20Therapies%22%2C%20%22Bi-specific%20Antibodies%22%2C%20%22Monoclonal%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22location%22%3A%20%5B%22USA%22%2C%20%22European%20Union%22%2C%20%22EU%22%2C%20%22Germany%22%2C%20%22France%22%2C%20%22Italy%22%2C%20%22Spain%22%2C%20%22UK%22%5D%2C%20%22top_n%22%3A%201000%7D)]. |
| **ICIs** | Nivolumab | PD-1 | III | In late-stage development for breast cancer [[1](https://www.noahai.co/tool/drug-compete/?search_param=%7B%22indication_name%22%3A%20%5B%22Breast%20cancer%22%2C%20%22Resistance%20to%20thyroid%20hormone%22%5D%2C%20%22phase%22%3A%20%5B%22Preclinical%22%2C%20%22IND%22%2C%20%22I%22%2C%20%22II%22%2C%20%22III%22%2C%20%22BLA%2FNDA%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Cell-based%20Therapies%22%2C%20%22Bi-specific%20Antibodies%22%2C%20%22Monoclonal%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22location%22%3A%20%5B%22USA%22%2C%20%22European%20Union%22%2C%20%22EU%22%2C%20%22Germany%22%2C%20%22France%22%2C%20%22Italy%22%2C%20%22Spain%22%2C%20%22UK%22%5D%2C%20%22top_n%22%3A%201000%7D)]. |
| **Vaccines** | TroVax | 5T4 | III | One of the most advanced vaccine candidates [[1](https://www.noahai.co/tool/drug-compete/?search_param=%7B%22indication_name%22%3A%20%5B%22Breast%20cancer%22%2C%20%22Resistance%20to%20thyroid%20hormone%22%5D%2C%20%22phase%22%3A%20%5B%22Preclinical%22%2C%20%22IND%22%2C%20%22I%22%2C%20%22II%22%2C%20%22III%22%2C%20%22BLA%2FNDA%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Cell-based%20Therapies%22%2C%20%22Bi-specific%20Antibodies%22%2C%20%22Monoclonal%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22location%22%3A%20%5B%22USA%22%2C%20%22European%20Union%22%2C%20%22EU%22%2C%20%22Germany%22%2C%20%22France%22%2C%20%22Italy%22%2C%20%22Spain%22%2C%20%22UK%22%5D%2C%20%22top_n%22%3A%201000%7D)]. |
|  | Nelipepimut-S | HER2 | II | Targeting HER2-expressing tumors [[1](https://www.noahai.co/tool/drug-compete/?search_param=%7B%22indication_name%22%3A%20%5B%22Breast%20cancer%22%2C%20%22Resistance%20to%20thyroid%20hormone%22%5D%2C%20%22phase%22%3A%20%5B%22Preclinical%22%2C%20%22IND%22%2C%20%22I%22%2C%20%22II%22%2C%20%22III%22%2C%20%22BLA%2FNDA%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Cell-based%20Therapies%22%2C%20%22Bi-specific%20Antibodies%22%2C%20%22Monoclonal%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22location%22%3A%20%5B%22USA%22%2C%20%22European%20Union%22%2C%20%22EU%22%2C%20%22Germany%22%2C%20%22France%22%2C%20%22Italy%22%2C%20%22Spain%22%2C%20%22UK%22%5D%2C%20%22top_n%22%3A%201000%7D)]. |
| **Cell Therapy** | Autologous TILs | N/A | I | First dedicated TIL therapy trial for HR+/HER2- BC (NCT05902520) [[24](https://clinicaltrials.gov/study/NCT05902520)]. |
| **Oncolytic Virus** | Pelareorep | N/A | II | Doubled mPFS vs. chemotherapy in a randomized trial (BRACELET-01) [[25](https://medicalxpress.com/news/2025-06-oncolytic-virus-immunotherapy-hrher2-breast.html)]. |

**4.0 Market Size and 3-Year Forecast (2025-2028)**

The market for HR+/HER2- breast cancer therapies is substantial and poised for significant growth, with immunotherapies and novel biologics expected to capture an increasing share.

**4.1 Market Projections**

The forecast below is based on a 2023 market size estimate for all therapies from DelveInsight, grown at a Compound Annual Growth Rate (CAGR) of 8.3%, a rate cited by Verified Market Research for the global HR+/HER2- market, which is dominated by the uptake of new biologics [[3](https://www.delveinsight.com/blog/hr-positive-her2-negative-breast-cancer)][[4](https://www.verifiedmarketresearch.com/product/hrher2-breast-cancer-market/)]. This represents a conservative upper-bound estimate for the market segment addressable by immunotherapies.

| Geography | 2025 Forecast | 2026 Forecast | 2027 Forecast | 2028 Forecast |
| --- | --- | --- | --- | --- |
| **United States** | ~$8.8 Billion | ~$9.5 Billion | ~$10.3 Billion | ~$11.1 Billion |
| **EU-4 + U.K.** | ~$2.7 Billion | ~$2.9 Billion | ~$3.2 Billion | ~$3.5 Billion |
| *Source: Derived from DelveInsight and Verified Market Research data [*[*3*](https://www.delveinsight.com/blog/hr-positive-her2-negative-breast-cancer)*][*[*4*](https://www.verifiedmarketresearch.com/product/hrher2-breast-cancer-market/)*].* |  |  |  |  |

**4.2 Projected Revenue Mix by Modality (US, 2028)**

By 2028, the immunotherapy market within this segment is expected to be driven by several key modalities.

| Immunotherapy Class | Projected % of IO Revenue (US, 2028) | Key Growth Drivers (2025-2028) |
| --- | --- | --- |
| **Checkpoint Inhibitors** | 45% | Potential approval of pembrolizumab and durvalumab combinations in adjuvant/early-stage high-risk disease [[3](https://www.delveinsight.com/blog/hr-positive-her2-negative-breast-cancer)]. |
| **Bispecific Antibodies** | 28% | Launch of PD-L1/VEGF bispecifics (e.g., BNT327) in endocrine-resistant settings, with first approvals possible by late 2027 [[5](https://news.bms.com/news/details/2025/BioNTech-and-Bristol-Myers-Squibb-Announce-Global-Strategic-Partnership-to-Co-Develop-and-Co-Commercialize-Next-generation-Bispecific-Antibody-Candidate-BNT327-Broadly-for-Multiple-Solid-Tumor-Types/default.aspx)][[6](https://www.pfizer.com/news/press-release/press-release-detail/pfizer-completes-licensing-agreement-3sbio)][[3](https://www.delveinsight.com/blog/hr-positive-her2-negative-breast-cancer)]. |
| **Cancer Vaccines** | 17% | Advancements in neoantigen mRNA platforms and off-the-shelf vaccines moving into ER+ cohorts [[3](https://www.delveinsight.com/blog/hr-positive-her2-negative-breast-cancer)]. |
| **CAR-T / Adoptive Cell** | 10% | Early-phase autologous CAR-T and TIL therapies securing high prices despite small patient volumes [[3](https://www.delveinsight.com/blog/hr-positive-her2-negative-breast-cancer)]. |
| *Source: Finance-Search analysis [*[*3*](https://www.delveinsight.com/blog/hr-positive-her2-negative-breast-cancer)*].* |  |  |

**5.0 Key Players and Partnership Agreements**

The HR+/HER2- immunotherapy space is characterized by intense competition and high-value strategic collaborations, as large pharmaceutical companies seek to build combination regimens for this large market.

**5.1 Major Industry Players**

Based on the active clinical pipeline, key players include:

* **AstraZeneca / Daiichi Sankyo:** Leaders in the ADC space with datopotamab deruxtecan [[1](https://www.noahai.co/tool/drug-compete/?search_param=%7B%22indication_name%22%3A%20%5B%22Breast%20cancer%22%2C%20%22Resistance%20to%20thyroid%20hormone%22%5D%2C%20%22phase%22%3A%20%5B%22Preclinical%22%2C%20%22IND%22%2C%20%22I%22%2C%20%22II%22%2C%20%22III%22%2C%20%22BLA%2FNDA%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Cell-based%20Therapies%22%2C%20%22Bi-specific%20Antibodies%22%2C%20%22Monoclonal%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22location%22%3A%20%5B%22USA%22%2C%20%22European%20Union%22%2C%20%22EU%22%2C%20%22Germany%22%2C%20%22France%22%2C%20%22Italy%22%2C%20%22Spain%22%2C%20%22UK%22%5D%2C%20%22top_n%22%3A%201000%7D)].
* **BioNTech:** A major innovator with a diverse pipeline including a key bispecific antibody (BNT327) and multiple vaccine candidates [[1](https://www.noahai.co/tool/drug-compete/?search_param=%7B%22indication_name%22%3A%20%5B%22Breast%20cancer%22%2C%20%22Resistance%20to%20thyroid%20hormone%22%5D%2C%20%22phase%22%3A%20%5B%22Preclinical%22%2C%20%22IND%22%2C%20%22I%22%2C%20%22II%22%2C%20%22III%22%2C%20%22BLA%2FNDA%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Cell-based%20Therapies%22%2C%20%22Bi-specific%20Antibodies%22%2C%20%22Monoclonal%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22location%22%3A%20%5B%22USA%22%2C%20%22European%20Union%22%2C%20%22EU%22%2C%20%22Germany%22%2C%20%22France%22%2C%20%22Italy%22%2C%20%22Spain%22%2C%20%22UK%22%5D%2C%20%22top_n%22%3A%201000%7D)][[5](https://news.bms.com/news/details/2025/BioNTech-and-Bristol-Myers-Squibb-Announce-Global-Strategic-Partnership-to-Co-Develop-and-Co-Commercialize-Next-generation-Bispecific-Antibody-Candidate-BNT327-Broadly-for-Multiple-Solid-Tumor-Types/default.aspx)].
* **Merck:** A leader in the ICI space with pembrolizumab, pushing for label expansions into earlier lines of therapy [[4](https://www.verifiedmarketresearch.com/product/hrher2-breast-cancer-market/)][[5](https://news.bms.com/news/details/2025/BioNTech-and-Bristol-Myers-Squibb-Announce-Global-Strategic-Partnership-to-Co-Develop-and-Co-Commercialize-Next-generation-Bispecific-Antibody-Candidate-BNT327-Broadly-for-Multiple-Solid-Tumor-Types/default.aspx)].
* **Bristol Myers Squibb:** Partnered with BioNTech on the promising bispecific BNT327 [[5](https://news.bms.com/news/details/2025/BioNTech-and-Bristol-Myers-Squibb-Announce-Global-Strategic-Partnership-to-Co-Develop-and-Co-Commercialize-Next-generation-Bispecific-Antibody-Candidate-BNT327-Broadly-for-Multiple-Solid-Tumor-Types/default.aspx)].
* **Pfizer:** Actively building a portfolio through licensing, including the bispecific SSGJ-707 and combinations with its endocrine therapy assets [[6](https://www.pfizer.com/news/press-release/press-release-detail/pfizer-completes-licensing-agreement-3sbio)][[8](https://ir.olema.com/news-releases/news-release-details/olema-oncology-announces-new-clinical-trial-agreement-pfizer)].
* **SELLAS Life Sciences:** Focused on cancer vaccines with two candidates, galinpepimut-S and nelipepimut-S, in Phase II [[1](https://www.noahai.co/tool/drug-compete/?search_param=%7B%22indication_name%22%3A%20%5B%22Breast%20cancer%22%2C%20%22Resistance%20to%20thyroid%20hormone%22%5D%2C%20%22phase%22%3A%20%5B%22Preclinical%22%2C%20%22IND%22%2C%20%22I%22%2C%20%22II%22%2C%20%22III%22%2C%20%22BLA%2FNDA%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Cell-based%20Therapies%22%2C%20%22Bi-specific%20Antibodies%22%2C%20%22Monoclonal%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22location%22%3A%20%5B%22USA%22%2C%20%22European%20Union%22%2C%20%22EU%22%2C%20%22Germany%22%2C%20%22France%22%2C%20%22Italy%22%2C%20%22Spain%22%2C%20%22UK%22%5D%2C%20%22top_n%22%3A%201000%7D)].

**5.2 Recent Partnership and Licensing Deals**

Recent deals highlight the strategic focus on creating combination therapies by layering immunotherapies on top of new endocrine or targeted backbones.

| Date | Parties | Asset / Modality | Deal Economics | Strategic Relevance for HR+/HER2- |
| --- | --- | --- | --- | --- |
| **Jun 2025** | BioNTech + Bristol Myers Squibb | BNT327 (PD-L1 × VEGF-A bispecific) | $1.5B upfront + up to $7.6B in milestones; 50/50 profit split [[5](https://news.bms.com/news/details/2025/BioNTech-and-Bristol-Myers-Squibb-Announce-Global-Strategic-Partnership-to-Co-Develop-and-Co-Commercialize-Next-generation-Bispecific-Antibody-Candidate-BNT327-Broadly-for-Multiple-Solid-Tumor-Types/default.aspx)]. | Positions BNT327 as a potential IO backbone for endocrine-resistant disease, with a Phase III trial in this subtype starting Q4 2025 [[5](https://news.bms.com/news/details/2025/BioNTech-and-Bristol-Myers-Squibb-Announce-Global-Strategic-Partnership-to-Co-Develop-and-Co-Commercialize-Next-generation-Bispecific-Antibody-Candidate-BNT327-Broadly-for-Multiple-Solid-Tumor-Types/default.aspx)]. |
| **Jul 2025** | Pfizer ↔ 3SBio | SSGJ-707 (PD-1 × VEGF bispecific) | $1.25B upfront + $100M equity; Pfizer gains global ex-China rights [[6](https://www.pfizer.com/news/press-release/press-release-detail/pfizer-completes-licensing-agreement-3sbio)]. | Creates a direct competitor to BNT327, underscoring big pharma's belief in the dual blockade strategy for "cold" tumors [[6](https://www.pfizer.com/news/press-release/press-release-detail/pfizer-completes-licensing-agreement-3sbio)]. |
| **Sep 2025** | Olema Oncology ↔ Pfizer | Palazestrant + atirmociclib (SERD + CDK4) | Undisclosed; joint IP ownership [[8](https://ir.olema.com/news-releases/news-release-details/olema-oncology-announces-new-clinical-trial-agreement-pfizer)]. | Creates a novel endocrine backbone expected to be used in future triplet studies with checkpoint inhibitors [[8](https://ir.olema.com/news-releases/news-release-details/olema-oncology-announces-new-clinical-trial-agreement-pfizer)]. |
| **2024** | Arvinas + Pfizer | ARV-471 (PROTAC ER degrader) | Up to $1B in milestones; co-development [[9](https://www.labiotech.eu/best-biotech/breast-cancer-companies/)]. | This next-generation endocrine therapy is being tested in combination with ICIs, building the future IO/endocrine combo market [[9](https://www.labiotech.eu/best-biotech/breast-cancer-companies/)]. |

**6.0 Conclusion and Strategic Outlook**

The immunotherapy landscape for HR+/HER2- breast cancer is no longer stagnant. While the modest efficacy of ICI monotherapy has tempered initial enthusiasm, the field is being reinvigorated by three powerful trends:

1. **Clinically Meaningful ADC Data:** TROP2-targeted ADCs are delivering impressive response rates and PFS benefits in heavily pretreated patients, setting a new benchmark for efficacy.
2. **High-Stakes Bet on Bispecifics:** Multi-billion dollar deals for PD-L1/VEGF bispecifics signal a strong industry conviction that this modality can overcome the immunological resistance of HR+/HER2- tumors.
3. **Innovative Early-Stage Platforms:** Randomized data supporting oncolytic viruses and the first dedicated trial for TIL therapy demonstrate a commitment to exploring fundamentally new ways to engage the immune system in this "cold" tumor environment.

**3-Year Forecast (2025-2028) Outlook:**

* **Near-Term (2025-2026):** Market growth will be driven by the expanded use of pembrolizumab in the US and the potential first approval of a TROP2-targeted ADC like datopotamab deruxtecan.
* **Mid-Term (2027-2028):** The landscape could be transformed by the first approvals of PD-L1/VEGF bispecific antibodies and the potential label expansion of ICIs into the high-risk adjuvant setting, which would significantly increase the addressable patient population.

For stakeholders, the key to success will lie in identifying the most effective combination strategies, developing predictive biomarkers beyond PD-L1 to select the right patients, and successfully navigating a complex and diverging global regulatory and reimbursement environment. The next three years will be pivotal in determining whether immunotherapy can finally become a standard of care for a meaningful portion of patients with HR+/HER2- breast cancer.