ESTHER,
diagnosed with ATTR amyloidosis, USA

2025 Rare Disease **Trend Report**

PERSPECTIVES FROM
HEALTHCARE PAYERS
AND EMPLOYERS

SIXTH EDITION

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SOPHIA,
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FOREWORD

The remarkable scientific progress under the backdrop of healthcare system evolution and economic challenges are what define the rare and specialty therapeutics landscape. These therapies often involve highly specialized manufacturing processes, unique trial designs, and difficult-to-reach patient populations, which contribute to complex reimbursement models and economic challenges. Despite these hurdles, the rare disease pipeline continues to expand. In 2025, 50% of all novel drug approvals were indicated for rare diseases.[1] As the growth of these innovative therapies expands treatment possibilities for patients with rare conditions, they are simultaneously providing stakeholders across the healthcare ecosystem with additional levers to help balance the promise of these life-enhancing advances with the challenges of affordability and access. The 2025 Alnylam Rare Disease Trend Report builds on previous trend reports' foundational insights, examining how payers and employers are seeking prudent strategies to support members' health and well-being while adapting to shifting cost burdens, evolving policy frameworks, and the growing complexities and intricacies of benefit design.

This report is published to foster open dialogue among payers, employers, providers, manufacturers, advocacy groups, and patients. By synthesizing perspectives from across the healthcare ecosystem, the 2025 edition aims to deepen understanding of emerging trends and challenges that must be addressed to sustainably improve patient access to rare disease products. Alnylam remains committed to advancing these discussions by equipping stakeholders with the insights and information they need to confidently navigate the evolving landscape and help ensure life-changing therapies reach those who need them.

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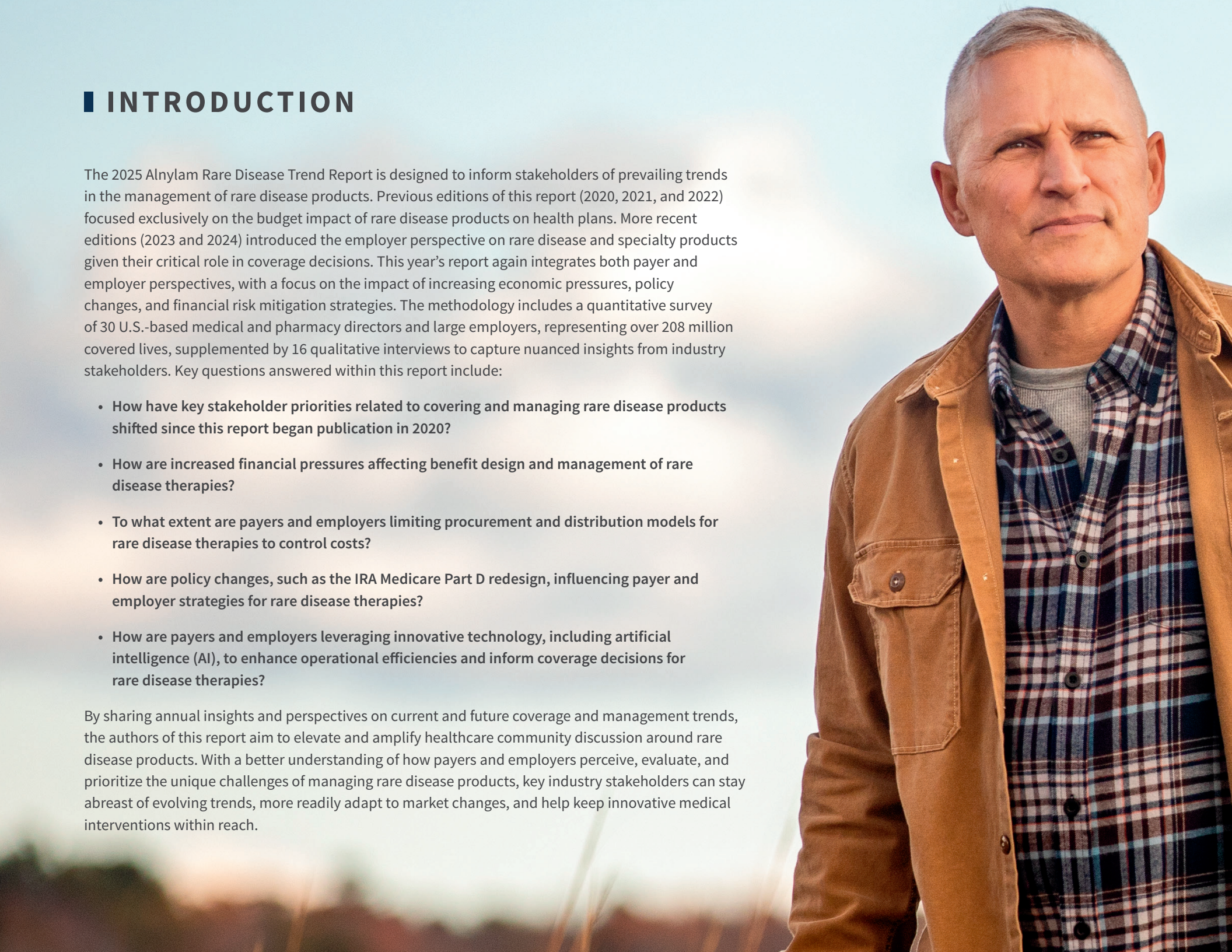
INTRODUCTION

The 2025 Alnylam Rare Disease Trend Report is designed to inform stakeholders of prevailing trends in the management of rare disease products. Previous editions of this report (2020, 2021, and 2022) focused exclusively on the budget impact of rare disease products on health plans. More recent editions (2023 and 2024) introduced the employer perspective on rare disease and specialty products given their critical role in coverage decisions. This year's report again integrates both payer and employer perspectives, with a focus on the impact of increasing economic pressures, policy changes, and financial risk mitigation strategies. The methodology includes a quantitative survey of 30 U.S.-based medical and pharmacy directors and large employers, representing over 208 million covered lives, supplemented by 16 qualitative interviews to capture nuanced insights from industry stakeholders. Key questions answered within this report include:

- **How have key stakeholder priorities related to covering and managing rare disease products shifted since this report began publication in 2020?**
- **How are increased financial pressures affecting benefit design and management of rare disease therapies?**
- **To what extent are payers and employers limiting procurement and distribution models for rare disease therapies to control costs?**
- **How are policy changes, such as the IRA Medicare Part D redesign, influencing payer and employer strategies for rare disease therapies?**
- **How are payers and employers leveraging innovative technology, including artificial intelligence (AI), to enhance operational efficiencies and inform coverage decisions for rare disease therapies?**

By sharing annual insights and perspectives on current and future coverage and management trends, the authors of this report aim to elevate and amplify healthcare community discussion around rare disease products. With a better understanding of how payers and employers perceive, evaluate, and prioritize the unique challenges of managing rare disease products, key industry stakeholders can stay abreast of evolving trends, more readily adapt to market changes, and help keep innovative medical interventions within reach.



This report was sponsored and developed by Alnylam Pharmaceuticals, Inc. Alnylam is a biopharmaceutical company leading the translation of RNA interference (RNAi) into a new class of approved and investigational medicines for rare and prevalent diseases.

KEY FINDINGS

1

PAYERS SAW A NOTABLE DECLINE IN OVERALL FINANCIAL PERFORMANCE IN 2024

Converging factors have contributed to this financial strain, including increased drug expenditures, rising medical costs due to service utilization, ongoing policy reforms, and broader macroeconomic challenges such as inflation. Drug spend has increased across all therapeutic areas, most prominently in obesity. Although other pressures may overshadow them, rare disease and specialty drug costs are key drivers of financial strain further compounding the burden on payers.

Payers' ability to manage these financial pressures varies based on their organizational structure (e.g., size, resources, degree of vertical integration) and, as a result, they are adopting varying management changes within rare disease.

2

GREATER PAYER FINANCIAL STRAIN IS DRIVING CHANGE IN RARE DISEASE MANAGEMENT

Many payers are tightening rare disease management through stricter utilization management. Smaller payers, including many regional health plans not affiliated with large national plans, are most acutely affected by growing financial pressures. As a result, many health plans are increasing documentation requirements and applying more detailed inclusion/exclusion criteria to rare disease therapies. They are also introducing more step requirements in competitive indications where multiple therapeutic alternatives exist.

In contrast, large national health plans and pharmacy benefit managers (PBMs) are better positioned to absorb these heightened financial pressures due to their scale and operational resources. As a result, some national health plans and PBMs are tightening prior authorization requirements for rare disease therapies, while others already managing rare disease restrictively are not making major changes to their management strategies.

3

MANY PAYERS ARE CONTROLLING COSTS THROUGH LIMITED SPECIALTY PHARMACY AND SITE OF CARE NETWORKS

Requiring certain rare and high-cost specialty products to be obtained through in-network specialty pharmacies allows for greater operational control, more visibility, and better reimbursement for payers. Larger, vertically-integrated payers are increasingly leveraging their operational efficiencies to contain costs through restricted specialty pharmacy procurement.

Many payers are also redirecting the administration of certain rare disease therapies away from more costly settings through site of care mandates in commercial health plans. When site of care strategies are not explicitly mandated, some health plans, including smaller regional and managed Medicaid payers, are using site of care initiatives and authorization strategies to guide rare and specialty therapy administration toward lower-cost settings such as physician offices and home health.

4

HEALTHCARE POLICY CHANGES ARE SUBSTANTIALLY INCREASING PAYERS' DRUG SPEND

Most notably, the recent Medicare Part D redesign has increased costs and reduced margins for payers due to an increase in the catastrophic coverage liability for Part D plans, which increased from 15% in 2023 to 60% in 2025. Patients also reached the catastrophic coverage phase faster than previous years due to the $2,000 out-of-pocket cap in 2025. Payers surveyed for the 2024 report anticipated taking a "wait-and-see" approach to the policy changes set to take effect in 2025, planning to hold off on re-evaluating strategies until then.

As a result of the realized increase in drug spend, some payers in the 2025 sample are implementing risk mitigation strategies. These include reducing Medicare Advantage plan offerings in certain regions, raising member premiums, restricting formularies using National Drug Code (NDC) blocks, and intensifying management efforts to control costs.

5

PAYERS ARE LEVERAGING TECHNOLOGY TO INCREASE EFFICIENCIES WITHIN ADMINISTRATIVE PROCESSES

Payers are using AI to streamline prior authorizations by scanning clinical documentation, auto-populating forms, and further optimizing the approval process. Beyond prior authorizations, innovative technologies are being applied to predictive modeling for claims patterns, underwriting, and benefit design. These tools are enabling increased accuracy in member expense forecasting, signaling a shift toward data-driven efficiency across the healthcare ecosystem. This shift reflects hypotheses outlined in the 2024 report, which anticipated that next-generation technologies would move beyond experimental use and begin driving operational efficiencies.

METHODOLOGY

Alnylam Pharmaceuticals, Inc., sponsored and developed this publication in partnership with their vendor, Guidehouse. The Commercial Health Group at Guidehouse is a leading global advisory consultancy that specializes in life sciences strategy and research services.

SURVEY DEVELOPMENT

A survey was developed to capture payer and employer sentiment on management of rare disease products. The survey was designed to assess current payer and employer practices, perspectives, and priorities, and gain insights into recent changes in the management of rare disease products as well as anticipated changes within the next plan year (2026), the next three to five plan years (2027–2031), and beyond (2031+).

The survey focused on similar themes as previous years to inform the report structure, including rare disease landscape, benefit design and utilization management, payer economics, distribution models, employer perspectives, and future trends, while also exploring themes related to payer-driven policy and technology. No specific products were assessed, although some may have been discussed in interviews as examples to further illustrate themes or trends. Potential respondents were screened for participation (see "Participant Selection and Demographics" below), and a total of 30 U.S.-based medical and pharmacy directors, employee benefit consultants (EBCs), and large employers meeting the predefined eligibility criteria were recruited to complete the survey and provided with the online link. Guidehouse partnered with a commercial vendor on Alnylam's behalf to recruit participants and transfer the survey to an online format.

RECRUITMENT AND FIELDING

Respondents were selected for relevant expertise and involvement in rare disease and specialty therapeutic product evaluation. Guidehouse informed respondents that data and insights would be aggregated, and respondent identities would remain anonymous. The authors then selected participants to ensure a mix of both medical and pharmacy directors from a variety of health plan types (e.g., commercial, Medicare Advantage, managed Medicaid affiliate), as well as a mix of stakeholders with national and regional purviews. In addition to payer respondents, the authors selected large employers and employee benefit consultant stakeholders to ensure a mix of self-funded and fully insured as well as unionized and non-unionized employer perspectives.

All participants completed the survey from September 19 to October 29, 2025. While survey respondents may choose to participate in the annual updates to the research, each sample of respondents should be considered an independent sample.

PARTICIPANT SELECTION AND DEMOGRAPHICS

Research participants were required to meet specific qualifying criteria to ensure the integrity of responses across topics. Specific prequalification criteria for payers and employers included:

- **Payers only: Current medical/pharmacy directors and/or chief data officer employed by a commercial, Medicare Advantage, or managed Medicaid payer, or a PBM;**
- **Employers/EBCs only: Current benefits directors or influential benefits decision-makers at large employer or EBC organizations with mix of self-funded and fully insured plan designs;**
- **All respondents: Past experience and current active involvement in policy development within their organization, including experience in medical and utilization management of policy development for rare disease products at their organization; and**

- **All respondents: Willingness and ability to discuss management approaches for rare products, such as new product evaluations, pharmacy and therapeutics (P&T) committee processes, innovative reimbursement model composition and implementation, distribution network determinations, and adoption of AI technology.**

QUALITATIVE INTERVIEWS

A set of individuals who completed the survey participated in interviews conducted over a 22-day period from October 15 to November 6, 2025. Fifteen respondents participated in 60-minute interviews to provide additional qualitative insight. To gain additional insights into the expected adoption of novel technological tools, a supplemental interview was held with a chief data officer (CDO) at a regional health plan. Guidehouse researchers conducted all interviews over the phone in a double-blind manner, such that no respondent knew the company supporting the research and no Alnylam employee knew which specific payer stakeholders were providing input. All interviewees provided consent for using their responses in the composition of this report.

Respondents who met all eligibility criteria and completed the survey and phone interview received honoraria according to fair market value calculations.

DATA ANALYSIS, REPORTING, AND LIMITATIONS

Guidehouse collected, analyzed, and reported survey and interview responses. Data was blinded and aggregated across the entire sample of respondents. Responses reflect each participant's views and self-reported claims of their organization's internal processes and operations. All statements and opinions contained within the report reflect responses received by payer and employer/EBC participants and do not necessarily reflect those of Alnylam or other reviewers.

PARTICIPANT SAMPLE PROFILE

Stakeholders with a strong understanding of rare and specialty product management, representing payers and employers across the United States, were selected to participate in primary research. In total, 24 payer stakeholders and six employer/EBC stakeholders were selected to complete the N=30 participant sample.

Of the 30 stakeholders selected to participate in the 2025 report, 30% represented regional health plans, 23% represented national health plans, 20% were PBMs, 20% represented large employers/EBCs, and 7% represented managed Medicaid, ensuring a mix of perspectives *(FIGURE 1)*. Payers who participated in the 2025 sample represented over 208 million total covered lives. Of the total covered lives represented by payers sampled, 57% represented the commercial book of business, 30% represented Medicare Advantage, and 13% represented managed Medicaid *(FIGURE 2)*. Regional health plans within the sample were selected to span across multiple geographic areas in the United States to ensure a representative sample.

Of the plans sampled, the percentage of commercial and Medicare Advantage rare disease drug spend was identical, with 55% under the medical benefit compared to 45% under the pharmacy benefit. For managed Medicaid plans, drug spend is slightly more pronounced within the medical benefit, with 61% of rare disease drug spend under the medical benefit compared to 39% under the pharmacy benefit.

Employer group stakeholders consisted of benefit leadership among large self-funded employers and EBCs. Of the 6 employer group stakeholders selected to participate in the 2025 report, 50% represented large employer groups and 50% represented EBCs to ensure a mix of employer perspectives *(FIGURE 3)*. Of the large employer stakeholders, 67% represented self-funded health plans while 33% represented a fully insured health plan. Within the same large employer stakeholder sample, 33% represented a majority unionized employee base, whereas 67% represented non-unionized employee bases.

FIGURE 1: **STAKEHOLDER SAMPLE PROFILE: RESEARCH SAMPLE MIX**

N=30 STAKEHOLDERS

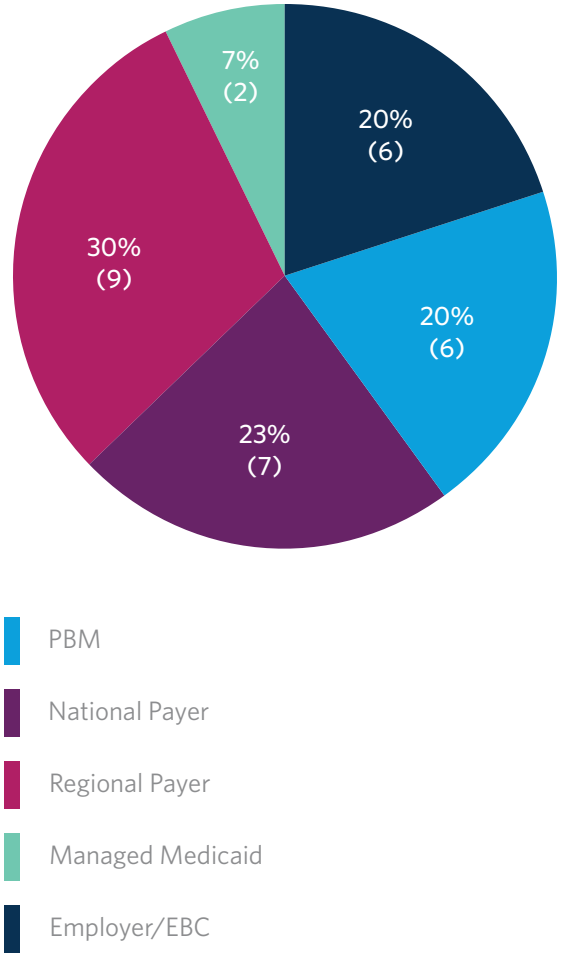
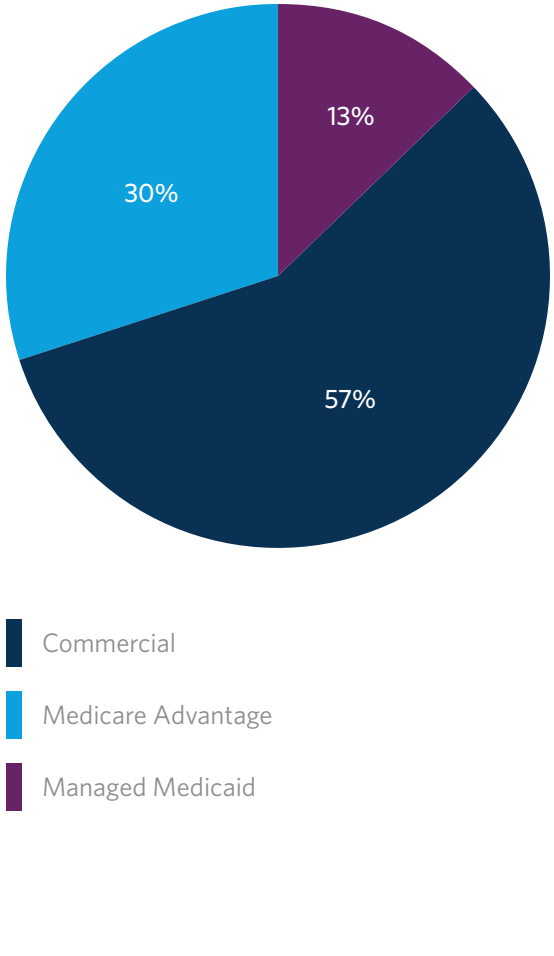


FIGURE 2: **PAYER SAMPLE COVERED LIVES MIX: COVERED LIVES MIX**

N=24 PAYERS; ~208M TOTAL COVERED LIVES



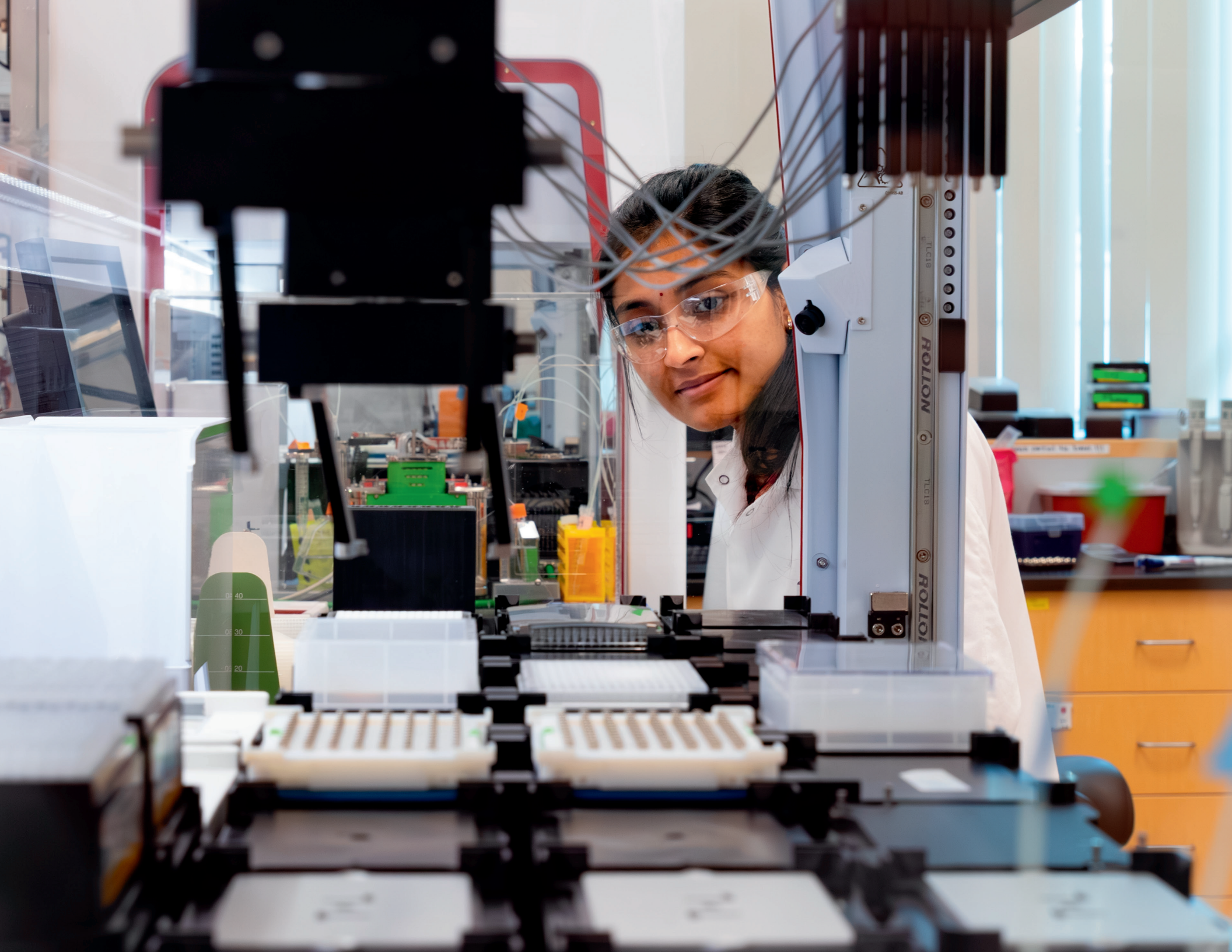
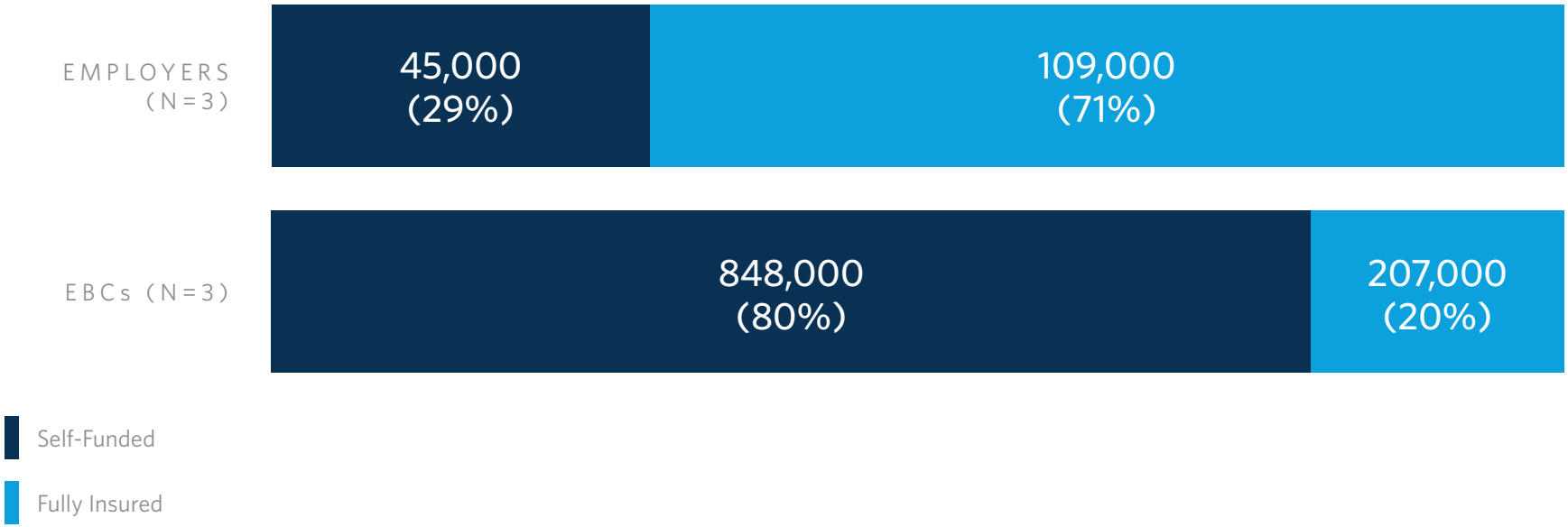

ROLLON

FIGURE 3: **EMPLOYER/EBC SAMPLE PROFILE: SELF-FUNDED VS FULLY INSURED PLANS**

N=6 EMPLOYER/EBC STAKEHOLDERS



SECTION 1:

RARE DISEASE LANDSCAPE

DRIVERS OF INCREASED FINANCIAL PRESSURES

Payers are facing a marked escalation in financial pressures in the rare disease space. Based on 2024 earnings reports, top health plans of varying sizes and revenue saw up to a 52% loss of net earnings year-over-year.

In the 2025 trend report respondent sample, U.S. payers across all segments reported intensified financial strain. Several cost drivers contributed to this, including rising drug spend, increased medical utilization and hospitalizations, and broader macroeconomic factors such as inflation. Payers reported an increase in drug spend across all therapeutic areas, but stated it was most notable within obesity, as the use of GLP-1 weight loss drugs continues to rapidly escalate. On top of changes in the therapeutic landscape, recent policy changes, such as the IRA Medicare Part D redesign, are often cited as shifting increased financial liability onto payers.

Payers' ability to manage these financial pressures varies based on their size and organizational resources. Larger, vertically-integrated national health plans and PBMs are better protected than smaller payers against these rising financial burdens but are taking steps to manage rising costs. In contrast, financial pressures are more keenly impacting smaller regional health plans unaffiliated with large national plans. As a result, these regional health plans are making more aggressive changes to management. Despite these measures aimed at curbing overall drug spend, rare and specialty therapies remain a growing source of financial concern.

DRIVERS OF RISING SPEND IN RARE DISEASE

Payers responsible for 99% of total member lives in this study noted an increase in rare disease and specialty drug spend over the past one to two years; only one small regional payer reported no change *(FIGURE 4)*. Several drivers are behind this increase. Foremost is the proliferation of new rare disease products, particularly one-time administered gene and cell therapies with multimillion-dollar price tags, which have fundamentally reshaped the cost landscape *(FIGURE 5)*. Additionally, payers consistently cite the "sticker shock" associated with the launch price of rare disease therapies, which is compounded by year-over-year price increases and limited ability to negotiate in this space. Advances in diagnostic technology and heightened disease awareness are enabling earlier and more frequent identification of rare conditions, increasing demand for specialized and often costly treatments. These converging factors underscore the urgency for payers to explore and adopt financial risk mitigation strategies to manage escalating costs.

FIGURE 4: **CHANGE IN RARE/SPECIALTY DRUG SPEND OVER THE PAST 1–2 YEARS**

PRESENTED AS % TOTAL LIVES IN PAYER SAMPLE (N=24)

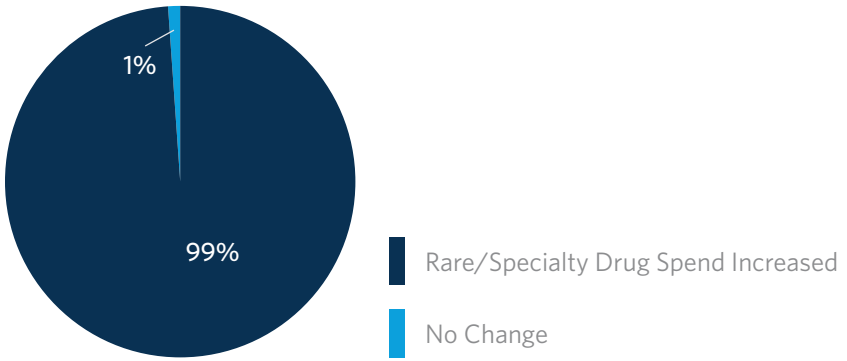
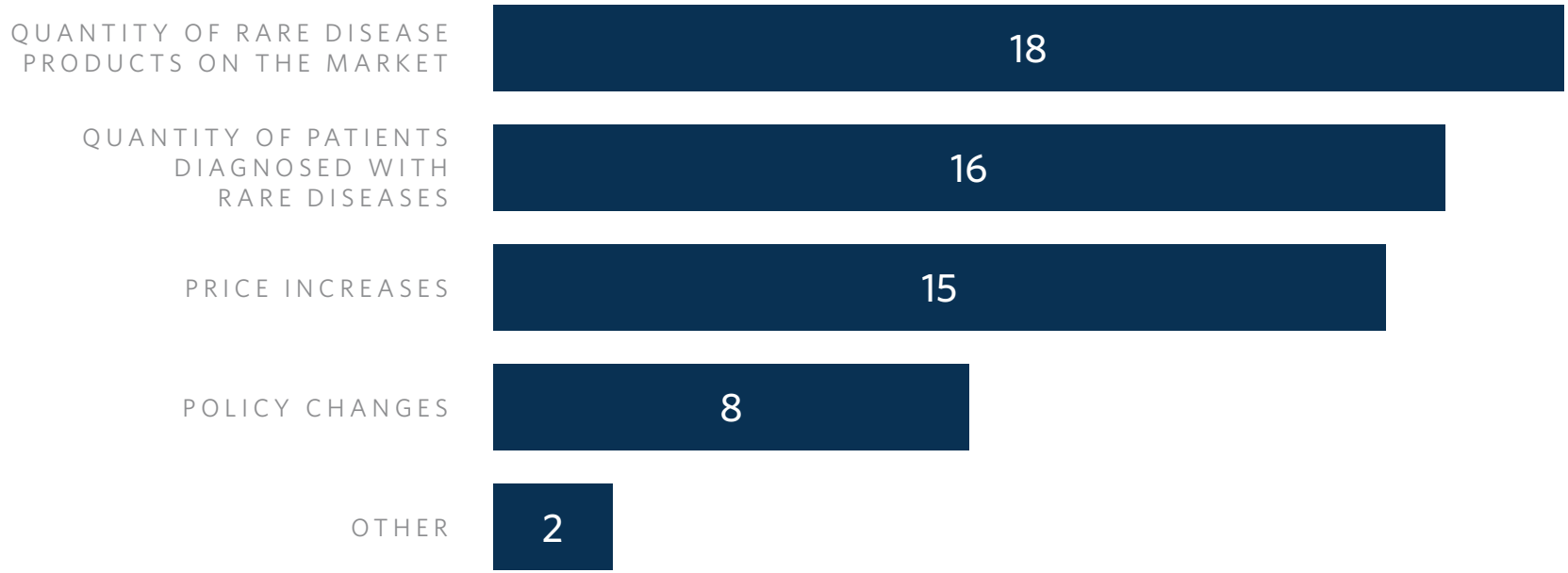


FIGURE 5: **DRIVERS OF INCREASED RARE DISEASE/SPECIALTY SPEND OVER PAST 1–2 YEARS**

PRESENTED AS COUNT OF PAYERS – MULTIPLE SELECT; N=24



"A main driver of increased financial pressure is extremely high-cost medications, and a lot of these medications fall into the rare disease category. Volume has also exploded compared to five or 10 years ago."

- MANAGED MEDICAID PAYER

"There's more available, a huge pipeline, earlier diagnosis, and a greater financial exposure. We are looking for ways to offset costs, whether it be through contracting or making prior authorization criteria more restrictive to ensure use in the most appropriate patients."

- REGIONAL PAYER

SECTION 2:

BENEFIT DESIGN AND UTILIZATION MANAGEMENT

VALUE DRIVERS ON ACCESS DECISION-MAKING

Looking at value drivers for rare disease access decision-making across the past five years, payers have consistently ranked product efficacy as the most influential factor in coverage decisions. Since 2023, efficacy, net price, and safety have remained the top three drivers shaping access strategies *(FIGURE 6)*. Overall, clinical outcomes continue to outweigh financial considerations for high-cost rare disease therapies, with four of the top five value drivers in the 2025 report rooted in clinical factors *(FIGURE 7)*. This pattern underscores payers' commitment to prioritizing therapies that deliver meaningful patient outcomes, even amid mounting financial pressures in an increasingly cost-conscious rare disease landscape.

This emphasis on clinical outcomes is shared across stakeholder groups. Payers place particular importance on therapies addressing unmet need, given the scarcity of disease-modifying treatments that provide significant clinical benefit for rare conditions. Durability, while ranked lower relative to other factors, emerged this year as a critical consideration for rare disease therapies in qualitative discussions, especially given the emergence of single-administration gene and cell therapies. Stakeholders highlighted durability as essential for ensuring long-term value and avoiding adverse budget impact from therapies that fail to deliver sustained benefit, which could force patients back to chronic or maintenance treatments. Payers frequently cited concerns with one-time therapies failing to live up to their promise as "cures" to many rare diseases.

Financial factors vary in importance by stakeholder type. Regional health plans and managed Medicaid payers, often managing smaller rare disease patient populations, place greater weight on net price and treatment cost offsets than national payers and PBMs. However, despite these differing financial priorities, payers across all segments continue to prioritize product efficacy over economic factors, reaffirming that patient outcomes remain central to coverage decisions even as financial pressures intensify.

> *"Unmet need can help increase our willingness to cover and pay for a drug. We look at it in terms of how effective the standard of care is. What is the remaining unmet need? Is it a disease-modifying treatment? Is it something to improve life expectancy? Overall, unmet need is very important."*
>
> **- NATIONAL PAYER**

> *"We are focused on durability for one-time treatments. If we're going to spend $1 million to $3 million for a one-time use drug, we want to see a near cure."*
>
> **- NATIONAL PAYER**

FIGURE 6: **2023–2025 VALUE DRIVER IMPACT ON ACCESS DECISION-MAKING FOR HIGH-COST AND RARE DISEASE**

CONTRACTING/ECONOMIC FOCUSED

= No Change ▲ Increase YoY ▼ Decrease YoY

Note on Graph: 2025 YoY increase relative to 2024

2023	2024	2025
EFFICACY	EFFICACY	EFFICACY =
SAFETY	NET PRICE	NET PRICE =
NET PRICE	SAFETY	SAFETY =
UNMET NEED	TREATMENT COST VS. SoC	UNMET NEED +1 ▲
TREATMENT COST VS. SoC	UNMET NEED	TA-SPECIFIC TREATMENT ALGORITHM +3 ▲
DIRECT TREATMENT COST OFFSETS	TOTAL BUDGET IMPACT	TREATMENT COST VS. SoC -2 ▼
TA-SPECIFIC TREATMENT ALGORITHM	DURABILITY	DURABILITY =
DURABILITY	TA-SPECIFIC TREATMENT ALGORITHM	TOTAL BUDGET IMPACT -2 ▼
INDIRECT TREATMENT COST OFFSETS	INDIRECT TREATMENT COST OFFSETS	DIRECT TREATMENT COST OFFSETS +1 ▲
	DIRECT TREATMENT COST OFFSETS	INDIRECT TREATMENT COST OFFSETS -1 ▼

FIGURE 7: **2025 VALUE DRIVER IMPACT ON ACCESS DECISION-MAKING FOR HIGH-COST AND RARE DISEASE**

CONTRACTING/ECONOMIC FOCUSED

= No Change ▲ Increase YoY ▼ Decrease YoY

Decreasing Level of Importance

	EMPLOYERS	PBMs	NATIONAL PAYERS	REGIONAL PAYERS	MANAGED MEDICAID
1	TOTAL BUDGET IMPACT *NEW*	EFFICACY =	EFFICACY =	EFFICACY =	EFFICACY =
2	NET PRICE *NEW*	SAFETY ▲	UNMET NEED ▲	NET PRICE =	NET PRICE =
3	TREATMENT COST VS. SoC *NEW*	DURABILITY ▲	TA-SPECIFIC TREATMENT ALGORITHM ▲	TREATMENT COST VS. SoC ▲	DIRECT TREATMENT COST OFFSETS ▲
4	EFFICACY *NEW*	TREATMENT COST VS. SoC =	NET PRICE ▼	SAFETY ▼	SAFETY ▼
5	DIRECT TREATMENT COST OFFSETS *NEW*	UNMET NEED =	TOTAL BUDGET IMPACT ▲	TA-SPECIFIC TREATMENT ALGORITHM ▲	INDIRECT TREATMENT COST OFFSETS ▲
6	SAFETY *NEW*	NET PRICE ▼	SAFETY ▼	DURABILITY ▲	TA-SPECIFIC TREATMENT ALGORITHM ▲
7	UNMET NEED *NEW*	TA-SPECIFIC TREATMENT ALGORITHM ▲	TREATMENT COST VS. SoC ▼	TOTAL BUDGET IMPACT ▼	DURABILITY ▼
8	INDIRECT TREATMENT COST OFFSETS *NEW*	TOTAL BUDGET IMPACT ▼	DURABILITY ▼	DIRECT TREATMENT COST OFFSETS ▲	TOTAL BUDGET IMPACT ▼
9	TA-SPECIFIC TREATMENT ALGORITHM *NEW*	DIRECT TREATMENT COST OFFSETS ▲	DIRECT TREATMENT COST OFFSETS ▲	UNMET NEED ▼	UNMET NEED ▼
10	DURABILITY *NEW*	INDIRECT TREATMENT COST OFFSETS ▼	INDIRECT TREATMENT COST OFFSETS ▲	INDIRECT TREATMENT COST OFFSETS ▼	TREATMENT COST VS. SoC ▼

MANAGEMENT OF RARE DISEASE PRODUCTS

To mitigate financial risk associated with increased spend, many payers are turning to more aggressive management strategies within rare disease than they have utilized in previous years. Given that the space has historically been managed closely, stakeholders reported looking to further tighten management wherever possible. In the 2025 sample, 93% of payers reported increasing their management of high-cost specialty and rare disease therapies over the past one to two years *(FIGURE 8)*. The degree and nature of these changes vary by organization size and structure.

Some national health plans and PBMs are increasingly restricting prior authorizations to pivotal trial inclusion and exclusion criteria for a broader range of rare disease products, requiring more frequent reauthorization intervals, and expanding the use of step therapy. Where steps were once used sparingly, rare disease drugs may now be subject to multiple steps, depending on available therapeutic alternatives. While formulary exclusions/non-coverage for rare disease drugs remain uncommon, national health plans and PBMs are signaling a willingness to exclude high-cost therapies with uncertain clinical benefit, safety concerns, or perceived inferior efficacy compared to competitors.

In many cases, smaller regional health plans are reaching even further than national payers and PBMs in adopting more restrictive prior authorization criteria and increased use of step therapy. Many regional payers are tightening requirements to include pivotal trial criteria, the presence of indication-specific biomarkers, and more extensive documentation, such as lab results and chart notes. Some are exploring custom formularies with seven to eight tiers, placing preferred and non-preferred specialty drugs on the highest tiers with the greatest member cost-sharing, albeit in limited situations.

Others are implementing “biosimilar-first” policies, requiring patients to try lower-cost options before progressing to more expensive therapies. This approach reflects the growing confidence payers have built through biosimilar use in other therapeutic areas, such as immunology, as safe and efficacious biosimilars begin to enter the rare disease space.

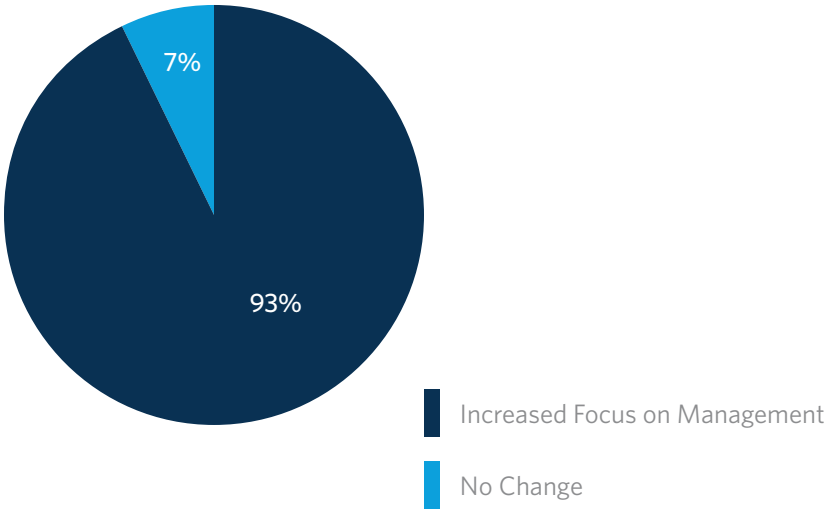
Already operating under restrictive frameworks, managed Medicaid plans continue to enforce rigorous prior authorization criteria, often aligned with pivotal trial inclusion/exclusion criteria and state-mandated requirements. Many states are moving toward standardized prior authorization criteria across Medicaid plans, aiming to streamline coverage decisions and provide equitable access while containing costs.

Employers are also making changes to address rising spend. Many employer groups are applying prior authorization criteria beyond label and increasing the use of step therapy where applicable within the rare disease space. In addition, many smaller and mid-sized employers are increasingly either excluding one-time administered cell and gene therapies entirely or carving them out under specialty benefit coverage.

While these measures help curb spending, they also underscore the growing challenge of managing rare and specialty therapies, which remain a disproportionate driver of cost growth. As payers across all segments intensify management, the balance between access and affordability remains at the forefront of industry strategy.

FIGURE 8: **CHANGE IN MANAGEMENT OF HIGH-COST AND RARE DISEASE PRODUCTS IN THE LAST 1–2 YEARS**

PRESENTED AS % TOTAL LIVES IN PAYER SEGMENTS (N=24)



CHANGES IN PHARMACY VS. MEDICAL BENEFIT ASSIGNMENT

For rare diseases, benefit assignment (i.e., medical or pharmacy) is primarily determined by route or site of administration. When this is unclear, payers tend to shift therapies to the pharmacy benefit. Large national health plans and PBMs cite cost-saving advantages of managing rare disease drugs under the pharmacy benefit, including greater opportunities for utilization management, higher rebate capture, enhanced claims tracking, and options for patient cost-sharing through formulary tiering. Regional health plans report additional benefits such as real-time prior authorization automation, higher rebate capture, and reduced cash flow burden.

This is consistent with the 2024 report's findings across payer segments. However, payers increasingly describe benefit assignment as a critical lever for cost containment. In some cases, they consider it as effective as contracting in mitigating the financial and operational burden of high-cost specialty and rare disease therapies. These strategies underscore how mounting financial pressures are driving innovation and adaptation in benefit management.

"We're focused on prior authorizations more than anything. Restrictive prior authorization has increased. Probably a slightly higher level of step edits if there are multiple therapies. We are definitely using these more in rare disease than we were a couple years ago."

- REGIONAL PAYER

"We are absolutely seeing a shift toward drugs being increasingly managed on the pharmacy benefit side... you have a lot of financial incentives with things like higher rebates, cost predictability, and real-time prior authorization integration with our pharmacy claims system."

- PBM

GROWING USE OF CROSS-BENEFIT MANAGEMENT

The ability to integrate and operationalize management across benefits has become critical for payers with the continued influx of rare disease therapies. Of all respondents in the 2025 sample, 82% report that their organization successfully manages across benefits, up from 68% in 2024 *(FIGURE 9)*. Another 12% of respondents in the 2025 sample indicated their organization is actively working toward implementing cross-benefit management. As payers increasingly recognize that siloed management is inadequate for the complex landscape of rare disease care, more plans are actively operationalizing cross-benefit strategies.

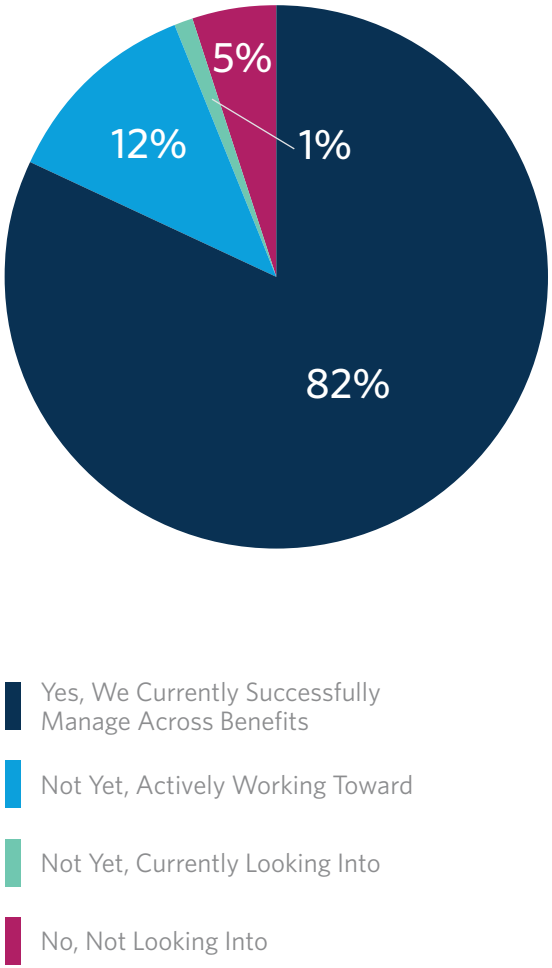
Payers consistently report enhanced coordination of step therapy and utilization management requirements across pharmacy and medical benefits. Many health plans now have the capability to operationalize a step through a pharmacy agent for a medical benefit product, a trend especially pronounced in competitive therapeutic areas with multiple routes of administration. Some plans have introduced combined benefit management drug lists to guide which therapies may be managed under either benefit, enabling more consistent cross-benefit decision-making. These approaches help ensure lower-cost or more accessible therapies are prioritized when payers perceive therapeutic assets across different benefits to hold similar efficacy and safety profiles.

Cross-benefit integration is most advanced among large vertically-integrated national health plans and PBMs, where aligned benefit reviews and streamlined processes enable consistent, coordinated decision-making. Regional and managed Medicaid health plans are also advancing these practices, using cross-benefit management to drive cost-effectiveness and support site of care strategies. Collectively, these efforts reflect a broader industry movement toward harmonized benefit design and greater operational efficiency.

> *"Managing across benefits also helps set the stage for site of care management, either soft steerage or hard restrictions, and other operational factors that are going to be important to help mitigate costs."*
>
> **- REGIONAL PAYER**

FIGURE 9: **USE OF CROSS-BENEFIT MANAGEMENT**

PRESENTED AS % TOTAL LIVES IN PAYER SEGMENTS (N=24)



2024

FIGURE 10: **MANAGEMENT OF RARE DISEASE INDICATION EXPANSIONS**

PRESENTED AS COUNT OF PAYERS - SINGLE RESPONSE; N=23

2025

FIGURE 11: **MANAGEMENT OF RARE DISEASE INDICATION EXPANSIONS**

PRESENTED AS COUNT OF PAYERS - MULTIPLE SELECT; N=24

Note on Survey Methodology: 2025 survey question allowed for "multiple select," whereas 2024 survey question limited response to one.

MANAGEMENT OF RARE DISEASE INDICATION EXPANSIONS

Management of rare diseases is rapidly evolving as therapies extend beyond traditional orphan populations into additional indications. While payers in the 2024 sample largely reported maintaining their established approaches for therapies with indication expansions, 2025 findings highlight a marked increase in management *(FIGURES 10 & 11)*. Payers are moving decisively away from legacy approaches and adopting tighter utilization management strategies. They are also taking steps to engage in more rigorous contract negotiations with manufacturers as products expand into broader populations. Payers are re-evaluating products against updated standards of care and developing indication-specific prior authorization criteria. Collectively, these actions reflect a more active and dynamic approach to rare disease management.

SECTION 3:

PAYER ECONOMICS

APPROACH TO TRADITIONAL CONTRACTING

Payers have historically faced challenges in contracting for rare disease therapies due to limited competition within many rare indications. Most rare disease therapies launch into indications with nonexistent or limited treatment options, leaving payers with minimal leverage to negotiate discounts or implement tiered formularies. This reduces the effectiveness of traditional contracting tools, such as rebates or preferred product status, since manufacturers face little pressure to offer price concessions.

As a result, contracting strategies in rare diseases have traditionally been less aggressive compared to more competitive therapeutic areas. However, payers in the 2025 sample reported a notable shift, citing increased competition in indications such as transthyretin-mediated amyloidosis (ATTR), Duchenne muscular dystrophy (DMD), familial chylomicronemia syndrome (FCS), hereditary angioedema (HAE), and spinal muscular atrophy (SMA), among others. As the set of available therapies for rare diseases has grown, payers are leaning more on contracting to manage costs, mirroring strategies used in broader therapeutic markets. Health plans typically begin by seeking deeper rebates on therapies within newly competitive rare disease categories. If rebate negotiations fail to meet their perceived value thresholds, payers often turn to utilization management tools such as step edits, prior authorization requirements, and preferential product placement on formularies to mitigate the additional budget impact.

Other specific contracting strategies are evolving to address the growing complexity of rare disease markets. Several payers indicated plans to expand formularies to include preferred and non-preferred specialty tiers, driven primarily by rebates and net pricing achieved through contracting. This expansion reflects a stronger emphasis on differentiating specialty products. Additionally, one regional health plan reported leveraging health technology assessments, such as evaluations from the Institute for the Clinical and Economic Review (ICER), to establish a baseline for negotiations on newly approved therapies.

Managed Medicaid payers surveyed in 2025 noted another significant trend in the management of rare disease drugs, highlighting that states are increasingly reclaiming control of specialty drugs to negotiate supplemental rebates directly with manufacturers. As of January 1, 2025, 40 U.S. states have value-based purchasing supplemental rebate agreements, compared to 16 in 2022.[2] This shift reflects a growing recognition that contracting remains one of the viable mechanisms for states to exert financial influence in a market where utilization controls are limited. Collectively, these strategies reinforce the continued reliance on contracting as a critical lever for cost containment in an increasingly competitive rare disease landscape.

> *"Once we get more than two [approved] drugs per MOA (mechanism of action), we look to get some contract value. And if we don't get rebates that match the value of the product, we start implementing step edits."*
>
> **- REGIONAL PAYER**

"We look at the competitive landscape by indication, and that's what we use as a basis for contracting. We also highly leverage ICER. If the manufacturer comes to market at X dollars, and ICER says it should be Y dollars, we ask the manufacturers to justify that price."

- REGIONAL PAYER

"A big trend is that many states are taking back management of specialty and rare disease drugs. They set the PA, negotiate pricing, and we just manage it with their criteria...the next step, which I guarantee is a few years down the road, is that all the states get together and negotiate with manufacturer on pricing."

- MANAGED MEDICAID

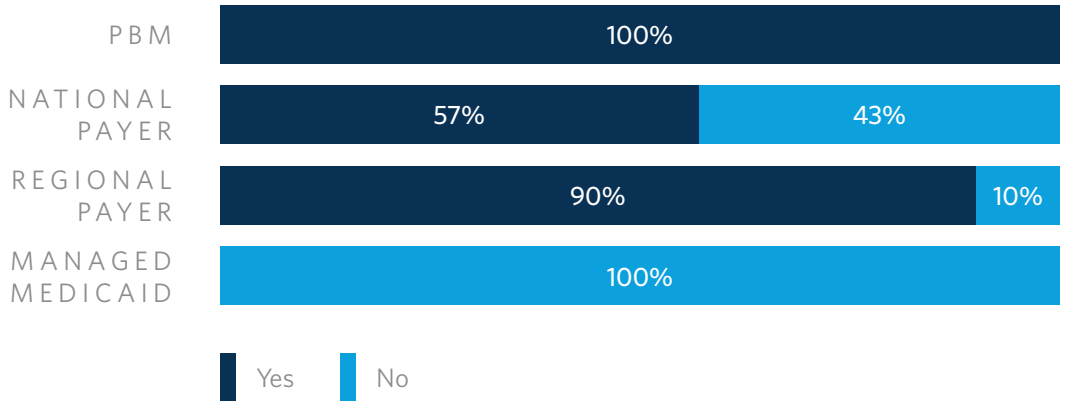
APPROACH TO INNOVATIVE CONTRACTING

In the 2022 and 2023 reports, payers projected that value-based agreements would become more widely used in rare disease contracting by 2025, particularly for high-cost cell and gene therapies. They anticipated robust adoption driven by improved data infrastructure, standardized outcome definitions, and greater manufacturer willingness to share risk, viewed as a critical safeguard given the limited competition within rare disease. While progress has been made, the reality in 2025 is more measured. Although the vast majority of payers in the 2025 sample report involvement in at least one value-based agreement, implementation remains limited to select one-time administered gene and cell therapies *(FIGURE 12)*.

Outcomes-based and warranty-style contracts are the most common value-based models in place today, but these generally remain exceptions in the rare disease landscape. Due to the limitations of innovative contracting, most payers rely on traditional contracting as their primary cost-control mechanism, signaling that the vision outlined in earlier reports has not fully materialized.

FIGURE 12: **CURRENT ENGAGEMENT IN INNOVATIVE CONTRACTING MODELS FOR RARE DISEASE PRODUCTS**

PRESENTED AS % TOTAL LIVES IN PAYER SEGMENTS; N=24



IMPLEMENTATION BARRIERS TO VALUE-BASED CONTRACTS

The gap between expectation and execution of innovative value-based contracts persists due to significant operational and structural challenges. Defining clinically meaningful and measurable outcomes remains complex, particularly for therapies with long-term efficacy profiles where durability is uncertain. Member churn and fragmented data systems complicate tracking patient data over extended periods, making it difficult to validate outcomes and enforce contract terms. Financial risk-sharing models face resistance because of uncertainty around treatment durability, the administrative burden of managing these agreements, and other ethical considerations. These hurdles, repeatedly highlighted in prior reports, continue to limit scalability.

Value-based implementation challenges are not unique to the rare disease space. In fact, low disease prevalence rates and low patient numbers were noted as barriers by payers, but least in relation to all other barriers in the 2025 sample *(FIGURE 13)*. This signals these challenges apply to all value-based agreements, agnostic of therapeutic area. Looking ahead, payers anticipate incremental growth in innovative contracting as more one-time administered high-cost therapies enter the market. However, widespread adoption will require overcoming several challenges. At a high level, this includes advances in data infrastructure, payer-manufacturer collaboration, and clearer regulatory frameworks. Operationally, it involves aligning on measurable outcomes, improving longitudinal data capture, and reducing administrative burden.

FIGURE 13: **CURRENT BARRIERS TO ESTABLISHING INNOVATIVE CONTRACTING MODELS FOR RARE DISEASE PRODUCTS**

PRESENTED AS COUNT OF PAYERS – MULTIPLE SELECT; N=24

SECTION 4:

DISTRIBUTION MODELS AND SITE OF CARE

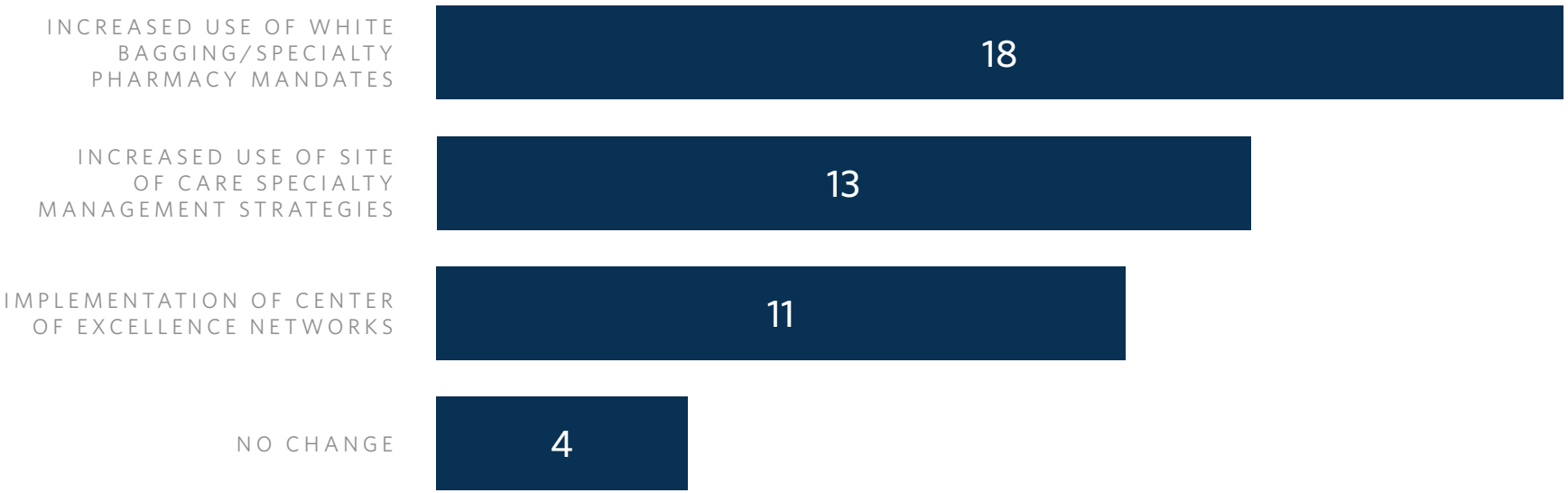
EVOLUTION OF RARE DISEASE DISTRIBUTION AND PROCUREMENT

Previous editions of this report anticipated payers would increasingly leverage specialty pharmacy requirements and site of care restrictions for rare disease therapies to maximize efficiencies and control costs. In 2022, most payers reported limited use of specialty pharmacy and site of care controls but projected significant growth in these strategies over the next three to five years. In 2023, vertically integrated national health plans and PBMs began piloting more assertive specialty pharmacy mandates and formalizing site of care policies. The 2024 report revealed further uptake, as a growing share of payers considered themselves vertically integrated and equipped to implement cost-containing procurement and administration strategies for many specialty and rare disease drugs.

By 2025, these trends have moved closer to full realization. A large majority of payers report increased use of white bagging (the required distribution of medications from a specialty pharmacy directly to a provider for administration) and site of care strategies for rare disease therapy administration *(FIGURE 14)*. Facing heightened financial pressures, payers are layering these advanced cost-control levers atop traditional management tactics.

FIGURE 14: **EVOLUTION OF APPROACH TO SPECIALTY/RARE DISEASE DISTRIBUTION AND PROCUREMENT OVER THE PAST 1–2 YEARS**

PRESENTED AS COUNT OF PAYERS – MULTIPLE SELECT; N=24



PREFERRED SPECIALTY PHARMACY PROCUREMENT AND DISTRIBUTION

Payers are routinely white bagging specialty and rare disease drugs under the medical benefit, requiring these therapies to be procured through specialty pharmacies. Many 2025 stakeholders noted this trend has rapidly increased in the past year, with regional payers noting a particular surge within the past six to eight months at the time of the research. In some instances, vertically-integrated organizations mandate procurement through their in-house specialty pharmacy, though this remains an exception. Stakeholders cited numerous incentives to white bag, including the ability to secure contracts with deeper pricing discounts compared to buy-and-bill. This approach also enhances operational control and visibility, allowing payers to pass cost savings onto members via cost-sharing adjustments.

Payers reported that some providers may prefer the white bagging model for rare disease and specialty therapies, as it allows them to avoid the financial cash flow exposure and administrative burden associated with buy-and-bill procurement. However, they noted this preference is not universal. Some hospital systems may seek greater utilization under buy-and-bill largely due to financial incentives of the 340B Drug Pricing Program.

Restrictions requiring prescriptions for rare disease therapies to be filled by a preferred specialty pharmacy are less common under the pharmacy benefit, though some national payers are beginning to apply these policies to a small subset of drugs with unique safety and handling risks. Specialty pharmacies offer adherence programs, patient education, and monitoring, which can improve member experience and outcomes for complex therapies.

> *"We require white bagging because we can buy medications cheaper than physician offices. The doctors aren't always thrilled, but we want to save the client money."*
>
> **- PBM**

APPROACH TO SITE OF CARE POLICIES

Under the medical benefit, site of care restrictions have likewise evolved as a key strategy for controlling costs and optimizing patient outcomes in rare disease therapy administration. Implementation approaches vary significantly by payer, largely influenced by organizational size and specific member needs *(FIGURE 15)*. National health plans typically enforce the most rigorous site of care mandates, leveraging operational scale and integrated networks to maximize cost savings and efficiency. These policies aim to redirect patients away from hospital outpatient departments toward lower-cost settings such as physician offices, ambulatory infusion centers, or home infusion. Criteria for these mandates often cite patient safety, clinical appropriateness, and improved operational efficiencies to support the site of care restrictions.

Regional health plans generally adopt a more flexible approach, favoring soft steerage through site of care initiatives rather than strict enforcement. Given their limited size, these payers generally have a heightened sensitivity to member dissatisfaction and therefore encourage, rather than mandate, the use of lower-cost sites. However, rising expenses are making soft steerage increasingly unsustainable, pushing regional plans toward more aggressive management even as tighter controls remain difficult to implement within local provider networks. Despite these constraints, regional plans share the

same core objectives as national payers, as they seek to maintain high standards for patient safety and outcomes while reducing dependence on hospital outpatient departments.

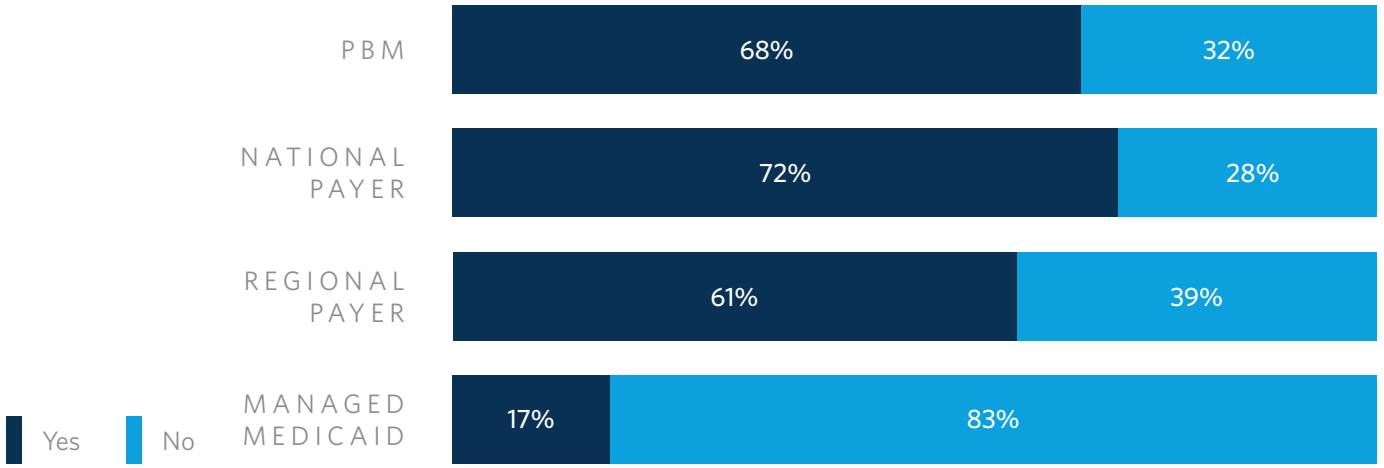
Managed Medicaid payers are the least likely to impose site of care restrictions, as state-level regulations and a focus on access for vulnerable populations require broader flexibility and case-by-case exceptions. When site of care mandates are applied, they often use an authorization process that evaluates patient status and therapy safety profiles. For patients with greater care needs or therapies with higher risk, site of care criteria are typically relaxed. Collectively, these strategies reflect a growing emphasis on aligning clinical appropriateness and patient satisfaction with cost efficiency across diverse payer segments.

> *"Number one, the goal is to steer away from the hospital outpatient department. Number two is to steer toward home infusion, especially for companies that are vertically integrated."*
>
> **- NATIONAL PAYER**

> *"We're utilizing certain kinds of operational cost control levers with site of care management, and it's become really critical. But we don't have any mandates in place, so I would call it a soft steerage, where we can triage patients between sites of care."*
>
> **- REGIONAL PAYER**

FIGURE 15: **USE OF SITE CARE MANAGEMENT STRATEGIES FOR HIGH COST THERAPIES**

PRESENTED AS % OF TOTAL LIVES IN PAYER SEGMENTS; N=24



SECTION 5:

EMPLOYER TRENDS

ONGOING SHIFT TOWARD SELF-FUNDED ARRANGEMENTS

Employer groups continue to show a slow but notable shift toward self-funded plan designs, driven by the desire for greater flexibility in benefit design and cost control, with self-funded models now accounting for 67% of all employer-sponsored health plans.[3] These plans are also increasingly being adopted by employers of all sizes that work closely with benefit consultants to customize rare disease coverage. This shift to self-funded health plans reflects employers' intent to proactively manage rising healthcare costs and maintain control over plan design, especially as rare disease therapies bring unpredictable financial exposure. In contrast, fully insured employers remain tied to standardized benefit packages managed by health plans and PBMs. This is often due to limited internal resources and greater risk aversion to catastrophic claims, which reduces their ability to tailor coverage for rare disease drugs.

EVOLVING EMPLOYER RISK MANAGEMENT TECHNIQUES

To address the volatility of claims associated with rare disease therapies, self-funded employers are continuing to adopt financial risk mitigation tools such as stop-loss insurance and reinsurance, a trend consistent with findings from the 2024 report *(FIGURE 16)*. These strategies provide a critical safety net against catastrophic claims. Payers report that underwriting and predictive analytics are being used to help employers assess exposure and guide coverage decisions for these therapies. While stop-loss remains the most common approach, employers are also exploring layered strategies, including selective coverage and optional riders, aiming to achieve better financial sustainability.

Carve-outs for rare disease therapies are emerging as an additional lever for employers seeking to manage financial risk. Payers note carve-outs allow employers to exclude certain ultra-high-cost therapies from their core benefit design, often shifting coverage responsibility to third-party programs or specialty vendors through a separate insurance policy. In the 2024 report, large self-funded employers anticipated a greater use of carve-outs for the broader class of rare disease products to better manage these risks. However, in 2025, their use remains focused on one-time cell and gene therapies.

Employers pursue carve-outs for rare disease drugs less commonly outside of cell and gene therapies, largely due to concerns about the administrative burden and potential impact on employee health outcomes. Payers reported small- to mid-size employers are more likely to carve out cell and gene therapies, since a one-time administered high-cost therapy may represent a sizable portion of their budget and threaten financial stability. In contrast, large employers are more likely to cover these therapies and utilize reinsurance or stop loss. This is likely due to their scale and ability to absorb financial shocks, along with their ability to navigate the complex administrative processes associated with these risk mitigation tools. Overall, carve-outs are viewed as a targeted solution for mitigating catastrophic financial exposure rather than a broad-based strategy for rare disease management.

"With more approvals coming through the pipeline, it's going to continue to put pressure on employers, and they are going to take measures like carve-outs, or carving out to a third party, or not covering at all."

- NATIONAL PAYER

Self-funded employers that actively manage rare disease therapies are adopting more aggressive utilization controls to help balance cost and access. These strategies most often include restricting pharmacy networks to reduce spend. They also involve implementing custom formularies that prioritize cost-effective options and increasing the use of step therapy protocols so lower-cost alternatives are tried first. Self-funded employers are also tightening clinical criteria for coverage, requiring more robust documentation and evidence of medical necessity for approval. These measures reflect a deliberate shift toward more structured benefit management among actively managed plans as specialty drug costs continue to rise.

"Self-funded employer groups are engaging in increased use of closed formularies, increased use of criteria, and increased use of steps, specifically through lower-cost therapies like biosimilars or generics, if they're available."

- REGIONAL PAYER

LEVERAGING EMPLOYEE BENEFIT CONSULTANTS

Employer groups continue to depend on EBCs to navigate the growing complexity of benefit design and the financial risks associated with rare disease coverage. EBCs help plan sponsors manage specialty and rare disease therapy costs through PBM contract optimization, prior authorization and clinical management, and financial protections such as stop-loss or reinsurance. For unionized employers, core plan design is often fixed due to collective bargaining agreements. However, EBCs help employers identify areas where some flexibility exists, such as in supplemental or third-party programs, to enhance benefits or manage costs without renegotiating the entire plan.

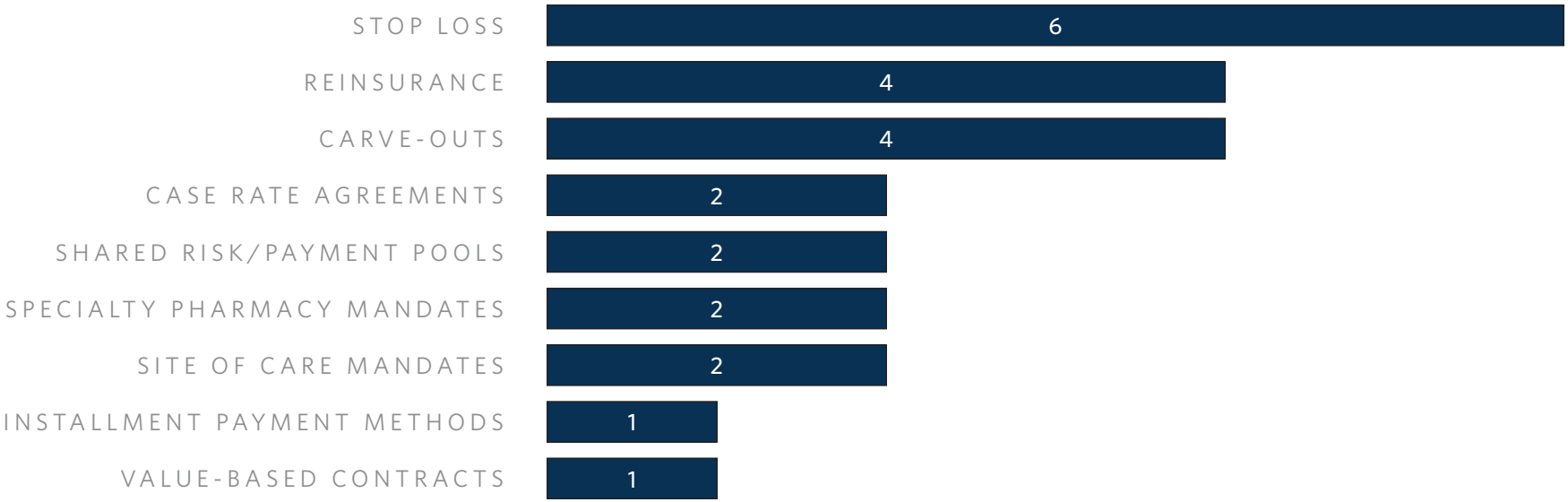
Employers also depend on EBCs to provide insights on market trends, emerging therapies, and competitive benchmarks, with EBCs often serving as the first point of evaluation for rare disease strategies. Once an employer decides to cover a drug class or adopt a new program, they typically collaborate with payers or third-party administrators. These partners help implement effective contracting and management strategies that help keep the plans competitive and financially sustainable.

"It starts at the plan sponsor level. If they decide yes, we are going to cover, then they're all in play, and it falls to the plan administrator to determine how to best manage the cost of this category."

- EMPLOYEE BENEFIT CONSULTANT

FIGURE 16: **EMPLOYER STRATEGIES TO MANAGE EXTREME HIGH-COST CLAIMS**

PRESENTED AS COUNT OF EMPLOYERS – MULTIPLE SELECT; N=6



ALYSSA,
gene positive for Huntington's Disease, USA

SECTION 6:

PAYER-DRIVEN POLICY

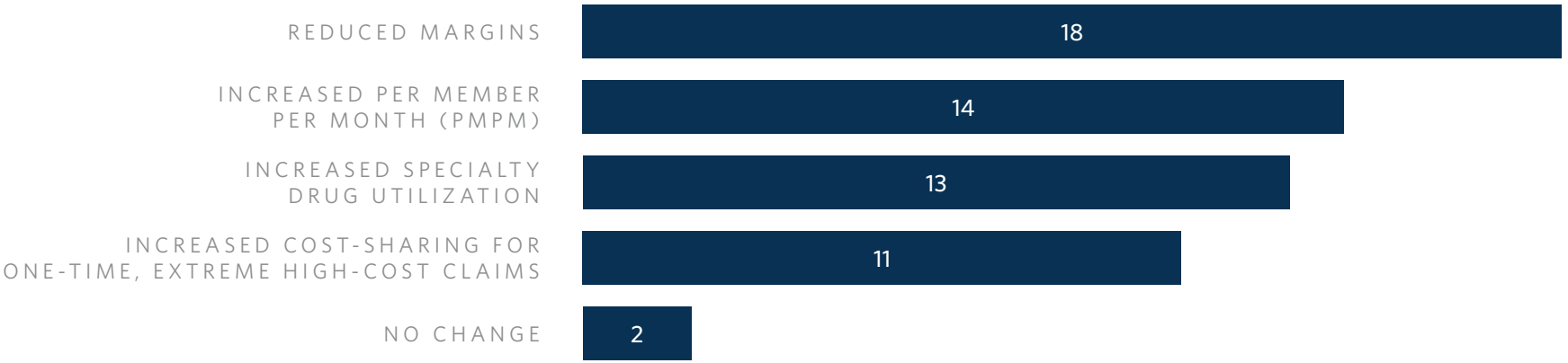
IMPACTS OF THE FULL MEDICARE PART D REDESIGN IMPLEMENTATION

The full implementation of the Inflation Reduction Act (IRA) Medicare Part D redesign took effect on January 1, 2025, and fundamentally reshaped the payer landscape by intensifying both financial pressures and operational complexity. The redesign substantially lowered Medicare patients' Part D out-of-pocket maximum and increased the payer share of costs in the catastrophic coverage phase. These policy changes have resulted in a significant rise in drug spend for payers offering Medicare Part D plans. At the same time, some stakeholders noted the reduced patient cost-sharing enabled individuals who previously could not afford specialty medications to access these therapies, potentially improving treatment adherence and outcomes. With the new $2,000 out-of-pocket cap for 2025, a substantially higher number of patients reached the catastrophic coverage phase than did with the $8,000 threshold in 2024.[4] Concurrently, as more patients entered the catastrophic coverage phase, payers' share of coverage rose to 60%, a sharp increase from 15% in 2023 and 20% in 2024.

Payers surveyed in 2025 noted their organizations were already experiencing reduced margins and increased per-member-per-month costs (PMPM), among other financial challenges from the increased liability in the Part D redesign *(FIGURE 17)*. While still in early stages, some stakeholders have also observed measurable spillover effects into the medical benefit, as payers reassess cross-benefit cost pressures. In response, many payer organizations in 2025 moved beyond the "wait and see" stance noted in the 2024 trend report and began implementing risk-mitigation strategies.

FIGURE 17: **EFFECTS OF MEDICARE PART D REDESIGN**

PRESENTED AS COUNT OF PAYERS – MULTIPLE SELECT; N=24



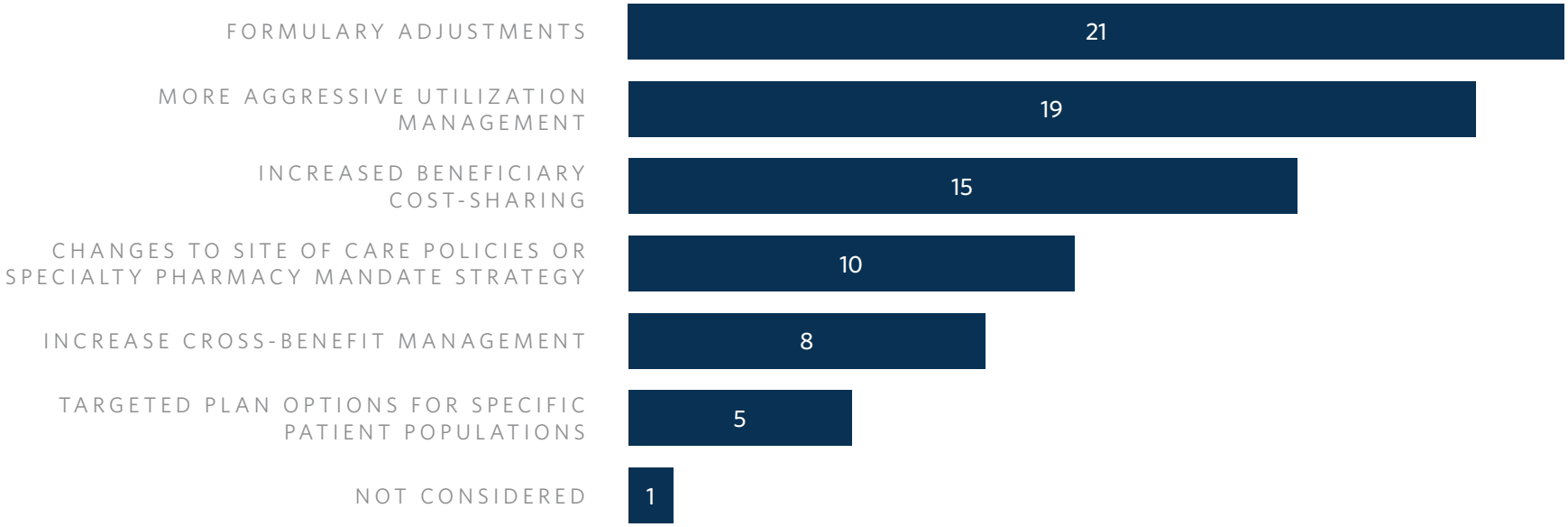
MEDICARE PART D REDESIGN MITIGATION STRATEGIES

Although the Medicare Part D redesign's most pronounced impacts have been in therapeutic areas like oncology and cardiology, the resulting financial risk mitigation strategies are increasingly shaping the management of rare disease therapies as well. Many payers have made formulary adjustments, including moving high-cost products to specialty tiers or removing them from formularies *(FIGURE 18)*. Many payers continue to adopt stringent utilization management tools to control costs for high-priced products, including expanded prior authorization, step therapy, and specialist documentation requirements.

Several organizations have reduced their Medicare Advantage plan offerings in regions where the new cost structure renders participation unsustainable, with some exiting these markets entirely. This strategic retrenchment reflects efforts by payers to limit exposure to the most severe financial pressures. Collectively, these actions reflect a decisive industry pivot toward increasingly restrictive management.

FIGURE 18: **STRATEGIES UNDER CONSIDERATION TO MITIGATE IMPACT OF PART D REDESIGN**

PRESENTED AS COUNT OF PAYERS – MULTIPLE SELECT; N=24



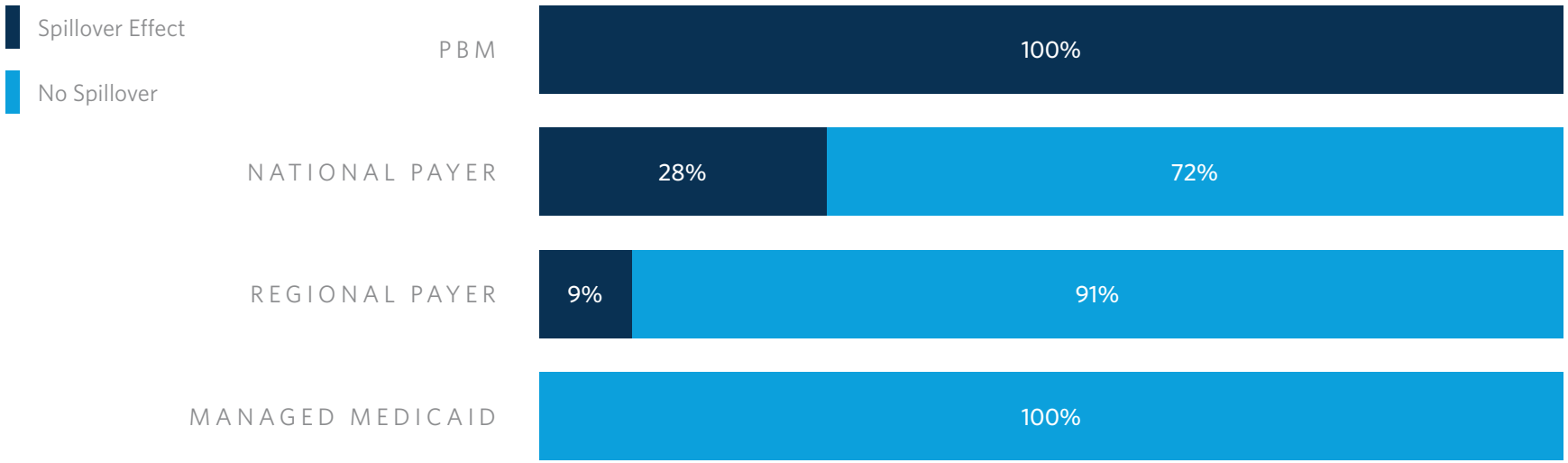
SPILLOVER EFFECTS ON COMMERCIAL PLANS AND EMPLOYER GROUPS

The financial impacts of the Part D redesign are also extending into the commercial market. As payers absorb higher liabilities in their Medicare Advantage books of business, some are tightening formularies, increasing cost-sharing, and raising premiums in commercial books of business to offset losses. This cross-segment impact is most notable among PBMs *(FIGURE 19)*. All PBM respondents in the 2025 report noted a spillover into commercial plan management due to the higher Medicare Advantage plan costs. The same is true for many EBCs who indicated many of their employer clients have seen drug costs rise, further highlighting how sweeping policy changes can drive broader shifts in benefit design and cost management strategies.

> *"With the $2,000 OOP max, the elimination of the coverage gap, the liability was shifted onto plans and manufacturers. We've made the most negative formulary changes to our formulary, maybe ever."*
>
> **- REGIONAL PAYER**

FIGURE 19: **SPILLOVER EFFECT OF MEDICARE PART D REDESIGN TO PAYERS' COMMERCIAL BOOK OF BUSINESS**

PRESENTED AS % TOTAL LIVES IN PAYER SEGMENTS; N=24



PAUL,
diagnosed with ATTR amyloidosis, UK

"When Medicare saves money, the cost differential is typically shifted onto employers. Employer cost shifting as a result of government program savings is a big problem for us."

- EMPLOYEE BENEFIT CONSULTANT

ADDITIONAL PAYER-DRIVEN POLICY CONSIDERATIONS

Beyond the IRA Medicare Part D redesign, payers are closely tracking emerging policy developments with the potential to significantly impact rare disease management. When interviewed in 2025, many payers and employers expressed uncertainty about policy changes that have yet to be implemented, but some offered forward-looking insights.

The "One Big Beautiful Bill Act" (OBBBA) is particularly relevant to managed Medicaid organizations, as it introduces new Medicaid eligibility and redetermination requirements. Beginning in 2027, certain beneficiaries must reapply for coverage every six months and complete at least 80 hours per month of work, community service, or vocational training. Stakeholders anticipate this change could lead to substantial fluctuations in Medicaid membership and funding, creating uncertainty and potentially disrupting continuity of care for patients, including those with time-sensitive rare disease treatment needs. Many payers expressed a desire to actively engage Medicaid beneficiaries at risk of losing coverage to help them navigate the new administrative requirements for enrollment.

Payers acknowledge the evolving policy landscape is difficult to monitor and has increased operational burden. Yet, most payers remain committed to avoiding overly restrictive management approaches unless necessary. Collectively, these shifting policy dynamics are prompting payers to remain vigilant and adaptable. They recognize the cumulative effect of these changes may require innovation in benefit design, contracting, and care management to help ensure sustainable access to rare disease treatments.

GABI,
diagnosed with ATTR amyloidosis,
Germany

SECTION 7:

TECHNOLOGY

EVOLVING APPLICATIONS OF TECHNOLOGY IN 2025

Technology adoption in the rare disease space became more widespread and operationalized in 2025 compared to previous years. While the 2024 report highlighted slow uptake primarily due to budget priorities, compliance uncertainties, and technical complications, artificial intelligence (AI) technology is now a core component of administrative processes. In 2025, 90% of payers and employers reported using AI technology to streamline administrative tasks that generally do not require human decision-making *(FIGURE 20)*.

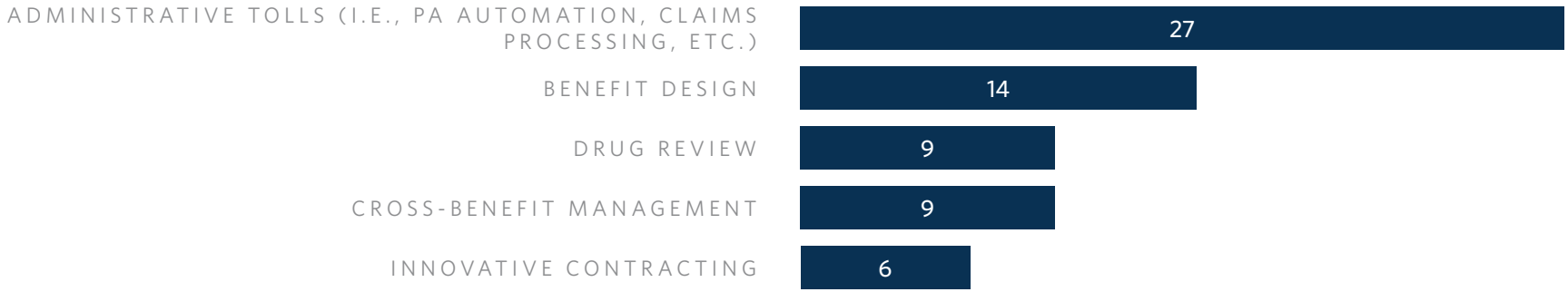
Most payers report using AI-driven tools for claims processing, prior authorization automation, and in certain cases, pre-approvals. However, they remain cautious about automating approvals in the rare disease space due to the high level of importance and subjectivity involved in such decisions. Payers also state that humans make all final decisions of a prior authorization request. This reflects ongoing disallowance to fully automate clinical or coverage determinations, reinforcing the 2024 sentiment that human judgment remains essential in these sensitive areas.

Though far less prevalent, benefit design emerged as the next most common application of technology, with some payers leveraging AI for predictive modeling related to disease progression and total cost of care. Some larger payers are now partnering with specialty care management vendors and leveraging predictive analytics and underwriting to identify high-risk members early, enabling more proactive interventions and resource allocation.

Differences in technology adoption are evident across payer types. Large national health plans and PBMs tend to be early adopters, integrating AI into their workflows with greater confidence and scale. Regional health plans use technology and AI in similar administrative applications as larger payers. However, due to their smaller size, more limited resources, and higher potential risk exposure, regional health plans are proceeding cautiously, monitoring how larger payers implement technology and how successful they are before investing themselves. Overall, 2025 report findings mark a turning point for payers, as technology evolves from basic automation to a strategic driver of efficiency and risk management, all while human oversight remains a critical safeguard in the rare disease space.

FIGURE 20: **APPLICATIONS OF TECHNOLOGY AT PAYER AND EMPLOYER ORGANIZATIONS**

PRESENTED AS COUNT – MULTIPLE SELECT; N=30



DATA STANDARDIZATION AND AUTOMATION IN RARE DISEASE MANAGEMENT

To further understand the evolving landscape of technology adoption in the rare disease space, a supplemental interview was conducted with a chief data officer (CDO) at a regional health plan. According to the CDO, payers in 2025 are modernizing legacy mainframe systems and strategically deploying AI, cloud-based platforms, and advanced data aggregation tools to address persistent challenges in rare disease management. A central goal for payers focuses on improving the interoperability of fragmented clinical and claims data across payers, providers, and health information exchanges to enable earlier patient identification. AI-driven data normalization is used to standardize this information by aligning different formats, codes, and terminology to help identify rare disease patients earlier and more reliably. Partnerships with data aggregators and the use of advanced natural language processing (NLP) help merge and enrich clinical and claims data, supporting more accurate risk modeling.

AI is also being applied to scenario modeling for benefit design and member engagement tools. Partnerships with data analytics organizations specializing in healthcare and life sciences enable payers to analyze small, complex patient populations with high accuracy, informing both internal guidelines and contracting strategies. Investments in member engagement platforms are complementing these innovations, leveraging automation and AI to simplify care coordination, personalize outreach, and support rare disease patients. Collectively, these efforts are fostering a more data-driven, collaborative, and patient-centered approach to rare disease management.

FUTURE USE OF TECHNOLOGY IN RARE DISEASE

Looking ahead, payers interviewed in 2025 anticipate AI will play a growing role in rare disease management, especially in areas such as analyzing claims data to uncover cost drivers and care patterns, reviewing real-world evidence (RWE), and generating total cost of care insights. Over the next one to three years, many expect AI to support functions like trend identification, claims-based recommendations, and even aspects of value-based contracting by tracking outcomes and financial performance. Meanwhile, employers generally foresee minimal changes ahead in the use of AI in coverage decisions, acknowledging potential benefits for financial predictability but emphasizing the ongoing need for human oversight.

Despite these advances, stakeholders continue to navigate ethical, compliance, and interoperability concerns. These factors are limiting broader adoption of AI and technology, especially in direct clinical decision-making. Across the board, consensus shows technology will serve as a powerful complement to—not a replacement for—human decision-makers as technology matures.

"We have been a pioneer in the AI space, but one thing is going to be very clear, AI will never deny the case. A medical director would have to review the case before a denial."

- NATIONAL PAYER

"We use AI tools to underwrite risk and assist with benefit design. We look at how fast people are getting through deductibles and how coinsurance is being maxed. Those tools can be very helpful and predictive."

- PBM

SECTION 8:

FUTURE RARE DISEASE TRENDS

INCREASING RARE DISEASE THERAPY APPROVALS

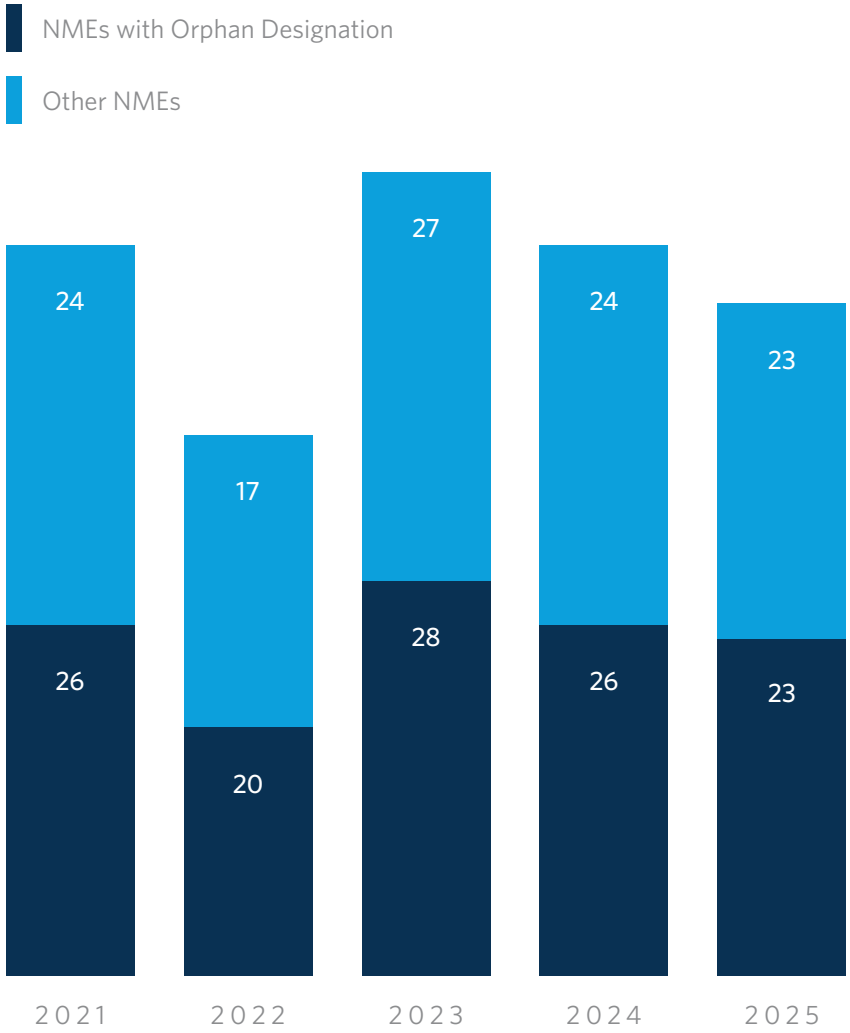
The rare disease therapy market continues to expand, with stakeholders identifying the growth in new product launches and indication expansions as the most significant trends shaping its future. Orphan drugs now consistently account for over half of new molecular entities, and this steady increase in approvals is expected to persist, driving stronger competition across certain rare indications and reshaping market dynamics *(FIGURE 21)*.

Payers recognize this new level of competition may provide them with more leverage for contracting. As more therapies are approved to treat the same rare condition with comparable efficacy, safety, and guideline support, traditional contracting and rebating strategies are set to play a larger role in the rare disease space. Payers and PBMs anticipate using their negotiating power to secure deeper discounts through access-based agreements and formulary preferencing. This evolving environment enhances payer influence and has the potential to broaden treatment options and improve affordability for patients.

"We are going to see more therapies for certain rare diseases. As competition increases, manufacturers will look to provide discounts to secure favorable access."

- NATIONAL PAYER

FIGURE 21: **FDA NOVEL DRUG APPROVALS (NEW MOLECULAR ENTITIES) BY YEAR[1,5-8]**



TIGHTENING PRIOR AUTHORIZATION AND SITE OF CARE MANAGEMENT

Payers expect to continue to apply more stringent utilization management to a growing number of rare disease therapies, particularly through the use of prior authorization and site of care restrictions. The evolution from prior authorization to label toward more restrictive inclusion/exclusion criteria and multi-step documentation reflects a wider industry shift toward maximizing clinical appropriateness.

Reauthorization requirements are also becoming more rigorous, with intervals and criteria increasingly defined by clinical trial data to ensure ongoing patient response and appropriate continuation of therapy. These heightened requirements will continue to impact prior authorization throughput and timing, driving increased staffing needs and accelerating the adoption of technology solutions to streamline and automate the review process.

Site of care requirements that steer patients away from high-cost hospital outpatient departments to lower-cost infusion centers or home settings are projected to expand, though their implementation will continue to depend on patient status, therapeutic safety, and specific state policy. As payers refine these strategies, many are investing in triage platforms and operational tools to help identify the most appropriate and cost-effective care setting for each patient. Collectively, these measures are designed to ensure access to rare disease therapies remains both clinically justified and financially sustainable.

> *"Product-specific evaluation is going to be reviewed under a microscope. If we're going to cover a drug that's six figures, we're going to have really detailed criteria to make sure it's used for the right patients."*
>
> **- NATIONAL PAYER**

GRACE,
diagnosed with PH1,
UK

SECTION 9:

CONCLUSION

The sixth annual Alnylam Rare Disease Trend report builds on prior years' research and analyses, offering a comprehensive view of how payers and employers are navigating the ever-evolving landscape of rare disease management. This year's findings underscore the intensifying financial strain on these stakeholders, driven by escalating costs, the expanding rare disease pipeline, and the cumulative impact of recent policy reforms and initiatives.

Payers and employers are closely monitoring the cumulative effects of ongoing regulatory changes, most notably the Inflation Reduction Act's Medicare Part D redesign due to the shift in cost-share contributions. Additional developments, such as new Medicaid redetermination requirements, expiration of enhanced premium tax credits for Affordable Care Act plans, and other recent public policy actions are expected to impact funding, formulary management, and patient access. The rapidly changing and uncertain policy environment is prompting stakeholders to re-evaluate their management strategies, with many anticipating additional shifts in benefit design and contracting in response to forthcoming policy developments. Future Alnylam Rare Disease Trend reports will continue to examine the impact of these changes and highlight the strategies payers and employers adopt in response.

As financial challenges increase, payers are adopting stricter cost-control strategies to provide access while managing risk. Payers are broadening their use of prior authorizations, expanding specialty pharmacy and site of care mandates, and in select cases, developing custom formularies with higher cost-sharing tiers. Employers are increasingly shifting toward self-funded arrangements and adopting risk mitigation tools, including carving out ultra-high-cost therapies and transferring coverage responsibility to third-party programs or specialty vendors. Benefit consultants continue to play a critical role in guiding plan design and helping employers navigate these intricate and complex decisions.

Technology adoption continues to accelerate, with AI now widely used for administrative functions such as claims processing and prior authorization automation. Larger payers are leveraging predictive analytics and data standardization to identify high-risk members and optimize resource allocation, while smaller organizations are cautiously expanding their use of digital tools. Although stakeholders anticipate further implementation of advanced technologies, human oversight remains essential, particularly in decision-making for rare disease therapies.

The Rare Disease Trend report offers insights to help U.S. payers, employers, and manufacturers anticipate, understand, and navigate emerging trends in rare disease management. In the next issue, the report will continue to explore how the growing rare disease pipeline, legislative policies, and technological advances are reshaping management and contracting strategies, as stakeholders work to balance patient access with affordability.

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GLOSSARY

1. **Reinsurance:** Insurance purchased by an insurance company from another insurer to reduce its risk exposure on policies it has issued.
2. **Rider:** An add-on or amendment to an insurance policy that provides additional coverage or modifies the terms of the original policy.
3. **Stop-loss insurance:** A financial protection mechanism that limits an insurer or employer's liability by capping the amount they pay for claims beyond a specified threshold.
4. **White bagging:** A payer practice where specialty medications are dispensed by an external pharmacy and shipped directly to a healthcare provider for administration to the patient.

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*A heartfelt thank you to **Folger Tuggle** for his continued contributions to the Alnylam Specialty & Rare Disease Trend Report. Throughout his distinguished career, Folger has been a passionate advocate for patient access to rare disease therapies. We are grateful for his service and wish him all the best in a well-deserved retirement.*

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