TRIANGLE INSIGHTS GROUP by Valeris

Levers for Launch: How Five Analog Brands Used Positioning, Advocacy, Evidence, and Access Levers for Launch and Beyond

CASE STUDY - VOL. 5 OF 5: KADCYLA

1 Entresto™ sacubitril/valsartan | 2 NUPLAZID™ (pimavanserin) tablets | 3 Repatha™ (evolocumab) | 4 Vyndamax™ (tafamidis) 61 mg capsules | 5 Kadcyla® ado-trastuzumab emtansine

OVERVIEW

This case study is the fifth volume of a five-part series that distills the essence of what to do when launching a pharmaceutical product. We curated five analog products and analyzed how they deployed four launch levers: **Positioning Strategy, Advocacy and Guideline Inclusion, Evidence Generation, and Market Access,** to create traction and sustain growth. Each case is mapped to a launch archetype: **Paradigm Shaper, First Mover, Late Challenger, Opportunist** to clarify context and actions taken.

Who should read this: Commercial, medical, market access, and analytics leaders who are preparing to launch a brand or have recently launched one.

How to use this series: Identify your product archetype → review lever playbooks from the most relevant analogs → adapt actions for your product as appropriate.

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INTRODUCTION

As referenced in the extended introduction provided in volume 1 of this case study series, this white paper series explores five examples of novel brands that shaped or reshaped their commercial trajectory through deliberate activation of key levers. Using a consistent framework, we examine each analog case through four strategic levers: **Positioning Strategy, Advocacy & Guideline Inclusion, Evidence Generation, and Market Access**.

Case Study 1 of 5 examined Entresto — a case where initial hesitation gave way to broad adoption after HCPs were convinced on the "therapy switch moment" for patients, payer friction was resolved, and guideline language updates were incorporated.

Case Study 2 of 5 examined Nuplazid — a launch where early advocacy and dynamic positioning drove clinical entrenchment and commercial success despite community hesitations on safety profile.

Case Study 3 of 5 examined Repatha — a product scenario which began as an access-constrained launch but was repositioned through outcomes validation and strategic pricing adjustments to unlock broader adoption.

Case Study 4 of 5 examined Vyndamax — a market-shaping breakthrough that turned a once-invisible disease into a defined, treatable condition through focused clinical education and advocacy-driven market engagement.

FIGURE 1.

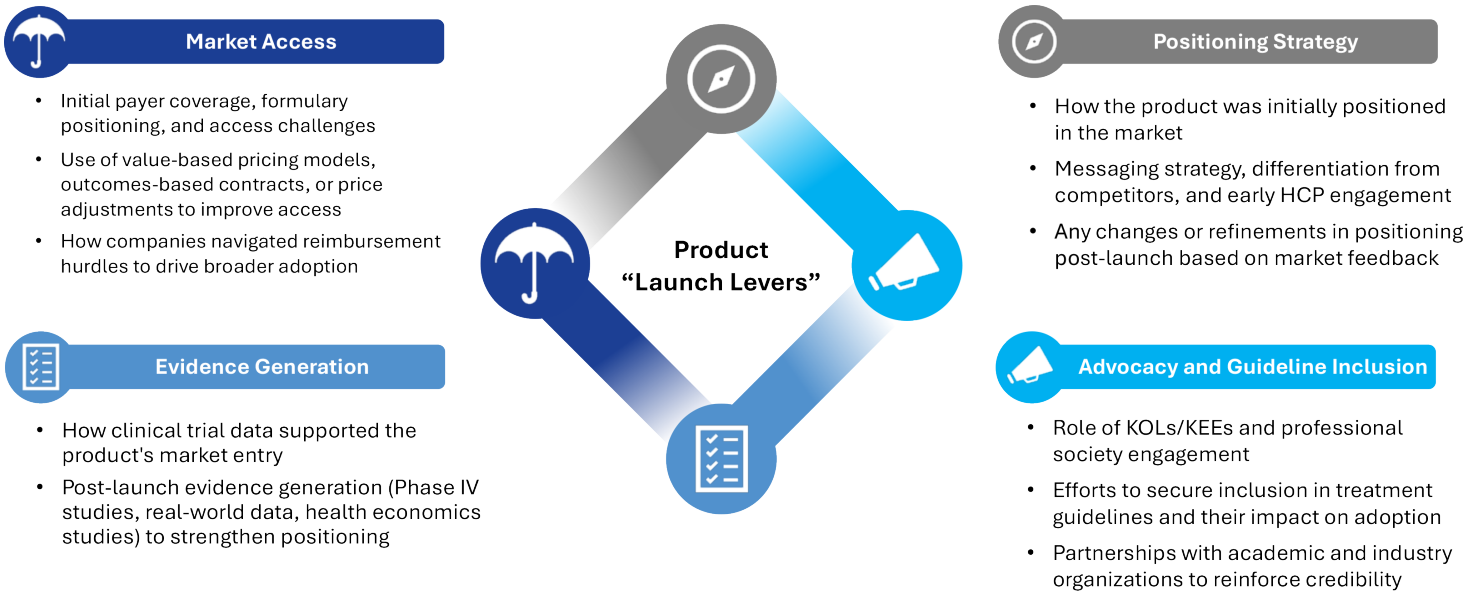


Figure 1. Overview of product "Launch Lever" categories in preparation for, at launch, and following launch.

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The five analog case studies featured in this series are categorized into distinct launch archetypes based on market maturity and product differentiation, providing additional context for the strategic levers activated at each stage of commercial evolution. By first identifying where your own product sits among the four archetypes, you will have appropriate context for how each upcoming case study, based on the archetype, can be considered as an analog.

FIGURE 2.

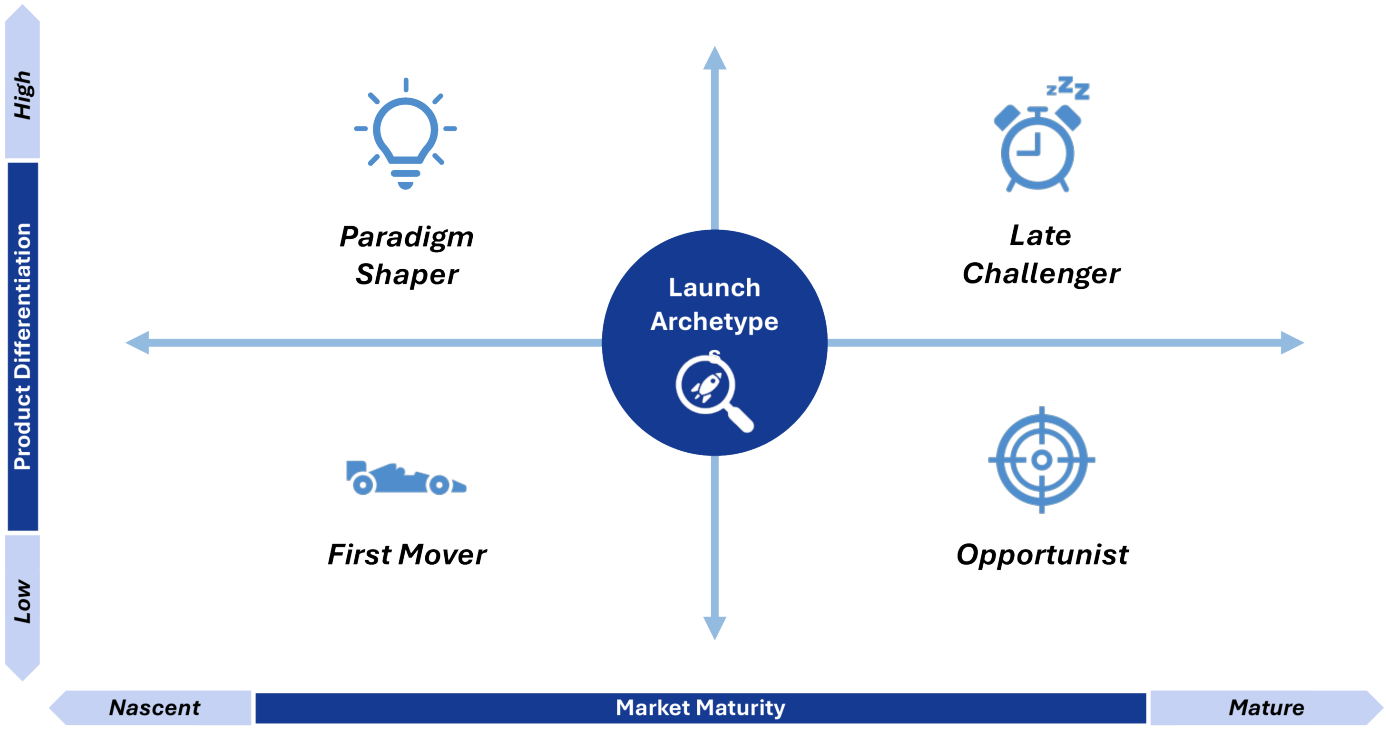


Figure 2. Illustrates four launch archetypes defined by the intersection of product differentiation and market maturity, highlighting the strategic contexts in which potential launch strategies may emerge

Note: Market maturity is defined by the degree of branded and generic competition within an indication

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We selected brands that (1) faced meaningful early adoption barriers, (2) executed targeted beachhead strategies, and (3) left a visible trail of levers used (positioning, advocacy/guidelines, evidence, access) that launch teams can adapt. The set spans cardiovascular, oncology, CNS, and rare disease to ensure breadth across therapeutic areas.

FIGURE 3.

Product	Disease Area	Mechanism of Action	Launch Archetype	Product Launch Overview
Entresto™ sacubitril/valsartan	HFrEF/HFpEF	ARNI	*Paradigm Shaper*	Entresto is a product in the cardiovascular space with a dual ARNI mechanism, representing a strong acceleration of market access and clinical uptake driven by **extensive evidence generation, real-world validation, and targeted market-shaping initiatives**
NUPLAZID™ (pimavanserin) tablets	PD Psychosis	Selective 5-HT_2A inverse agonist	*First Mover*	Nuplazid is a therapy in the Parkinson's disease psychosis space with a selective 5-HT_2A inverse agonist mechanism, representing a differentiated CNS launch that overcame early resistance through **focused clinical education and advocacy-driven market engagement**
Repatha™ (evolocumab)	LDL-C	PCSK9 inhibitor mAb	*Late Challenger*	Repatha is a therapy in the cardiovascular space with a PCSK9-inhibiting mechanism, representing a clinically differentiated but **access-sensitive launch that was repositioned successfully through outcomes validation and strategic pricing realignment**
Vyndamax™ (tafamidis)	ATTR-CM	TTR Stabilizer	*Paradigm Shaper*	Vyndaqel/Vyndamax is a therapy in the rare disease cardiovascular space with a transthyretin-stabilizing mechanism, representing a market-shaping breakthrough that turned a **once-invisible disease** into a defined, treatable condition through focused **clinical education and advocacy-driven market engagement**
Kadcyla	HER2+ breast cancer	HER2+ ADC	*Late Challenger*	Kadcyla is a therapy in the breast cancer space with a HER2+ antibody-drug conjugate mechanism, representing a case of functional innovation that required **post-launch evidence and strategic repositioning to unlock its full commercial potential**

Figure 3. Provides an overview of the five analog products analyzed in this series, highlighting their therapeutic area, mechanism of action, launch archetype, and a brief launch overview

Note: The five analog products featured in the table above are categorized using launch archetypes, which help frame each asset's initial market context.

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CASE STUDY 5: KADCYLA

FIGURE 4.

Kadcyla® ado-trastuzumab emtansine

Product Overview

- Kadcyla (ado-trastuzumab emtansine), launched by Genentech/Roche in 2013 as the first FDA-approved HER2-targeted antibody–drug conjugate for HER2+ breast cancer
  - *It was positioned as a targeted, single-agent option for patients with previously treated metastatic disease, later expanding (post-KATHERINE) to the adjuvant setting for residual disease after neoadjuvant therapy*
- Kadcyla earned rapid uptake in the second-line setting by anchoring to clear superiority vs. SoC, then broadened reach to the adjuvant setting
  - *Kadcyla secured durable standard-of-care status in adjuvant residual disease and maintained a defined role in metastatic care, remaining embedded in U.S. guidelines and pathways even as the metastatic landscape evolved with new approvals*

Market Phases: ***Kadcyla's performance in the market from launch in 2013 to present can be segmented into four phases:***

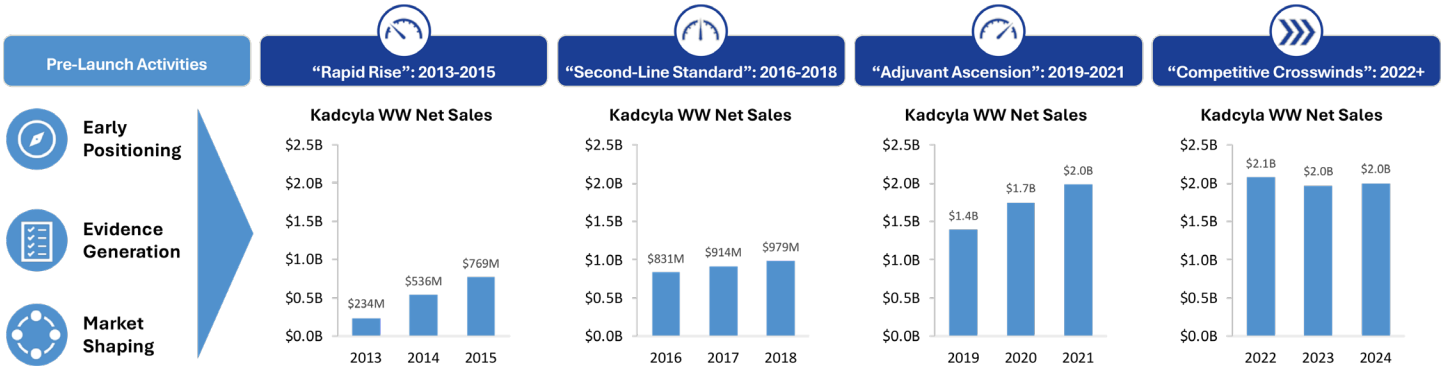


Figure 4. Overview of Kadcyla's commercial performance, segmented by revenue growth phases

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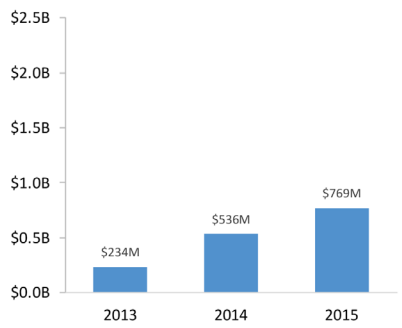
FIGURE 5.

"Rapid Rise": 2013-2015

Growth Phase Overview

Kadcyla launched as a first-in-class HER2-targeted ADC, debuting for previously treated metastatic breast cancer and earning rapid uptake off the strength of EMILIA/TH3RESA and manageable safety profile

Kadcyla WW Net Sales



Key Takeaway: A first-in-class therapy can scale fast when pivotal data, cogent positioning, and access support are all set up at the time of launch.

Positioning Strategy

Kadcyla's at-launch positioning was based primarily on its headline differentiation vs. capecitabine+lapatinib (EMILIA) and physician's choice in pre-treated patients (TH3RESA)

- Focused materials spotlighted the progression-free survival and overall survival deltas compared to standard of care
- Genentech also infused positioning with references to the simplistic Q3W dosing regimen and a communicated a clear safety management playbook to proactively address the label box warnings

Advocacy & Guideline Inclusion

In collaboration with Genentech, KOLS and cooperative groups quickly legitimized the ADC mechanism, with NCCN compendia incorporating Kadcyla for post-trastuzumab/taxane metastatic breast cancer

- Global enthusiasm, such as presentations at ESMO on Kadcyla's clinical benefit, reinforced US prescriber confidence as formal guideline and clinical pathways were still under development

Evidence Generation

Kadcyla's robust at-launch evidence package demonstrated clear superiority vs. capecitabine+lapatinib (EMILIA) and physicians choice in pre-treated patients (TH3RESA), anchoring Kadcyla as the preferred anchor therapy for 2L mBC

- Because the initial front-line trial (MARIANNE) ultimately did not hit endpoints, Genentech focused its market presence on second-line, where its data was strongest
- Additionally, Genentech invest in a Phase IIIb safety extension study (KAMILLA) to confirm the product's manageable safety profile in HER2+ advanced breast cancer

Market Access & Pricing Strategy

Genentech supported post-launch access with robust hub support (Access Solutions) to provide J-code / buy-and-bill reimbursement clarity for hospital/office infusion centers, as well as copay assistance for patients

- Prior authorizations for Kadcyla typically centered on the label criteria, requiring documentation of HER2+ BC, prior trastuzumab+taxane, and documentation of progression/recurrence within 6 months of adjuvant completion

Perceived Effort Level: High | High-mod | Mod-low | Low

Figure 5. Overview of Kadcyla's commercial performance "Rapid Rise" phase

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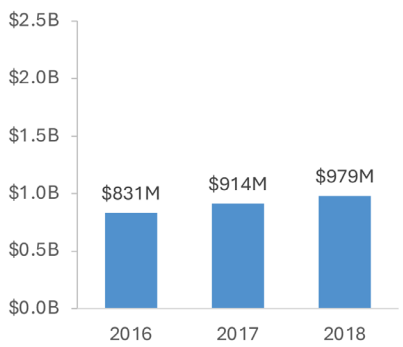
FIGURE 6.

"Second-Line Standard": 2016-2018

Growth Phase Overview

Kadcyla settled as second-line standard behind trastuzumab+pertuzumab+taxane; MARIANNE's non-superiority snuffed frontline aspirations but cemented the 2L entrenchment with broad community adoption.

Kadcyla WW Net Sales



Key Takeaway: Clear sequencing and pathway standardization can entrench a therapy even without frontline superiority.

Positioning Strategy

As the front-line dual treatment "blockade" spread, Genentech sharpened positioning with consistent messaging around continuity of HER2 targeting and improved tolerability vs. chemotherapy

- Leveraging also the familiarity of the trastuzumab backbone, Kadcyla became the clean, trusted 2L workhorse therapy after dual blockade front-line treatment (pertuzumab-taxane regimens)

Advocacy & Guideline Inclusion

In further endorsements of Kadcyla, KOLs clarified the appropriate patients for the drug, which was supported by codified clinical pathways (e.g., ViaOncology) to communicate sequencing in HER2+ BC

- Pathway committees aligned on first-line → second-line transitions, entrenching T-DM1 as the clear second-line standard
- NCCN compendia were consistent with KOL presentations and roadshows in translating Kadcyla's trial results to practical utilization recommendations

Evidence Generation

While Genentech did not invest directly in any additional trials during this period, in-market utilization metrics and the ongoing Phase IIIb safety extension (KAMILLA) conveyed marketplace confidence in the asset

- As trial evidence matured into real world validation, prescribers became even more comfortable with the supporting evidence behind Kadcyla

Market Access & Pricing Strategy

Front-line access dynamics changed as biosimilar versions of trastuzumab were approved in 2017 (e.g., Ogivri), nudging payers to revisit total cost of care and appropriate pathways and sequencing

- Kadcyla remained the only ADC approved for second line mBC, which allowed it to retain its price and access (PA to label / NCCN guidelines) despite genericization within the market

Perceived Effort Level: High | High-mod | Mod-low | Low

Figure 6. Overview of Kadcyla's commercial performance "Second-Line Standard" phase

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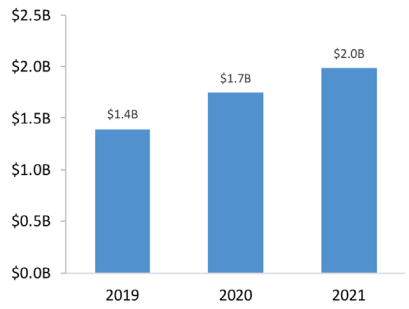
FIGURE 7.

"Adjuvant Ascension": 2019-2021

Growth Phase Overview

Powerful data from the KATHERINE trial flipped Kadcyla from a metastatic 2L workhorse to an adjuvant standard for residual invasive disease after neoadjuvant therapy, expanding reach and strategic durability

Kadcyla WW Net Sales



Key Takeaway: The most tried-and-true route to durable adoption is to generate definitive data in a precisely defined, high-risk patient niche.

Positioning Strategy

Post-KATHERINE and FDA's May 2019 approval, Genentech repositioned Kadcyla from 2L mBC to a curative-intent adjuvant for HER2+ patients with residual disease after neoadjuvant taxane+trastuzumab-based therapy

- Messaging from Genentech rapidly pivoted to risk reduction (~50% lower risk of invasive recurrence/death vs. trastuzumab) and defined a clear duration of use (14 cycles)
- In addition to provider-geared positioning, Genentech bolstered messaging with patient-friendly materials reframing the drug for curative care rather than a later-line option

Advocacy & Guideline Inclusion

Genentech engaged with guideline bodies to quickly disseminate updates on the adjuvant relevance of Kadcyla; ASCO's 2020 focused update and NCCN compendia formalized adjuvant trastuzumab emtansine (T-DM1) for residual disease

- Oncology clinical pathways almost immediately mirrored guideline updates, informing treatment sequencing within payer organizations and codifying adjuvant trastuzumab emtansine as the default for residual disease

Evidence Generation

KATHERINE (NEJM 2019) cut invasive disease recurrence/death risk by ~50% vs trastuzumab; subsequent analyses and RWE reinforced benefit across subgroups and clarified safety in adjuvant practice

- Genentech's investment in a definitive head-to-head trial vs. trastuzumab (adjuvant SoC) enabled rapid expansion into the adjuvant setting, significantly broadening Kadcyla's reach beyond its well-established 2L usage

Market Access & Pricing Strategy

Adjuvant expansion increased total eligible patient months but came with tighter cycle caps (12–14 cycles) in payer policies and pathway documents

- HER2+ economics (most significantly the availability of biosimilar trastuzumab) kept payers attentive to national and global guidelines, as well as oncology pathways and sequencing, but the H2H data mitigated cross-price comparison
- Genentech also supported educational programs to pharmacy leaders on drug wastage (JW/JZ modifiers) to align with payer-implemented cycle cap requirements

Perceived Effort Level: High | High-mod | Mod-low | Low

Figure 7. Overview of Kadcyla's commercial performance "Adjuvant Ascension" phase

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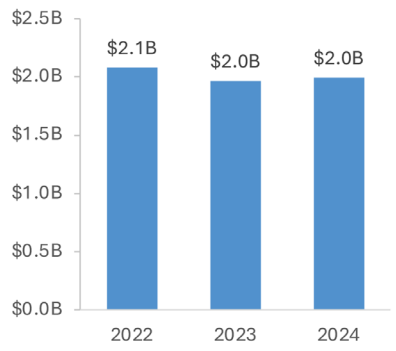
FIGURE 8.

"Competitive Crosswinds": 2022-present

Growth Phase Overview

Enhertu (T-DXd) outperformed T-DM1 and became the preferred 2L mBC standard, while Kadcyla entrenched adjuvant leadership—but 2025 results signal a potential adjuvant challenge ahead.

Kadcyla WW Net Sales



Key Takeaway: Late life-cycle sales can be preserved by an intentional focus on where the data is strongest and leveraging mature real-world evidence to defend against competitive threats.

Positioning Strategy

With DESTINY-Breast03 showing superior PFS/OS for T-DXd vs T-DM1, U.S. NCCN updates and expert commentary moved T-DXd to preferred 2L - Genentech's counter-positioning leaned hard into adjuvant durability

- Genentech emphasized the adjuvant benefit of Kadcyla (now with recent 2025 OS data in hand) to strengthen market position within a niche where Enhertu is weaker
- Genentech effectively ceded 2L mBC to AZ/Enhertu, with 2L positioning focused solely on ineligible/contraindicated patients for T-DXd

Advocacy & Guideline Inclusion

NCCN and expert panels shifted 2L mBC preference to T-DXd post-DB-03, while ASCO/NCCN maintained adjuvant T-DM1 for residual disease (until potential revisions based on DESTINY-Breast05)

- With Enhertu's superiority driving 2L guideline updates, Genentech's focus was to ensure guideline bodies remained up-to-date for the adjuvant setting and reflected the real-world efficacy and tolerability of Kadcyla

Evidence Generation

Extension data from KATHERINE in 2025, which provided overall survival efficacy on top of PFS, strengthened Kadcyla's adjuvant credibility alongside a growing body of real-world evidence

- The maturity of Kadcyla's evidence package – both in terms of real-world safety and efficacy in the adjuvant setting – will be Genentech's last line of defense against Enhertu, which showed positive interim data from DESTINY-Breast05 in 2025 that threatens Kadcyla's adjuvant market position

Market Access & Pricing Strategy

Payers increasingly prefer T-DXd in 2L mBC pathways; Kadcyla appears in later lines or contraindication scenarios, with prior authorizations reflecting line-of-therapy and safety fit

- Despite weakening access in 2L mBC, Genentech persisted with clear education around billing/coding and vial reconciliation (JZ/JW) to avoid denials, as well as hub support to maintain affordability

Perceived Effort Level: High | High-mod | Mod-low | Low

Figure 8. Overview of Kadcyla's commercial performance "Competitive Crosswinds" phase

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CLOSING

What to consider for your product based on learnings from Kadcyla:

1. **Own a Precise Moment**
   Practice-changing data in a narrowly defined, high-risk niche beats broad but ambiguous superiority claims.

2. **Play Where You Can Win**
   When competitors are superior within one segment, anchor your brand where evidence is indisputable and receptivity is highest.

3. **Safety is a Strategy**
   Predictable adverse event management and clean clinic workflows can counter more potent but riskier alternatives.

4. **Pathways are Power**
   Guideline compendia plus pathway integration drive real access faster than price moves alone, especially in high-cost indications where payer scrutiny is highest.

5. **Prepare for the Next Readout**
   Build switch plans and messaging bridges before the rival trial reads out particularly if competitive intelligence suggests stronger data from debuting entrants.

SERIES SEGUE

This wraps Case Study 5 of 5 (Kadcyla) — a case of functional innovation that required post-launch evidence and strategic repositioning to unlock its full commercial potential.

A collective reflection of the five presented case studies will be provided in a coming update to ensure key learnings across these analogs are captured.

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