WHITE PAPER

How market competition is changing the game in rare disease diagnosis

The influence of market events on patient outcomes

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The diagnosis of rare diseases, which represents a critical juncture in the patient journey, is often best described as a "diagnostic odyssey." Patients and their families frequently endure years of uncertainty, undergoing myriad tests and consultations before reaching a definitive diagnosis. The average time to obtain an accurate diagnosis is between six and nine years, with patients often consulting seven or more specialists before receiving an accurate diagnosis.

Tragically, about 30% of children with rare disease die before the age of five. Given the complexity of these disorders, the need for timely and accurate diagnosis is crucial for effective management and improved patient outcomes.

Rare disease awareness proves crucial for improving diagnosis rates

Despite scientific advancements and increased information sharing, particularly in recent years through online resources, the challenges to timely and accurate diagnoses persist. In a 2019 NORD survey, about 50% of the patients and caregivers attributed diagnostic delays to a lack of disease awareness, and 42% believed that limited medical specialization caused delays.

Some of the key reasons attributed to these delays include:

- Healthcare professionals (HCPs) struggling to link symptoms, especially when they span multiple organ systems
- Extended waiting times for consultation with specialists
- The need for more precise testing

The market appears to be an important factor in diagnosis rates. In this white paper, we'll look at how various market events influence the diagnosis rates of rare diseases, with a specific focus on market competitiveness, including the introduction of first-in-class products and subsequent product launches.

More companies in the market means more attention to rare disease—and more resources

The market for rare disease treatments is expanding rapidly and becoming even more competitive as the number of pharmaceutical company entrants increases. This competition can drive innovation and improve treatment options. It can also lead to more awareness campaigns, which help patients and healthcare providers stay informed about new diagnostic tools and treatments.

In the past decade, the diagnosis rates for competitive rare indications have increased. To understand this evolution, the factors contributing to the increase in diagnosis rates have been analyzed across two key areas: one where competition has gradually intensified and another where an indication became competitive in a relatively short span of time.

Increased market competition drives rare disease diagnosis improvements

Spinal muscular atrophy (SMA), Duchenne muscular dystrophy (DMD) and amyotrophic lateral sclerosis (ALS) are all indications that have gradually become competitive over the years. The number of patients diagnosed with these indications has steadily increased over the past decade, particularly following the launch of products targeting these conditions.

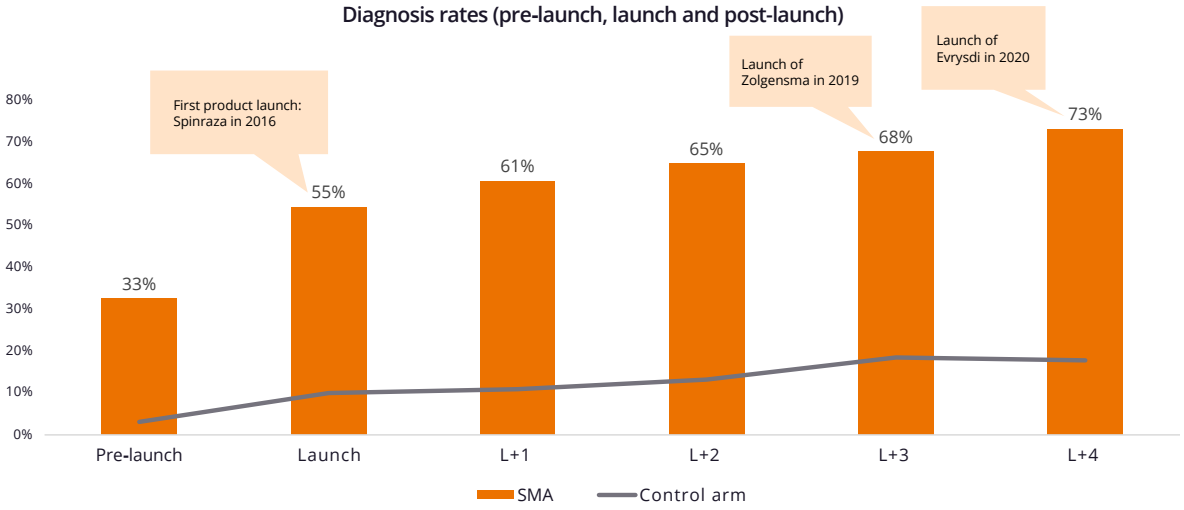
In the case of SMA, the diagnosis rate increased from around 30% in 2015 to 55% in 2016, according to our analysis of data from Komodo Health that is used throughout this white paper. This increase coincided with the launch of Spinraza, the first disease-modifying therapy approved for SMA. Spinraza addressed a critical need for patients who had no approved treatments previously. And Biogen, the manufacturer, made significant efforts in raising awareness about the treatment. As the awareness for the treatment increased, so too did the diagnosis rate for SMA.

Limited awareness among primary care HCPs about the early signs of SMA led to delayed referrals to specialists. For SMA patients, the average age of disease onset was around 2.7 years, while the average age of diagnosis was 4.34 years, indicating an average diagnostic delay of nearly 1.5 years. Since 2017, the average time to diagnosis of SMA has decreased due to both new products entering the market and also an increase in patients identified via prenatal screening or newborn screening.

Significant increases in diagnosis rates have been observed in the time period analyzed in Figure 1, which we attribute to the launch of new products and initiatives by companies aimed at raising disease awareness.

FIGURE 1:

Evolution of diagnosis rates for SMA with gradual ramp up in competition (2015-2020)



Note:
"Control arm" refers to the average of diagnosis rates registered by osteogenesis imperfecta (OI) and Angelman syndrome, two rare indications with ICD codes but no marketed products yet.

DMD and ALS have also seen increasing diagnosis rates with increasing competition. In the case of DMD, the introduction of exon skipping therapies such as Vyondys 53, Viltepso and Amondys 45 helped increase the diagnosis rate. After the launch of Exondys 51 (in 2016) and Vyondys 53 (in 2019), the diagnosis rate jumped—from 21% in 2018 to 59% in 2019.

Similarly, in ALS, the diagnosis rate jumped from 34% in 2015 to 76% in 2016. This significant improvement occurred just one year before the launch of Radicava, which was approved nearly 20 years after the first product Riluzole (1995).

TABLE 1:

Evolution of diagnosis rates for rare indications with gradual ramp-up in competition (2015-2020)

Indications	L-2	L-1	Launch (L)	L+1	L+2	L+3	L+4
DMD	-	1%	**1%**	2%	21%	**59%**	**60%**
ALS	34%	76%	**82%**	85%	87%	85%	86%
SMA	-	33%	**55%**	61%	65%	**68%**	**73%**

Note: Bold numbers indicate the year of product approvals for each indication.

Accelerated competitive environment

IgA nephropathy (IgAN), paroxysmal nocturnal hemoglobinuria (PNH) and myasthenia gravis (MG) are all indications that became competitive in a short span of time. In this accelerated competitive environment, the combination of company forces builds the market by increasing disease awareness among HCPs and patients.

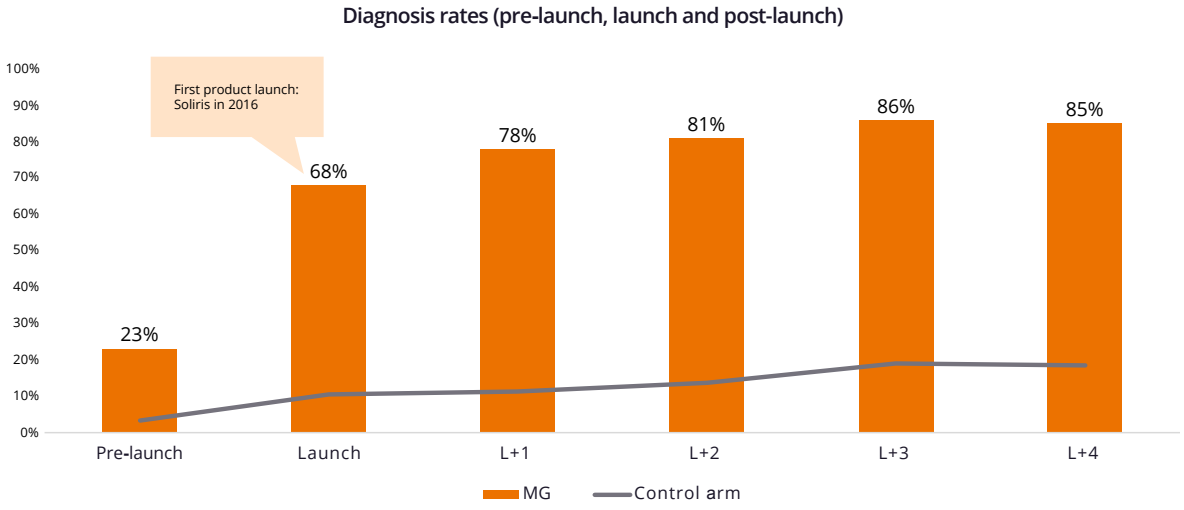
In the case of MG, the diagnosis rate jumped from 23% in 2015 to 68% in 2016, with the launch of its first marketed product, Soliris. The market remained relatively quiet after the launch of Soliris in 2016; however, the subsequent launches of Vyvgart and Ultomiris in 2022, Rystiggo in 2023 and Zilbrysq in 2024 saw competition on the rise and witnessed an increased diagnosis rate of 90%.

The increase in the diagnosis rate for MG can be attributed to various initiatives. For instance, Argenx's initiative to launch its awareness campaign began in 2022 with a virtual conference, light-up nights around the country, the debut of a patient-focused website "MG United" and a documentary series focused on the lives and challenges of three people living with MG.

There was a significant increase in the diagnosis rate for MG in the time period analyzed in Figure 2.

FIGURE 2:

Evolution of diagnosis rates for MG with accelerated ramp-up in competition (2015-2020)



Other indications such as IgAN and PNH also saw higher diagnosis rates as the result of an accelerated competitive environment. In the case of PNH, the diagnosis rates increased from 20% in 2015 to 53% in 2019, owing to the launch of Ultomiris in 2019. This was followed by Empaveli in 2021 and Voydeya, Fabhalta and Piasky in 2024, which further increased the diagnosis rate to 59%. Similarly, for IgAN, the diagnosis rate jumped from 4% in 2015 to 20% in 2022, with the launch of Tarpeyo in 2022. This was followed by Filspari in 2023, which led to an increase in the diagnosis rate to 26%.

TABLE 2:

Evolution of diagnosis rates for rare indications with accelerated competitive environment

Indications	Pre-launch	L-2	L-1	Launch (L)	L+1	L+2	L+3	L+4
IgAN	4%	19%	20%	20%	26%	-	-	-
PNH	20%	44%	49%	53%	57%	58%	59%	59%
MG	-	-	23%	68%	78%	81%	86%	85%

Note: Pre-launch for IgAN is (L-7) and PNH is (L-4).

Rare indications with first-to-market and only launched products

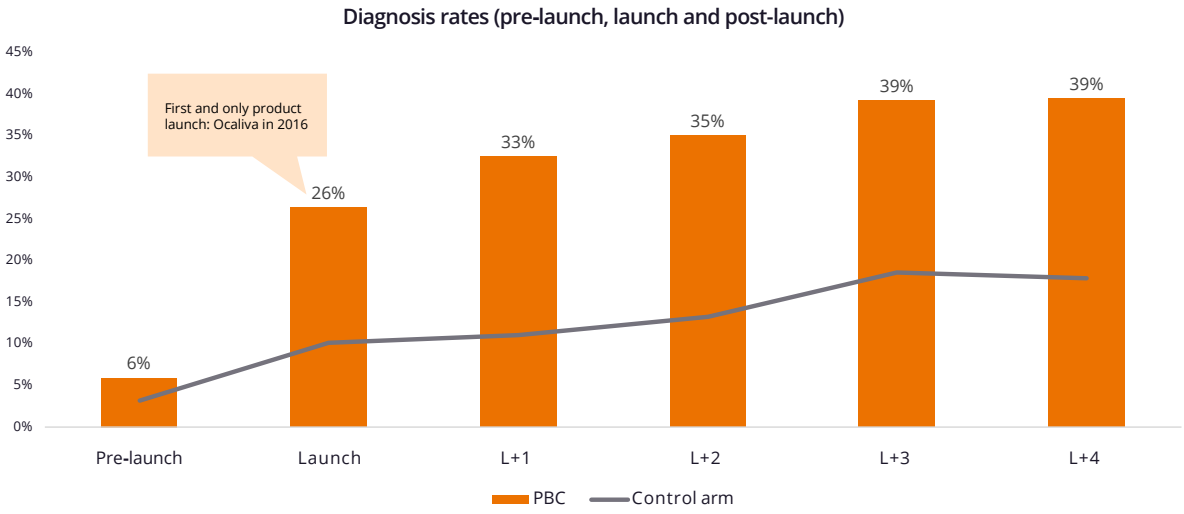
Friedreich ataxia (FA), erythropoietic protoporphyria (EPP) and primary biliary cirrhosis (PBC) are indications with only one approved therapy. And yet, all of these have also seen an increase in their diagnosis rates.

In the case of PBC, the diagnosis rate increased from 6% in 2015 to 26% in 2016, following the launch of Ocaliva. This growth can be attributed to initiatives by Intercept Pharmaceuticals, such as a series of live and virtual educational events in 2016 to raise PBC awareness among healthcare providers and patients. Moreover, in 2017, the company partnered with the Global Liver Institute to develop and distribute educational materials, aimed to standardize diagnostic criteria and improve the overall understanding of PBC.

The increasing trend for diagnosis rates for indications with first and only product launches in the market has been observed in the time period analyzed in Figure 3.

FIGURE 3:

Evolution of diagnosis rates for PBC with first and only product launches (2015-2020)



A similar trend has been witnessed in other indications. When Scenesse was approved to treat EPP, there was a significant increase in diagnostic rates—from 6% in 2015 to 24% in 2019. The approval of Skyclarys to treat FA marked a significant milestone in diagnosis, seeing the rate of 1% in 2019 increase to 34% in 2023. The pivotal trial for Skyclarys' approval demonstrated the drug's efficacy and brought together a community of patients, researchers and clinicians, fostering a more robust diagnostic network.

TABLE 3:

Evolution of diagnosis rates for rare indications with first and only product launches

Indications	Pre-launch	L-2	L-1	Launch (L)	L+1	L+2	L+3	L+4
FA	1%	29%	32%	34%	23%	-	-	-
EPP	6%	24%	25%	24%	24%	31%	30%	32%
PBC	-	-	6%	26%	33%	35%	39%	39%

Note: Pre-launch for FA and EPP is (L-4).

Rare indications with an ICD 10 code but no marketed products yet

On the other hand, there are rare indications that lack any launched product in the market but do have a defined diagnostic ICD 10 code. The diagnosis rates for these cases remain below 20%, unable to climb further.

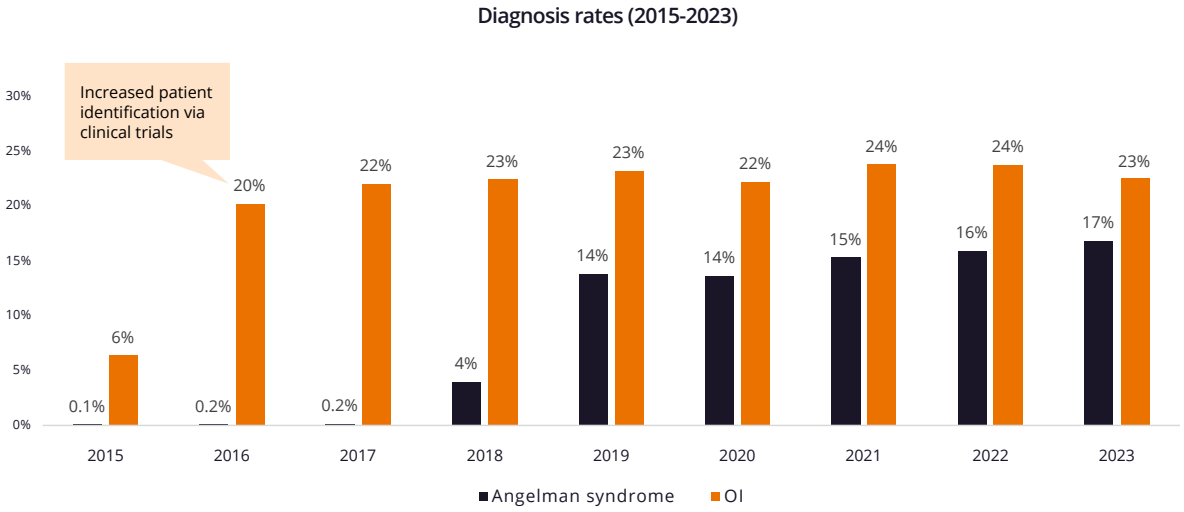
OI, for instance, has no marketed products, and the diagnosis rate has hovered steady around 20%. It jumped from 6% in 2015 to 20% in 2016—attributed to the identification of patients through clinical trial studies. During this time, there was a significant push in research and clinical trials aimed at increasing scientific understanding and treating OI. After 2016, however, the diagnosis rate has remained unchanged, largely due to the lack of any commercial activity in the market, such as new product approval.

Similarly, in the case of Angelman syndrome, a rare genetic disorder affecting the nervous system, the diagnosis rate has remained steady at 14%-15% after a jump from 0.1% in 2015 to 14% in 2019, driven by advancements in research and clinical trials. In August 2024, actor Colin Farrell opened up about his son, who was diagnosed with Angelman syndrome, and cofounded a foundation to support research and raise awareness about the condition—which is expected to play a crucial role in improving the diagnosis rates and increase public awareness.

Although no marketed products are currently available for Angelman syndrome, an initial increase in diagnosis rates for rare indications has been observed from 2015 to 2016 (see Figure 4).

FIGURE 4:

Evolution of diagnosis rates for rare indications with ICD 10 codes and no launched product



Rapid market competition growth enhances rare disease diagnosis

The synergy between market competition and product innovation plays a pivotal role in transforming the diagnostic landscape for rare diseases, ensuring that more patients receive the care they need at the earliest possible stage. Moreover, continued investment in research, supportive policies and innovative technologies will be key to addressing the challenges and seizing the opportunities in rare disease diagnostics.

The introduction of new products not only enhances awareness among healthcare professionals but also drives advancements in diagnostic technologies. As companies strive to differentiate their offerings, they invest in educational initiatives and diagnostic tools that facilitate early and accurate detection. This competitive drive fosters a more informed medical community and empowers patients with timely diagnoses, ultimately improving patient outcomes.

About the authors

Jason Yaffe is the lead of ZS's global rare disease practice. Jason extends ZS's unparalleled domain expertise to organizations large and small in the development and commercialization of therapeutics for over 350 million patients. Under Jason's leadership in the last year, the rare disease practice has supported 87 clients and 50% of global rare disease launches.

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