

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

CASE STUDY - VOL. 2 OF 5: NUPLAZID























#### **OVERVIEW**

This whitepaper is the second 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

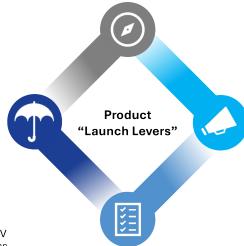
As referenced in the extended introduction provided in volume 1 of this case study series, this white paper series explores five examples of novel brands that shaped or reshaped their commercial trajectory through deliberate activation of key levers. Using a consistent framework, we examine each analog 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.

#### FIGURE 1.

### Initial payer coverage, formulary

· How companies navigated reimbursement



### **Market Access**

- positioning, and access challenges
- Use of value-based pricing models, outcomes-based contracts, or price adjustments to improve access
- hurdles to drive broader adontion

#### **Evidence Generation**

- · How clinical trial data supported the product's market entry
- Post-launch evidence generation (Phase IV studies, real-world data, health economics studies) to strengthen positioning

### **Positioning Strategy**

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

### **Advocacy and Guideline Inclusion**

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

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



### FIGURE 2.

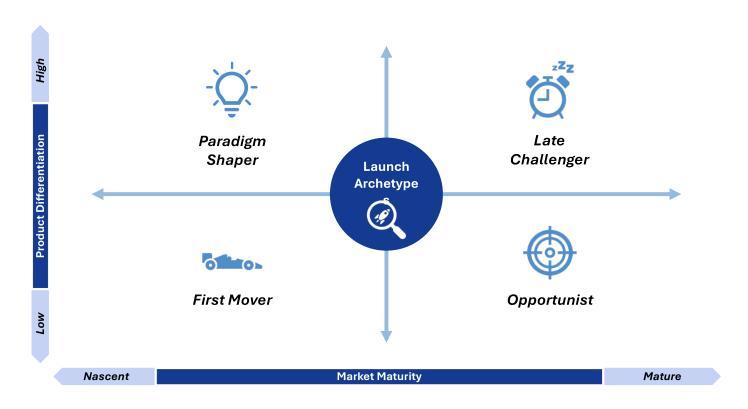


Figure 2. Illustrates four launch archetypes defined by the intersection of product differentiation and market maturity, highlighting the strategic contexts in which potential launch strategies may emerge

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
<b>Entresto</b> ™ sacubirril/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
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 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>
🎝 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.



#### **CASE STUDY 2: NUPLAZID**

#### FIGURE 4.

### \_\_\_NUPLAZID® (pimavanserin) 34mg capsules

#### **Product Overview**

- Nuplazid (pimavanserin), launched by Acadia in 2016 as the first and only FDA-approved therapy for Parkinson's disease psychosis (PDP)
  - It was positioned as a breakthrough for addressing hallucinations and delusions in Parkinson's patients without worsening motor symptoms, aiming to displace widespread off-label use of atypical antipsychotic
- Despite strong clinical need, Nuplazid's early adoption was tempered by safety scrutiny, physician inertia, and payer restrictions
  - Through transparent communication, intensive advocacy, targeted evidence generation, and robust patient access programs, Acadia stabilized Nuplazid's trajectory and established it as the standard of care in PDP

## **Market Phases:** Nuplazid's performance in the market from launch in 2016 to present can be segmented into four phases:

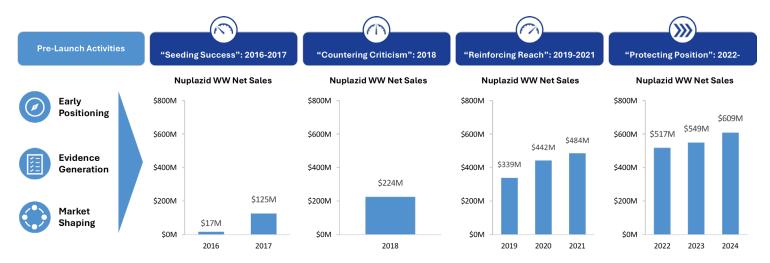


Figure 4. Overview of Nuplazid's commercial performance, segmented by revenue growth phases

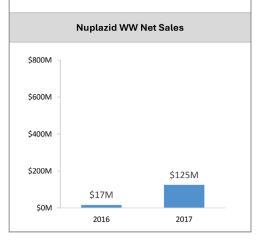


#### FIGURE 5.

#### "Seeding Success": 2016-2017

#### **Growth Phase Overview**

Nuplazid launched as the first FDA-approved therapy for Parkinson's psychosis, gaining steady early uptake by positioning itself as a first-in-class therapy in a high unmet need indication, engaging with KOLS, and securing access on Medicare plans



**Key Takeaway:** Acadia's launch strategy "planted the seeds" for uptake by positioning Nuplazid as the first and only solution for PDP, backed by KOL endorsement and robust patient support programs.

#### **Positioning Strategy**

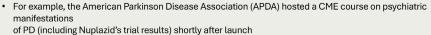
Acadia positioned Nuplazid as a breakthrough, first-in-class 5-HT2A inverse agonist for Parkinson's disease psychosis, emphasizing the lack of approved therapies and high unmet need within the indication, as well its breakthrough therapy designation

- Messaging centered around Nuplazid as the "first and only" FDA-approved PDP therapy (standard of care at launch was off-label antipsychotics)
- Acadia deployed consistent promotional narratives educating clinicians on the burden of psychosis within Parkinson's disease and offering Nuplazid as a targeted therapy where previously only off-label, suboptimal treatments were available.

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

among movement disorder specialists

Surrounding Nuplazid's launch, KOL networks partnered with Parkinson's advocacy groups and CME programs to promote awareness of PDP and drive early adoption of Nuplazid



While guidelines were not formally updated to include Nuplazid during these initial years, Acadia's advocacy
efforts laid the foundation for future guideline uptake and began to establish Nuplazid as a clinically viable option

#### **Evidence Generation**

Nuplazid was approved based on its third pivotal trial after two failed attempts (safety concerns) — at launch, Acadia focused on communicating the benefit of the clinical trial data rather than generating new evidence

Acadia continued an open-label study extension post commercialization, but early efforts were centered
around Nuplazid's existing evidence package and driving real-world use to gain trust among specialists

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

Nuplazid faced modest early access hurdles (PA across plans, but no ST) given its high list price (~\$24k/year) – Acadia invested heavily in patient support to overcome access friction, and focused on Medicare plans as an early access beachhead

Notably, Acadia launched the 'Acadia Connect' hub to offer benefits verification, PA assistance, and 14-day supplies of the drug to certain patients

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

Figure 5. Overview of Nuplazid's commercial performance "Seeding Success" phase

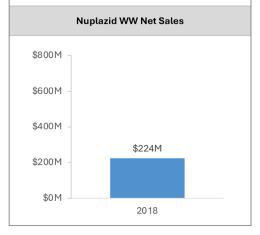


#### FIGURE 6.

#### "Countering Criticism": 2018

#### **Growth Phase Overview**

A wave of media scrutiny and FDA review over postmarketing safety concerns temporarily slowed adoption, forcing Acadia into a defensive, transparency-driven strategy to restore trust and stabilize growth.



Key Takeaway: Faced with external scrutiny,
Acadia pivoted to a transparency-based
approach, enlisting credible voices and
leveraging internal data to preserve physician
trust and strong access

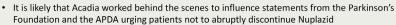
#### **Positioning Strategy**

In response to high-profile media backlash around the safety concerns of Nuplazid – pointing to the adverse events and deaths in the Nuplazid clinical trial – Acadia pivoted to a defensive positioning strategy to stabilize market uncertainties around the product

- The recalibrated messaging strategy from Acadia emphasized Nuplazid's benefits within its intended context (i.e., on label PDP, not for general dementia related psychosis)
- Additionally, Acadia reinforced the notion that Nuplazid's known risks are outweighed by its benefits for appropriate patients

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

Acadia ramped up its PDP community engagement in order to counterbalance uncertainty surrounding Nuplazid's safety profile



- Acadia emphasized and amplified the FDA communication from late 2018 that "no new or unexpected safety risks had been discovered"
- Continued advocacy group partnerships, like that with the Michael J. Fox Foundation, highlighted the FDA's conclusion and continued to reference that data indicating that Nuplazid was as-safe-as other medications that treat psychosis

#### **Evidence Generation**

In addition to finalizing plans for Phase IV and post-market studies, Acadia conducted internal analyses gathering data to alleviate the negative perception around Nuplazid's mortality risk

The FDA's analysis in 2018 included – alongside the trial data and the FDA adverse event reporting system –
Acadia's own post-marketing safety surveillance, all of which pointed to the frailty of advanced Parkinson's
patients as the cause for reported deaths (rather than concerns implicating Nuplazid)

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

Despite widespread safety concerns, Nuplazid's access remained stable (no new utilization management was added), and Acadia bolstered its patient support efforts

• By 2018, prescriptions of Nuplazid were available for a \$0 copay for patients with commercial insurance

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

Figure 6. Overview of Nuplazid's commercial performance "Countering Criticism" phase

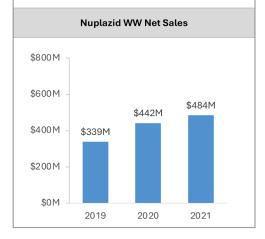


#### FIGURE 7.

#### "Reinforcing Reach": 2019-2021

#### **Growth Phase Overview**

Market confidence rebounded as Nuplazid became embedded in practice guidelines, while Acadia pursued ambitious evidence-generation and label-expansion efforts and bolstered PSPs to broaden the brand's impact.



Key Takeaway: In the wake of market headwinds, Acadia's continued investment into evidence generation and value proposition communication translated to Nuplazid's entrenchment into PDP treatment practice

#### **Positioning Strategy**

After weathering the storm of the 2018 backlash, Acadia shifted to more expansive positioning, highlighting Nuplazid as an essential, integrated part of Parkinson's care, not just an innovative niche therapy

 Using emerging data that earlier PDP intervention could delay nursing home placement, Acadia encouraged providers to consider Nuplazid early in PDP rather than waiting until psychosis became disruptive

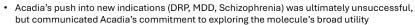
#### Advocacy & Guideline Inclusion

Following from the extensive community engagement post-launch, Nuplazid gained critical endorsements in 2019-2021 that secured its position as an essential "standard practice" first-line therapy for treatment of PDP

- The International Parkinson and Movement Disorder Society and the American Geriatrics Society
  updated their guidelines in 2019 to specifically endorse pimavanserin, and downgraded antipsychootics
  (e.g., quetiapine) especially in geriatric patients
- Acadia continued to ramp up its advocacy efforts, sponsoring symposia at key conferences (AAB, APA, MDS) to share new data, published narrative reviews in collaboration with experts, and continued CME programs to educate on the use of Nuplazid

#### **Evidence Generation**

Acadia invested heavily in Phase II-III label expansion studies – all of which were unsuccessful – and continued to gather real-world outcomes and safety data to support the long-term clinical rational of the product



 Alongside clinical trials, Acadia published a large Medicare claims analysis showing a reduction in long-term care admission associated with Nuplazid, as well affirming the lack of new safety signals in 2020 now with 4 years of post-market data

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

As Nuplazid's utilization became entrenched, Acadia leveraged health-economics evidence to maintain access and further expanded its patient support programs

- By ~2020, Nuplazid was covered by virtually all Part D and commercial plans with a prior auth
- Acadia expanded its patient access programs to ensure that 90% or more of patients had a copay of <\$10

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



Figure 7. Overview of Nuplazid's commercial performance "Reinforcing Reach" phase



#### FIGURE 8.

#### "Protecting Position": 2022-present

#### **Growth Phase Overview**

With market penetration plateauing within the limited PDP patient pool and no direct competitors, Acadia shifted to sustaining Nuplazid's adoption through refined positioning and targeted evidence



Key Takeaway: In the wake of market headwinds, Acadia's continued investment into evidence generation and value proposition communication translated to Nuplazid's entrenchment into PDP treatment practice

#### **Positioning Strategy**

With Nuplazid entrenched as the standard-of-care for PDP, Acadia's emphasis was on specific patient subsets that may have been undertreated, in addition to a focus on long-term benefits and quality of life

- In 2023, Nuplazid received a label updated clarifying that the drug is approved for patients "with or without dementia," which Acadia leveraged to drive confidence for utilization within the PDP dementia patient subgroup
- More recent campaigns aim to communicate the value of Nuplazid on the "trajectory of Parkinson's care"

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

Acadia's advocacy efforts in recent years have been focused on sustaining support rather than driving awareness, with the majority of key guideline organizations and scientific groups clearly endorsing Nuplazid

 Continued advocacy and community engagement helped support use of Nuplazid in the longterm care setting (e.g., nursing homes) which have been traditionally encouraged to minimize antipsychotic use

#### **Evidence Generation**

Even as Nuplazid reached commercial maturity, Acadia continued to invest in evidence generation with head-to-head studies and additional long-term outcomes and safety monitoring

- An investigator initiated study, published in 2024, showed the head-to-head benefit of Nuplazid vs. quetiapine
- Acadia published follow-up studies on mortality and long-term safety in PDP, with data published in 2023 showing that patients on Nuplazid have a lower mortality risk compared to other antipsychotics

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

Acadia's access efforts continue to be focused on maintaining broad access and justifying the premium pricing of Nuplazid (WAC approaching ~\$40k/year)

 Nuplazid continues to be covered broadly across Medicare and Commercial plans, and programs like Acadia Connect and \$0 copay provision remain in place to keep patients on therapy

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

Figure 8. Overview of Nuplazid's commercial performance "Protecting Position" phase



#### **CLOSING**

#### What to consider for your product based on learnings from Nuplazid:

#### 1. Create Conversation Early on the Need to Treat

Define the exact patient profile that exhibits clear unmet need and a need to treat from the start. This helps overcome entrenched off-label habits and accelerates adoption of a new standard.

#### 2. Enlist Champions and Build Credibility

Activate trusted KOLs and advocacy groups to validate the benefit–risk and carry the message during moments of skepticism. Independent voices stabilize confidence more effectively than company-led promotion.

#### 3. Data is Your Defense (and Offense)

Continually generate and share evidence — from RWE to head-to-head comparisons — to defend against scrutiny and reinforce value. Transparent data use transforms potential threats into opportunities for differentiation and credibility.

#### 4. Access is as Critical as Efficacy

Premium-priced therapies must be paired with intensive payer engagement and robust patient support to remove financial friction. If cost blocks treatment, clinical innovation alone will not secure uptake.

#### 5. Adapt and Evolve the Launch

Each phase of a product's lifecycle demands recalibration of levers — from safety-focused messaging to refined positioning in new subgroups. Treat launch as a multi-year process that requires flexibility to sustain momentum.

#### **SERIES SEGUE**

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

Case Study 3 will examine 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.