Rare Disease

Year in Review 2025

2025 has been a year of progress in the rare disease (RD) space. At CRA, we continue to leverage our cross-functional expertise in strategy, policy, analytics, and litigation to deliver holistic solutions and uncover new opportunities for our clients. Over the past five years, our Rare Disease Initiative Team has supported more than 700 projects – nearly 150 of them in 2025 alone – covering a wide range of therapeutic areas and modalities.

CRA was more active than ever this year in sharing insights at leading global events such as the World Orphan Drug Congress (WODC) and ISPOR, and publishing thought leadership to spark dialogue on the future of RD innovation.

This review captures the scope of our contributions and the impact of our partnerships. We look forward to continued collaboration as we navigate and shape the future of the RD space.

Sincerely,

Dr. Greg Bell, Group Vice President and Global Practice Leader, Life Sciences, CRA

Over the past year, the CRA Rare Disease Initiative Team continued to strengthen our role as a trusted partner to organizations supporting and advancing care and access for people living with rare conditions. A key focus has been proactively anticipating and responding to rapidly evolving global trends, such as the rollout of the Joint Clinical Assessment (JCA) in Europe, policy shifts in the United States like the evolving implications of the Most Favored Nation (MFN) Executive Order, as well as significant changes impacting access and pricing landscapes in China and other emerging markets.

Throughout the year, we worked closely with leading experts, including former payers and other key stakeholders, to develop thought-provoking perspectives that critically examine how emerging trends could influence RD innovation and uptake. At the same time, we maintained our commitment to delivering high-quality work across engagements, reinforcing strong cross-functional collaboration within and beyond our team. As we look to 2026, we remain committed to helping RD organizations navigate uncertainty, identify new opportunities, and ultimately improve patient outcomes.

Dr. Bhavesh Patel, Principal, Lead for CRA's global Rare Disease Initiative

Engagement highlights

In the past five years, CRA has completed >700 projects focused on RDs. In this section, we highlight some of our more unique 2025 engagements spanning strategy, policy, analytics, and expert witness work, leveraging our expertise across functions on a number of projects.

Assessment of rare lysosomal storage disorder landscape to inform clinical trial and pricing & access strategy of a new gene therapy

Conducted an in-depth landscape assessment to identify unmet needs, evidence requirements, and recommended clinical trial designs, and developed pricing and reimbursement scenarios across markets to balance access, risks, and contracting trade-offs.

European JCA Population, Intervention, Comparison, Outcome (PICO) simulation and evidence development

Supported development of an evidence generation plan for two orphan drugs to prepare for JCA submission and downstream health technology assessment and pricing negotiations. Identified and simulated PICOs and developed actions to optimize access outcomes.

European policy forum and white paper on coordinated care for Rett Syndrome

Convened a Policy Forum at the European Parliament to present findings from a white paper on coordinated care pathways for Rett syndrome in Europe. The paper was co-authored by CRA with Rett Syndrome Europe, European Brain Council, and Acadia Pharmaceuticals Inc., and included practical policy recommendations to ensure timely, coordinated, and high-quality care for every person living with Rett Syndrome across Europe.

Payer value proposition and draft pricing guidance for a novel therapy targeting an ultra-rare genetic disease

Built a knowledge base on RD analogues and launch strategy to inform development of a novel therapy. Identified payer value drivers, evidence generation needs, and country-specific insights to develop a compelling value narrative and provided early pricing guidance.

Mock negotiations for the pediatric expansion of an ultra-rare disease treatment

Supported negotiation strategy development across key European and Middle East markets by designing and facilitating in-person mock negotiations for a pediatric expansion of an ultra-rare therapy. Identified competitor differentiators, payer value drivers, and objection mitigation strategies, integrating current and emerging payer trends into negotiations.

Commercial and development trade secrets litigation support in PAH

Supported a matter regarding the alleged trade secrets theft of commercial and development materials for pulmonary arterial hypertension (PAH). Plaintiff alleged that an executive took confidential materials to a competitor, accelerating their commercialization and development efforts and assisting in their financing activities.

EU SMA care landscape assessment to inform product go-to-market strategy

Informed the go-to-market strategy for a new spinal muscular atrophy (SMA) infusion therapy in Germany and France through multi-stakeholder interviews. Assessed care coordination, patient support services, treatment journey pain points, and perceptions of the product among clinicians, patients, caregivers, and patient advocacy groups.

Quantification of patient journey to inform strategic planning for a rare genetic disorder

Conducted a comprehensive patient journey analysis for a rare genetic disorder to support US launch planning. Mapped provider networks, referrals, specialty involvement, and diagnostics to build enhanced databases of healthcare professionals and develop cross-sectional and longitudinal patient-level datasets to assess care dynamics and market evolution.

Conferences and events

In 2025, CRA's Rare Disease Initiative Team attended several RD conferences and events, most notably World Orphan Drug Congress (WODC) EU and ISPOR Europe.

World Orphan Drug Congress EU

Dr Michele Pistollato and **Dr Súil Delgado-Collins** hosted a panel session titled "Every Newborn Counts: The Quest for Equitable Newborn Screening in Europe." The central theme was the urgent need to dismantle the "postcode lottery" that currently dictates a child's access to early diagnosis and care based on their country of birth. The session featured a multi-stakeholder discussion involving experts representing European patient advocacy communities, former Members of the European Parliament and Ministry of Health, and the industry associations.

Cecile Matthews and **Chris Jones** hosted a panel session titled "From Clinical Evidence to Equitable Access: Navigating Joint Clinical Assessment in Rare Diseases" with stakeholders representing patients, political institutions, and industry. A short presentation covered the key outputs of a JCA simulation conducted by CRA for Alexion, as well as the potential opportunities and challenges posed by the JCA for patient access. The panel highlighted the urgent need for a more clearly structured and pragmatic approach to the JCA, with greater involvement from patients to ensure JCA reports are feasible to conduct in the designated timelines, while remaining useful to national organizations.

ISPOR

Andras Ruppert presented the results of an analysis of access and pricing outcomes of RD products in Germany, leveraging CRA's proprietary RAre Disease Assessment Review database (RADAR). The analysis showed that G-BA benefit ratings have the largest
impact on achievable GKV rebates, but that patient numbers, free list prices set by the manufacturers, and other factors have an impact on negotiated prices. Additionally, the data suggest a relationship between manufacturer-set list prices of products in their launch indication in Germany and the previously established US Wholesale Acquisition Cost (WAC) for the same product. Read the full posters **here**.

Content dinner and interactive roundtable

In April 2025, CRA's Life Sciences Practice hosted an event on the "Emergence of competitive rare diseases" with opening remarks from leading industry experts. Facilitated by **Kira Gordon** and **Bhavesh Patel**, roundtable participants assessed how commercialization strategies have been impacted as rare indications have evolved, and how to maximize value and optimize price & access as either a new entrant or an incumbent in an increasingly competitive RD environment. Read the full insights on the CRA website, **here**.

Rare disease live webinar

CRA hosted a webinar organized by **Bhavesh Patel** and **Toby Veale** with leading European payer experts to discuss the increasingly competitive RD landscape and its implications for pricing and market access. The panelists highlighted several key trends and learnings, including a shift in HTA and reimbursement systems away from "automatically" awarding premium or favorable pricing for orphan drugs towards requiring robust comparative evidence and demonstrated incremental value. As competition intensifies in RDs, experts emphasized that unmet need alone can no longer justify premium pricing and the shift in payers' focus from willingness to pay (WTP) for a single orphan drug to WTP for the competitive RD in its entirety. Read the full insights on the CRA website, **here**.

News and trends

Throughout 2025, CRA has been monitoring and analyzing movements and trends in the RD space. Here, we highlight some of the major news stories from the year, as well as some key trends we have identified.

Rare disease news

In 2025, the focus on controlling medicine spending continued, with risks of increased price pressure, notably with the draft **2026 Social Security Financing Bill in France**. In Germany, discussions are ongoing regarding the (partial) removal of **orphan drug benefits**, with the risk that only treatments in ultra-rare indications and with demonstrated benefits versus standard of care would remain eligible for non-quantifiable ratings. In Italy, the revised **innovation criteria** require robust comparative evidence and pre-planned real-world data collection. Meanwhile, in the UK, the NICE agreed to raise the **cost-effectiveness threshold** from £20-30k to £25-35k per QALY, which could open the door to more innovative RD medicines. As part of a trade agreement with the US, the UK secured a 0% import tariff on pharmaceuticals, while the US agreed not to apply its **Most Favored Nation (MFN)** pricing rules to UK drugs. 2025 was also the year of the first **JCAs**, with roughly half of the products under review being RD medicines, and marked a big step towards the finalization of the EU pharmaceutical legislation.

We saw a series of targeted acquisitions in the RD space in 2025, as major players strengthened portfolios through selective, high-impact deals. **Novartis acquired Avidity** for $12 billion, securing an RNA-therapeutics platform with late-stage neuromuscular programs, with the stated objective of becoming a leader in neuromuscular diseases. **Sanofi moved to acquire Blueprint Medicines** in a ~$9 billion transaction, reinforcing its position in systemic mastocytosis and rare immunology.

Key trends and issues to watch in 2026

New FDA regulatory pathway: *In 2025, the FDA introduced the Rare Disease Evidence Principles (RDEP), allowing the approval of treatments for ultra-rare diseases based on smaller, flexible evidence packages. First approvals under this framework are expected in 2026. While this could accelerate access, approvals are likely to come with stricter post-marketing commitments, and reliance on non-traditional evidence introduces some regulatory uncertainty.*

Challenges for rare disease treatment access in Europe: *Future changes in European regulations may create higher hurdles for RD therapies. In Germany, there is a growing risk that orphan drug designation (ODD) benefits could be removed or restricted, as sickness funds push for stricter criteria to limit spending. In France, the proposed Social Security Financing Bill is expected to increase price pressure on medicines and strengthen incentives for generics and biosimilars. Together, these changes could slow market access, reduce reimbursement, and create additional challenges for RD treatments.*

Impact of JCAs: *Approximately half of the products already submitted for JCA are RD therapies, with the first outcomes expected in Q1 2026, ahead of the full rollout for all RD products in 2028. There remain risks that real-world evidence and external control arms may not be fully recognized within the JCA framework, with more pronounced implications for pricing, market access, and PMA outcomes in markets with less structured HTA processes that rely heavily on JCA.*

Most Favored Nation (MFN) impact on ex-US pricing: *The impact of the MFN order on orphan drugs (ODs) may be limited, given the relatively smaller price differentials between the US and reference countries. However, unless the MFN mechanism is repealed or fundamentally altered, adjustments are likely to be required within the US healthcare system or in reference markets to accommodate the new pricing framework, as we have seen in the UK with the ICER thresholds adjustment. Without such changes, there is a real risk that patient access could be adversely affected.*

Growing competition in rare diseases: *Competition in RDs is intensifying, with more conditions now having multiple approved therapies and EU payers no longer granting "automatic" premium pricing based on orphan status alone. As such, payers increasingly expect clear comparative value and differentiation, even in ultra-rare settings. In the US, similar pressures are emerging through heightened scrutiny of clinical benefit and pricing. Together, these shifts mean manufacturers must prepare for true competitive launch environments rather than relying solely on orphan-drug incentives.*

Key publications

Throughout 2025, we have explored key topics in the RD field. Here, we present some of our publications that highlight important developments and insights from the year.

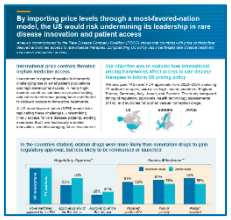
Navigating competitive arenas in rare disease

CRA published a multi-format content series exploring the **emergence of competitive categories in rare disease**, challenges and opportunities, and critical success factors for clients. Implications for pricing and market access were discussed in a webinar with leading European payer experts.

Read more >

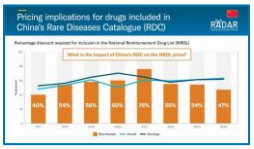
The impact of price controls on rare disease medicines access and lessons for the United States

In this analysis of 142 novel FDA-approved drugs between 2022 and 2024, including 74 orphan therapies, we found that **orphan drugs were more likely to be approved by international regulators than nonorphan drugs**, but less likely to be reimbursed or launched, and faced longer delays to patient access. Read more >



Pricing implications for drugs included in China's Rare Diseases Catalogue (RDC)

China's RDC plays a growing role in shaping awareness, investment, and access to therapies for RDs in China. With the 2023 update expanding the list of nonhereditary conditions and rare cancers, its influence is increasing. CRA's latest analysis examines **how RDC inclusion impacts National Reimbursement Drug List (NRDL) pricing**, revealing subtle but important implications for price negotiations. Read more >



The economic cost of living with a rare disease in Japan

CRA quantified the total economic cost of 64 RDs in Japan with **one of the largest patient surveys**. The study concluded that the total economic cost of people living with rare disease (PLWRD) in Japan is significant and exceeds that of other leading causes of death in Japan. Read more >

Trends in HTA outcomes and pricing in France and Germany

Using ***RADAR*, CRA's orphan drug data repository** which includes all orphan drugs granted EMA or FDA approval from 2013 to 2024, new analyses have been published on:

- Factors impacting GKV rebates for RD products in Germany: Read more >
- Evolution of manufacturer-set list prices and GKV rebates for RD products in Germany: Read more >
- Comparison of prices achieved by RD products indicated for oncology vs. prices achieved by non-oncology RD products in France: Read more >

Future outlook

In 2026, we expect the RD landscape to continue shifting as policymakers intensify cost-containment efforts and raise expectations for evidence generation. In Europe, the first wave of JCA reports will provide critical learnings for future orphan drugs navigating the process. Tightening orphan-drug criteria in key markets and reduction of the market exclusivity incentives through the draft European General Pharmaceutical Legislation create growing challenges for manufacturers.

At the same time, increasingly crowded RD classes in the US are prompting payers to adopt more active and differentiated management strategies, influencing access pathways even for orphan-designated therapies. Adding to this complexity, the anticipated increase in the number of cell and gene therapy approvals will test whether healthcare systems can manage the financial challenges these high-cost treatments present, even if restricted to rare indications.

CRA will continue to engage on these themes throughout 2026, including at WODC 2026, the World EPA Congress, and the Asembia AXS26 Summit, where we will discuss how payers are managing competitive orphan drug categories and strategies to optimize access in this evolving environment.

If you would like to discuss how CRA can support you in this space, please reach out to Dr. Bhavesh Patel (bpatel@crai.com) and CRA's global Rare Disease Initiative Team.

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