

Forecasting Rare Disease:

The Benefits of a Market Archetype Approach

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WHITE PAPER

Introduction

Forecasting the commercial potential of rare disease assets is high stakes. Small differences in assumptions have an outsized impact on forecasted revenues due to small patient populations. Unique rare disease forecasting challenges include:

- **Limited Published Epidemiology:**

Existing prevalence estimates are often outdated and subject to sample bias (e.g., based on advocacy cohorts or centers of excellence), which can over- or under-represent undiagnosed, less engaged, or milder patient segments. In many cases, estimates capture only a subset of a heterogeneous disease, limiting their utility for commercial planning

- **Evolving Diagnosis & Treatment Dynamics:**

Rates of diagnosis and treatment can shift rapidly in response to new product launches, updated clinical guidelines, heightened provider awareness, and expanded access to genetic or biomarker testing. These fluctuations complicate forecasting and require continuous assumption validation

- **Influence of Access Dynamics:** The access environment (e.g., payer policies, site-of-care limitations, infrastructure constraints) can materially accelerate or constrain uptake. Small changes in coverage criteria or utilization management can meaningfully alter the realized patient population

These challenges make it difficult to develop a credible picture of today's diagnosed and treated populations and tomorrow's addressable opportunity. Forecasts must not only interpret and reconcile fragmented literature and claims data but also anticipate how patient awareness, diagnostic pathways, and activation strategies will evolve.

Key questions include:

- *What is the true size of the addressable patient pool? What share remains undiagnosed, concentrated in centers of excellence, or sitting on the sidelines due to lack of effective treatment?*
- *Where are patients dropping out of the journey, and why? Is it during the diagnostic odyssey, accessing specialists, adopting advanced treatment, or continuing with treatment?*
- *Which strategic levers, whether through awareness, diagnostic support, patient activation, and/or evidence generation, will be essential to unlock growth and drive the commercial opportunity?*

- *How might payer behavior (e.g., outcomes uncertainty, UM, evidence expectations) create inflection points that can be incorporated into modeling accurately and at the correct time?*

Without addressing these questions rigorously, forecasts may be misaligned with strategy, complicating alignment on asset value and organizational resourcing.

Market Archetype Approach to Rare Disease Forecasting

Approaching rare disease forecasting from an archetype approach allows us to focus assumptions and sensitivities on the core levers relevant to the target indications.

Diagnosis-Limited Archetype

Key characteristics:

- Misdiagnosed or undiagnosed due to low awareness or limited access to diagnostics, often with no specific diagnostic code available
- Even when diagnosed, patients often absorb the burden of educating their care team
- May be genetically driven but are often later onset and less severe in presentation
- Symptomatic patients are managed with generics or intensive self-care routines

Core Challenge:

Estimating the latent patient pool and modeling how awareness campaigns, diagnostic tools, and referral pathway improvements can expand the market.

Illustrative Analogs

- **Transthyretin amyloidosis (ATTR):** Awareness and noninvasive diagnostic tools (PYP scans, genetic testing) dramatically increased diagnosed prevalence once effective therapies emerged
- **Alpha-1 antitrypsin deficiency (AATD):** Growth has been driven by targeted HCP education and expanded screening programs
- **Lysosomal storage disorders (e.g., Fabry, Pompe):** Also historically underdiagnosed, newborn screening and genetic testing has expanded identified patients

Constrained Growth Archetype

Key characteristics:

- Established diagnosed population based on genetic testing, or clear diagnostic criteria
- Uptake constrained by lack of screening, utilization in subsets, or access restraints
- Health system capacity constraints related to gene therapy adoption (e.g., center accreditation, bed availability, conditioning regimen, historic failures)

Core Challenge:

Developing high impact strategies to counter constraining forces and modeling impact on adoption

Illustrative Analogs

- **Duchenne muscular dystrophy (DMD):** Although most patients are identified through established diagnostic pathways, early therapies demonstrated limited efficacy, and payer skepticism regarding cost-benefit slowed adoption and constrained initial market growth
- **Spinal muscular atrophy (SMA):** The introduction of gene and antisense therapies rapidly expanded the treated population; while newborn screening and access barriers initially constrained uptake, these challenges have largely been mitigated over time
- **Sickle-cell disease (SCD):** Newborn screening has increased diagnosis rates, but adoption of gene therapies remains limited by treatment infrastructure, access constraints, and uncertainty around long-term outcomes, while other therapeutics face hurdles related to dosing burden, modest efficacy, and payer resistance

Mature Market Archetype

Key characteristics:

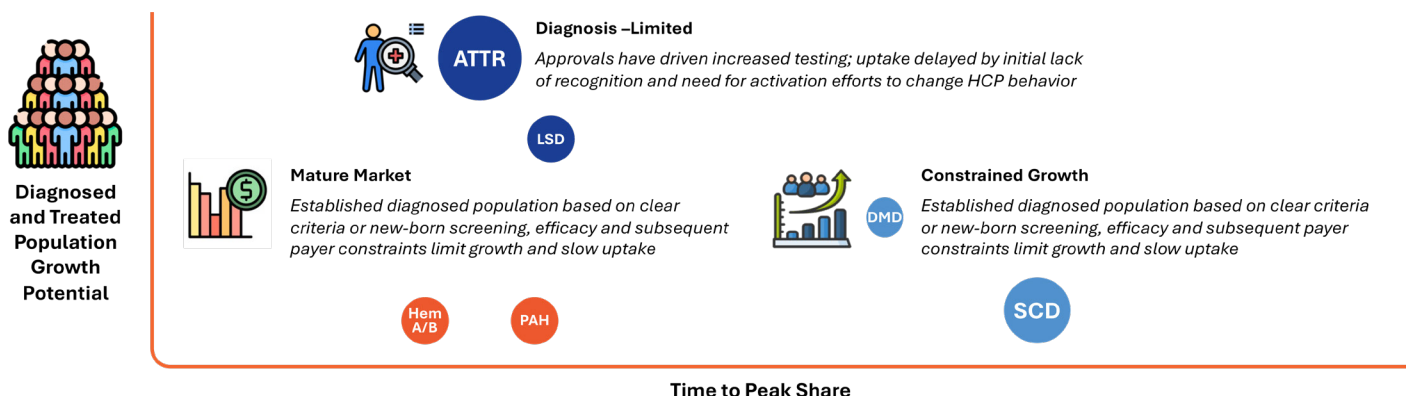
- High diagnosis and treatment rates driven by long-standing awareness, established diagnostic pathways, and multiple available therapies
- Market growth driven primarily by differentiation among late entrants rather than expansion of the patient pool
- Rebate walls and formulary entrenchment can create payer challenges for late entrants attempting to define differentiation

Core Challenge: Identifying credible levers for differentiation - improved tolerability, convenience, combination potential, or evidence in underserved patient subsets - to capture share in a well-defined market

Illustrative Analogs

- **Pulmonary arterial hypertension (PAH):** A mature market shaped by decades of commercial activity; late entrants are primarily differentiated through novel delivery modalities (e.g., oral, inhaled) and combination strategies. Growth has plateaued as most eligible patients are already treated
- **Hemophilia A/B:** A market with near-universal diagnosis and well-established care infrastructure. Successive innovation waves have emphasized treatment convenience and durability, with uptake delayed as HCPs and payers awaited real-world evidence from switching studies and indirect treatment comparisons
- **Paroxysmal nocturnal hemoglobinuria (PNH):** Soliris (Alexion) defined the market; later entrants like Ultomiris leveraged extended dosing intervals and improved convenience rather than new patient growth, while biosimilar and complement-pathway competition now focus on pricing and administration advantage

Figure 1. Rare Disease Market Growth and Penetration by Archetype



The Triangle Insights Group Approach: Building a Defensible, Insights-Driven View of Rare Disease Opportunity

Capturing value in rare disease markets requires more than epidemiology and optimism. At Triangle Insights Group, we blend quantitative rigor, analog-driven benchmarks, and strategic commercial insight to build a credible, investor-ready view of a commercial opportunity as well as a roadmap to realize it.

Our approach translates ambiguity into advantage, delivering actionable outputs that connect forecast potential directly to launch strategy, resource allocation, and organizational focus:

- **Patient Journey & Diagnostic Pathway Mapping:**

Granular analysis of where patients fall out of the journey, who influences progression, and what interventions can accelerate diagnosis and treatment, enabling smarter investment and higher yield on activation spend

- **Commercial Opportunity Assessment and Forecasting:** Robust models that synthesize published epidemiology, real-world claims, and registry insights,

all pressure-tested through relevant analogs to anticipate growth trajectories, adoption dynamics,

and barriers to uptake. Outputs include realistic adoption curves and evidence-based assumptions informed by targeted market research

- **Market Access landscape:** Enabled by our proprietary Policy Reporter database, identifies detailed review of access policies for the competitive set and/or analogs to understand relationship between clinical data package, label, pricing, and utilization management likely to influence product positioning and market share
- **Commercial Lever Prioritization & Launch Roadmap:** A quantified view of which levers matter most and when. We provide a prioritized roadmap to focus commercial resources where they will drive measurable acceleration in adoption and unlock full market value

In rare disease, opportunity is defined not only by the asset, but by the ecosystem. This is inclusive of diagnostics, infrastructure, payer behavior, awareness, and real-world evidence. Triangle Insights helps clients see that ecosystem clearly, forecast credibly, and invest intelligently.

Organizations seeking to strengthen their rare disease strategy, validate market potential, or prepare for launch are encouraged to engage with our partner team. Reach out to learn how Triangle Insights can offer customized support for strategic needs in rare disease and adjacent therapeutic areas.

Figure 2. From Data to Direction: A Rare Disease Commercial Assessment Framework

