

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

CASE STUDY - VOL. 1 OF 5: ENTRESTO







(pimavanserin) tablets













# **OVERVIEW**

This case study initiates 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.

Authors: Vaibhav Shrishail, William Sheehan, and Wes Yanowitch



# INTRODUCTION

Pharmaceutical product launches have never been more complex—or more critical to get right. In today's environment, marked by heightened payer scrutiny, therapeutic crowding, and compressed timelines for demonstrating value, even promising therapies often face slow uptake and missed forecasts in their earliest months. Without early traction, even clinically strong therapies risk falling behind, making launch execution not just a starting point, but a make-or-break moment for long-term success.

Several high-profile assets that stumbled early have gone on to become commercial successes, often through the identification and activation of strategic beachheads (e.g., concentrating on a guideline-backed sub-population, removing a single high-friction access barrier, or generating real-world validation that resolves prescriber ambiguity). This series demonstrates how assets found their beachheads for launch and pulled the right levers to achieve commercial success.

We identified 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.

#### FIGURE 1.

# **Market Access** · Initial payer coverage, formulary positioning, and access challenges in the market · Use of value-based pricing models, outcomes-based contracts, or price adjustments to improve access · How companies navigated **Product** reimbursement hurdles to drive market feedback "Launch Levers" broader adoption Evidence Generation How clinical trial data supported the society engagement product's market entry • Post-launch evidence generation (Phase IV

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

# **Positioning Strategy**

- How the product was initially positioned
- Messaging strategy, differentiation from competitors, and early HCP engagement
- Any changes or refinements in positioning post-launch based on

# **Advocacy and Guideline Inclusion**

- Role of KOLs/KEEs and professional
- Efforts to secure inclusion in treatment guidelines and their impact on adoption
- Partnerships with academic and industry organizations to reinforce credibility

studies, real-world data, health economics studies) to strengthen positioning



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.

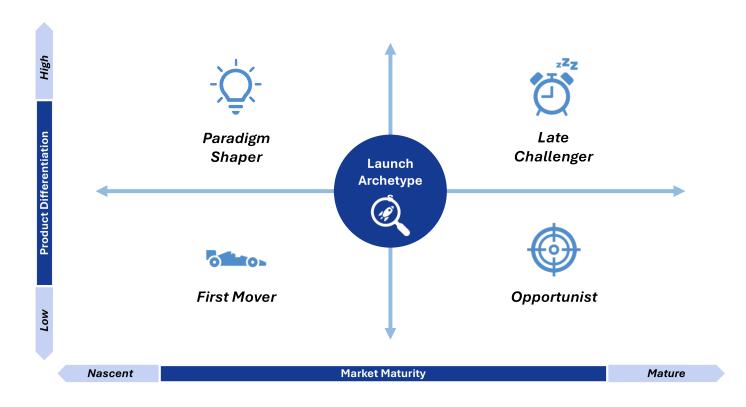


Figure 2. Illustrates four launch archetypes defined by the intersection of product differentiation and market maturity, highlighting the strategic contexts in which potential launch strategies may emerge

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



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, realworld validation, and targeted market-shaping initiatives
NUPLAZÍD (pimavanserin) tablets	PD Psychosis	Selective 5-HT <sub>2</sub> A inverse agonist	First Mover	Nuplazid is a therapy in the Parkinson's disease psychosis space with a selective 5-HT <sub>2</sub> A inverse agonist mechanism, representing a differentiated CNS launch that overcame early resistance through focused clinical education and advocacy-driven market engagement
<b>Repatha</b> (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 transthyretinstabilizing mechanism, representing a marketshaping breakthrough that turned a <b>once-invisible disease</b> into a defined, treatable condition through focused <b>clinical education and advocacy-driven market engagement</b>
擬 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



# **CASE STUDY 1: ENTRESTO**

# FIGURE 4.



#### **Product Overview**

- Entresto (sacubitril/valsartan), launched by Novartis in 2015, introducing a novel therapy for heart failure with reduced ejection fraction (HFrEF)
  - It was hailed as a "game-changer" for chronic heart failure and intended to replace decades-old ACE inhibitors/ARBs as the new standard of care
- Despite industry enthusiasm, Entresto's initial uptake fell short of expectations, and Novartis encountered significant commercial headwinds in the first two years
  - Through deliberate strategic repositioning, extensive advocacy efforts, evidence generation, and improved market access, Novartis transformed Entresto into a blockbuster therapy

# Market Phases: Entresto's performance in the market from launch in 2015 to 2024 can be segmented into four phases:



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



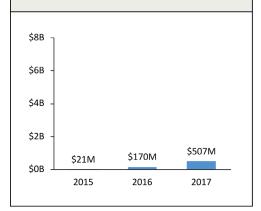
# FIGURE 5.

# "Lagging Launch": 2015-2017

#### **Growth Phase Overview**

Despite robust clinical outcomes, Entresto's initial adoption was slow due to positioning challenges, payer skepticism, and physician reluctance to switch from established treatments

# **Entresto WW Net Sales**



Key Takeaway: Entresto's early adoption was hindered by misaligned positioning and payer resistance, resulting in it missing its 2016 sales target (i.e., falling ~\$30M short of its internal forecasts)

# **Positioning Strategy**

Entresto's early positioning fragmented the brand narrative and fueled physician hesitation, with alarmist disease awareness campaigns, unclear messaging around its fixed-dose combination, and limited familiarity with neprilysin inhibition all contributing to slow early adoption

- · Early disease awareness campaigns were perceived as alarmist by HCPs, compounding physician hesitation to adopt a novel MOA (neprilysin inhibition)
- Novartis' initial positioning fragmented the product narrative, emphasizing its fixed-dose components (sacubitril and valsartan) rather than presenting Entresto as a unified, superior alternative to ACE inhibitors

#### **Advocacy & Guideline Inclusion**



While securing early strong guideline recommendations is crucial for influencing physician prescribing behavior, real-world adoption can still lag if payer and HCP concerns remain

- Early efforts such as the "Rise Above HF" campaign (2016) raised disease awareness but failed to translate into prescription growth
- Partnerships with organizations like the AHA ("Better Hearts Better Cities" in 2017) began to build the foundation for stronger advocacy alignment

#### **Evidence Generation**



While strong Phase III data is essential, early investment in post-launch evidence

Entresto's approval was based on the PARADIGM-HF trial, which showed superiority (compared to a RAS inhibitor) in reducing the risk of the combined endpoint of cardiovascular death or hospitalization for heart failure, based on a time-to-event analysis

# **Market Access & Pricing Strategy**

Lack of upfront payer engagement and economic justification can significantly delay broad market access

- · In 2015-17, Entresto was either not covered or heavily disadvantaged by most commercial payers, with many insurers requiring step-through therapy with an ACE inhibitor before covering Entresto
- That said, Novartis' efforts in 2015 & 2016 to reach outcomes-based contractual agreements with Aetna and Cigna precipitated Entresto's improved access

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

Figure 5. Overview of Entresto's commercial performance "Lagging Launch" phase

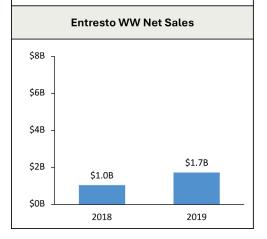


# FIGURE 6.

# "Galvanizing Growth": 2018-2019

#### **Growth Phase Overview**

Novartis recalibrated its approach, driving a surge in adoption through a refined messaging strategy, expanded evidence, and payer engagement



**Key Takeaway:** Novartis paired evidence generation with aggressive contracting and patient assistance programs to achieve broad coverage

# **Positioning Strategy**

Reframing the brand story to align with emotion and long-term evidence helped Entresto overcome early adoption barriers

 The brand narrative shifted from fear-based messaging to a more emotional, patient-centric campaign: "Entrust Your Heart to Entresto," emphasizing trust and long-term benefits

# **Advocacy & Guideline Inclusion**

By strategically engaging with guideline authors and sponsoring awareness initiatives, Novartis was able to significantly boost prescriber confidence

- In preparation for Entresto's HFpEF approval, Novartis maintained partnerships with guideline authors and continued sponsoring guideline adherence initiatives (e.g., Novartis had already contracted ~40% of AHA/ACC guideline authors in 2016/17)
- By 2019, Entresto had been included in heart failure guidelines and recommended as a Class I (strong) therapy, reinforcing physician confidence

# **Evidence Generation**

Post-launch clinical data was critical to strengthening physician confidence and payer acceptance

- Four Phase IV studies completed in 2018 demonstrated Entresto's effectiveness in real-world settings
- Parallel HFpEF trials, completed in 2019, positioned Entresto for future expansion Into adjacent heart failure populations (achieved approval in 2021)

#### **Market Access & Pricing Strategy**

Demonstrating economic value to payers was instrumental in removing early access barriers

- Entresto's commercial success in 2018 & 2019 was positively impacted by an increase in coverage and widespread removal of prior authorizations that restricted the product's use
- By 2019, Entresto was covered with no PA on most plans due to long-term evidence on cost savings and additional evidence in HFpEF

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

Figure 6. Overview of Entresto's commercial performance "Galvanizing Growth" phase



# FIGURE 7.

# "Securing Success": 2020-2021

#### **Growth Phase Overview**

With secured guideline inclusion across several indications, growing evidence, and improved market access, Entresto benefited from a leadership position



Key Takeaway: Continued evidence generation and strong guideline endorsements solidified Entresto's market positioning

# **Positioning Strategy**

Novartis maintained a consistent global strategy, reinforcing the positive message and positioning from the previous phase (e.g., "galvanizing growth"), while allowing for regional adaptations to support continued growth

• For example, in regions like Japan, positioning following approvals for HFrEF/HTN, emphasized Entresto as a tool with diet and exercise

# **Advocacy & Guideline Inclusion**

Continued collaborations with academic centers and guideline committees reinforced Entresto's role in standard care

• "Implement-HF" (2020) and "TRANSFORM" (2021) focused on adherence to the guidelines and helped reverse the COVID-driven downturn in new Rx

#### **Evidence Generation**

Despite challenges (e.g., SGLT2i HF launch, COVID-19), Novartis entrenched Entresto sales (i.e., leveraging the Phase IV data and a pediatric approval), showing the value of a strong evidence package in mitigating market uncertainties

One Phase-IV study comparing against valsartan was stopped due to COVID, and a Phase-III post-MI study did not hit endpoints

# **Market Access & Pricing Strategy**

Downward pressure following competitive approvals can be further mitigated by sustained evidence generation and pharmacoeconomic research

- By 2020, Entresto was covered with no PA on most major plans (based on available data)
- Real-world evidence from a Prime Therapeutics partnership demonstrated Entresto's costeffectiveness, enabling Novartis to remove prior authorization requirements from Cigna's commercial and Medicare plans by 2021

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

Figure 7. Overview of Entresto's commercial performance "Securing Success" phase



# FIGURE 8.

# "Continuing Commitment": 2022-2024

#### **Growth Phase Overview**

Facing intensifying competition from SGLT2 inhibitors, Novartis continued investing in Entresto's brand equity and market leadership



**Key Takeaway:** Competitive pressures intensified, but strategic messaging and ongoing evidence efforts helped Novartis to maintain Entresto's market leadership

# **Positioning Strategy**

Competitive messaging evolved to emphasize Entresto's broad applicability across chronic heart failure populations, reinforcing its distinct positioning against emerging therapies

 Novartis ramped up competitive positioning (given SGLT2i approvals) and communicated a broad application within heart failure and across ejection fraction

# **Advocacy & Guideline Inclusion**

Novartis prioritized continued partnerships with leading academic and professional organizations to ensure Entresto remained a cornerstone of guideline-directed medical therapy

 Initiatives included partnerships with academic institutions (e.g., Duke, Stanford), web resources for HCPs, and the Lp(a) Discovery project helped streamline HF diagnosis and bolstered guideline relationships

#### **Evidence Generation**

Recognizing the importance of real-world data in the market, Novartis invested in additional HFpEF and long-term outcomes studies to reinforce Entresto's sustained value

 In 2022-23, several follow-on pEF studies and rEF safety studies bolstered the perception of Entresto among HCPs

#### **Market Access & Pricing Strategy**

As market dynamics evolved, Novartis leveraged label expansions to maintain payer support and create additional growth opportunities for Entresto

 Novartis preserved favorable U.S. access while adapting pricing strategies internationally (e.g., price adjustments in China and Japan following indication expansions into hypertension)

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

Figure 8. Overview of Entresto's commercial performance "Continuing Commitment" phase



# **CLOSING**

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

# 1. Characterize the "who and when" on day one.

Make the decision easy: spell out the exact patient profile, the setting of care, and the plan for a switch from existing standard of care.

#### 2. Remove the top payer hurdles urgently.

Attack the most common prior authorization and step edit hurdles for HCPs early with targeted contracts and patient support programs. Give clinics prior authorization aids and benefits verification support to enable ease of prescribing.

# 3. Publish proof that answers key anticipated questions.

Prioritize studies and RWE data that clarifies questions raised by HCPs and other key stakeholders (initiation timing, safety/tolerability in typical patients, etc.). Share the proof of data to key adopters and market movers.

#### 4. Turn proof into rules of care.

Convert new data into momentum for guideline language and clinical document updates so the new default includes use of the product. Leverage this product inclusion to drive widespread adoption.

#### 5. Reframe when new classes enter.

When novel competitors surge, adjust positioning to retain your product as a core element of standard of care alongside new entrants. Update message maps, prescribing sequences, and access materials to show paths where products can be used together.

# **SERIES SEGUE**

This wraps Case Study 1 of 5 (Entresto)—a case where initial hesitation gave way to broad adoption once the switch moment, payer friction, and guideline language were all identified and acted upon.

Case Study 2 (Nuplazid) looks at a new challenge: a differentiated CNS launch that overcame early resistance through focused clinical education and advocacy-driven market engagement. We look forward to presenting the next case study in our upcoming entry.