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Innovative Financing for Novel Therapies

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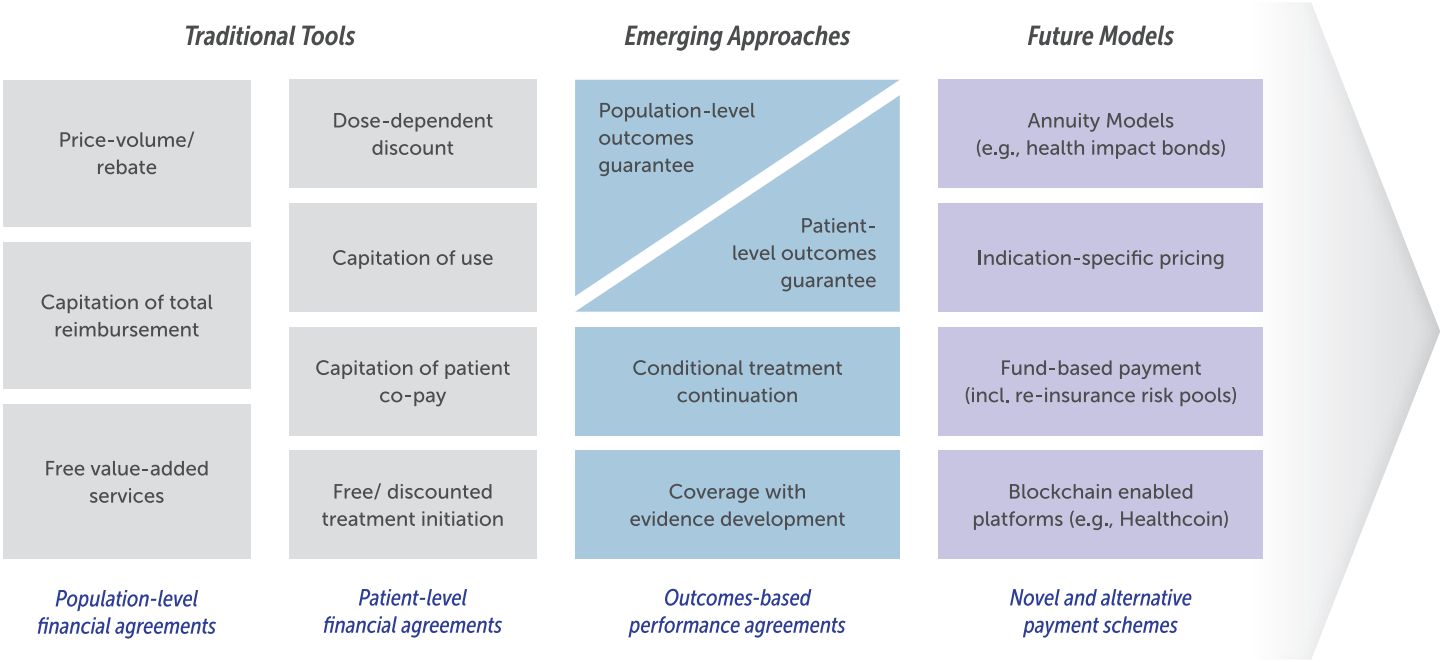
The Advent of Transformative Medicines as a Driver for Payment Innovation

- The advent of transformative and gene therapies has amplified affordability concerns among payers, providers and patients. Stakeholders agree that both funding and delivery systems are inadequate to deal with a wave of future cures. Until recently, little had changed in the thinking about how to pay for and deliver these therapeutic innovations.
- With respect to gene therapies, different US payer types are variably exposed to three core risks:
  - *Actuarial uncertainty (how many eligible patients will be in our insurance pool?)*
  - *Therapeutic performance (how do we assess long-term, real-world effectiveness of treatments?)*
  - *Payment timing (how do we administer payment given plan switching and beneficiary migration?)*
- Health plans conduct individual risk assessments: Broadly speaking, smaller beneficiary numbers result in higher financial exposure on a per-patient cost basis and comparatively greater operational challenges given the need for highly specialized treatment knowledge. Some small commercial payers, self-insured employers, MA Advantage and Medicaid can be expected to see a higher impact than larger commercial payers and Medicare Fee-for-Service. Insurance risks vary further across therapy modalities for the different target populations in question. Payers think that multiple payment solutions are required to mitigate the impact of a proliferation in transformative high-cost therapies – but few concrete mechanisms exist today.

Figure 1.

Range of payment innovations



Case in Point: How to value, how to pay for cures?

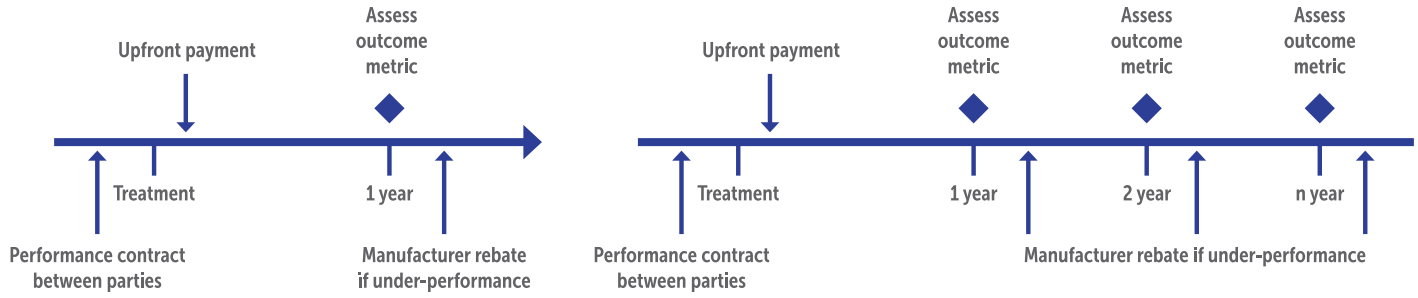
- Zolgensma, approved in May 2019, was the first gene therapy to cure young children with spinal muscular atrophy (SMA), a rare genetic disease. While some investigations exposed data manipulations in Zolgensma's pre-clinical research, the FDA highlighted that human clinical trial data support its efficacy and justify its place in the market. It was priced by Novartis/ AveXis at over $2M for an injection administered once, while the therapy value accrues over a patient's lifetime. The disconnect between payment and outcomes reveals a fundamental challenge to the current 'pay-as-you-go' funding approach.
- The lifetime savings potential is exceptional in terms of reducing the burden of mortality, disability and overall treatment costs. But collapsing decades worth of potential cost-offsets into the single, one-time administration produces extra-ordinary upfront budget pressure on payers.
- The cumulative effect of curative therapies across multiple conditions is likely going to put increasing strain on the current structure. Another compounding challenge for health systems' value determination here is the lack of long-term durability data at launch, a performance outcome measure that the clinical trial research can't capture. In view of the evidence, are we right to assess these therapies under the same criteria we established decades ago to manage the much more predictable cost of chronic conditions? In the case of Zolgensma, "ICER" estimated a value-based price to be between $1.2M and up to $2.1M (assuming an alternative thresholds of $100,000 to $150,000 per life year gained). But once we move beyond the hurdle of defining a value-based price to the question of paying for these cures, a corresponding set of alternative reimbursement models, so-called 'precision financing' schemes for precision cures, is required to assure affordability and reimbursement.

Milestone-based Outcomes Contracts for Payment Innovation

- Performance-based contracts involve an upfront payment and reception of refunds over either the short-term (<1 year) or long-term (e.g. five years) and can help to reduce the risk around a variability in response and to limit treatment costs.
- Developers may rebate based on nonresponse rates in individual patients, pay a discount based on performance within a population, or pay for additional treatment costs associated with suboptimal responses to therapy. Common deal parameters include (a) the adjustments of an additional rebate (above a base rebate) proportionate to pre-defined outcomes metrics; (b) financial guarantees to pay for plan beneficiaries who missed an outcomes performance threshold (e.g., cost for impacted members pharmacy spend related to the product, total pharmacy costs of all utilized products relating to the condition, hospitalization costs, also for all patients on product if population-level); or c) total cost-of-care guarantees for patients on the manufacturer's product (e.g., on a per episode-basis or population-based per member per month) with applied outcomes data to adjust for the negotiated risk share of either payout (shortfall of the guarantee) or shared savings (in excess of guarantee).

Figure 2.

Simplified modalities of milestone-based outcomes contracts across the short-term (1 year), and multi-year horizon



CURRENT STATE

- Different types of outcomes-based agreements (OBAs), such as with adjustments on individual or population-based outcomes metrics, are currently used in less than 10% of covered lives, as perceived by respondents in this survey. As Certara has documented in a series of OBA whitepapers over the past three years, the recent rise of risk-sharing agreements in the US is clear evidence that outcomes-based contracting has become a reality in the marketplace, but we should stress that it is neither the norm nor the panacea for a majority of pharmaceutical reimbursement.
- We also note that only 1 in 3 surveyed MCOs with OBA experience today is satisfied with the agreements they have seen put in place by their organization. 35% of payer respondents cc currently have, or have had, an OBA (see figure below). All of these payers note that they have obtained value for money and have renewed, or will seek to renew these OBAs and similar types in the future.

Figure 3.

Payers who have past or current experience with outcomes-based contracts

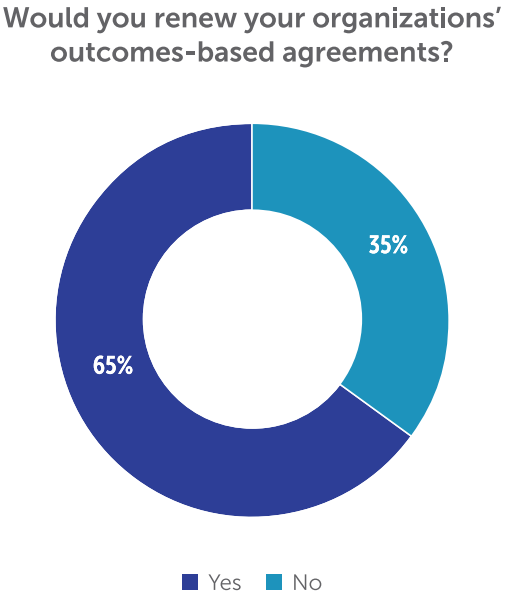


Figure 4.

Challenges with the implementation of value-based agreements

Stakeholder-cited challenges with OBA implementation

- Assessing risk upfront due to uncertainties around real world performance.
- Managing lack of control (over outcome, proper dosing, product use, adherence…).
- Finding adequate time horizons in fragmented, multi-payer insurance market.
- Managing resource requirements to set up and adjudicate compared to traditional rebates and discounts.
- Leveraging data infrastructure adequately for measuring/monitoring relevant outcomes.
- Reaching contractual agreements b/w all stakeholders.
- Managing risk of potentially burdening physicians with uncompensated data collection.

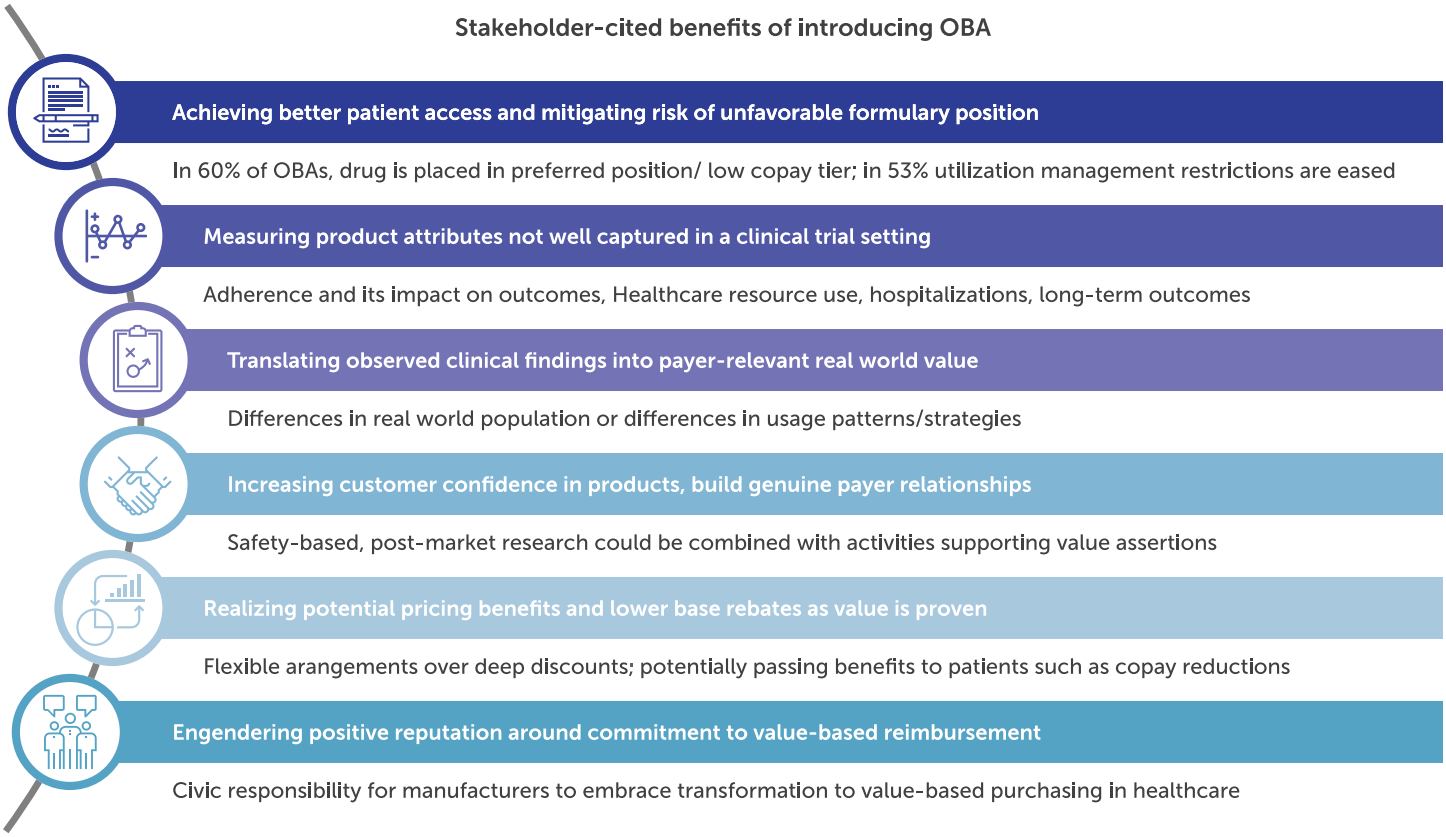


Figure 5.

Benefits associated with offering value-based contracting options

FUTURE EXPECTATIONS

- When asked about their likelihood for renewal, contracts are expected to be renewed for national plans. Only IDNs are moderately confident to expand OBA use beyond pilots.
- Additional qualitative feedback also indicates why the current types of OBA have seen limited scale, frequently citing lack of resources and lack of manufacturer' commitment to more meaningful areas of implementation. Developers also must agree to a set of measurable and obtainable outcomes which can be challenging in several disease states.
- Given the need for third-party adjudication services, and data and analytics infrastructure to track patients over time (across payers and providers), we do not expect a large-scale uptake within the next three years. These steps add to the already costly administration and legal complexity. At the same time, developers are well advised to be prepared for the emerging payer environment where meaningful commitment to value in the real world, not RCT simply results, will be the marker of differentiation.

- Following our results, there is still an opening for developers to further adopt alternative models – but it remains restricted to IDN archetypes within the next three years.
- We believe that regulatory clarity would serve as a key enabler: CMS could provide reasonable accommodation for best-price and other government price reporting, the OIG could advance anti-kickback statues to define explicit safe harbors, and FDA could further specify communication guidelines to enable appropriate communication between payers and developers. There have been encouraging proposals by the OIG and CMS for new AKS and Stark protections for value-based agreements on the provider site currently pending at OMB, but such arrangements explicitly exclude manufacturers of drugs, medical equipment, prosthetics, orthotics or supplies.

Figure 6.

Outcomes based agreement with financial adjustment based on performance in population (Commercial)

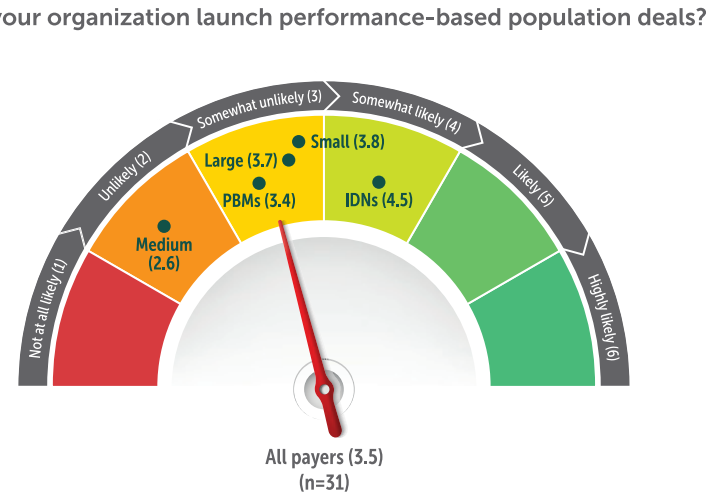


Figure 7.

Outcomes based agreement with financial adjustment based on performance in individual patients (Commercial)

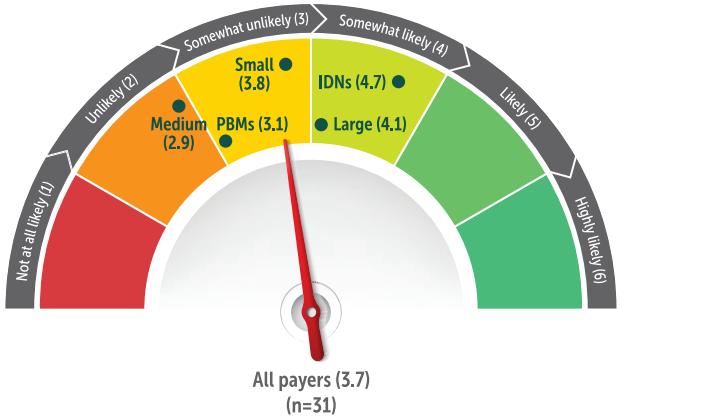
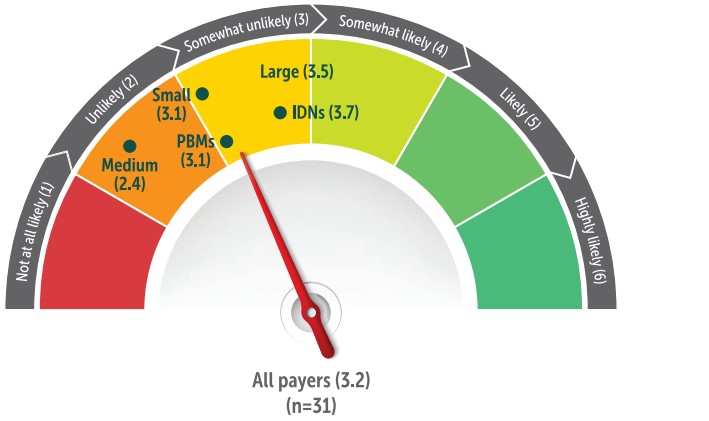


Figure 8.

Outcomes based agreement with financial adjustment based on performance in individual patients (Commercial)



Annuities Payments/ installment Financing

- The objective of annuity financing (which can be combined with outcomes measures) is to spread the cost of a therapy over a fixed time frame thus smoothing the scheduling of payments. This would help tackle the immediate budget pressures in the first year faced by smaller insurance pools and partially mitigate the actuarial risk around patient backlogs and individual high-cost cases. Typically, the timeframe is based on the durability of response in the trial; many payers would want to see five years. This currently faces a major implementation obstacle in terms of patient potability.

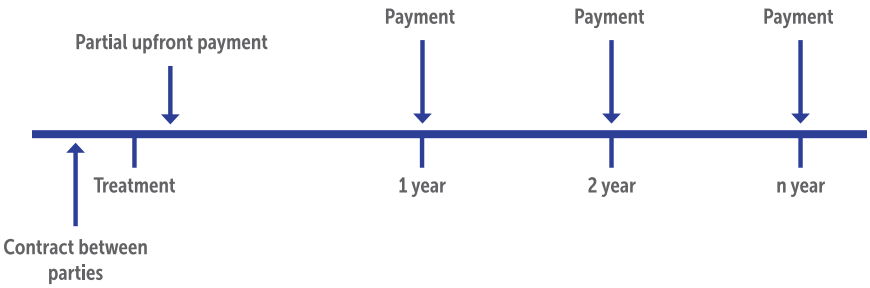


Figure 8.

Simplified modalities for multi-year installment payments

CURRENT STATE

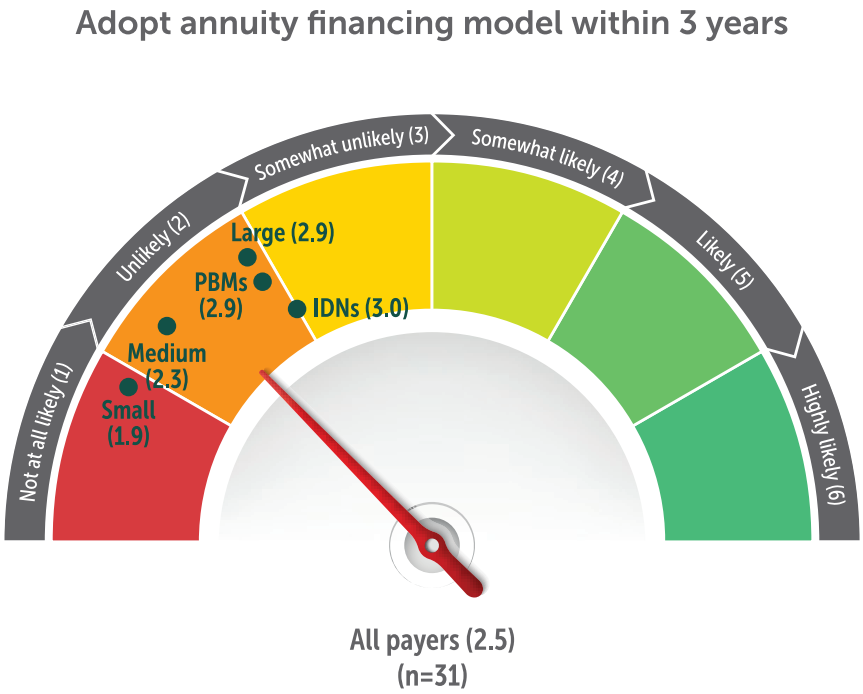
- Currently, no payers report using annuity financing arrangements. Policymakers have hitherto made no tangible commitment to developing an infrastructure for annuity financing or to enabling long-term, value-based pharmaceutical reimbursement.

FUTURE EXPECTATIONS

- We note that the bi-partisan legislation from the Senate Finance Committee (Grassley/Widen) would enable Medicaid plans to amortize the cost of delivering curative gene therapy over time.
- Given the multi-year contract horizon, open questions around patient tracking, pricing regulation and accounting issues persist and payer interest in adopting these payment options is muted.

Figure 9.

Interest in adopting annuity payment model within the next 3 years (Commercial)

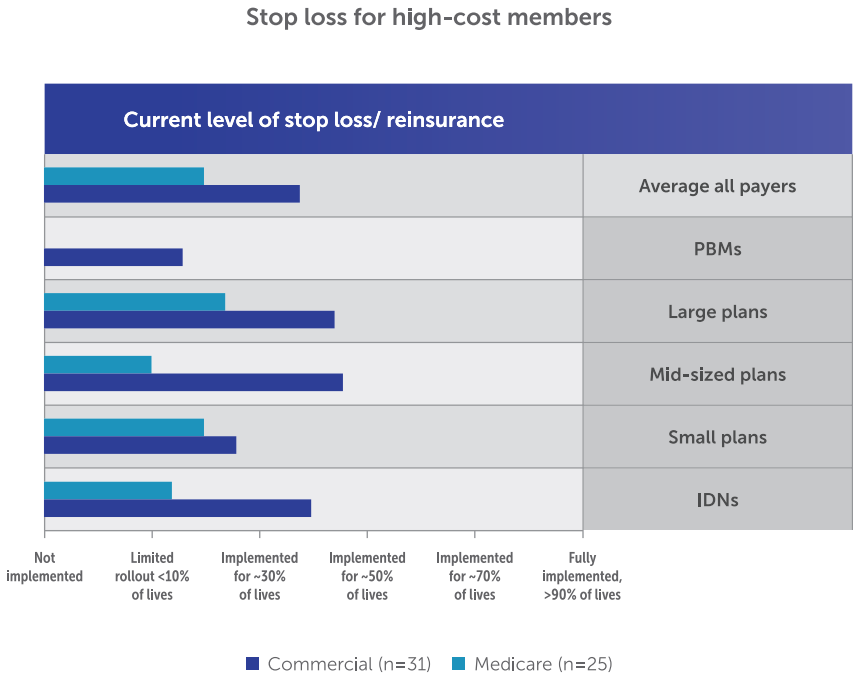


Reinsurance / Stop loss

CURRENT STATE

- Reinsurance (e.g. purchased by payers) and stop loss insurance (e.g. purchased by self-funded employer organizations) is currently employed to manage the actuarial risk of single plan-year contracts. For example, payers pay the third-party insurer per member per month (PMPM) to assume the risk for unexpected events above a certain cost threshold.

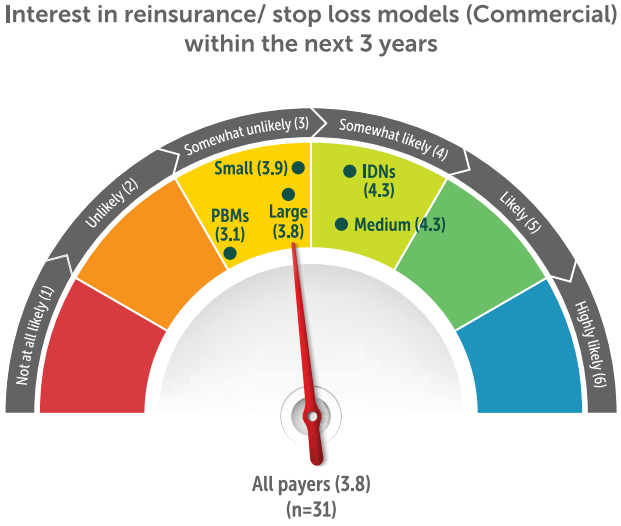
Figure 10.
Payers' current level of implementing re-insurance and stop loss insurance



FUTURE EXPECTATIONS

- Applied to the context of transformative therapies, the reinsurance/stop loss approach could work well in incident populations but faces challenges in multi-year agreements since high-cost claimants will have to be disclosed to re-insurers and are often "lasered out" of future policies which focus specifically on insuring unknown and unexpected financial risk.
- We observe that interest in growing annuity models is fairly significant among commercial payers at "somewhat likely" with IDNs and Midsized payers most interested and PBMs being "rather unlikely" to implement within the next three years.

Figure 11.
Interest in reinsurance/ stop loss models (Commercial) within the next 3 years



Subscription-based Pricing

CURRENT STATE

- Following the principle of a subscription, the approach also called the "Netflix model" aims at ensuring patient access to a therapy for a given population at a predictable cost. In 2019 Medicaid state payers Louisiana and Washington decided to reimburse the manufacturers Gilead and AbbVie, respectively, based on fixed amounts for multi-year-periods for HCV drugs.
- Currently, no payers have implemented subscription-based pricing across Commercial or Medicare lives.
- The set-up of the governing contract follows a public 'winner takes all' auction in which the lowest bidder earns the right to supply product for the agreed-on license. In the two US cases, the auction seems to have resembled more of a confidential negotiation process led by the state payers with each of the three competing bidders. Price tenders remain unpublished, but our researched estimates of the accepted agreements in the US are provided in figure 12.
- Subscription licensing models fall in line with alternative approaches that de-link innovation from unit pricing, following the rationale that any additionally treated patient does not represent a higher cost to payers who, in turn, would avoid limiting access restrictions otherwise necessary to protect their budgets.

FUTURE EXPECTATIONS

- Going forward, only 13% of payers[dd], are somewhat interested in adopting subscription-based pricing models for Commercial plans.
- There is little interest of implementing such a financing model on the Medicare side with only 2 respondents somewhat likely to explore this financing option for Medicare plans.
- In Medicaid, the states of Oklahoma, Michigan and Colorado reported to have evaluated this approach.

Figure 12.

Current subscription model in the US market (Medicaid)

	LOUISIANA (2019)	WASHINGTON (2019)
Awarded manufacturer	Asegua (Gilead subsidary)	AbbVie
Bidders	3 – AbbVie, Gilead, Merck	3 – AbbVie, Gilead, Merck
Lump sum amount total	$290M – potential	$321M – contracted
Payment modality	Up to $58M per year	Upfront
Duration	5 years contracted	4 years, 2-year extension option
Patients targeted	31,000 (2024) / 10,000 (2020)	30,000 (2023)
Price per patient targeted	$9,354	$10,700
2018 Medicaid price	$24,363	$24,363
Expected discount over best price	61%	56%
Additional details	Modified licensing – fixed/ unit price until cap, unlimited pricing thereafter	AbbVie commits to patient identification, outreach, diagnosis

[dd] *n=4, representing 52M Commercial lives*

Implications for Developers

- Despite heightened excitement around innovative financing models, MCOs in the US see comparatively little to no current use. Thus, we see few immediate opportunities for the adoption among private insurers. This is partially due to beneficiary switching at the end of the plan year that doesn't allow for the continuity in the treatment population that the approaches require while unit-level reporting requirements are legal and administrative barriers.
- Propositions such as licensing models have unquestionable public heath value as long as no further treatment innovation is to be expected in the category. By nature, this limits the model to indications and categories where continued R&D can be sacrificed for budget surety such as curative therapies.
- While some tactical benefits may sound appealing to manufacturers at first sight – e.g. annual recurring revenue and cashflow certainty, reduced COGS etc – the shift may be indicated for a limited set of competitive scenarios, e.g. for a hold on a patient pool that is diminishing when competitive differentiation is unable to open the funnel. As figure 13 shows in a simple simulation, properly accounting for the potential loss of the entire segment as a result of the auction or bidding process limits the commercial rationale of pushing for licensing models in most scenarios.
- Under any circumstance, developers need to make sure to have a superior understanding of the prevalence within the state population and gauge the price-volume accordingly. If the increase in volume reduces a defined contribution margin (driving up COGS) at a decreasing net price and the resulting decline in profitability for the entire market appears to be greater than forgoing sales in that state's Medicaid segment, they should re-consider. If they proceed, they must define what share of the delta they can claim to take home given the product's value delivered to the entire patient population.
- For any non-traditional pricing agreement, successful developers are supported by a multi-disciplinary pricing steering committee and have provisioned for monitoring and adjudication systems.

Figure 13.

Simplified scenario for licensing options and revenue risk: Not always "win-win"

Scenarios for adopting a Netflix-model

Unit-based sales (conventional model Treatment cost: $30,000/patient Annual patient pool for condition: 8,000	**Subscription model** Lump sum: 190M Annual patient pool: 14,000			
Market scenario 1	Product A: 40%	Product B: 40%	Product C: 20%	
New TRx starts	(3,200 pts)	(3,200 pts)	(1,600 pts)	
Expected revenues (conventional model)	$96M	$96M	$48M	
Likely subscription revenue	$57M	$57M	$57M	
Market scenario 2	Product D: 66%	Product E: 17%	Product F: 17%	
New TRx starts	(5,280 pts)	(1,360 pts)	(1,360 pts)	
Expected revenues (conventional model)	$158M	$40.8M	$40.8M	
Likely subscription revenue	$57M	$57M	$57M	
Market scenario 3	Product G: 30%	Product H: 20%	Product I: 15%	Product J: 35%
New TRx starts	(2,400 pts)	(1,600 pts)	(1,200 pts)	(2,800 pts)
Expected revenues (conventional model)	$72M	$48M	$36M	$84M
Likely subscription revenue	$47.5M	$47.5M	$47.5M	$47.5M

01

In this simplified Medicaid example, we're assuming a state payer wants to see net savings of $50M on its annual expenditures for the category, but in turn expect a 75% demand surge given the removal of utilization restrictions limiting patient access under current pricing. The assumption seem reasonable looking at conceptual and recently discussed models in Louisiana and Washington.

02

Given that the bidding process is not public, manufacturers cannot pre-determine their success in the process – even though revenues under the lump sum would be guaranteed, the risk is significant as only one market participant will be rewarded.

03

For the 10 firms in our simulation, only those with products with a preference share of less than 20% fare better under the subscription model if we apply a probability-weighted revenue forecast. In 60% of the situations, the traditional unit sales provide higher expected revenues, with a significantly higher overall revenue in each case.

Emergence of Novel Entities to Manage Orphan Benefits? [55]

A few collaborative efforts have lately put the development of so-called 'precision financing' schemes for precision cures on the public policy agenda. One of the more prominent multi-stakeholder initiatives in the US was launched at the Massachusetts Institute of Technology (MIT). Their Financing and Reimbursement of Cures (FoCUS) project has recently presented a set of alternative reimbursement models based on "Design Lab" workshops, primary research, financial modeling and case study analyses.

The aim is to advance a practical toolkit that helps drive early adoption and enables payers to guarantee patient access to novel therapies. For the future state of transformative therapy commercialization, the colleagues at MIT imagine the possible emergence of novel provider-administrator entities to support and administer novel financing models. These intermediaries, so-called Gene Therapy Administrators or Orphan Reinsurer and Benefits Managers (ORBM), could combine the risk-bearing of reinsurers with the therapy contracting capabilities of PBMs, and the provider network building, and medical management capabilities of insurers (Figure 15).

While no such dedicated vendor exists today, third parties are already providing these services. Additional capabilities such as specialty pharmacy distribution could hypothetically, be added as well. Below is an overview presented by the MIT initiative as a first step of conceptualizing the promise of an inter-mediating entity. However, the specific confines of the business model behind the ORBM are yet to be fully fleshed out.

Figure 14.

Possible relational construct of the new ORBM entity proposed by FoCUS

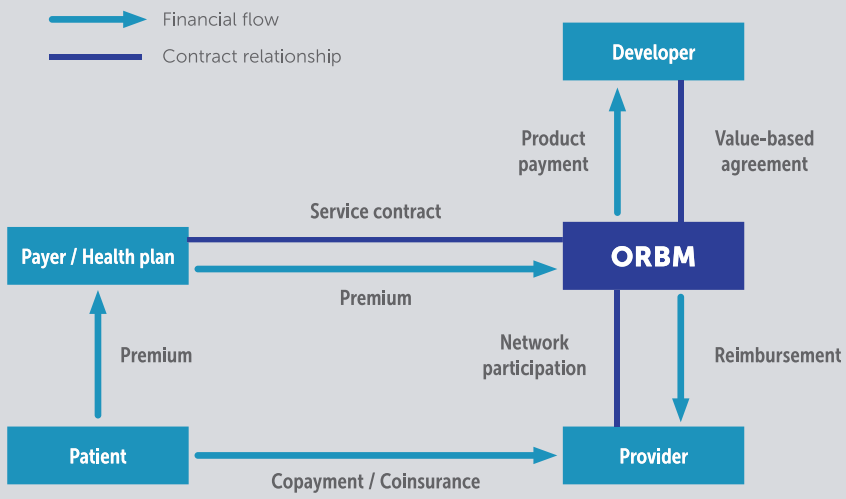


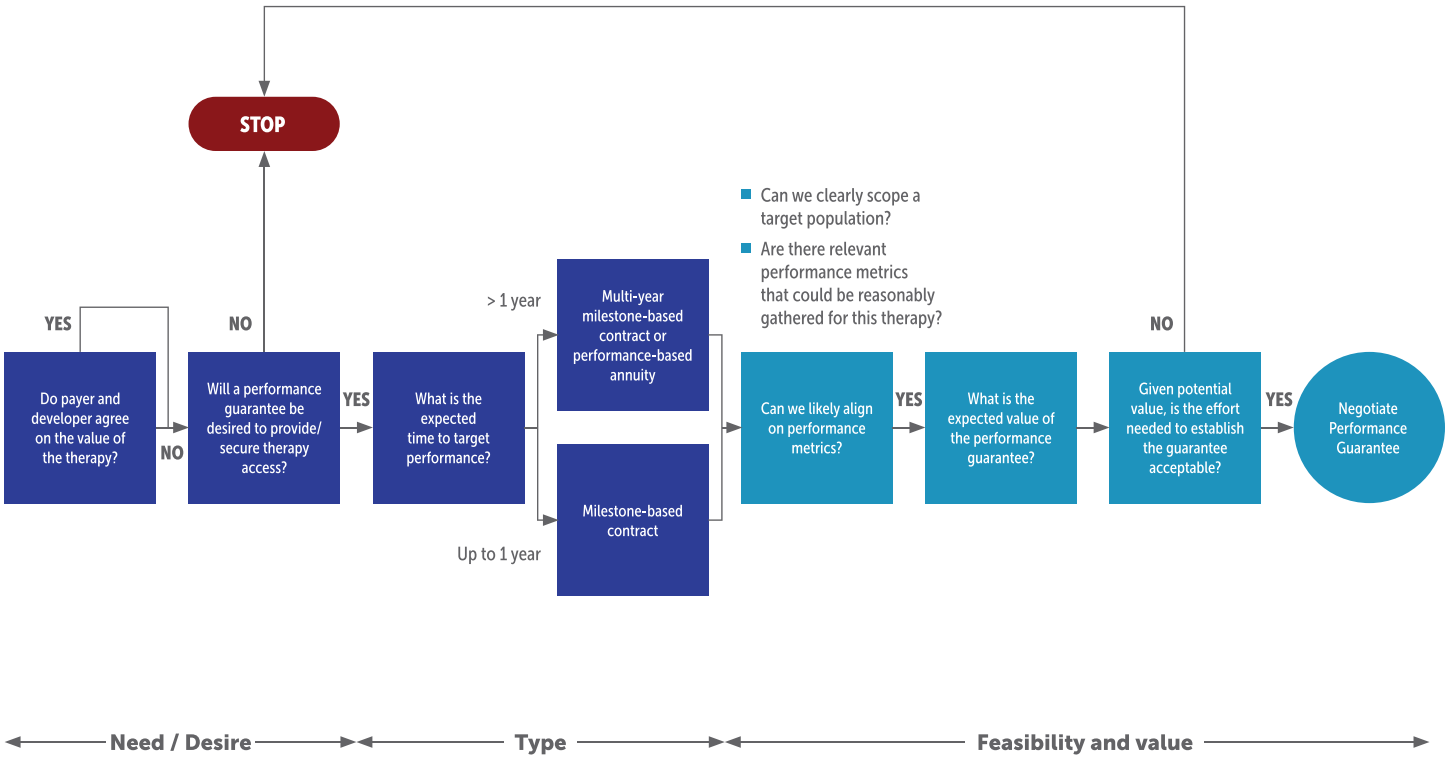
Figure 15.

Conceptualizting the new entitiy of the Orphan Benefit Manager (proposed by Trustheim et al, 2018)

ORBM Function	Full service	Pharmacy Benefit Manager	Specialty pharmacy	Reinsurer
Carve out / Pool risk				
Underwriting: Premium setting	✔			✔
Pool and Bear actuarial risk	✔			✔
Payment financing to developers and payers	✔	✔		
Claim adjudication and reimbursement	✔	✔		
Contracting				
Contracting with developers	✔	✔	✔	
Patient eligibility and utilization management	✔	✔	✔	
Product reimbursement	✔	✔		
Patient data collection for performance contract	✔	✔		
Adjudicate any performance criteria	✔	✔	✔	
Collect and distribute performance-based rebates and/or payments	✔	✔		
Patient mobility management/contract	✔	✔		
Care Coordination Services				
Provider network management	✔			

Figure 16.

Decision-making paths (Focus initiative) [56]



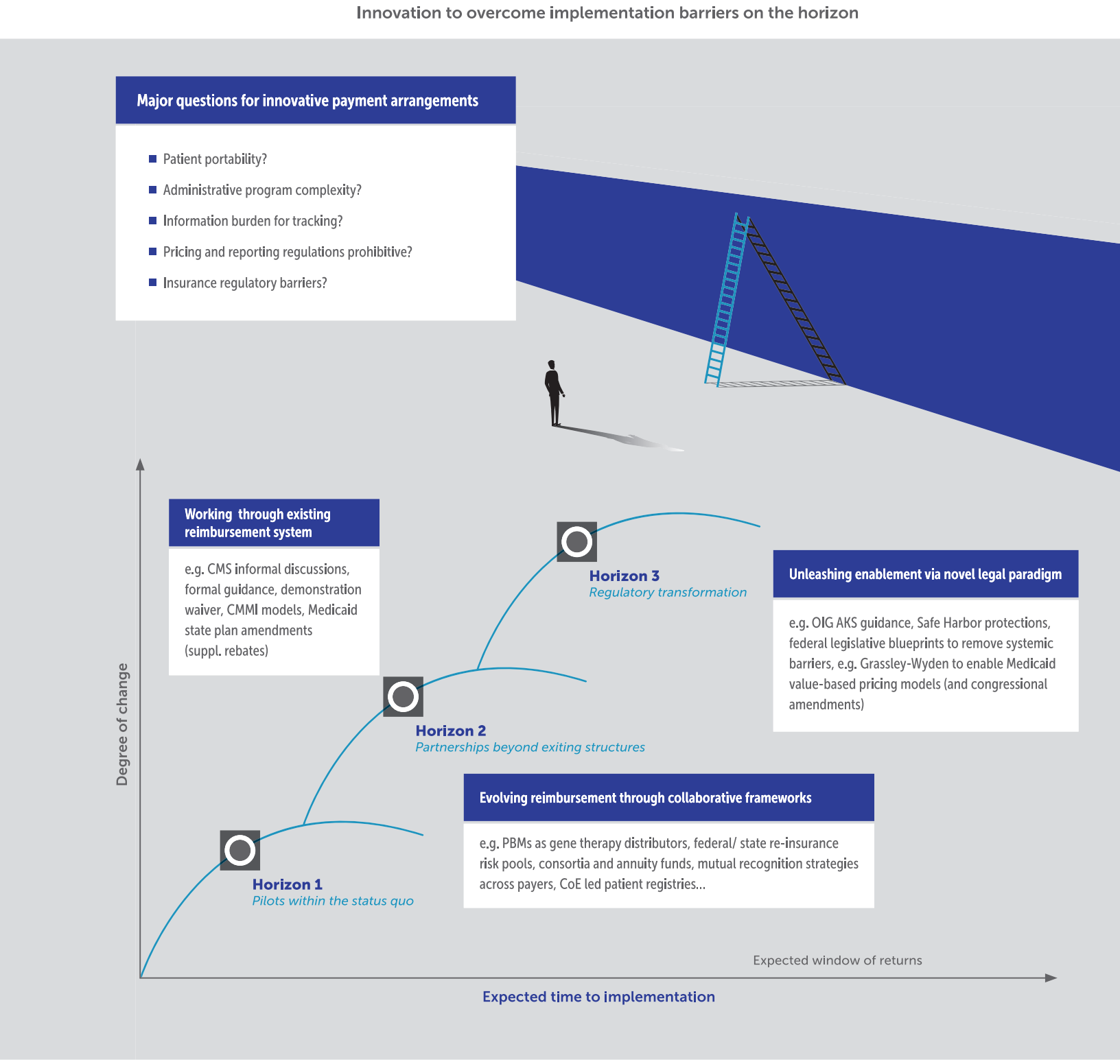
A critical question for the future of innovative contracting is whether any of the negotiated financial benefits between manufacturer and payer will ever reach the patients and how can we operationalize that.

– MAXIMILIAN VARGAS, Sr. Director, Certara

56 Trusheim, M. et al., Improving Management of Gene and Cell Therapies, Pharmaceutical Executive (Sep. 10, 2018), accessed 6/18/2019.

Figure 17.

Barriers to adoption of novel financing arrangements, and innovative horizons to overcome them



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