Rare Disease
Year in Review 2022

Charles River Associates

As more investments have been made in developing and commercializing treatments for rare diseases, the experience and expertise of our CRA teams have grown. The number of client projects undertaken by CRA consultants in rare diseases now exceeds 600 in the last five years and constitutes over 20% of our total client projects. In the past year alone, we have completed over 120 projects on rare diseases, covering everything from neurology to rare oncology. In addition, our consultants have presented at events, including World Orphan Drug Congresses (US and Europe), ISPOR, and PMSA, and written over 60 published thought leadership articles covering rare disease issues.

We are delighted to present this review to showcase our activities, capabilities, and experience in rare diseases and look forward to working with you in this expanding and exciting space in the years ahead.

Sincerely,

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

It has been an exciting and fruitful year for the CRA Rare Disease Initiative team. In celebration of Rare Disease Day 2022, we launched #RDSpotlight, a series that provides updates on recent trends and developments, insights and thought leadership, and highlights of our key engagements across strategy, policy, and litigation in rare disease. We continued to strengthen our presence and position as a strategic thought partner in rare disease by innovating and enhancing our offerings and capabilities, disseminating pertinent content, and building relationships. Of note, our team has been gathering opinions on the future of rare disease through Project LEOPARD (Long-term Evolution & Outlook for Patient Access in Rare Disease) and developing RADAR (Rare Disease Assessment Reviews), a central source of knowledge for orphan drug assessments across key geographies. With rare disease being a key area of focus for CRA, the RD Initiative team will continue to build upon the depth and breadth of our experience to partner with organizations connecting patients to the care they need.

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

Engagement highlights

CRA has conducted over 600 projects in Rare Diseases since 2017. Here, we share some of the more unique engagements from across our strategy, policy, and litigation teams this year

Supporting countries assess and respond to orphan policy trends at national level across Europe

Review of the changing orphan policy landscape at national level across Europe and consideration of possible future policy scenarios that could occur at EU level. Supporting local Government Affairs and Market Access teams in their responses to policy changes through development of an Impact Assessment template piloted in working sessions with the local teams.

Navigating the complexities of rare disease evidence generation and assessment

Assessment of rare disease HTA and P&R decisions to determine key impact and success factors in different market and product scenarios, ultimately supporting the client with strategic planning for evidence generation, value justification, and implementation.

Modeling the impact of participating in cross-country collaborations for novel gene therapies

Development of a quantitative model to simulate the client's potential participation in BeNeLuxAI and FiNoSe to illustrate the risks and benefits for pipeline gene therapies in terms of speed and breadth of access, expected price discounts, and overall revenue.

Estimating profits for rare disease biosimilar launch

Assessment of lost profits due to a cancelled development agreement to launch a 505(b)(2) of a high-spend rare disease drug. Components included examining generic entries of analogs for rare disease uptake and pricing. Assumptions were found to be in line with assessments by the development partner.

Concentration of Care analysis using patient-level claims data to support product launch

Analysis of Longitudinal Access and Adjudicated Data (LAAD) to create a patient and physician database and interactive PowerBI dashboard, for validation of client's target list and definition of launch strategy.

PMA diligence assessment for device complement to gene therapy

Gauge of value proposition and attainable price and access for an administration device system to be used for delivering a gene therapy to patients.

Developing guidance for management of adverse events in recently approved treatment

Development, completion, and summary of an expert panel integrating a modified Delphi approach to collect best practice on using a new treatment and managing side effects, and publication of guidance.

Thought leadership

CRA continues to be at the forefront of thought leadership in rare diseases. Here, we highlight some key pieces from 2022

Project LEOPARD

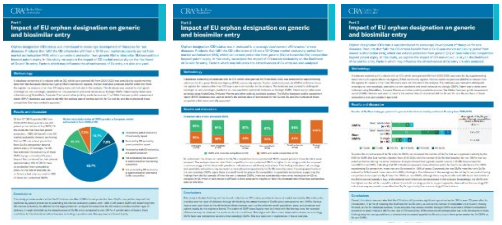
Cécile Matthews, **Dr. Bhavesh Patel**, **Lev Gerlovin**, and others explore what we can expect for patient access in established, or competitive, rare diseases, and how life sciences companies can successfully navigate the future environment for this category of rare disease. Watch the video **here.**

Gene therapy competitive dynamics: Winner takes all?

Andrew Parece and **Matthew Majewski** explore the unique competitive dynamics presented by the curative promise of gene therapies. Read the full article **here.**

Impact of EU orphan designation on generic and biosimilar entry

Steve Kelly, **Dr. Bhavesh Patel**, and others present an analysis of the opportunities offered by Orphan Drug status in terms of competitive landscapes post-launch. View the infographics **here**.



A landscape assessment of newborn screening in Europe

Tim Wilsdon and others present a comparative analysis of policies governing updates to newborn screening (NBS) panels and the role of stakeholders involved in this process in 30 European countries, demonstrating the need for policy changes to make NBS programs more patient-focused and fit for purpose. Read the full article **here**.

How does rare disease prevalence impact drug pricing in England?

Cécile Matthews, **Dr. Eva Marchese**, and others explore how the value of disease rarity is captured in health technology assessments (HTAs) in England, with a focus on orphan drugs for chronic conditions. Read the full article **here**.

Conferences

CRA was a proud sponsor of both WODC US and EU in 2022

World Orphan Drug Congress

WODC US: At the US meeting, **Lev Gerlovin** and **Dr. Bhavesh Patel** presented "Project LEOPARD: Future expectations for pricing, access, & commercialization for orphan drugs". The focus of the session was on major critical success factors for manufacturers over the next 5-10 years, in the context of trends within the RD space.

CRA also launched our new data analytics platform, Healthcare Claims Analytics Platform (HCAP) at WODC US. HCAP is a modular, dynamic, data-visualization tool that provides streamlined analysis of patient-, Health Care Practitioner (HCP)-, and Health Care Organization (HCO)-level data to support decision making and insight generation.

In addition, **Mark Trusheim**, a Strategic Director at MIT NEWDIGS where he co-leads the Financing and reimbursement of Cures in the US (FoCUS) Project and a consultant affiliated with CRA, led a rousing discussion of pricing issues for rare disease, comparing initiatives in the US with those in the EU.

WODC EU: Building on the session at WODC US, **Cécile Matthews** and **Dr. Bhavesh Patel** presented "Project LEOPARD: A dive into future critical success factors". Based on the three CSFs identified as 'top of mind' for manufacturers at WODC US, the session explored key areas of focus for manufacturers and how these might differ among different categories of rare disease.

CRA's policy work was also a major focus, with **Dr. Michele Pistollato** presenting a session titled "Policy perspectives: Can the care for patients with rare diseases be improved?"

ISPOR

At ISPOR, **Cécile Matthews** and **Charlotte Capdevila** presented an overview of the French ATU reform one year on. The analysis concluded that the AAP remains an attractive program, despite ongoing limitations regarding evidence requirements for RD products.

Key trends and insights

Some of the key trends and discussion points identified at this year's conferences included:

- Interest and research in rare disease **precision medicine to identify target patients** and optimize value.
- Discussions on the potential **wave of gene therapies** with a need for robust evidence and/or ability to use **innovative contracting** around durability.
- A drive for more equitable **access to rare disease diagnosis and treatment** through continued efforts around **newborn screening**, e.g., recommended uniform screening panel (RUSP) across US.
- Uncertainties on impact of upcoming **European Union-level joint clinical assessments** (JCAs) expected to expand to ODs in 2028 and general risks of a **deteriorating incentives environment** for orphan drugs in Europe.
- Importance of **early access schemes and support for innovation** in rare disease, including a holistic approach to **evidence development beyond RCTs.**

News and trends

Throughout 2022, CRA has been monitoring and analyzing movements and trends in the RD space. Here, we are pleased to highlight some of the major news stories from the year, as well as some key trends we have identified.

RD News

Gene therapies continued to experience mixed success in 2022. In February, the NHS in England reached a deal for the **roll-out of Libmeldy at a list price of £2.8 million**, reportedly the most expensive drug in the world at the time. After being forced to withdraw the GTx from the European market in 2021, Bluebird Bio achieved **FDA approval for Zynteglo** in August, pricing the therapy at US$2.8 million, a record for US drug pricing which was broken in November by **CSL Behring and uniQure's launch of Hemgenix at US$3.5 million**. Challenges remain however, especially in ultra-rare diseases such as Ada-Scid, where Strimvelis became a loss-making product for Orchard Therapeutics, resulting in a **takeover by Fondazione Telethon,** who are appealing for support to keep the drug available. **Zolgensma's sales also slowed in 2022** as use shifted primarily to incident cases, illustrating a dynamic which future GTx products will have to navigate.

Significant changes to the landscape included the **launch of the FDA's Accelerating Rare disease Cures (ARC) Program**, while future changes were signaled by **EFPIA's and EURORDIS' joint statement containing proposals for HTA and P&R reform** across Europe in June and the finalization of the European Commission's impact assessment for **EU orphan drug legislation reform**.

Finally, several 2022 reports have highlighted how far there still is to go in our understanding and treatment of rare diseases. However, new technologies are increasingly pushing the **discovery** and **diagnosis** of conditions; eventually, more patients would be able to access treatment.

Key trends and issues to watch in 2023

More innovative targeted/curative therapies and diagnostics: Currently, **~800 therapies** are in development to treat rare diseases. OD share of global R&D pipeline value is expected to jump from 16% in 2022 to **29% in 2024.**

More RD patients receiving treatment, including disease-modifying treatment: The orphan drug market is **growing over twice as fast as the non-orphan market**; by 2026, OD sales are predicted to account 20% of all prescription drug sales, with increasing competition among manufacturers.

Evolution in pathways and policies: Several markets are introducing **novel pathways** (*Netherlands – NEB-ZIN Parallel Procedure and Orphan Drug Access Protocol*) or **developing existing programs** (*UK – Cancer Drugs Fund/Innovative Medicines Fund* and *France – Early/Compassionate Access schemes*) which may **facilitate faster access for RD products.**

Increasing budget impact concern and payer management: **More orphan products are undergoing stricter assessment** (*Germany – reduction in orphan drug revenue threshold from EUR 50 million to EUR 20-30 million for full HTA; France – new criteria for cost-effectiveness evaluation for products with applications for ASMR I, II, or III; US – Inflation Reduction Act impacts on orphan drugs with multiple indications through Drug Price Negotiation Program; Canada – PMPRB pricing guideline revision including greater consideration of pharmacoeconomic value and a larger IRP basket*).

The **US Inflation Reduction Act** coming into force could have significant impacts on price and access across the sector; although orphan drugs for a single rare disease are currently exempt from the Drug Price Negotiation Program, those with multiple indications could be included. You can read CRA's three-part analysis of the IRA, looking at **access**, **pricing & reimbursement**, and **patient cost-sharing** reforms, on our **website**.

Future outlook

In 2023, CRA's rare disease consultants are looking forward to continuing to support our clients as they navigate the rapidly-evolving rare disease space. New in-house offerings, including our Healthcare Claims Analytics Platform (HCAP) as well as a rare disease pricing framework and RADAR, a new analysis tool for orphan drug pricing and HTA outcomes, will allow us to continue delivering high-quality and highly specific insights across our rare disease engagements. We also will continue to closely monitor the ongoing changes in the landscape and look forward to sharing our assessment of the impacts that these may have on the industry going forward.

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 the Rare Disease Initiative team. We would love to hear from you.

Have a wonderful holiday season and we look forward to connecting in 2023!

Gregory K. Bell
Group Vice President and
Life Sciences Practice Leader
Boston
+1-617-425-3357
gbell@crai.com

Bhavesh Patel
Principal
Cambridge
+44-1223-78-3909
bpatel@crai.com