Avalere eBook

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Rare Disease Biotech Landscape

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Introduction

To learn more about how Avalere can help you with clinical development planning, value, and access strategies for rare and ultra-rare disease assets, **connect with us**.

Rare diseases are not so rare. This is a commonly used phrase in the rare disease community. There are more than 10,000 known rare conditions that affect more than 30 million Americans and more than 400 million people worldwide. This diverse and complex disease area poses challenges not only to patients but their caregivers, regulators, pharmaceutical manufacturers, policymakers, and other stakeholders. Considering that less than 10% of these conditions have any treatment options available, there is a significant unmet need in this space.

In this edition of the eBook, Avalere Health experts discuss issues and considerations associated with rare-disease drug development, ex-US policy considerations, US federal and state-level programs and initiatives, the economic burden associated with rare diseases, and opportunities for a cohesive quality strategy in these conditions.

*Avalere is part of Avalere Health's global Advisory team. We build seamless strategies that anticipate and adapt to the latest industry trends, ensuring optimal outcomes for **EVERY PATIENT POSSIBLE**.

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Manufacturer Considerations for Rare-Disease Drug Development

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The development and launch of rare disease therapies require tailored strategies that account for unique patient journeys and the broader evolving landscape.

Drug manufacturers bringing therapies to market for rare diseases face challenges typically unseen with therapies for more prevalent conditions. These challenges span multiple stages—from clinical development through commercialization—and require coordinated efforts from medical affairs, health economics and outcomes research, policy, advocacy, and market access functions to execute successful evidence planning, stakeholder engagement, and patient access strategy.

Evidence Strategy: Defining Value and Identifying Appropriate Research Design

Defining value through a patient-centered lens is critical for all conditions but is especially important for rare disease treatment, as patients encounter disease impacts that don't routinely occur in non-rare populations. For example, adults with rare diseases are more likely to travel or relocate to be near specialists, incurring direct costs such as transportation and temporary lodging and indirect costs such as lost workdays or lost career opportunities. Spouses, other family members, or parents of children with a rare condition may have to change or prematurely end their careers to become full-time caregivers, resulting in major financial implications for the entire family. Limited research exists on these impacts and how to quantify them, which is needed to support more holistic value assessments.

Conducting research in the rare-disease space necessitates creative approaches to study design and recruitment to accommodate the small participant pools. Comparative effectiveness studies can be challenging with small patient populations, so innovative approaches, such as studies looking at total disease burden and the effect of existing therapies on patient- and caregiver-centered disease impacts can provide important

Patient Populations	• Thousands of rare diseases fragmented into small patient populations make it more onerous to understand the clinical manifestations and patient impacts of each rare disease. • Small patient populations also pose challenges for clinical trial recruitment, where issues around equity, access to care, and representation may be exacerbated due to lacking availability of trial sites. • Rare diseases with high prevalence in specific markets or populations may make development for some conditions less attractive or more challenging.
Diagnostic Journey	• The diagnostic journey for patients with rare diseases is long compared to more common diseases, with a high likelihood of initial misdiagnosis. • Patients and their caregivers may face additional cost burdens associated with testing and treatment options. • Delayed diagnosis can result in diagnosis at a later stage, with greater impacts on the patient; this is especially relevant for conditions that have cumulative, non-recoverable, degenerative impact. • Patients with the same condition may receive care in different specialties, presenting challenges for quantifying patient numbers and having clear view of their care pathway; access to specialist tests may be highly variable across markets.
Care Navigation	• The lack of approved treatments for most rare diseases poses ethical challenges with placebo arms in randomized control trials, requiring innovative approaches to control groups and use of real-world data. • Patients may face delays in receiving care as they navigate insurance coverage and support programs for high-cost drugs with small target patient populations. • Different treatment pathways across markets (e.g., Asia and Pacific regions) may impact how patients access care.
Treatment Options	• Specialists who have the experience and knowledge to diagnose and treat a rare condition are usually only located at major academic medical centers. • A lack of expertise among local providers and healthcare systems may result in delayed diagnosis, disruptions in treatment, or inappropriate care. • Rare diseases have disproportionate and severe impacts on children and require significant time and resources from caregivers. • Different treatment options for heterogenous disease manifestations may make it hard to be specific about the standard of care. • In many markets ex-US, demonstrating clinical benefit versus standard of care (and not placebo) is required, making it more challenging to robustly demonstrate added value and secure target pricing.

context and perspective for payers. Further, manufacturers can capture longitudinal data to assess real-world safety and efficacy for new modalities of drug delivery and mechanisms of action that take place at the cellular and genetic level using patient registries and patient-reported outcomes. Endpoints in clinical trials can be designed in anticipation of potentially innovative contracting strategies and the outcomes that will need to be tracked from real-world data. For providers and health plans, few quality measures specific to rare disease

and suited to this purpose are available. Because of the small populations, the impact of any one rare disease on the general population's quality outcomes is minimal. Patients with rare conditions share similar challenges that, when considered in aggregate, affect quality outcomes such as readmissions, adverse events, and the total cost of care, and can have a major impact on a provider's or plan's performance in quality-driven payment programs.

US Market Access Considerations

Developers of rare disease treatments must navigate a complex regulatory and commercialization landscape. Manufacturers often take on higher research and development (R&D) costs due to small clinical trial population size and difficulties in identifying and validating endpoints, especially in heterogeneous rare diseases, which poses additional barriers to manufacturers who already must navigate the changing policy environment (e.g., Inflation Reduction Act implementation). The Food and Drug Administration (FDA) recognizes these challenges and continues to invest in various programs focused on rare diseases that could help advance endpoint development and validation, promote innovative study designs, and enhance patient identification.

Patient access to available treatments may be a more significant challenge in the rare disease space given the diagnostic odyssey patients experience before receiving a correct diagnosis. For pediatric patient populations, newborn screening is available, but not all conditions are included, and due to budgetary constraints not all states screen for diseases on the Recommended Uniform Screening Panel (RUSP) or additional diseases outside the RUSP. Conditions not detected by newborn screening or those manifesting in adolescence and adulthood may be detected by novel testing approaches, such as whole genome or exome sequencing, but utilization management requirements may restrict patient access to these diagnostic tools, further delaying access to treatment.

Patient support resources needed in the rare disease space require a more tailored approach to address the unique challenges faced by patients and caregivers. Manufacturers may need to develop more patient-support education and resources about specific rare diseases. Demand for care coordination and case management support services may be even higher for rare diseases compared to non-rare diseases. Additionally, caregiver support resources and programs that mitigate breaks in care and disruption in therapy—such as bridge programs and site-of-care locators—are also important to consider for access. Once patients begin treatment, resources that enable tracking adherence and persistence also become critical as part of a robust suite of patient support offerings.

In addition, price sensitivities, driven by the need to balance R&D efforts with the associated return on investment, differ in the rare-disease space as compared to more common diseases.

Downstream impacts include more restrictive utilization management by payers, who often replicate clinical trial inclusion/exclusion criteria in their formulary designs. Payers may also want to see the total cost of care when evaluating a product, but total cost of care may not be widely studied or is poorly understood for many rare diseases. To address some of these issues, manufacturers may need to develop strategies early in the clinical development process for engaging payers, providers, and other key stakeholders.

Federal and State Policy Opportunities

Federal and state policies shape the rare disease landscape, influencing patient access and the broader R&D environment. Given the unique care journey and high-cost burden that patients with rare diseases and their families often face, policies may provide flexibilities and enable novel approaches to support access to treatments and drug development, or create specific policy exemptions for rare disease treatments in instances where patients could be adversely affected.

Federal and state policymakers are increasingly pursuing efforts to reduce cost exposure and improve patient access across the unique rare disease care journey (e.g., patient support and reimbursement for ancillary costs associated with **traveling to treatment centers**, limiting use of **copay accumulator** and maximizer programs). Meanwhile, **Medicare drug price negotiation** aims to reduce costs for high-spending drugs but could have adverse implications for rare-disease drug development due to the **orphan drug exclusion's** limitation that only enables a drug to qualify with a single rare-disease designation.

More than half of states have created **rare-disease advisory councils**. As novel treatments continue to emerge, opportunities exist to bolster and expedite efforts that shorten the diagnostic and treatment journey for patients, such as through newborn screening. Meanwhile, several states have been active in implementing **prescription-drug affordability review boards** aimed at reducing state costs for a subset of high-cost drugs, many of which could implicate rare disease treatments if not otherwise carved out of the policy. Looking ahead, federal flexibilities for novel financing arrangements through the **value-based purchasing rule**, combined with efforts from the Center for Medicare & Medicaid Innovation and state-driven initiatives, signal growing opportunity for stakeholders to engage in innovative models aimed at improving access and outcomes for patients.

The Impact of European Policy and Advocacy on Progress in Rare Disease

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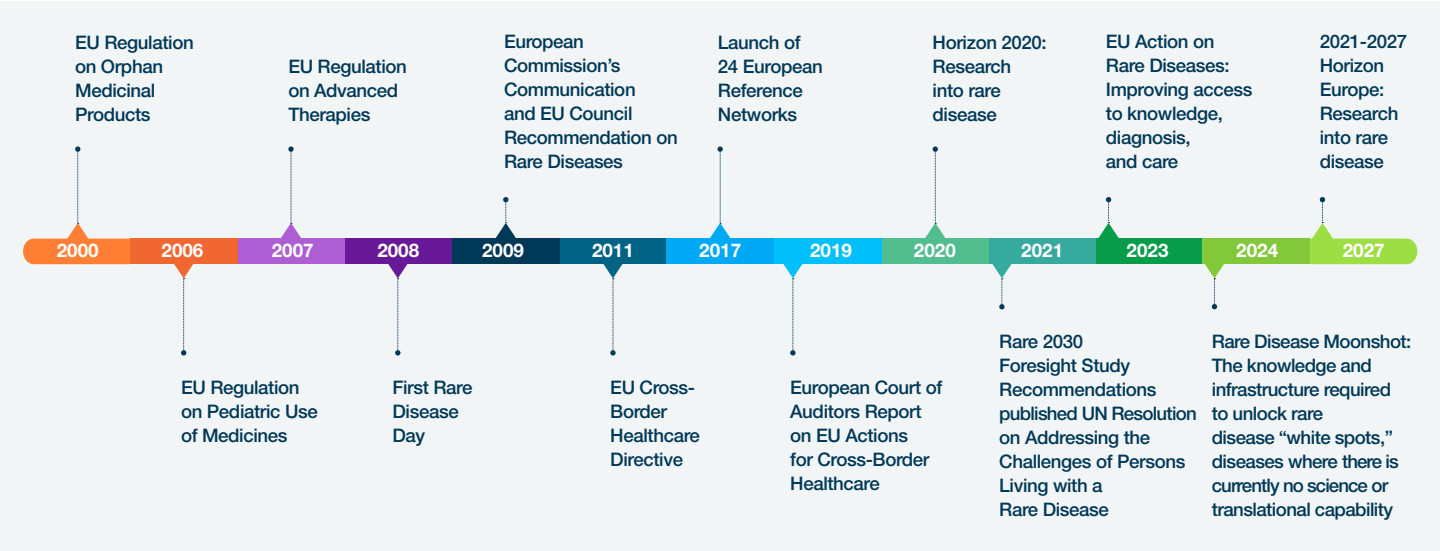
Up to 36 million people across Europe and more than 400 million globally are living with a rare disease.

It is widely understood that patients and their families face a number of challenges in accessing diagnosis and appropriate, timely treatment. Healthcare professionals are also faced with challenges with the availability of care for their patients, appropriate treatment, and access to suitable guidelines. Finally, investigators and researchers face challenges with research and development (R&D) in the rare disease space due to the small patient pool and limited funding for research.

EU policy and advocacy play a key role in overcoming these challenges; over the past two decades, policy changes and the introduction of awareness campaigns have increased the availability of treatment for patients with a rare disease. For example, in 2000, the implementation of the Orphan Medicinal Products Regulation, which provides incentives for pharmaceutical companies to invest in rare disease treatments, led to the approval of more than 200 orphan drugs in the EU. Since 2000, a number of policies and initiatives have helped increase awareness and stimulate investment to encourage the development of innovative treatments in the rare disease space. The following timeline highlights the key policies, awareness initiatives, and funding programs implemented to help elevate the standard of care for rare diseases.

Funding for research is an essential driver of innovation in the treatment of rare diseases. The availability of funding has been facilitated in part by the EU's research and innovation framework programs, such as Horizon 2020 and Horizon 2021-2027, which emphasize developing treatment and diagnostics via innovative collaborative research. The European Reference Networks (ERNs)—virtual networks of healthcare providers across Europe—have also played a key role in elevating the rare disease agenda. The first 24 ERNs were launched in 2017, with more than 900 specialized healthcare units from over 300 hospitals across 26 member states. The ERNs work via virtual advisory boards, collaborating to

Policies, Awareness Initiatives, and Funding Programs Across the EU Since 2000



review patient cases, diagnosis, and treatment and to share knowledge and experience with colleagues and patient groups. They also work on research projects, setting up disease registries, and developing clinical guidelines. As of 2024, the number of ERN members has grown to more than 1,600 located in 382 hospitals across 27 member states and Norway.

In 2023, the EU published its action plan for rare diseases, which aims to improve the diagnosis, care, and treatment of patients with rare diseases through the pooling of resources and collaboration.

The Rare Disease Moonshot program is another example of the coordination of policymakers, advocacy groups, and public and private partnerships in shaping the environment to promote advances in rare diseases. The program was established to foster collaboration between public and private organizations to support research in disease areas where there are no treatment options and where no R&D is currently taking place. The program has identified three key areas where public-private collaboration was thought to add most value:

- Optimizing the translational research ecosystem to accelerate translation
- Modernizing clinical trials (design, conduct, and regulatory sciences) to make them more suitable for very small populations
- Supporting infrastructure to shorten the path to diagnosis and treatment

The Rare Disease Moonshot program is uniquely positioned to leverage public-private collaborations to help amplify the patient voice. The program aims to achieve this by building partnerships with patient groups and helping build communities to collect vital data.

However, in order for this collaboration to be successful, stakeholders from patient groups, healthcare professionals, academics, drug and technology manufacturers, and regulators must work in collaboration to ensure that the correct data are collected and the program is truly multidisciplinary.

Patients and patient advocacy groups have also played a vital role in raising the profile of rare diseases. The first Rare Disease Day was marked in 2008, with patients, charities, and public and private organizations celebrating innovation or highlighting gaps in research and access to care. As a key stakeholder, patients add a unique perspective to research and market access endeavors. Between 2006 and 2016, the number of clinical trials focused on rare disease **increased by 88%**.

Despite the increase in awareness, drug development, and regulatory improvement, the rare disease market continues to face issues such as patient access and affordability. Navigating policies and engaging various stakeholders can be difficult. In recent years, with the introduction of gene therapies, which are potentially curative for rare diseases but come with a premium price, companies are faced with complex market access challenges.

Individual markets in Europe have specific routes or considerations for the assessment of orphan drugs for reimbursement and pricing – globally, many markets have policies to speed up access to treatments for rare diseases. For example, National Institute for Health and Care Excellence (NICE) is in the process of revising the NICE Highly Specialised Technologies (HST) Programme **routing criteria** to clarify the circumstances under which new technologies will be eligible for review within the HST Programme. **Sweden's TLV** (Tandvårds- och läkemedelsförmånsverket; Dental and Pharmaceutical Benefits Agency) is moving to take greater consideration of patient numbers and sales value in decision-making to increase access to medicines for patients with very severe and rare health conditions, with the intention to accept a higher cost in relation to benefit compared with medicines for more common conditions. In Germany, the G-BA (Gemeinsamer Bundesausschuss; Federal Joint Committee) benefit assessment of orphan drugs is such that additional medical benefit has already been proven by the regulatory approval of the drug, therefore the categories of "no additional benefit" and "less benefit" are omitted, and a favorable initial outcome is achieved, which impacts pricing. A full benefit assessment is only triggered when the €30 million sales threshold has been exceeded.

The lack of a consistent route to access for orphan drugs across Europe necessitates gaining an understanding of the relevant routes and the health technology assessment evidentiary requirements to achieve optimal access and pricing in these markets.

Newborn Screening: US Landscape and Rare Disease Developments

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Novel approaches to newborn screening of rare diseases could shape the future of federal and state screening guidelines.

Newborn screening (NBS) is a public health program that helps identify rare conditions that may affect a child's long-term health or survival. The overarching goal of this federal program is to allow early treatment, leading to reduction or elimination of the disease symptoms and its downstream impacts. About 4 million babies born in the United States are screened at birth each year. Through NBS, approximately 13,000 children are identified annually with a congenital condition (condition that is present at birth) such as a rare metabolic, endocrine, hemoglobin, and "other" (hearing and congenital heart disease) disorder.

All states are required to operate an NBS program. State public health programs are encouraged to screen for disorders included in the national Recommended Uniform Screening Panel (RUSP), but it is up to individual states to determine which conditions will be included on their screening panels.

Recommended Uniform Screening Panel

The federal Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC) issues the RUSP and advises the Health and Human Services (HHS) Secretary on the most appropriate application of the NBS tests, technologies, policies, and guidelines.

The RUSP is a list of disorders that the Secretary recommends for states to screen as part of their state universal NBS programs. The panel includes 38 primary and 26 secondary rare conditions that can be detected either through laboratory screening of dried blood spots or point-of-care screening. According to Health Resources and Services Administration (HRSA), "non-grandfathered health plans are required to cover screenings included in the HRSA-supported comprehensive guidelines without charging a co-payment, co-insurance, or deductible for plan years beginning on or after the date that is one year from the Secretary's adoption of the condition for screening."

Adding a condition to the RUSP is a multistep process that may take more than one year to complete. To add a condition to the RUSP, requestors must submit a comprehensive evidence package. The committee will then review and hold a preliminary vote on the recommendation, followed by external expert review of the evidence, after which the committee will review again and vote on the final recommendation to be adopted by the HHS Secretary.

RUSP Alignment Legislation

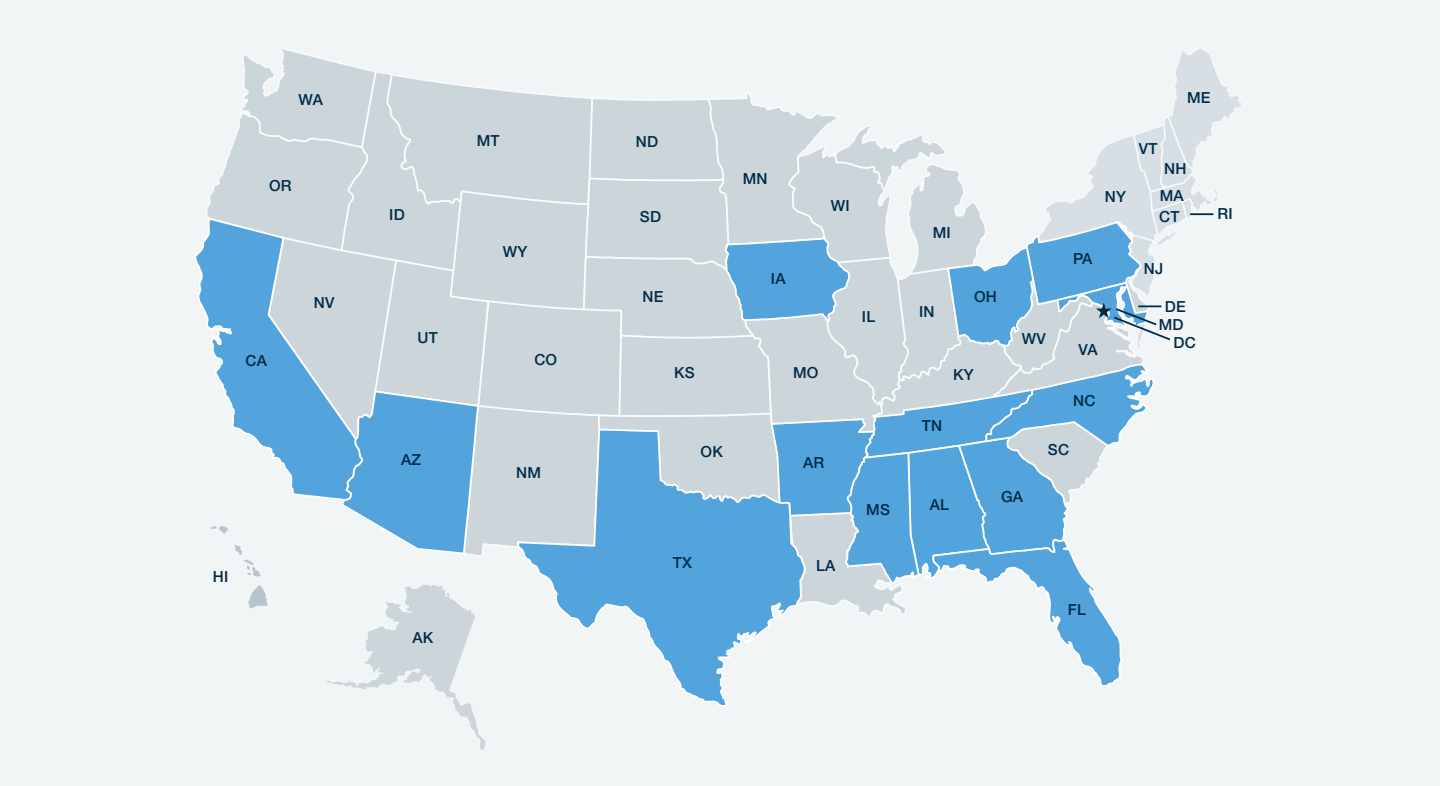
Several states have laws that align their NBS program with RUSP, meaning that their state will screen newborns for any condition on the RUSP, implement a timeline for including a condition to the state panel, and ensure appropriate resource allocation to meet the recommendations. These laws expedite the process of adding disorders included on the RUSP to state panels once they are approved by the ACHDNC. There are currently 14 states that have enacted RUSP alignment legislation, with Tennessee and Alabama being the most recent (Figure 1).

Table 1: Characteristics of NBS Programs

	Federal RUSP	State NBS Program
Scope	National	State
Enforcement	Recommended	Regulated
Number of Conditions	38 primary and 26 secondary conditions	Between 33 and 75
Funding	HRSA	State-determined fees; health insurance; Medicaid/Children's Health Insurance Program
Time to Add a New Condition	From 21 months to 10 years	Several months to several years
Level of Engagement to Add a New Condition	High	Varies by state

Stakeholders interested in adding a rare disease to the NBS panel have two potential avenues: request a condition to be added to the RUSP at the federal level or engage with individual states to have a disease added to the state NBS program.

Figure 1: States with RUSP-Aligned Newborn Screening Laws



Novel Approaches to Newborn Screening

It takes an average of 4.8 years for a patient with a rare or ultra-rare condition to receive an accurate diagnosis, and they may have to visit more than seven specialists during this process. Of more than 10,000 known rare diseases, RUSP includes only 64.

Many researchers identify a need to reduce the duration of patients' diagnostic odyssey through implementation of novel approaches to NBS, such as rapid genomic sequencing. Multiple studies are evaluating the impact of adding genomic sequencing to NBS. In the United States, these studies include BeginNGS, BabySeq, and Early Check. Ex-US programs include 100,000 Genomes Project in the United Kingdom, Initiative on Rare and Undiagnosed Diseases in Japan, Genomics Health Futures Mission in Australia, and the Saudi Human Genome Program in Saudi Arabia.

There are several implications of genomic sequencing, including ethical considerations (e.g., privacy, types of results to be returned to parents, psychological impacts of knowing the results), impact on the overall healthcare system, implementation, governance, and social determinants of health. The initial results of the studies indicate that some of these impacts may not be realized if genomic sequencing is implemented on a larger scale, though further studies are required.

Rare Disease Advisory Councils: Opportunities for Engagement

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Stakeholders should seek to engage with RDACs to develop a better understanding of rare disease care access, treatment, and populations in different states.

Background

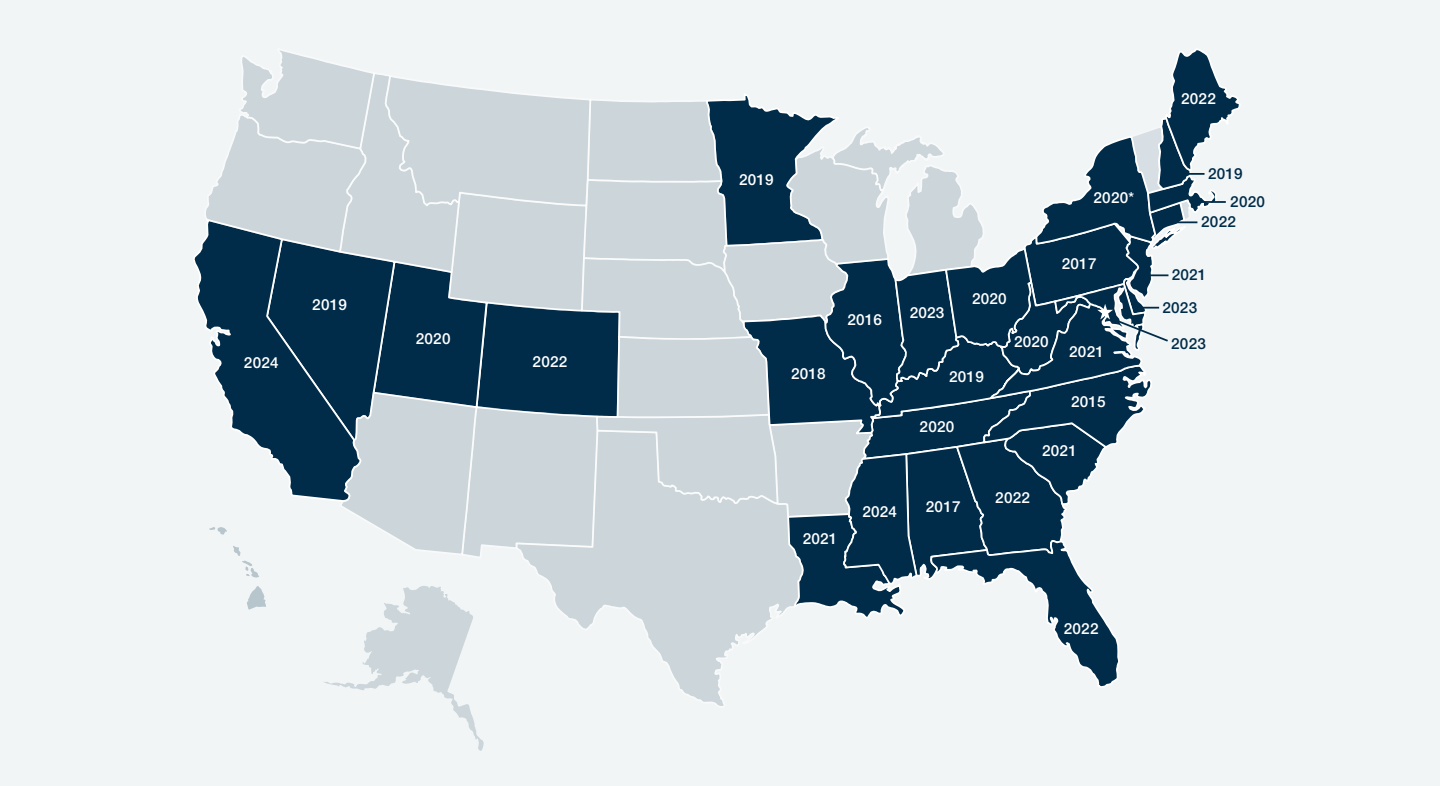
About 30 million people in the United States suffer from rare diseases and 95% of rare diseases lack a Food and Drug Administration-approved treatment. There are over 10,000 types of rare or genetic diseases, which makes it difficult for government officials and policymakers to understand the unique needs of the rare disease community.

To help rare disease communities navigate these challenges, many state legislatures have created Rare Disease Advisory Councils (RDACs), which help states refer rare disease patients to specialists, evaluate treatments, improve awareness of rare diseases, and create strategies that stakeholders (e.g., health providers, payers, advocacy organizations) can implement to improve the quality of care and health outcomes for patients with rare diseases. There are currently 28 RDACs, with the first created in 2015 in North Carolina, and one rare disease advisory working group in New York. In September 2024, California became the most recent state to sign an RDAC into law.

There are substantial differences across RDACs, with each state determining the composition, function, responsibilities, state funding mechanism, and size of their council. RDAC members include a variety of rare disease stakeholders, including patients, patient advocates, providers, caregivers, researchers, biotech industry representatives, state government officials, and health insurance representatives.

RDACs often work in conjunction with rare disease organizations such as patient advocacy groups, the National Organization for Rare Disorders, and other stakeholders in the rare disease community (e.g., academic medical centers). These partnerships help RDACs identify state-specific issues (e.g., barriers to treatment) for the rare disease community and enable them to provide comprehensive recommendations

Figure 2. Map of RDACs by Year Established



*New York Rare Disease Working Group is not an official RDAC.

through engagement with relevant stakeholders. Given RDACs' limited resources, partnering with different stakeholders can also provide funding for various programs to assist patients with rare diseases and execute councils' goals.

Function of RDACs

Given the number of rare diseases, it is difficult for government officials and policymakers to understand the unique needs of the rare disease community. This can hinder treatment options, result in high out-of-pocket costs, limit access to specialists, and cause delays in diagnosis and treatment. In evaluating and addressing state-specific barriers to care, RDACs can bridge the gap between legislators, health departments, and the rare disease community.

RDACs conduct surveys to assess the needs of the rare disease community, publish resources for patients and families, and consult with experts to improve access and quality of care for patients, among other activities. Some RDACs also hold public meetings on their current priorities.

RDAC Limitations

Although RDACs can be valuable resources for understanding state-specific rare disease landscapes in the state, they do have limitations. RDACs are advisory bodies, meaning that they can provide recommendations to policymakers, but do not have authority to set policy. The amount of funding and resources RDACs receive also differs across states, and many RDACs do not receive state appropriations. It is important

for stakeholders to understand the differences in funding, activity, and organization between RDACs in different states to plan engagement opportunities. Additionally, the structure and goals of RDACs can differ by state, which make it imperative for stakeholders to understand the resources, capabilities, and support that an RDAC has prior to engagement.

Opportunities for Engagement

Engaging with RDACs can help stakeholders better understand the patient demographics and barriers to care for rare disease in a particular state. Furthermore, RDACs often have strong relationships with prominent rare disease medical centers and state-based patient organizations, which could help stakeholders identify partners to engage and improve health outcomes for patients with rare diseases. Additionally, through communications with RDACs, stakeholders may have opportunities to help promote the creation of more RDACs and assist in policymaker education to understand the intricacies of the rare disease **diagnostic odyssey** and patient journey.

Assessing the Total Economic Burden of Rare Disease

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Innovative research methods can be used to measure the total burden of rare disease, including direct medical costs, indirect costs, and overall life impacts.

Avalere Health experts developed a whitepaper describing the opportunity and importance of measuring the total economic impact of diseases, particularly for rare diseases. First, experts present a case for considering the total economic burden of rare disease, then explore the current state of evidence on the burden of rare diseases, concluding with real-world application of total economic impact research. The proposed hybrid study approach builds upon a prior assessment by the EveryLife Foundation on the economic burden of 379 rare diseases, which can be used as a springboard for studying the disease-specific social and economic burden of a single rare disease. The team selected generalized myasthenia gravis (gMG) as a case study to measure direct and indirect non-medical costs based on Avalere's foundational research on patient- and caregiver-centered life impacts. A previous mixed-methods analysis found that financial and occupational impacts ranked highly among the eight impacts studied—emotional, financial, occupational, physical, planning & autonomy, safety, sleep, and social—elevating the importance of economic impacts.

The figure on the next page details potential components of total economic burden to be studied to better understand the true cost of these conditions, such as the significant out-of-pocket costs, labor and productivity impacts, and broader societal impacts. Understanding the true burden of rare diseases can help policymakers and the public better recognize the extent of the individual, family, and social impacts and allocate resources accordingly.

Despite the challenges of calculating the total burden of disease (especially for heterogeneous populations), robust and well-designed research can offer useful insights and context for patients, caregivers, payers, health technology assessment bodies, healthcare providers, policymakers, manufacturers, researchers, and society.

Potential Components of a Total Economic Burden Study for Rare Diseases

[Access the whitepaper here.]

The State of Quality in Rare Disease

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Avalere Health assessed quality measurement, quality improvement, and value-based initiatives in rare disease and the opportunity for a cohesive quality strategy.

Individuals with rare diseases face unique clinical circumstances that put them at increased risk for poor health outcomes and adverse events. For example, there is limited evidence on how best to deliver care for some rare diseases and specialized providers may only be available at major academic medical centers, which represents a significant barrier to accessing appropriate care. If a provider is less familiar with the patient's rare condition, care decisions for other health needs may not consider the impact on the disease's exacerbation or progression. These factors create unique challenges for achieving optimal quality: care that is safe, effective, efficient, equitable, timely, and patient-centered.

To determine whether and to what degree the core commonalities of rare disease care needs are addressed by existing quality improvement efforts and to identify opportunities to enhance rare disease care quality, Avalere conducted a landscape analysis of the existing quality measures, value-based care programs, and quality improvement initiatives. The targeted search aimed to identify major features of the quality landscape specific to rare diseases such as quality measures, improvement programs, and evidence-based care guidelines. Avalere used multiple tools, including UpToDate®, and publicly available resources.

Avalere identified 34 active quality measures, 17 quality improvement programs, and 26 evidence-based care guidelines focused on rare diseases. The Up-to-Date database alone has more than 850 disease-specific care guidelines. The few existing quality improvement programs and patient registries for rare diseases were spearheaded by patient advocacy groups, with the predominant focus on expediting time to diagnosis for individuals with rare diseases. Other improvement efforts focused on establishing specialized treatment centers designed to mitigate geographic barriers to treatment. Quality measures developed for rare diseases are not widely used or found in high-

profile quality payment programs, and many measures have been discontinued or were never integrated into the Centers for Medicare and Medicaid Services' reporting programs.

There is a clear opportunity for stakeholders to consider rare diseases collectively rather than individually. There are more than 10,000 rare diseases that together affect an estimated 25–30 million Americans, a population size rivaling those of the most common chronic conditions. Developing quality improvement initiatives, building rare disease common care guidelines, or implementing quality measures are strategies relevant for multiple stakeholders, and could have significant impact in improving care for these patients.

Access the white paper here.

Table 2. Rare Disease Quality Improvement Programs

Program/Initiative Name	Organization	Focus
NORD Rare Disease Centers of Excellence	National Organization for Rare Disorders (NORD)	Diagnosis, care coordination
Myasthenia Gravis Foundation of America (MGFA) Global Patient Registry	MGFA	Research
Axon Registry	American Academy of Neurology (AAN)	Research
Rare Disease Registry Program	National Center for Advancing Translational Sciences	Research
Newborn Screening Quality Assurance Program	Centers for Disease Control	Research
National Pediatric Cardiology Quality Improvement Collaborative (NPC-QIC)	NPC-QIC	Transitions of care
RARE Toolkit	Global Genes	Diagnosis, patient education
ThinkALS Toolkit	Amyotrophic Lateral Sclerosis (ALS) Association	Diagnosis
Genetic Disorder of Mucociliary Clearance Consortium	National Center for Advancing Translational Sciences	Diagnosis
Cystic Fibrosis Foundation Care Centers	Cystic Fibrosis Foundation	Care coordination
Congenital Heart Defects Toolkit	Centers for Disease Control and Prevention's Congenital Heart Public Health Consortium	Care coordination, transition of care
ACCESS Telemedicine Model	University of New Mexico Health Sciences Center	Value-based care, access to care
Merit-Based Incentive Payment System (MIPS) Value Pathway: Supportive Care for Neurodegenerative Conditions	Centers for Medicare & Medicaid Services (CMS)	Shared decision making
Coordination of Rare Diseases at Sanford	Sanford Health	Research
The Global Paroxysmal Nocturnal Hemoglobinuria (PNH) Patient Registry	The Aplastic Anemia and Myelodysplastic Syndromes International Foundation	Research
Congressionally Directed Bone Marrow Failure Research Program	The Aplastic Anemia and Myelodysplastic Syndromes International Foundation	Research
Lysosomal Acid Lipase Deficiency (LAL-D) Registry	Alexion	Research

Webinar

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Join Our Rare Disease Day Webinar

February 28 / 10 AM ET / 3 PM GMT

Video Series

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Avalere's Insights on Rare Disease

Explore examples of our collaboration with rare disease stakeholders to develop practical solutions and achieve meaningful outcomes for patients. ⟶

Case Studies

See More

Case Study

IRA Modeling

Utilization Analysis and IRA Volume Model Development for Three Products in Rare Autoimmune Conditions

Challenge

In anticipation of Part D redesign implementation and shifting volume trends in Medicare for key portfolio products, the client sought a strategic partner to understand how portfolio products are being accessed in Medicare and how the IRA may shift stakeholder economics over time and, as a result, stakeholder behavior.

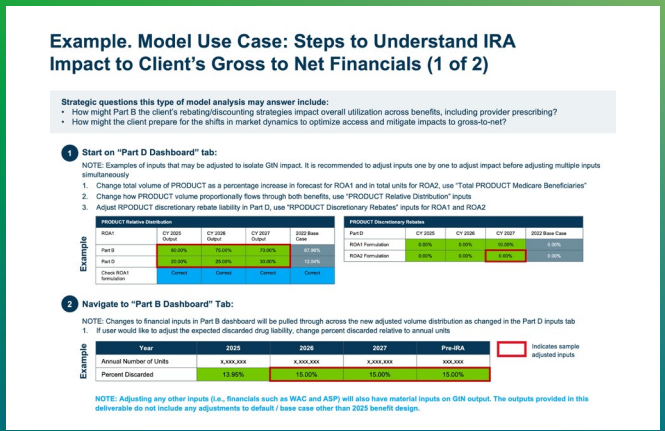
Solution

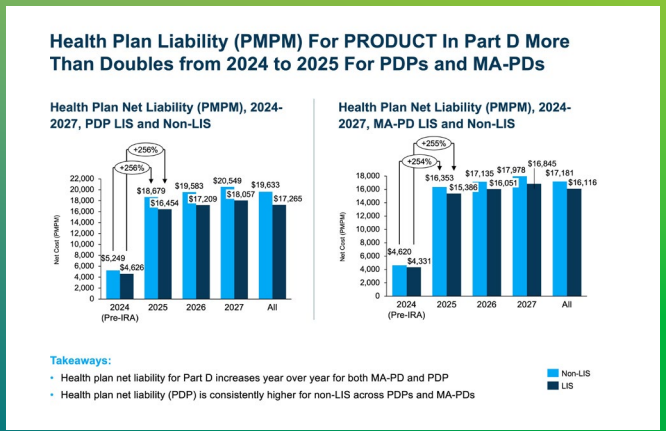
- We conducted several claims analyses to identify market trends and develop two bespoke flexible-input IRA models.
- Then, we used 100% Medicare claims data to build a flexible model that leverages inputs such as product utilization, share between Part B and Part D and demand elasticities to understand resulting client's GtN, shifts in plan liability, and patient OOP pre- and post-IRA.
- We provided numerous trainings to the client's teams to ensure internal comfort with leveraging models as a strategic tool.

Results

The client was provided with a tool that would support internal forecasting and channel strategy planning, particularly around how product utilization in Parts B and D could impact access. Results were used to inform IRA scenario planning workshop.

GtN: Gross-to-Net;
IRA: Inflation Reduction Act;
OOP: Out-of-Pocket





Case Study

IRA Modeling & Workshop

IRA Volume Model Development and Workshop for Three Products in Rare Autoimmune Conditions

Challenge

The client sought a strategic partner to leverage and assess results of the IRA models developed for the client's products to understand implications for 2025-2027 strategic planning, focused on mitigation strategies and tactics to seize opportunities arising from IRA reform.

Solution

We convened a cross-functional expert panel, including senior SMEs with direct clinical, actuarial, and health plan experiences to assess scenarios that may arise for each portfolio product. Key considerations addressed as part of the workshops included:

- Understanding most likely plan responses to Part D Redesign, specifically considering liability of the client's products from modeling task;
- Considering potential impacts to patient access;
- Strategizing potential client's tactics that could mitigate impacts to product access based on stakeholder (e.g., payer) behavioral shifts resulting from IRA, focused on channel and site of care strategy;
- Considering impact of biosimilar entry

Results

We provided tactical and tangible insights to inform how the client can prepare to adapt market access strategies in a changing policy environment.

IRA: Inflation Reduction Act;
SME: Subject Matter Expert

Case Study

Value-Based Contract Design and Validation

Avalere Supported a Client to Identify and Evaluate Potential VBC Approaches for a Rare Disease Asset

Challenge

An R&D biotech company was preparing to transition to a commercial company. In preparing for a launch of an asset for an ultra-rare disease with subsequent label expansion to a broader population, the client sought Avalere's support to design VBC constructs and test them with a panel of payer experts.

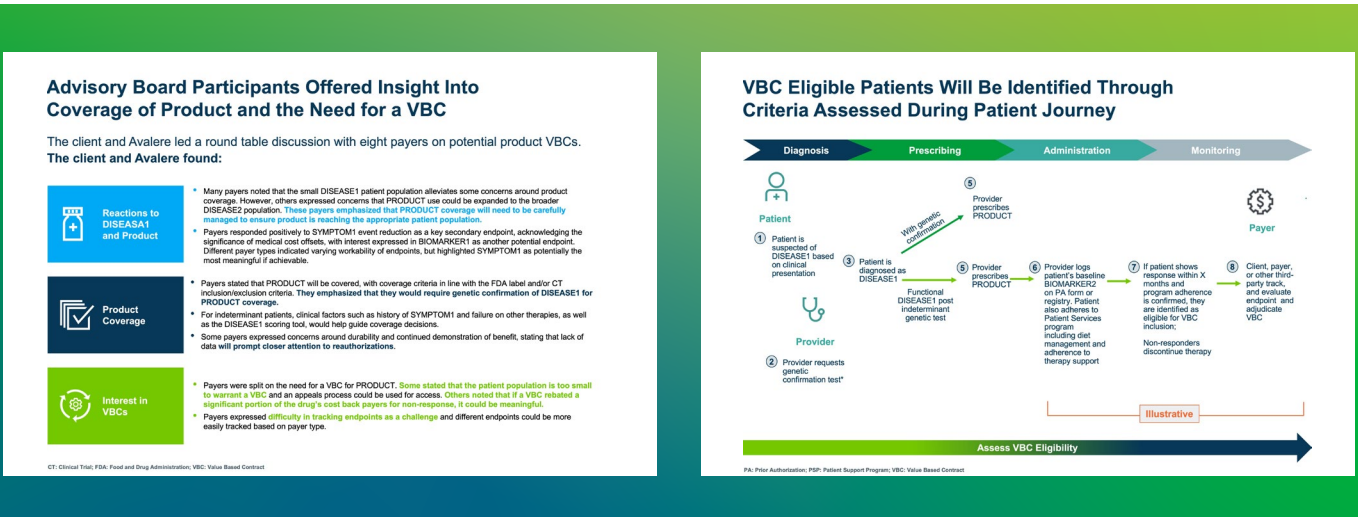
Solution

- We reviewed client provided materials, including CDP, SAP, scientific publications, previously conducted market research, etc.
- Leveraging background information and close collaboration with the client's internal KOL, we identified VBC metrics that were used to develop VBC constructs, which were tested with external payers during the 2-day advisory board meeting.

Results

As the client was preparing for a commercial phase, we leveraged the insights from this engagement to help the organization in determining launch and access strategies for its first fully commercialized asset.

CDP: Clinical Development Plan;
KOL: Key Opinion Leader;
SAP: Statistical Analysis Plan;
VBC: Value-Based Contract



Case Study

Market Access and Contracting Strategy

Avalere Assessed Hemophilia Market Dynamics to Inform SP Contracting Strategy for Pipeline Product

HTC: Hemophilia Treatment Center;
PBM: Pharmacy Benefit Manager;
SP: Specialty Pharmacy

Challenge

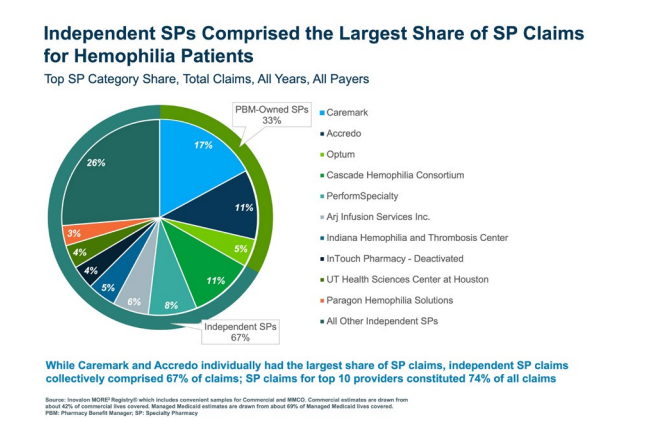
A client sought to better understand hemophilia market dynamics and explore contracting options with independent and PBM-owned specialty pharmacies (SPs) for a pipeline hemophilia product.

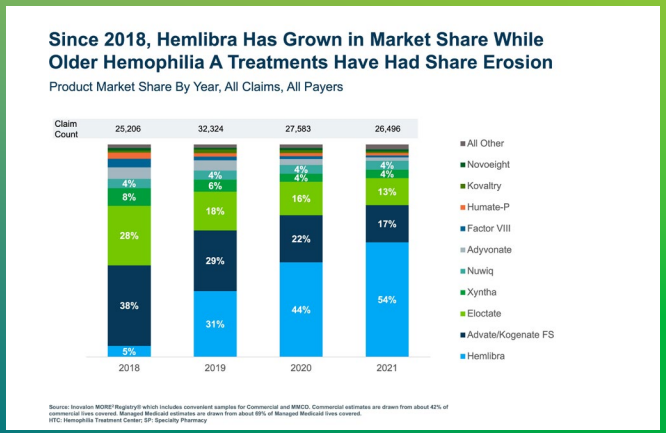
Solution

- We leveraged claims to assess market share of competitor products and to identify top sites (HTCs and SPs) that bill for hemophilia products.
- We then conducted primary research with key stakeholders at top sites to supplement claims findings and to identify 5 potential contracting options.
- Leveraging claims analysis and primary research findings, we identified contracting options and assessed those options against metrics such as patient support services, contracting/discounting considerations, and access to patient volume.

Results

The client used these findings to educate internal stakeholders on the current state of hemophilia market and implement alternative approaches to working through independent SPs with a focus on hemophilia treatment.





Case Study

Patient Journey Mapping & Resource Utilization

Avalere Outlined the Patient Journey to Support Commercialization of a New Treatment

Challenge

A client wanted to understand the patient journey and resource utilization following FDA approval of their new therapy for a rare autoimmune disease.

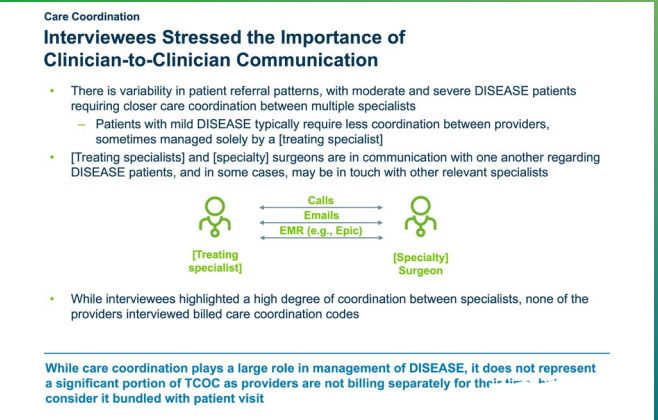
Solution

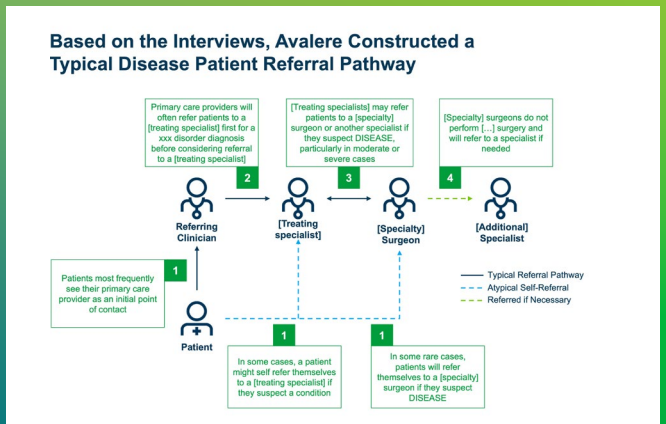
- We conducted provider interviews to identify components of the patient journey related to diagnosis, treatment, and subsequent monitoring of patient disease progression.
- We synthesized the key findings from primary research into a resource utilization map that displayed the patient journey and potential barriers to infused treatments to inform how coverage and reimbursement may impact the client's product.

Results

We outlined the disease's clinical course and the potential TCOC for 4 treatment scenarios which displayed the value of developing a TCOC model for differing patient populations. The client leveraged these findings to build an economic model to reimbursement via public and commercial payers.

FDA: Food and Drug Administration;
TCOC: Total Cost of Care





Case Study

EU Market Access Strategy and Roadmap for SBS-IF

Avalere Health Developed, and Pressure-Tested Through Primary Research, a European Market Access Strategy and Evidence Generation Roadmap in SBS-IF

CSFs: Critical Success Factors;
HTA: Health Technology Assessment;
SBS-IF: Short Bowel Syndrome with Intestinal Failure

Challenge

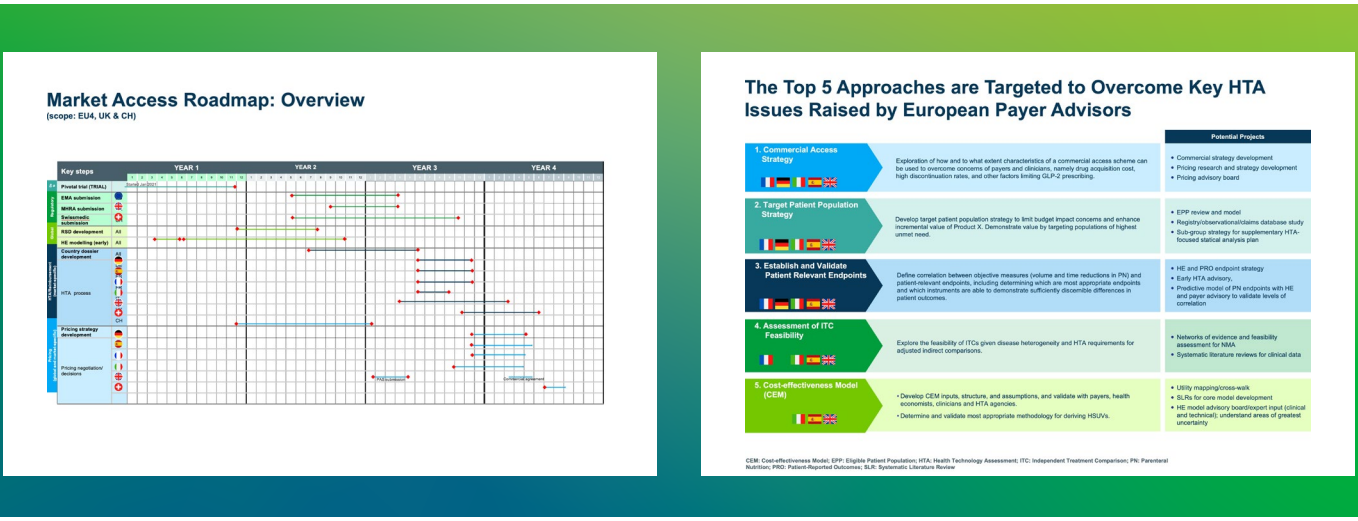
A US-based client had a drug in clinical trials to treat a rare, chronic and life-threatening condition with low disease awareness outside of specialist centers. The client was seeking to develop a European market access strategy and evidence generation roadmap to guide their small team and prioritize limited resources.

Solution

- We summarized the disease landscape through desk research to highlight likely market access drivers and barriers, summarized through a series of strategic imperatives, CSFs, and associated evidence generation recommendations.
- We pressure-tested core elements of the market access strategy and evidence plan with European clinicians and payers to refine outputs across markets of interest.
- We tailored the market access roadmap and recommendations to each of the markets of interest.

Results

The core and market-specific recommendations informed the client's European strategy and prioritization of evidence generation activities. The roadmap allowed the client to understand the cross- utilization of evidence and plan its submissions to HTA bodies.



Case Study

Multi-stakeholder Disease Area Assessment in AATD

Avalere Health Developed a Holistic Landscape Assessment for AATD to Support the Potential Commercialization of a Newly Acquired Asset

Challenge

Following acquisition of a product being developed for a rare, inherited condition with high unmet need, our client sought to assess the potential value against multiple stakeholder expectations in core markets.

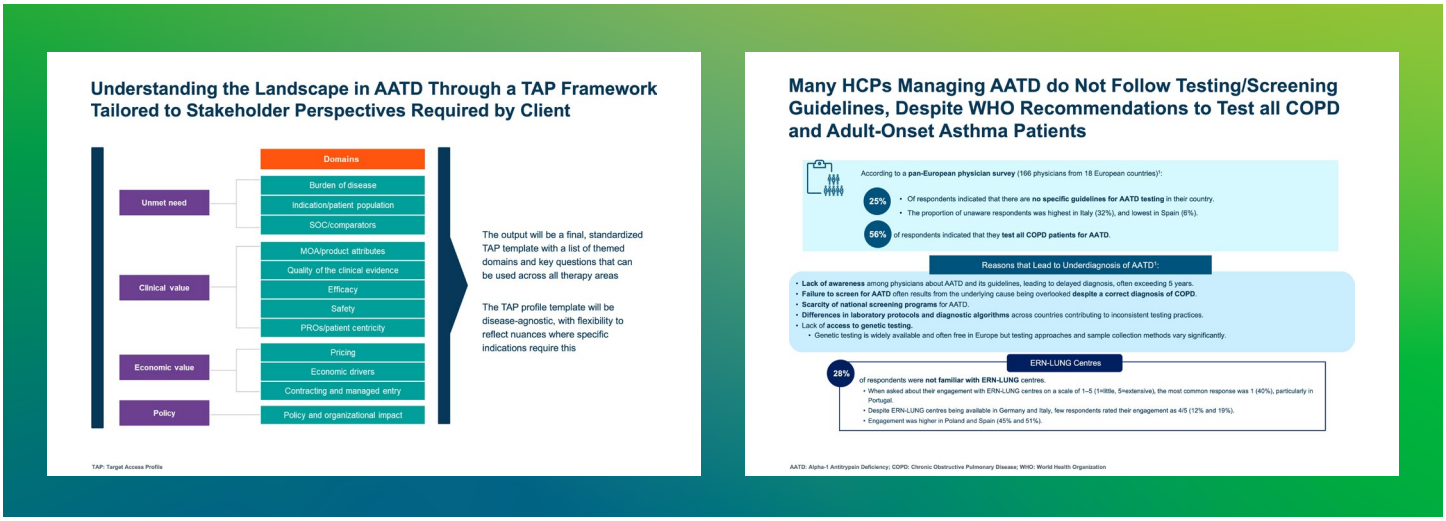
Solution

- We developed a Target Access Profile (TAP) to characterize the access landscape in AATD as the foundation for an evidence gap analysis for commercial development.
- We considered the perspectives of multiple stakeholders including clinical, regulatory, patient, policy, and payers.
- The multistakeholder TAP was refined with input from the client's cross-functional teams in a facilitated workshop.
- Our evidence generation recommendations were used to validate internal evidence activities and prioritize development of the evidence generation plan.

Results

Findings and insights from the TAP and consolidated evidence plan facilitated our client's cross-functional strategy needed to optimize the commercialization plan of the acquired asset.

AATD: Alpha-1 Antitrypsin Deficiency;
TAP: Target Access Profile



Case Study

Commercial Potential and Value Proposition Development

Avalere Health Assessed the Access Potential and Pricing Opportunity for a Novel Monoclonal Antibody in a Rare Chronic Inflammatory Disease

APAC: Asia Pacific;
BD&L: Business Development & Licensing

Challenge

The client sought to understand the commercial potential of a novel monoclonal antibody licensed for commercialization in select APAC markets, given likely competitive pressure at launch.

Solution

- We established a clear understanding of the rare disease ecosystem characterizing the local clinical practices, funding and reimbursement pathways through secondary research.
- Based on the asset target profile, we generated a hypothesis of potential risk and opportunity with knowledge gaps to support identification of priority topics for expert validation.
- We conducted in-depth interviews with relevant payer and clinician experts. Payer- and clinician-specific discussion guides were tailored to deep dive into local clinical practices, perception of unmet need, clinical value of asset profile, validation of reimbursement and funding routes, and establishing price potential, keeping in view the evolving competitive landscape.

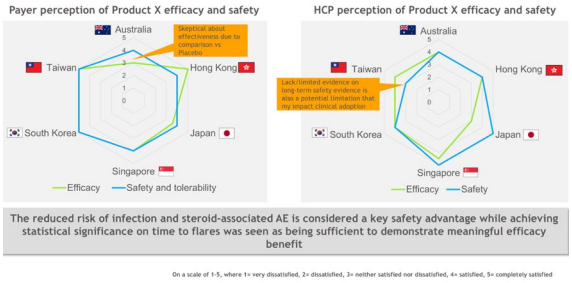
Results

The client gained a clear understanding of risks and opportunities of in-licensing the asset and commercializing in APAC markets that supported future BD&L discussions and local launch planning.

Rare Disease Pathways Can Support Reimbursement in Some Markets However Access Strategy will be Impacted by Product Y Launching Prior to Product X

Reimbursement considerations	Australia	Hong Kong	Japan	Singapore	South Korea	Taiwan
P&R pathway	No rare disease pathway applies (LSDP not applicable as disease is not life-threatening)	No rare disease pathway although expedited regulatory approval possible	Disease X categorized as intractable disease with high unmet need- orphan drug premium and protections apply	Not eligible for rare disease fund Standard pathway will apply	Eligible for Pharmacoeconomic waiver	Expedited regulatory approval and funding if orphan drug designation (ODD) is achieved
Funding mix	Public only	Private (PHI/OOP market)	Public only	Public/OOP mixed opportunity	Predominantly public	Predominantly public
Decision drivers	• Cost effectiveness or cost minimization outcome • RSA	• HCP adoption and patient affordability/WTP (Very limited set of rare diseases receive public subsidy)	• Both cost calculation and similar treatment pricing methods may apply • High-Cost Medical Expense Benefit will support limiting OOP costs • Likely exempt from CEA repricing	• Cost effectiveness outcome • Clinician adoption and patient affordability/WTP	• Pharmacoeconomic evidence (CEA and BIA) • RSA • Limited disease understanding hinders payer perception • Limited global launches delay access	• BIA dictates funding decisions • RSA
Impact of Product Y launching first	Product Y will be direct comparator only if reimbursed; cost minimization approach may apply	No impact	'Similar treatment' pricing method vs Product Y will apply	Product Y will be direct comparator if SOC; restricted opportunity in the public market if Product Y is reimbursed	Product Y will be direct comparator, cannot avail PE waiver	Support establishing orphan drug designation for Disease X will benefit Product X

Safety and Efficacy Profile of Product X was Largely Seen Favorably Across Expert Types and Markets



The reduced risk of infection and steroid-associated AE is considered a key safety advantage while achieving statistical significance on time to flares was seen as being sufficient to demonstrate meaningful efficacy benefit

On a scale of 1-5, where 1= very dissatisfied, 2= dissatisfied, 3= neither satisfied nor dissatisfied, 4= satisfied, 5= completely satisfied

Case Study

Price-Based Risk Assessment to Inform Go/No-Go Decision for Ex-US Market Entry

Avalere Health Provided Insights on Pricing and Access and Their Impact on Revenue Forecasting to Drive a Launch Go/No-Go decision

Challenge

The client had an asset in development for the treatment of TED and wanted to inform near-term corporate development and investment decisions that require an updated point of view on the commercial opportunity ex-US.

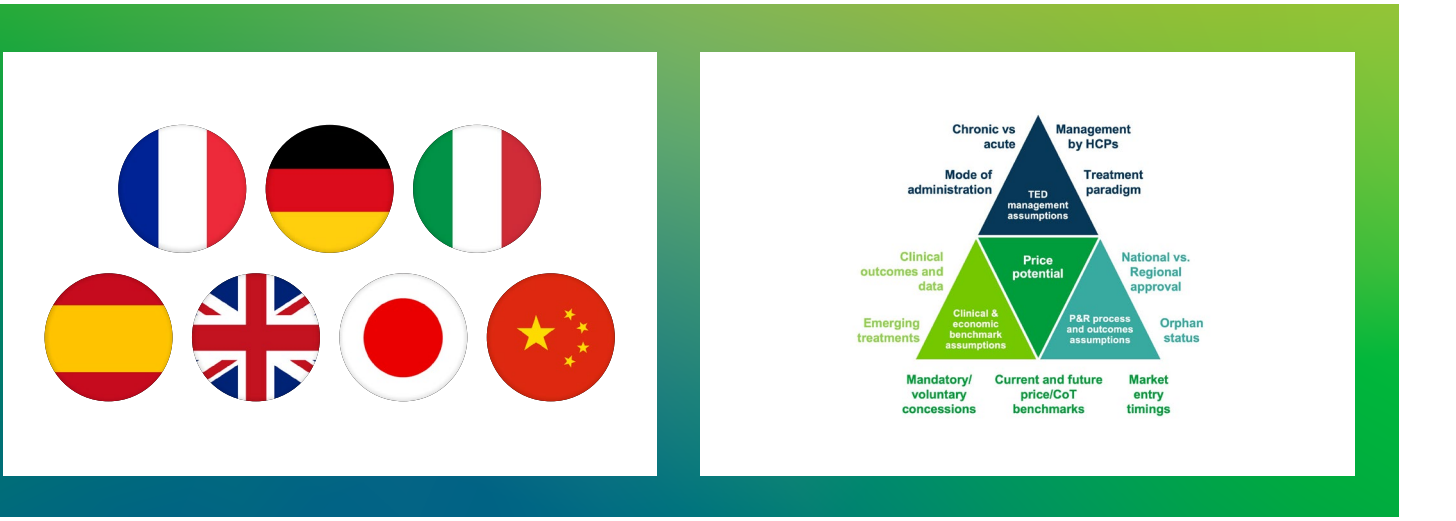
Solution

- We leveraged an abbreviated approach as used by the national reimbursement bodies and payers to review a new product and its price potential, including identifying appropriate clinical and price comparators, evaluating the available evidence for comparative effectiveness, assessing additional treatment/ pathway costs, determining a likely price band for each market.
- We determined two reimbursement scenarios (conservative vs optimistic) based on different data requirements to optimize price, reimbursement, and market access.

Results

The client gained insights that informed clinical development and corporate development decisions in the near term, and commercial planning decisions in the mid-to-longer term. An overview of the ex-US commercial opportunity allowed the client to provide recommendations on go/no-go decisions to its board of directors.

TED: Thyroid Eye Disease



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The miraculous happens when we decide every person is within reach.

At Avalere Health our goal is to ensure every patient is identified, supported, treated, and cared for. Equally.

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A healthcare consulting firm for more than 20 years, Avalere partners with leading life sciences companies, health plans, providers, and investors to bring innovative, data-driven solutions to today's most complex healthcare challenges.

Avalere is part of **Avalere Health**, a global strategic partner, perfectly formed to solve the biggest challenges in healthcare – at pace and at scale.

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About Avalere Health

Guided by a single mission to make **EVERY PATIENT POSSIBLE**, our Advisory, Medical, and Marketing capabilities move as one to ensure no patient is left behind.

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