Rare Expertise

WHITE PAPER

Defining the Disease

The Science-First Strategy for Biopharma Commercial Success — with case studies in SMA, Gaucher Disease, and Hereditary ATTR Amyloidosis

A Rare Expertise White Paper

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For biopharma brand marketers, medical affairs & commercial leadership

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SECTION 01

Executive Summary

For nearly half a century, one commercial strategy has proven itself more durable, more defensible, and more aligned with both science and patient need than any other approach in biopharma marketing: define the disease first, and let the product follow.

This white paper argues that the most successful pharmaceutical launches — particularly in rare and complex diseases — are not built on brand identity. They are built on biological understanding. When marketers, medical affairs professionals, and commercial leaders invest in teaching the world what a disease truly is — its mechanism, its molecular drivers, its patient phenotypes — they create the context in which a drug's value becomes self-evident.

Drawing on 45 years of experience in the pharmaceutical industry, beginning at Pfizer, and illustrated through three compelling rare disease case studies (Spinal Muscular Atrophy, Gaucher Disease, and Hereditary Transthyretin Amyloidosis), this paper presents a framework for science-based commercial strategy that is as applicable to a pipeline asset as it is to a launched product.

> KEY THESIS
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> **The most powerful commercial act a biopharma company can perform is not to sell a drug — it is to define the disease that drug was built to treat. Market education precedes market creation. Science-based disease definition is both the right thing to do for patients and the smartest long-term commercial strategy.**

SECTION 02

Introduction: The Brand Trap

Spend enough time in biopharma marketing — and I have — and you will observe a recurring pattern. A company develops a genuinely innovative drug. Scientists have spent a decade understanding a previously poorly characterized disease, identifying its

molecular root cause, and engineering a therapeutic to address it. Then the drug moves into commercialization, and something goes wrong.

The marketers arrive. They conduct market research. They test messages with physicians. They develop a brand name, a visual identity, a tagline. The drug becomes a brand. And in that transformation, something vital is often lost: the science itself.

HCPs hear about features and benefits. They see before-and-after patient vignettes. They receive speakers' bureau decks heavy with clinical trial endpoints and light on biology. The drug is positioned against competitors. The conversation becomes commercial rather than scientific. And physicians — particularly in rare diseases, where diagnosis is uncertain and disease understanding is shallow — are left without the conceptual framework they need to recognize patients, make confident diagnoses, and understand why a particular therapy is appropriate.

This white paper makes the case for a different approach — one I observed working brilliantly early in my career and have seen validated again and again, most dramatically in the rare disease space. The approach is simple to state and demanding to execute: before you market a drug, define the disease.

Define it by its mechanism of action. Define it by the cell or protein or pathway it targets. Define it by the patient phenotype it produces. Build a scientific narrative that makes the disease real, coherent, and recognizable — and then show how your product addresses it at the level of biology. When you do this well, the commercial strategy and the scientific strategy are the same strategy.

You cannot sell a drug to a physician who doesn't know the patient is sick. ***First, you must teach them the disease.***

SECTION 03

Part I: What It Means to “Define a Disease”

The Concept Explained

Defining a disease, in this context, does not mean simply publishing a clinical definition or an ICD code. It means constructing a coherent biological narrative that explains:

- What is going wrong at the molecular or cellular level (the mechanism)
- Which patients are affected and how they can be identified (the phenotype)
- Why symptoms manifest when and how they do (the pathophysiology)
- What the natural history looks like if the disease is untreated (the urgency)
- Where intervention is most likely to modify the disease course (the therapeutic rationale)

This kind of disease definition work is rigorous. It requires deep collaboration between commercial teams, medical affairs, and the scientific community. It often involves sponsoring or supporting natural history studies, biomarker research, patient registries, and medical education programs. It is not cheap, and it is not fast. But it pays dividends that a brand campaign simply cannot.

Why Rare Diseases Are the Ideal Laboratory

Rare diseases are the ideal setting in which to observe this strategy at work — and at its most critical. In rare diseases, the barriers to diagnosis are enormous. Most rare diseases take between 4 and 8 years to diagnose from symptom onset. Many rare disease specialists have seen only a handful of cases in their careers. Primary care physicians may never see a case at all.

In this environment, a brand campaign is nearly useless. A physician who doesn't recognize that a patient's constellation of symptoms represents a coherent, diagnosable condition will not prescribe — cannot prescribe — no matter how many times they see a logo or hear a tagline. What they need is education: a framework for understanding the disease that allows them to recognize it in their practice.

When a biopharma company provides that framework — when it funds natural history studies, publishes diagnostic criteria, creates disease awareness tools, and trains specialists — it becomes the defining authority on that disease. It earns a scientific credibility that is essentially impossible

to buy with advertising. And when its drug is approved, it occupies a position in the HCP's mind that is inseparable from their understanding of the disease itself.

FACTOR	BRAND-FIRST APPROACH	DISEASE-FIRST APPROACH
HCP experience	Hears product messages before understanding the disease; may not recognize patients; adoption is slow and uncertain	Understands the disease deeply, recognizes patients confidently, sees the product as the logical scientific response
Short-term outcome	May generate earlier buzz	Generates earlier diagnoses and appropriate prescribing
Long-term outcome	Positioning fades without differentiation	Creates durable franchise; defines the standard of care
Risk profile	High risk of repositioning, losing differentiation	The scientific framework itself is a moat

SECTION 04

Part II: The Framework in Practice — The Four Pillars

Across the cases observed over four decades, disease-defining commercial strategies share four structural pillars. These are not sequential steps but concurrent, mutually reinforcing investments.

Pillar 1: Biological Narrative Development

The foundation of the strategy is a scientifically rigorous, accessible narrative that explains the disease at the mechanistic level. This narrative should be able to answer the question: “If a smart internist who last studied this in medical school reads this, will they finish with a clear mental model of what is going wrong in these patients?”

The biological narrative typically covers the relevant pathway, cell type, or protein; how dysfunction in that system produces the clinical manifestations; and what the downstream consequences of continued disease progression are. It should be grounded in published

science, co-developed with leading KOLs, and presented in language that is accessible without being reductive.

Pillar 2: Patient Phenotype Definition

Once the biology is clear, the commercial team must work with medical experts to define the patient. Who has this disease? What do they look like at presentation? What symptoms or lab findings or biomarkers should trigger suspicion? In rare diseases especially, early diagnosis is transformative — and enabling early diagnosis requires giving clinicians a vivid, memorable picture of the patient.

Patient phenotype definition often involves publishing or supporting natural history studies, creating diagnostic algorithms or screening tools, and developing patient case vignettes that bring the clinical reality to life. It also increasingly involves patient advocacy — because patients and their families are often the most powerful diagnostic catalysts of all.

Pillar 3: The Therapeutic Rationale Bridge

This is the step that most directly connects disease education to commercial strategy. Once the biological narrative is established and the patient is defined, the therapeutic rationale is the bridge: given what we now understand about this disease, here is why this specific intervention — at this specific point in the pathway — is scientifically sound.

When this bridge is built carefully, the drug's value proposition emerges organically from the science. The physician doesn't need to be “sold” on the drug; they simply need to understand the disease. The drug is the logical conclusion of the scientific argument.

Pillar 4: Community and Ecosystem Building

The final pillar is the creation of a community around the disease. This includes establishing or supporting patient registries, funding disease-specific research, sponsoring subspecialty meetings, engaging patient advocacy organizations, and developing diagnostic centers of excellence.

Companies that build this ecosystem early — often years before their drug is approved — are extraordinarily difficult to displace. They are not merely selling a product; they are the infrastructure of the disease's scientific and clinical world.

SECTION 05

Part III: Case Studies in Rare Disease

The following three case studies illustrate the disease-defining strategy as it has played out in different rare disease contexts, across different eras, with different molecular targets and commercial structures. Each demonstrates a core dimension of the framework.

CASE STUDY

Spinal Muscular Atrophy — Defining a Disease by Its Genetic Root

DISEASE: SMA · COMPANY: BIOGEN / AVEXIS (NOVARTIS) · DRUGS: SPINRAZA (NUSINERSEN) / ZOLGENSMA (ONASEMNOGENE)

The Disease Before Definition

For most of the 20th century, Spinal Muscular Atrophy was understood primarily in clinical terms: a spectrum of progressive neuromuscular weakness, classified by age of onset and motor milestone achievement into Types 1 through 4. The biology was poorly understood, the prognosis was grim particularly for Type 1, and there was no treatment.

The critical inflection point came in 1995, when the SMN1 gene on chromosome 5q was identified as the causative gene. Suddenly, SMA had a molecular identity: a disease of insufficient Survival Motor Neuron (SMN) protein, arising from deletion or mutation of the SMN1 gene, partially compensated by the nearly identical SMN2 gene whose exon 7 is predominantly spliced out.

The Biology-First Commercial Architecture

The companies that would eventually develop Spinraza and Zolgensma did not begin with brand strategy. They began with biology. Years before approval, Biogen invested in natural history studies, helped fund newborn screening pilots, and supported development of validated functional motor scale assessment tools — building the diagnostic and monitoring infrastructure of the disease itself.

The scientific education platform centered on a beautifully clear explanation: SMN2 is a backup gene that almost works. Nusinersen is an antisense oligonucleotide that corrects the splicing error in SMN2, causing it to produce more full-length SMN protein. Given how early in life motor

neurons are lost, earlier intervention produces dramatically better outcomes.

> *SMA became the model for what newborn screening plus disease-defining science can accomplish: a generation of children treated before they lose a single motor neuron.*

The Result

When Spinraza was approved by the FDA in December 2016 — the first approved treatment for SMA — it launched into a community that already understood the disease at a molecular level, had access to validated outcome measures, and had newborn screening programs beginning to identify presymptomatic patients. The commercial ecosystem had been built through scientific investment; the brand campaign was almost secondary. The subsequent approval of Zolgensma further validated the framework: because the disease had been so thoroughly defined at the genetic level, the therapeutic rationale for gene replacement was immediately intelligible to the clinical community.

CASE STUDY

Gaucher Disease — Defining a Disease by Its Enzymatic Defect

DISEASE: GAUCHER DISEASE (TYPE 1) · COMPANY: GENZYME (NOW SANOFI) · DRUG: CEREDASE / CEREZYME (IMIGLUCERASE)

The Pioneering Case

The story of Gaucher disease and Genzyme is, in many respects, the founding case study of rare disease commercialization — and it is a pure expression of the disease-defining strategy. Gaucher disease is the most common lysosomal storage disorder, caused by deficient activity of the enzyme glucocerebrosidase, leading to accumulation of glucocerebroside primarily in macrophages of the liver, spleen, and bone marrow.

Before Genzyme, Gaucher disease was known to exist but was dramatically underdiagnosed. Many patients with hepatosplenomegaly, bone pain, thrombocytopenia, and fatigue had gone years or decades without a correct diagnosis. The disease had no approved treatment, and the

patient community was small, dispersed, and largely invisible to the broader medical world.

Building the Disease Framework

Genzyme's founder, Henri Termeer, made a strategic decision that would define the company: before worrying about market size, build the disease framework. Genzyme invested heavily in establishing diagnostic testing infrastructure, educating hematologists, gastroenterologists, and pediatricians on the clinical presentation of Gaucher disease, and supporting patient registries.

The Gaucher disease patient registry, established by Genzyme in 1991 and later formalized as the International Collaborative Gaucher Group (ICGG) registry, became one of the most important disease characterization tools in rare disease history — enrolling thousands of patients globally, generating dozens of publications, and providing the evidence base for treatment guidelines.

Commercial Outcomes and Lasting Legacy

Cerezyme, approved in 1994, became one of the most commercially successful rare disease drugs in history — at one point generating over $1 billion annually from a patient population estimated at fewer than 20,000 patients worldwide.

> *Science and service, not brand loyalty, created the moat.*

LESSON FOR MARKETERS

The Gaucher case shows that disease definition is not just a pre-launch activity. The Genzyme registry, built post-approval, continued generating scientific value and commercial stickiness for decades. Disease definition is an ongoing investment, not a campaign.

CASE STUDY

Hereditary ATTR Amyloidosis — Defining a Disease Hidden in Plain Sight

DISEASE: HATTR AMYLOIDOSIS · COMPANIES: PFIZER / ALNYLAM · DRUGS: TAFAMIDIS (VYNDAQEL) / PATISIRAN (ONPATTRO)

A Disease That Was Hiding

Hereditary transthyretin (hATTR) amyloidosis is a particularly instructive example of disease-defining strategy because it involves a condition that was, for decades, systematically misdiagnosed or undiagnosed. In patients with pathogenic variants of the TTR gene, the transport protein misfolds and forms amyloid fibrils that deposit in peripheral nerves, the heart, and other organs.

The disease was known to neurologists who recognized the hereditary neuropathy cases, but the cardiac manifestation was almost completely unrecognized in the broader cardiology community. Patients with thickened hearts, heart failure with preserved ejection fraction, and low-voltage ECGs were being diagnosed with hypertensive heart disease, “senile” amyloidosis, or hypertrophic cardiomyopathy.

Pfizer and the Cardiac Amyloidosis Education Campaign

The commercialization of tafamidis (a TTR stabilizer that prevents misfolding) required, above all else, making cardiologists aware that this disease existed and that they were seeing it in their practices without recognizing it. Pfizer undertook one of the most systematic disease awareness campaigns in recent rare disease history — and worked with the scientific community to validate non-invasive diagnostic approaches, particularly technetium pyrophosphate (Tc-PYP) scintigraphy, that could identify ATTR cardiomyopathy without requiring cardiac biopsy.

Alnylam and the RNA Interference Story

Contemporaneously, Alnylam pursued an entirely different therapeutic approach — RNA interference with patisiran to silence TTR gene expression in the liver, reducing production of misfolded protein at the source. The existence of two mechanistically distinct therapies — a stabilizer and a silencer — actually enriched the disease education ecosystem, creating a richer scientific conversation around hATTR than either company could have generated alone.

> *In hATTR, the most important commercial act was not a product launch. It was teaching cardiologists to look for a disease they had always been seeing but never recognizing.*

SECTION 06

Part IV: Implementing Disease-Defining Strategy

The disease-defining strategy is not an abstract philosophy. It translates into specific organizational decisions, resource allocations, and cross-functional activities. The following framework is intended to guide commercial leaders, medical affairs professionals, and brand teams who want to implement this approach.

Phase 1: Disease Characterization (Pre-Phase 3 / Pre-Approval)

This phase begins before the drug exists in marketable form, ideally in Phase 2 or even earlier. The goal is to establish the scientific foundation on which the commercial strategy will be built.

- Commission or partner on natural history studies to characterize disease progression, identify biomarkers, and establish the burden of untreated disease
- Identify and map patient phenotypes, including underdiagnosed or misdiagnosed populations
- Engage KOLs as scientific collaborators, not just speakers — build genuine intellectual partnerships
- Identify diagnostic gaps and begin developing or validating diagnostic tools
- Begin supporting patient advocacy organizations with disease education resources

Phase 2: Diagnostic Enablement (12–24 Months Pre-Launch)

This phase focuses on creating the infrastructure that enables physicians to find patients. A launched drug with no diagnostic pathway is commercially ineffective regardless of its efficacy profile.

- Develop clinical decision support tools, diagnostic algorithms, and screening checklists
- Support newborn screening programs (where applicable)
- Establish referral pathways from primary care to specialists
- Create CME programs focused on disease recognition, not drug features
- Launch or support patient registries

Phase 3: Launch and Beyond — Science as Sustained Commercial Infrastructure

At launch, the commercial and medical affairs activities intensify, but the scientific foundation built in earlier phases now does much of the commercial work. The ongoing investment is in deepening the disease knowledge base, not simply selling the drug.

- Continue natural history and real-world evidence programs to characterize long-term outcomes
- Publish and present data that refines patient identification and therapeutic sequencing
- Build centers of excellence or disease-specific clinics where possible
- Invest in physician fellowship programs in the relevant subspecialty
- Engage payers with disease burden data and patient phenotype characterization, not just drug efficacy data

> THE MEDICAL AFFAIRS-COMMERCIAL ALIGNMENT IMPERATIVE
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> In the rare disease examples above, the most successful organizations were those in which medical affairs was not merely a compliance function but a strategic driver. When medical affairs leads disease education with commercial awareness, and commercial teams respect the scientific rigor required to execute it credibly, the result is a coherent disease-ownership strategy that neither team could build alone.

SECTION 07

Part V: The Competitive and Ethical Dimensions

Why This Strategy Is Commercially Superior

Some commercial leaders resist the disease-defining approach because it feels slow, expensive, and diffuse. This perception is mistaken. The disease-defining strategy is not just ethically preferable; it is commercially superior on every time horizon that matters.

COMMERCIAL DIMENSION	WHY DISEASE-DEFINING WINS
Defensibility	A company that owns the disease definition occupies a position competitors must enter on your terms. The scientific framework itself becomes a competitive moat.
Payer credibility	Disease burden data and natural history studies provide the evidence base for value arguments that brand campaigns cannot supply.
Physician trust	A company that has invested in understanding the disease earns credibility with specialists that advertising cannot purchase.
Regulatory relationships	Companies with natural history data and registries are better positioned for accelerated pathways and expanded indications.
Pipeline extension	Thorough disease definition naturally surfaces opportunities for pipeline expansion. The scientific investment compounds commercially.

The Ethical Case

It would be incomplete to discuss this strategy without acknowledging its ethical dimension. In rare diseases especially, the gap between disease biology and clinical recognition causes profound patient suffering. Patients spend years — sometimes decades — being misdiagnosed or undiagnosed, undergoing unnecessary procedures, losing function that might have been preserved with earlier intervention.

A biopharma company that invests in disease definition — that makes the disease recognizable, creates diagnostic tools, trains physicians, and supports patient communities — is not merely marketing effectively. It is fulfilling a moral obligation that comes with operating at the intersection

of science and patient need. The alignment of scientific purpose and commercial interest is not accidental — it is the design principle of the strategy.

SECTION 08

Conclusion: Back to First Principles

There is a version of pharmaceutical marketing that is purely transactional: find a prescriber, deliver a message, generate a script. This approach has its place, particularly in primary care and commodity markets. But it is deeply inadequate for the kinds of diseases — rare, complex, biologically defined — that increasingly represent both the scientific frontier and the commercial opportunity in biopharma.

The message for biopharma brand marketers, medical affairs professionals, and commercial leaders is this: your most powerful commercial asset is not your brand. It is your science. Define the disease. Educate the community. Show physicians the patients they have been missing. Demonstrate, with unambiguous biological clarity, why your product addresses the root cause of what you have taught them to recognize. The commercial strategy and the scientific strategy, when properly integrated, are not two strategies. They are one.

The most powerful pharmaceutical brand is not a name or a logo. ***It is the disease itself,*** understood so thoroughly that no competitor can enter the conversation without entering on your terms.

SECTION 09

Appendix: Summary of Case Studies

DISEASE	COMPANY / DRUG	CORE BIOLOGY	KEY LESSON
Spinal Muscular Atrophy	Biogen / AveXis (Novartis) Spinraza, Zolgensma	SMN1 gene deletion/mutation causing SMN protein deficiency; loss of motor neurons	Genetic disease definition enables newborn screening, enabling pre-symptomatic treatment
Gaucher Disease (Type 1)	Genzyme (now Sanofi) Cerezyme	Glucocerebrosidase deficiency; glucocerebroside accumulation in macrophages	Post-approval registry and community infrastructure sustained competitive advantage against later entrants
Hereditary ATTR Amyloidosis	Pfizer / Alnylam Tafamidis, Patisiran	TTR gene variants cause protein misfolding and amyloid deposition; cardiac and neurological manifestations	Diagnostic tool development (non-invasive testing) was as strategically important as the drug itself

Rare Expertise

Rare Expertise is a strategic consultancy focused on helping companies developing and marketing products for patients with rare diseases. Our mission is to shorten the diagnostic and treatment journey in people with rare diseases through better education.

Rare Expertise and the Rare Medical Network work at the intersection of rare disease knowledge, clinical practice, and trusted professional networks. Our focus is on supporting healthcare professionals with credible information and access to expertise — when it matters most.

FOUNDED

Rare Expertise was founded in 2015 by Jack Davis and Jeff Sweeney, who are parents of children with rare diseases, and who both have extensive professional experience in marketing communications and medical education in rare disease markets.