THE PRICE OF ACCESS

INNOVATIVE PRICING AND OUTCOMES-BASED MODELS FOR PHARMACEUTICALS

CONTENTS

“TO COPE WITH THESE CHALLENGES, ALL HEALTHCARE SYSTEMS AND THE RESPECTIVE PAYORS AIM TO LOWER COSTS. [...] MANUFACTURERS ON THE CONTRARY [...] WANT TO ACHIEVE MARKET ACCESS FOR THEIR THERAPIES.”

01

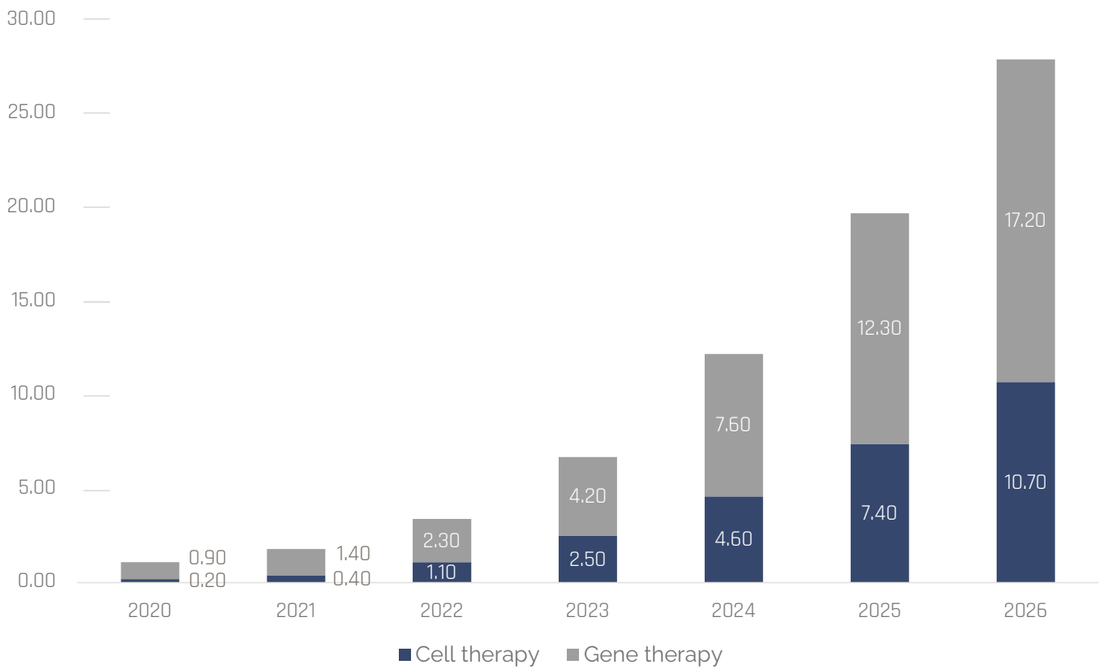
CHALLENGES IN TODAY’S HEALTHCARE SYSTEMS

For many years, healthcare systems worldwide have been grappling with rising expenditures and the risk of overextending their budgets.

If healthcare expenditures continue to grow at consistently high rates, the proportion of healthcare spending relative to GDP will significantly increase. A recent study concluded that if this trend persists and the growth of healthcare expenditure keeps surpassing overall GDP growth, US healthcare spending could reach 20% of the GDP at the start of the new decade. [31]

Pharmaceutical spending is often labeled as the most important cost-driver in healthcare. While even this statement is highly debatable, an increasing number of traditionally costly oncological or immunological treatments seem to support this argument. Just to name a few, mega-blockbusters such as Keytruda® or Humira®, and the ubiquitously discussed GLP-1 receptor agonist franchises Ozempic® / Wegovy® and Mounjaro® /

FIGURE 1: SALES DEVELOPMENT OF CELL & GENE THERAPIES FROM 2020-2026 IN € BILLION. [10]



Zepbound® fuel these allegations even further. Another widely discussed factor is the rise of innovative yet costly cell and gene therapies over the past ten years and their promise to cure devastating diseases. Prices exceeding $1 million for one-time administered curative drugs have frequently sparked controversy.

Nonetheless, it is obvious that the pharmaceutical industry needs to refinance new drug developments and everything that failed along the way. In highly prevalent indications such as diabetes, clinical trial programs can cost billions of dollars due to increasing regulatory demands and associated patient numbers. Not only in prevalent indications but also in rare diseases with very low patient numbers, research and development costs must be recouped while costs must be shouldered by only those few patients and their payors.

In recent years, the number of Investigational New Drug (IND) applications for Advanced Therapeutic Medicinal Products (ATMP) [16] has increased drastically to a peak of 666 in 2020 coming from about 200 applications 20 years ago. [3] With an increasing number of expected approvals, these innovative gene, cell, and tissue therapies alone are expected to generate sales of almost €28 billion in 2026 compared to only €7 billion in 2023 (see Figure 1).[1] [10]

Besides all the benefits ATMPs may bring to the patient, they also come with a set of challenges for pricing and reimbursement:

[1] One Euro equals about 1,10 US Dollars as of March 2025

1) Traditionally, costs for chronic diseases are spread over the patient's lifetime with drug costs being reimbursed in a bill-and-pay manner. The longer the patient lives, the more expensive the total treatment will be. For curative ATMPs, the same bill-and-pay approach – a one-off payment – would result in a considerable budget impact in a short time frame, typically one financial year. The logic behind this is that all costs associated with the previously used chronic treatment of the disease, especially direct medical costs, would be aggregated and charged at once because curing the disease would prevent future chronic treatment costs.

2) Payors as well as patients face uncertainty about the outcomes of many newly approved innovative breakthrough therapies. Accelerated approval, which is granted for high unmet need indications, often comes with uncertainty but also improves patient access to potentially lifesaving therapies. These high unmet need indications are often rare diseases treated with orphan drugs. They frequently come with the limitation of missing or having limited comparator data: On the one hand, treatments that can be used as an active comparator arm might not yet exist. On the other hand, the use of placebo controls in life-threatening diseases is regarded as unethical. When limited data is available, post-marketing requirements such as patient registries will be imposed on the drug's manufacturer, which comes with significant additional expenses.

FIGURE 2: CONFLICTING INTERESTS OF INDUSTRY AND PAYORS.

To cope with these challenges, all healthcare systems and the respective payors aim to lower costs and the pharmaceuticals' budget impact – in other words: cost containment. Planning budgets and making them sustainable goes hand in hand with this. Manufacturers on the contrary, and despite outcome uncertainty, want to achieve market access for their costly therapies (see Figure 2). This imposes the question of how both parties could find agreements with mutual benefit.

As one approach, innovative and outcomes-based pricing models (IOPM) have emerged over the past decade as potential remedies and compromises between industry and payors. These alternative pricing schemes entail risk-sharing to better balance payor risk and manufacturer risk and can be – but do not have to be – outcomes-based. More ATMP approvals and the increasing usage of IOPMs in current practice in major pharma markets necessitates an overview of their application over the course of time. 2024 has also demonstrated that this topic is still highly relevant with approvals of innovative costly therapies such as Beqvez®, Lenmeldy® (Libmeldy® in the EU), Kebilidi®, or Amtagvi®. Therefore, this publication aims to:

1) Provide an overview of different IOPMs

2) Explore and assess IOPM application in case studies across indications and markets

3) Discuss IOPM key learnings, implications, and give an outlook on future use

EXISTING METHODOLOGIES AND PRINCIPLES FOR INNOVATIVE AND OUTCOMES-BASED PRICING MODELS

Although the name might imply that innovative and outcomes-based pricing models are a recent phenomenon, related approaches were already in use 100 years ago.

Emerson's Bromo-Seltzer was a pain drug used against headaches (see Figure 3) and already had an – in today's words – innovative outcomes-based approach. In the early 20th century, Emerson's Bromo-Seltzer's refund guarantee was used as a warranty for patients based on an outcomes component which was entirely patient-subjective. If patients were not satisfied with the pain relief, they could receive a full refund.

The term innovative and outcomes-based pricing models usually refers to so-called risk-sharing agreements. These reimbursement schemes can be divided either into various financial-based agreements or a set of different outcomes-based agreements. (see Figure 5).

02

FIGURE 3: INNOVATIVE AND OUTCOMES-BASED PRICING MODELS: INNOVATION OR REINCARNATION?

OUTCOMES-BASED AGREEMENTS

All outcomes-based agreements have a specified outcome component (e.g., survival, function, biomarker, or quality of life) that is directly linked to the drug's reimbursement. This means that the manufacturer will be penalized for and bear the risk of treatment failure. Depending on the exact formulation of the model, different risk distributions between manufacturer and payor can be discussed conceptually (see Figure 4).

If an agreed-upon outcome is met, the costs of the drug will be fully reimbursed by the respective payor. If outcomes are not met or only to a certain degree, there are several possible reimbursement scenarios, depending on the contract and its terms. For example:

1) Partial refund:
Refund of a fraction of the drug's costs dependent on the extent of achieved outcomes

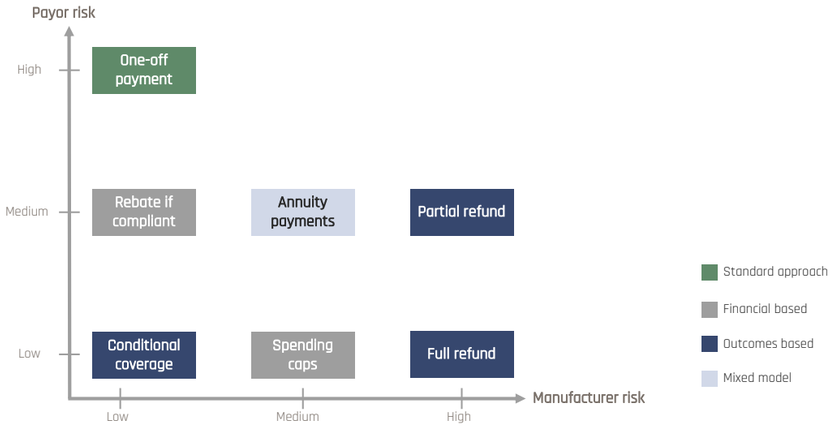
2) Full refund:
Refund of the drug costs to payors and costs incurred to patients (co-payment, etc.)

3) Provision of the matching amount of drug:
Remaining drug doses will be covered by the manufacturer after the defined cap is utilized

4) Coverage from a certain threshold:
Drug costs are covered if defined efficacy thresholds surpassed

5) Coverage of induced medical costs:
Coverage of costs associated with the treatment such as diagnostics, administration, aids, etc.

FIGURE 4: RISK DISTRIBUTION OF SELECTED INNOVATIVE AND OUTCOMES-BASED PRICING MODELS



Typically, payors like public or private insurance companies or governments would receive the mentioned refunds. In some cases, patients also get reimbursed for expenses related to their treatment such as co-payments for drugs, accommodation, or transport charges. Examples of this include the drugs Xalkori® and Alunbrig® in Non-Small Cell Lung Cancer (NSCLC).

Conditional reimbursement is another crucial type of reimbursement, which is tied to the submission of additional evidence. Conditions for payments could include a long-term extension of an ongoing trial, a new phase IV trial (real-world evidence, RWE), or the establishment of a patient registry. The example of Zolgensma® in spinal muscular atrophy (SMA) gives an overview of required evidence generation in Germany. Furthermore, conditional treatment continuation would mean that the treatment would only be prolonged if it is likely to show further benefit.

FINANCIAL-BASED AGREEMENTS

While not a major focus area of this publication, financial-based agreements can be split into population- and patient-level models. Population-level means that a certain population (e.g., specified indication, location, insurance membership) is covered by the agreement. Such models entail rebates, the coverage of co-payments, and volume agreements / expenditure caps. One such model design is the subscription model, also called the "Netflix model" where insurers pay a certain amount upfront for having access to an unlimited drug supply for their patient population or a lump sum for a certain drug volume. In Chapter 3, subscription models will be further explored using the case of the Hepatitis C drugs Epclusa® and Mavyret® in the US or Luxturna® for retinal dystrophy in Italy.

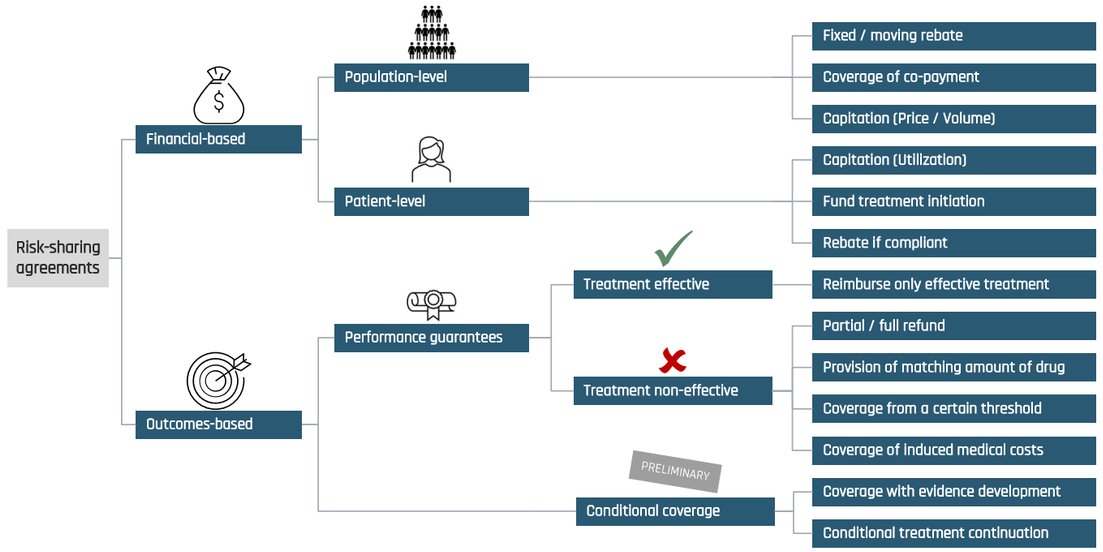
Another frequently used agreement utilizes staggered payments (also called overtime or annuity payments) where the drug's costs are split over an agreed period. Examples of this approach encompass Zynteglo® for the treatment of beta-thalassemia or Zolgensma® in SMA.

Agreements on a patient level can also entail e.g., expenditure caps, but also funding the initiation of treatment (Entresto® in chronic heart failure), or rebates depending on compliance. [26]

Although the financial- and outcomes-based models have different characteristics, they are not always mutually exclusive. Instead, models can be combined as desired which will also become evident in the discussed case studies. Additionally, different combinations can be agreed upon within each sphere of financial- and outcomes-based models. For instance, CAR (chimeric antigen receptors) T cell therapies included both performance guarantees as well as evidence generation obligations.

At this point, the terms outcomes-based vs. value-based should be briefly explained. The quintessential difference between outcomes-based and value-based reimbursement is that the former is mainly seen from the payor perspective vs. value-based which can have different perspectives, depending on the type of stakeholder. Value-based reimbursement promises to lower spending for payors, better health outcomes for patients, and a more efficient healthcare system, resulting in an overall benefit for society. For example, a cured or healthier patient would potentially cause less future medical costs borne by the insurer and might also be able to contribute back to society by participating in work life again.

FIGURE 5: OVERVIEW OF INNOVATIVE PRICING MODELS [26]



“THE WAY RISK IS SHARED BETWEEN THE PAYOR AND THE MANUFACTURER CAN VARY GREATLY BASED ON THE SPECIFICS OF THE CONTRACT. THE KEY FACTOR IN DETERMINING HOW THE RISK IS ALLOCATED IS THE REIMBURSEMENT-DEFINING OUTCOME.”

03

CASE STUDIES FOR INNOVATIVE AND OUTCOMES-BASED PRICING MODELS IN THE US AND EUROPE

In the following sections, multifaceted case studies of drugs with innovative and outcomes-based pricing models are explained and discussed. Additionally, regional differences between the US and European countries such as Germany, France, the United Kingdom, Italy, and Spain are highlighted.

KYMRIAH® AND YESCARTA® IN ALL AND B-CELL LYMPHOMA

One of the most prominent and early examples of IOPMs are the CAR T cell therapies Kymriah® by Novartis and Yescarta® by Gilead. Kymriah® which received FDA breakthrough designation and FDA approval in 2017 is indicated for Acute Lymphoblastic Leukemia (ALL), B-cell lymphoma, and follicular lymphoma. [23]

It quickly became evident that Novartis was pushing towards outcomes-based agreements in the US and worldwide – using similar but not the same approaches. In the US, agreements for ALL were concluded with specialized centers that were relieved from bearing the drug's cost at their own risk. Novartis did this by billing the drug only after an assessment of the patient's response (after 30 days of treatment initiation) and providing the drug free of charge if the patient did not respond to the treatment in this timeframe. [30]

Key learnings Kymriah® and Yescarta®

It is important to consider all stakeholders in the process: payors, manufacturers as well as intermediaries / service providers. Hospitals can be relieved from high upfront purchasing costs by adjusting the billing scheme.

With a list price of €320,000, Kymriah® was one of the most expensive therapies launched in Germany to that date following EMA approval in 2018. This price was only partially paid if the patient died due to blood cancer within a certain (confidential) time frame. The exact rebate remained confidential as well. [14, 17]

Similar to the US, only certified hospitals in Germany carry out CAR T cell therapies. To avoid an overburden of drug costs to these hospitals, Kymriah® applied to and received the so-called NUB status ("Neue Untersuchungs- und Behandlungsmethoden; new examination and treatment methods"). NUB status offers costly treatments to be reimbursed extra-budgetary on top of the DRG (Diagnosis Related Group) reimbursement, consequently, assisting to regularly integrate the treatment in the respective DRG. [43] Moreover, Novartis was mandated to deliver additional Real-World Evidence. [46]

Reimbursement remuneration for Yescarta® was similar: payors would receive a rebate if the patient died soon after treatment. Thus, the drug received a similar NUB status as Kymriah®.

In the UK, Yescarta® was also subject to generate additional evidence after being reimbursed through the Cancer Drug Fund. This resembles the French procedure where both drugs received market access through an early access program required to deliver additional evidence for a reassessment once per year. Furthermore, the agreements specified which aspects would be relevant for reimbursement: survival, remission status, disease progression, and adverse events. [46]

While the reimbursement in Italy and Spain has also been based on results, a slightly different approach has been chosen using staggered payments. In Italy, Kymriah® was reimbursed in three installments at infusion, 6 months, and 12 months. Gilead shouldered some more risk because the first of three installments was only paid for after 6 months. Payments were stopped if the treatments showed failure within the specified time frames. In Spain, staggered payments were applied, and the treatment response was assessed at 12 and 18 months. [27, 30, 46].

XALKORI® AND ALUNBRIG® IN NSCLC

What a drug in a competitive environment can attempt, Pfizer demonstrated with Xalkori® and Takeda with Alunbrig® in NSCLC in the US. Both drugs received accelerated approval, Xalkori® in 2011 and Alunbrig® in 2017. List prices were about $19,000 per month for Xalkori® and about $17,000 for Alunbrig® and both companies marketed their products as value-based. Pfizer offered full refunds for insurers and patients if Xalkori® lacked efficacy and the expected benefits within the first three months. [50]

Similarly, Alunbrig® also added treatment discontinuation due to tolerability (and efficacy) as reasons for refunds. While efficacy would usually be the key criterion to choose a therapy, IOPMs can still become a differentiating factor in a market with similar effective and similar-priced drugs. A well-defined outcomes-based agreement can help to achieve a preferred status by insurers as they might face fewer costs and risk in the case of ineffective therapies.

Nevertheless, one could argue that the three-month timeframe is too short for a meaningful assessment because most patients might show some level of improvement within this agreed-upon short timeframe. Importantly, Alunbrig® also showed superiority versus Xalkori® expaning its label which might have had a larger impact on sales than an IOPM alone.

Key learnings Xalkori® and Alunbrig®

In a competitive market, the better outcomes-based model can become a driver for success.

Also noteworthy for the Xalkori® example is that Pfizer could bypass the Medicaid best-price regulation as they have contracted an insurance company to pay refunds. As Pfizer reimbursed the drug's price via the contracted insurance, Medicaid legislation's claim of "the lowest price available from the manufacturer" became invalid or inapplicable. [22]

EPCLUSA® AND MAVYRET® IN HEPATITIS C

Another interesting and relevant model used in the US is the population subscription / Netflix model. The states of Louisiana and Washington subscribed their Medicaid enrollees to two

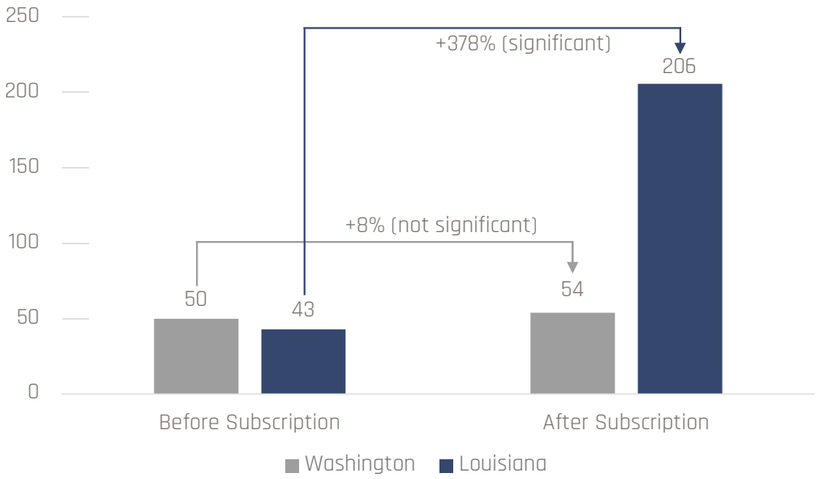
different Hepatitis C drugs, namely Epclusa® (Gilead) in Louisiana and Mavyret® (AbbVie) in Washington. The drugs were chosen based on the cheapest offer (Epclusa®) and the best-perceived portfolio (Mavyret®). For the respective drugs, the states made an upfront payment to gain "unlimited" access to them instead of paying for the prescribed volume. The aim in Louisiana has been to treat 31,000 patients within the next decade because only 3% of 40,000 patients were treated in 2018.

Key learnings Epclusa® and Mavyret®

Population-based models can boost prescriptions and improve the patients' access but might limit the business opportunities for manufacturers while assuring a predictable cash flow.

But how did the programs impact the states' Hepatitis C cases? As Louisiana was relatively restrictive with regards to Hepatitis C pioneer Sovaldi® approved in 2017 due to its high one-time treatment costs of $84,000, there was a high proportion of untreated patients. Until 2019, Sovaldi® was only reimbursed for patients with already severely damaged livers right before progressing to cirrhosis. A steep increase in reported chronic Hepatitis C cases of 99% – most likely due to screening efforts – from 2017 to 2018 in Louisiana followed a decline of 42% from 2018 to 2019. In Washington on the contrary, the prescription restrictions were lifted already in 2016. These prior policies still had an impact on the Netflix model: A tremendous difference between both states can be seen regarding the change in prescription numbers displayed in Figure 6. In Louisiana, prescriptions rose by a dramatic 378% showing an enormous catch-up effect while Washington only saw an insignificant increase of about 8%. [5, 29]

FIGURE 6: CHANGE IN MEDICAID-COVERED HEPATITIS C QUARTERLY PRESCRIPTION FILLS PER 100,000 ENROLLEES



LUXTURNA® IN RETINAL DYSTROPHY

In 2017, Luxturna® by Spark Therapeutics / Novartis, a drug to treat retinal dystrophy, was launched in the US, one year later in the EU, and only in 2023 in Japan. The US price tag was $850,000 ($425,000 per eye) and came with several particularities. First, the manufacturer contracted directly with insurers so that hospitals did not have to purchase the drug before approaching insurers for reimbursement. This helped to de-risk hospital budget planning. Second, Spark Therapeutics / Novartis offered to split the drug price into several installments to limit the annual budget impact with pharmacy benefit managers serving as intermediaries. Third and most importantly, the reimbursement was outcomes-based: Spark Therapeutics / Novartis committed to pay a rebate if short- (30-90 days) and long-term (30 months) endpoints were missed. Pre-defined endpoints included full-field light sensitivity threshold (FST) testing scores. FST measures the patients' residual visual function, thus determining the overall improvement over time with the treatment.

In contrast to the US, Italy applied a mainly financial-based model. Within two years, reimbursement for 60 patients was secured for €21.6 million including early access costs. However, if the budget exceeded this threshold, Novartis was mandated to pay the surplus back. The benefits of such a model are twofold from the manufacturer's perspective, given the high treatment cost: 1) Novartis secured its revenue, though limited to the above-mentioned. 2) Novartis achieved market access by offering financial security to insurers and might have the possibility to expand coverage later. [11, 19]

Key learnings Luxturna®

Using specific outcomes and measuring them in the short and long term offers transparency to all stakeholders, thus enhancing trust in pharma companies and healthcare systems.

ZOLGENSMA® IN SPINAL MUSCULAR ATROPHY

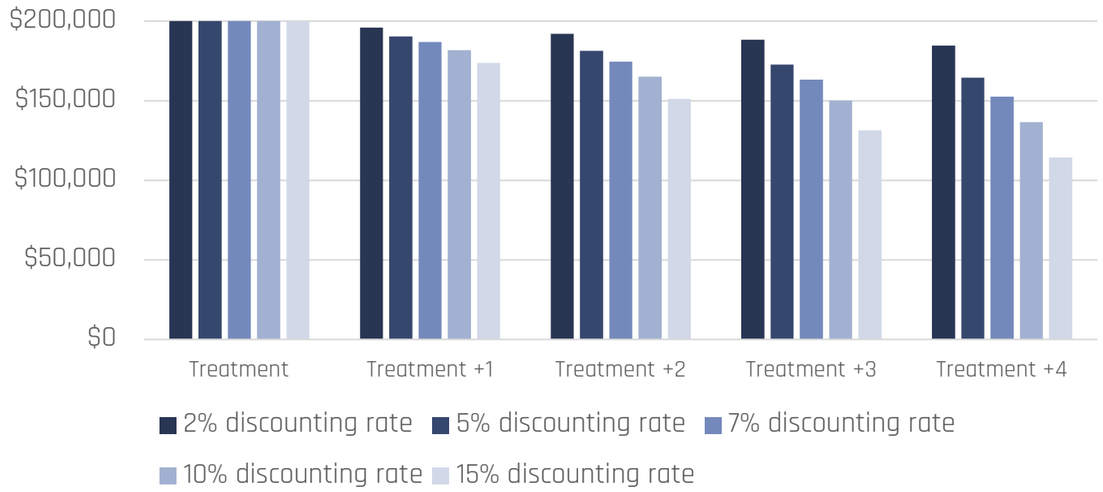
A drug widely criticized for its price and access strategy is the often life-saving drug, Novartis' Zolgensma®. It was approved and launched in 2019 for a rare neuromuscular disease, spinal muscular atrophy (SMA) with an incidence of 1-2 in 10,000 newborns. Novartis added Zolgensma® to its portfolio by acquiring Avexis in 2018. Zolgensma® offers and promises a cure to patients as a one-off treatment by replacing the faulty gene sequence causing the disease while Spinraza® by Biogen approved in 2016 offers a chronic treatment option. This chronic treatment, however, does not promise to address the root cause but instead to improve the course of the disease.

As it was FDA and EMA approved with limited medium- and longer-term data, additional evidence generation was required (see German example in the info box below). The price of about $2 million was split over the years as payment over time when positive treatment effects were sustained. Else the costs would be (partially) reimbursed. The responsible body in Germany, the Federal Joint Committee (Gemeinsamer Bundesausschuss, G-BA), defined various patient-relevant endpoints that longer-term data should show – the first of its kind since the introduction of the additional-benefit appraisal in Germany. [24, 39]

Info Box – Real World Evidence Generation for Zolgensma® in Germany

- The number of deaths as mortality endpoint
- For morbidity:
  - Motor function with age-appropriate measures
  - Development of motor milestones according to WHO
  - Respiratory functioning and (permanent) artificial ventilation
  - Bulbar functioning (swallowing, speaking, need for non-oral nutrition)
  - Complications (pain, orthopedic complications)
- For safety:
  - Severe adverse events
  - Adverse events leading to hospitalizations
  - Severe specific adverse events: hepatoxicity, cardiac events, inflammation of spinal ganglion cells, renal toxicity, and hydrocephalus
- Administering Physicians: participation in data collection

FIGURE 7: INCREMENTAL NET PRESENT VALUE OF FIVE ANNUITY PAYMENTS WITH VARYING DISCOUNTING RATES.



For a hypothetical treatment priced at $1,000,000, the total net present value (NPV) for the manufacturer varies depending on the reimbursement method. If the price was fully reimbursed at treatment, the NPV would be $1,000,000. If, however, the price was split into e.g., five annuities, the incremental NPV per annuity would reduce dramatically (see Figure 7) depending on the used discounting interest rate. The total NPV reduces accordingly (see Figure 8).

It should also be highlighted, despite the high costs of $2 million, that the treatment can still be cost-effective. Compared to Spinraza®, Zolgensma® shows a favorable cost-effectiveness profile (see Figure 9). Already after five years, Spinraza® would cost more than Zolgensma® and also has less favorable outcomes. Nevertheless, if a drug is compared to a cost-ineffective drug such as Spinraza®, the conclusion of cost-effectiveness is also not always straightforward. Furthermore, it became common to treat patients who received Zolgensma® with Spinraza® or Evrysdi® by Roche with 6-figure annual treatment costs additionally as the combination seems promising. This would have a detrimental effect on Zolgensma's® cost-effectiveness as it was assumed to replace those chronic treatments entirely. New upcoming drugs such as Scholar Rock's apitegromab offer a mechanism of action complementing Spinraza® and Evrysdi® and might improve outcomes even further. Nonetheless, this would again result in higher annual treatment costs.

Also other European countries like Italy and Spain either split the payment or contracted outcomes-based. Italy split the payment into five with patient assessments before each additional

FIGURE 8: TOTAL NET PRESENT VALUE OF ONE-OFF PAYMENT VS. DISCOUNTED ANNUITY PAYMENTS FOR 5 ANNUITIES.

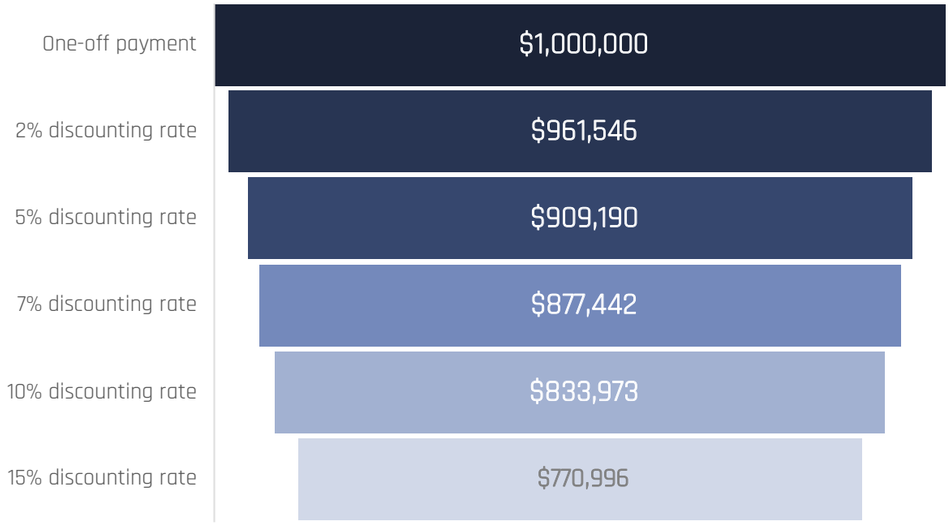
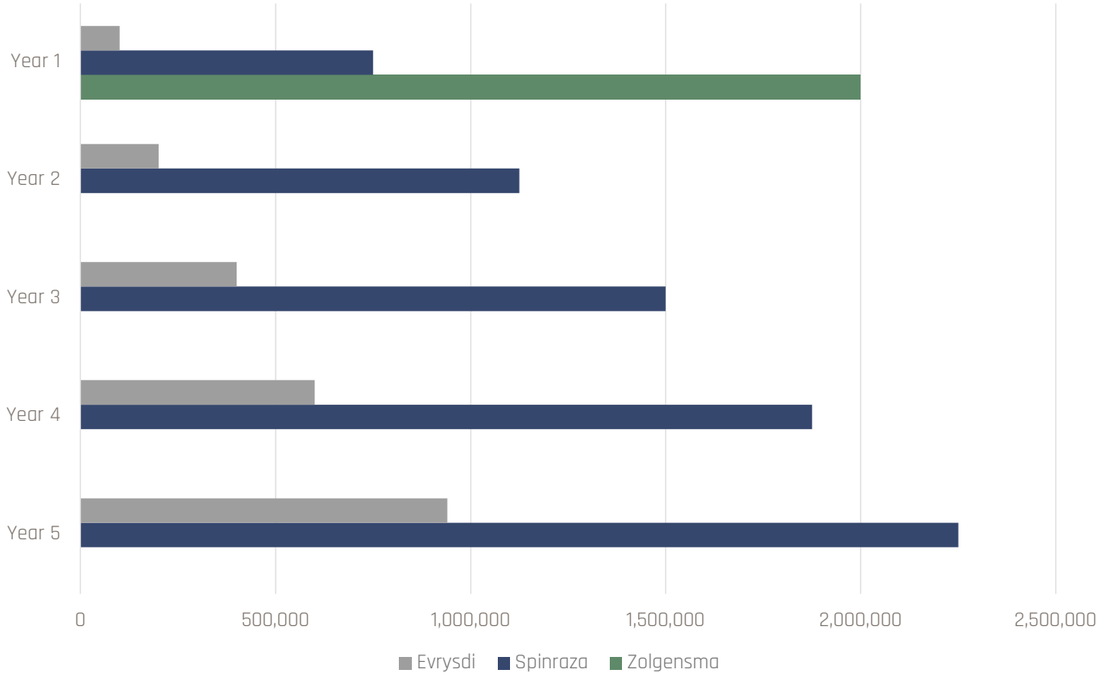


FIGURE 9: CUMULATIVE COSTS OVER TIME OF ZOLGENSMA®, SPINRAZA®, AND EVRYSDI® IN COMPARISON [USD]*



[2] Costs for Evrysdi® vary significantly based on the patient's weight. Patients younger than 2 years cost less than $100,000 and older patients up to $350,000. For comparability with Zolgensma®, early treatment and an increase over time is assumed.

payment. In Spain, the reimbursement was also linked to treatment results and obtained market access via a managed entry agreement. In the UK, the National Health Service (NHS) also agreed to reimburse Zolgensma® with a substantial (confidential) rebate while refraining from waiting for the final NICE guidance. [18, 20, 36]

Key learnings Zolgensma®

Generating additional evidence and showing sustained effect is relevant for most one-off (curative) therapies in a rare disease setting; The comparison of standard lifetime therapy costs and the NPV calculation for annuity payments is crucial to assess the opportunity.

ENTRESTO® IN CHRONIC HEART FAILURE

Often when ATMPs come to market, they are the first treatments changing the course of a condition with significant improvements, sometimes even have curative potential, and no serious competitors. An early outcomes-based example not following this rule is Entresto® indicated for acute and chronic heart failure. This drug entered a highly genericized primary care market in 2016 having cheap drugs such as enalapril as comparators. Entresto® not only had to compete against well-established drugs but also against their daily price of less than $1 per day. Entresto® launched with a daily price of about $12 in the US and offered outcomes-based agreements to Aetna and Cigna clients first. Even though this price seemed high for observers, trial data and the promise of saving overall healthcare expenditure were a convincing argument for payors – initial sales however only rose slowly. Novartis offered an outcomes-based agreement based on heart failure hospitalizations. If real-life data showed higher numbers in hospitalizations than seen in study outcomes, Novartis would reduce the price or increase rebates. The concept of tying reimbursement to outcomes deemed beneficial to payors as hospitalizations due to heart failure cause significant medical costs.

To overcome prescriber reluctance in the first place and further foster the drug's uptake in the US, Novartis kicked off patient assistance programs covering patient co-payments, free trial prescriptions for the first month, and free patient support programs e.g. to promote a healthier lifestyle. This move additionally increased the number of prescriptions by making Entresto® more acceptable to prescribers.

In 2023, Entresto® reached another two milestones: 1) extended data protection by receiving approval for children with heart failure, and 2) became Novartis' bestselling drug by generating a revenue of about $6 billion. [28, 33, 40, 41, 42]

Key learnings Entresto®

Hard endpoints from trials such as hospitalizations (significant financial burden for payors) can be a good baseline and starting point in RWE settings. In certain circumstances, even a genericized market can be conquered with innovation.

REPATHA® IN HYPERLIPIDEMIA

The way risk is shared between the payor and the manufacturer can vary greatly based on the specifics of the contract. The key factor in determining how the risk is allocated is the reimbursement-defining outcome. An interesting example is Amgen's outcomes-based deal for Repatha®, indicated for hyperlipidemia aiding to prevent certain cardiovascular events. If events such as heart attacks or strokes occurred while on treatment, Amgen agreed to refund the reimbursement (for patients insured under Harvard Pilgrim Healthcare). The risk Amgen takes here is limited as only 4.5 events in 100 patient years were observed. In addition to this agreement, the price was reduced according to the Institute for Clinical and Economic Review (ICER) assessment and Amgen agreed to lower out-of-pocket costs for patients aiming to facilitate patient access – travel expenses or accommodation would also be covered by the manufacturer for receiving the treatment. [2, 47]

Key learnings Repatha®

Defining the exact outcome is critical as it determines the risk distribution between the payor and manufacturer.

3. Case studies for Innovative and Outcomes-based Pricing Models in the US and Europe

ZYNTEGLO® IN BETA THALASSEMIA

Genetic disorders such as beta thalassemia can have tremendously high lifetime treatment costs with available chronic treatment options. This becomes relevant for pricing potentially curative treatments as the Zolgensma® case has shown. In beta thalassemia, the lifetime costs for transfusions and other treatments would amount to more than $6M per patient. Bluebird Bio's gene therapy Zynteglo® can cure Beta Thalassemia by replacing a defective gene relevant to hemoglobin synthesis. This works by genetically modifying the patient's stem cells, making the patient its own stem cell donor. When curing the disease, patients no longer need burdensome blood transfusions that used to be administered in frequent intervals. The price tag for the cure is $2.8M in the US but still, the company claims to be cost-effective for the 800 – 850 potentially treatable patients. Here, however, discounting the future costs applies similarly to Figure 8 – spending millions on a treatment today could theoretically exceed discounted costs in the future; the NPV calculation would improve decision-making here. [44]

Key learnings Zynteglo®

Even with a positive cost-effectiveness claim, there is no guarantee that payors and manufacturers reach an agreement. A drug lacking acknowledgment of adding value versus existing treatments can lead to access gaps and less innovation for patients.

Outcomes-based terms agreed in the US for Zynteglo® include Bluebird to refund 80% of Zynteglo's costs (paid upfront) if two years post-therapy, patients remained uncured and still needed blood transfusions. Clinical evidence showed that 90% of treated patients responded sufficiently to the treatment and thus, the refund would only apply to about 10% of the treated patients. While annuity payments and outcomes-dependency had also been planned for Germany, Bluebird withdrew Zynteglo® from the market. Bluebird felt compelled to do so due to the lack of price agreement between the German statutory health insurance and Bluebird: "[...] reimbursement negotiations in Germany did not result in a price for Zynteglo® that reflects the value of this one-time gene therapy with potential life-long benefit [...]" according to Bluebird. Bluebird offered five annual installments of €315,000 while the German statutory health insurance body proposed a significantly lower total price of €630,000. Bluebird found the offer unacceptable, claiming the deal is a business loss as the major costs of production and delivery to patients would remain uncompensated. Consequently, patients in Germany were deprived of a potentially life-changing drug while continuing to experience frequent burdensome blood transfusions. [4, 8, 30]

ROCTAVIAN® IN HEMOPHILIA A AND BEQVEZ® IN HEMOPHILIA B

Staying within the field of costly hematology products: The gene therapy Roctavian® by BioMarin is indicated for the treatment of hemophilia A replacing factor VIII, EMA approved in late 2022, followed by FDA in June 2023 with costs of $2.9 million. The company justifies the price based on costs of about $800,000 per patient per year for the already approved preventative drug Hemlibra® (Roche). And indeed, even with the high price tag, the ICER institute calculated that Roctavian® is cost-effective by increasing QALYs and reducing the lifetime costs by several million dollars. However, the duration of the effect remains undetermined and is a crucial factor to conclude on the long-term benefits. This is why BioMarin accepted a relatively strict outcomes-based risk-sharing agreement in the US.

The agreement entails that if patients were non-responders, BioMarin would reimburse the full wholesale acquisition costs. If efficacy was lost within four years of therapy, the price would be partially refunded. Interestingly, in Europe, the warranty is offered for a longer duration of 5-8 years as stated by a BioMarin representative. Nonetheless, the success of Roctavian® including its adoption still needs to be determined, especially given other available treatment options which differentiates this case from most other ones described here. [7, 32, 35]

Key learnings Roctavian® and Beqvez®

Customized strategic approaches per market and flexibility lead to success in both market access and commercially, e.g. considering the duration of warranties.

Pfizer also offered a warranty program for the 2024 approved virus-based gene therapy Beqvez® in hemophilia B which is licensed from Spark Therapeutics. Equal to BioMarin's approach, Pfizer would reimburse costs of Beqvez® if no durable treatment effect was achieved and the patient would still rely on factor IX infusions. Although only approved in April 2024, Pfizer decided in February 2025 to discontinue Beqvez® moving away from gene therapies and stating that interest by patients and physicians was very limited. [53]

ELEVIDYS® IN DUCHENNE MUSCULAR DYSTROPHY

In contrast to all previous examples, Elevidys® for the treatment of Duchenne muscular dystrophy (DMD) developed by Sarepta and co-marketed by Roche, purposefully does not follow an outcomes-based approach. The drug received FDA accelerated approval in June 2023 with a price of $3.2M. According to CEO Douglas Ingram, the drug would still be cost-effective for $5-13M due to the tremendously high costs of chronic treatment. Instead of applying an outcomes-based model, another "innovative concept" will be found to reimburse the drug. He argued that only a restricted patient population will have access to the drug, consequently resulting in the budget impact being manageable. As such, some manufacturers do not perceive currently used models as sufficient but are still aware of the necessity of different than standard payment mechanisms. Despite the claims of being cost-effective, the drug failed to meet the primary endpoint (North Star Ambulatory Assessment 52 weeks after treatment) in their confirmatory phase III EMBARK trial end of October 2023. Compared to placebo, the functional improvement was insignificant. Secondary endpoints of motor functioning, however, improved significantly which made Sarepta confident to gain a label expansion. In June 2024 they eventually received the expansion for patients aged four and above irrespective of ambulatory status – confirmatory trial data for certain sub-populations pending. It will be interesting to observe the impact of recent trial data on pricing and reimbursement and whether projected peak sales of $4 billion will be feasible. [6, 21, 34, 49]

Key learnings Elevidys®

Companies do not want to follow a "one-size-fits-all approach" as some companies develop their own innovative pricing model strategies to reach their targets and achieve success. Sometimes, companies do neither pursue outcomes-based approaches nor financial-based models.

CASGEVY® AND LYFGENIA® IN SICKLE CELL DISEASE

ATMPs presently heavily discussed include the first CRISPR gene-editing therapies: Casgevy® (exa-cel) by Vertex and CRISPR Therapeutics and Lyfgenia® (Lovo-cel) by Bluebird Bio. They were FDA-approved in December 2023 for sickle cell disease. While the viral-based gene therapy Lyfgenia® is priced at $3.1M, the CRISPR therapy Casgevy® is priced lower at $2.2M; both are almost within the range of ICER's cost-effectiveness threshold of $1.35M up to $2M. Considering confidential rebates, achieving cost-effectiveness seems realistic. With these two treatments for sickle cell disease, it also becomes apparent that pricing decisions can become a competitive advantage or disadvantage. While innovative drugs for rare diseases can often find fertile ground for monopolies, competition between two or more companies (in this case an established company vs. a newcomer) can lead to decreasing prices. [15]

Key learnings Casgevy® and Lyfgenia®

Even with highly innovative methods such as gene editing and with prices well above $1M, pricing decisions can become a building block of the competitive strategy.

casgevy™ (exagamglogene autotemcel) suspension for IV infusion

lyfgenia™ (lovotibeglogene autotemcel) suspension for IV infusion

EXCURSUS DRUG PRICING IN JAPAN

Japan is the third largest pharma market worldwide and hence, quite an attractive market for pharmaceutical companies from a revenue perspective. Despite being attractive, Japan was known for a long time to be a challenging country for accessing the market, especially for ex-Japan companies. Consequently, patients in Japan either did not receive innovative drugs at all or a few years later than patients in the US and EU. Considering the relevance of this market and recent regulatory modifications enabling companies and their innovative products to achieve easier and quicker market access, it is interesting and necessary to have a closer look at Japan. This excursus gives an overview of the pricing system in Japan and elaborates on the market's particularities through selected case studies of innovative drugs.

Prices of pharmaceuticals in Japan are determined when entering the market for the first time but are also frequently re-assessed. For new drugs, pricing can follow two approaches depending on the availability of comparable drugs (see Figure 10).

1) Comparable in this context means comparable regarding e.g., efficacy and effect, mechanism of action, composition and chemical structure as well as dosage form and administration. Depending on the drug's innovative character, additional premiums can be awarded (see Figure 11). However, if the innovation remains unacknowledged by the responsible body, the price is supposed to be not higher than the comparator drugs' price. [1]

2) If comparable drugs are unavailable, the price of new drugs is determined using a cost-plus calculation. This includes costs for material, labor, manufacturing, sales, distribution, research, profit, and tax. For innovative drugs, additional premiums can apply, corrected with a factor based on the cost disclosure rate of the manufacturer. This rate is defined as disclosed costs as a share of total product costs. For example, a disclosure level of more than 80% would result in the full awarded premium while a cost disclosure of less than 50% would result in only 20% of the awarded premium. [1]

FIGURE 10: JAPANESE PRICING SYSTEM FOR NEW DRUGS

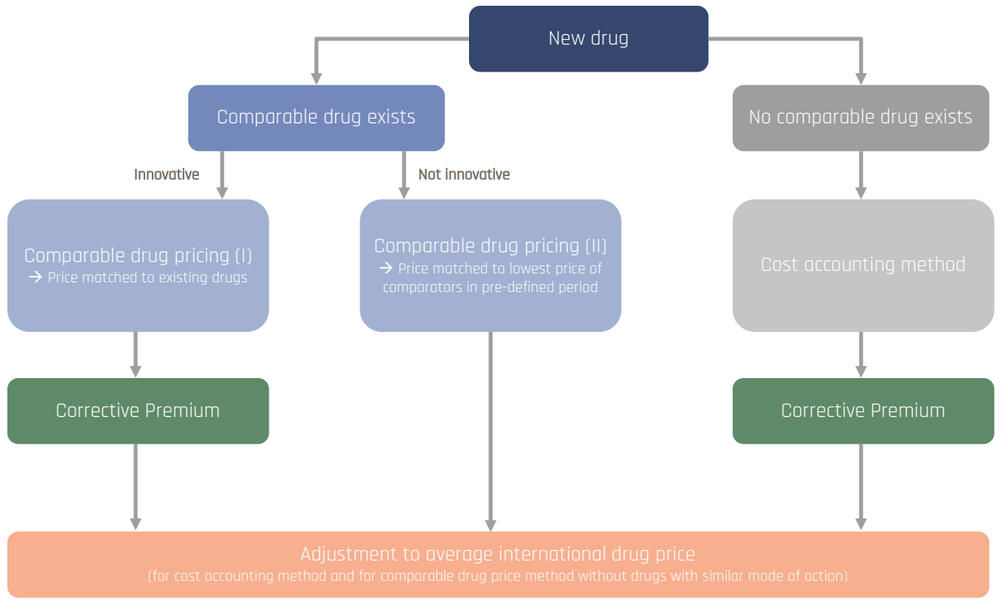


FIGURE 11: PRICE PREMIUMS FOR INNOVATIVE DRUGS IN JAPAN

Premium	*Description*	*Range*
Innovativeness	New mechanism of action, high efficacy or safety, improvement of disease treatment	70-120%
Usefulness	High efficacy or safety, improvement of disease treatment	5-60%
Marketability	Orphan drugs, etc.	5%, 10-20%
Pediatric	Explicit inclusion of pediatric populations	5-20%
Sakigake Review Designation Scheme	Approval obtained in Japan ahead of other countries	10-20%
Specific Use	High unmet need, no marketability or pediatric premium and comparator without marketability premium	5-20%

Luxturna®, an innovative drug without comparators at launch, was only approved in Japan in June 2023, followed by launch in August 2023, six and five years later than in the US and EU, respectively. Luxturna® received a 45% premium for its therapeutic usefulness, e.g. clinically valuable mechanism of action and improved treatment for the disease. Additionally, a 10% marketability premium was granted as being an orphan drug. However, both the premiums were not fully granted due to the cost disclosure rate of below 50%. The effective launch price was about $340,000 per eye, making it the second most expensive drug after Zolgensma® at that point in time. The revenue and profit success story for Luxturna® in Japan remains to be observed as the launch has been relatively recent and only a handful of patients have been treated. [13]

Similarly, Kymriah® was also assessed as a first-in-class drug using the cost-based method in 2019. Kymriah® received a premium of only 35% due to the disclosed costs of less than 50%, resulting in an effective premium of 7% only (20% of 35%). Also noteworthy is that Novartis aimed to become the very first outcomes-based reimbursed treatment, only being paid for if patients responded.

Different from the cost-plus calculation is the comparative pricing method. Zolgensma® was priced in Japan by comparing it with the already available Spinraza®. The price base was one full treatment cycle of 11 vials of Spinraza®. In addition to the base price, a premium of 50% for the therapeutic usefulness of the product was granted. Furthermore, a 10% premium was awarded for the fast-track status, thus making

Zolgensma®, the most expensive drug in Japan up until that year. [45]

As stated earlier in the Zolgensma® case study, it is important to consider which comparator is used for cost-effectiveness analyses. Comparing a new drug (Zolgensma®) to a non-cost-effective drug (Spinraza®) can have critical consequences on the cost-effectiveness appraisal of the new drug. For drugs that are already on the market and intending to control drug spending, Japan introduced the possibility of re-assessments (cost-effectiveness assessments). If Zolgensma® was assessed and considering its good cost-effectiveness compared to Spinraza®, it would most likely not suffer price reductions. For other drugs discussed in the chapters before, it would be different. Again, Kymriah® and Yescarta® took a special role in Japan because they were the first drugs to undergo the cost-effectiveness assessment. In 2021, Kymriah® received a 4.3% price reduction followed by the same reduction for Yescarta® soon after. [12, 38]

The cost-effectiveness system works similarly as in other markets where these analyses were performed before Japan introduced them. For example, Incremental Cost Effectiveness Ratios (ICER) which determine the incremental benefit of a drug vs. the incremental costs of a drug are utilized. Usually, ICER is expressed as costs per Quality Adjusted Life Year (QALY) which also Japan utilizes.

But there are also some particularities of the Japanese system:

01 The assessment does not influence whether a drug should be reimbursed or not, but which price would be appropriate for it.

02 The assessment is usually only performed for costly drugs or the ones with a large market size / high sales.

03 In general, pediatric-only drugs and drugs for rare diseases are exempt from this regulation.

04 Cost-effectiveness thresholds differ by indication. Usually, the threshold is about $30,000 per QALY but e.g. for cancer drugs it is higher at about $50,000 per QALY.

05 Prices can also be corrected upwards if medical expenses are reduced overall.

In summary, the Japanese pricing system rewards innovation by granting different price premiums and uses similar assessment approaches as European countries. Nevertheless, price disclosure obligations reduce the market's attractiveness. Time will demonstrate whether manufacturers will consider Japan as an attractive market for early launches and supply patients with cutting-edge pharmaceuticals and whether the government's aim of fostering access to innovation will be fruitful. If not, it might be necessary to adjust regulation and further increase the market's openness for innovation.

“CONSIDERING THE ROLE OF BOTH THE PAYOR AND PHARMACEUTICAL COMPANY, THE NATURE OF CONCLUDED AGREEMENTS SHOULD BE SYMBIOTIC AND FAIR FOR BOTH PARTIES. [....] IF ONE STATEMENT COULD SUMMARIZE THE LEARNINGS, IT WOULD BE: NO ONE-SIZE-FITS-ALL.”

04

LEARNINGS & OUTLOOK

Whether it is a financial- or outcomes-based model or a combination of both, there are always important factors that determine and impact the model’s success.

Considering the role of both the payor and pharmaceutical company, the nature of concluded agreements should be symbiotic and fair for both parties. Symbiotic agreements involve fostering patient health, treatments at prices affordable for payors, while the industry being able to achieve market access, recoup their investments, and being able to make reasonable profits to invest in the discovery and development of innovative drugs. Thus, the balance between the advantages and disadvantages of each model and between both parties should be kept. Figure 12 gives a condensed non-exhaustive overview of selected innovative and outcomes-based pricing models covering perspectives from the industry and the payor.

FIGURE 12: ADVANTAGES AND DISADVANTAGES OF SELECTED INNOVATIVE AND OUTCOMES-BASED PRICING MODELS.

Model	Perspective Pharma	Perspective Payor
Subscription model	⊕ Exclusivity for product / positioning ⊕ Predictable sales volume	⊕ Improves insurer budget planning ⊕ Limit budget impact ⊕ Wide access for insured population improving health
	⊖ High rebates & price competition	⊖ Dependence on one supplier and low flexibility
Annuity payments	⊕ Constant cash flow	⊕ Decrease the upfront budget burden
	⊖ Annuity decreases NPV	⊖ Budget commitment
Partial / full refund	⊕ Confidentiality ⊕ Public opinion	⊕ Value for money
	⊖ Outcomes can be influenced by non-drug factors ⊖ Performing of outcome measurements	⊖ Bureaucracy
Coverage with evidence generation	⊕ Early access	⊕ Decision criteria ⊕ Ensures benefit
	⊖ Costs of evidence generation ⊖ Late failure ⊖ Regulatory risks	⊖ Bureaucracy

The real-life examples analyzed in this work contributed to understanding the potential of innovative and outcomes-based pricing models by giving context to pure theory. If one statement could summarize the learnings, it would be: "no one-size-fits-all". It is critical to acknowledge the importance of tailor-made approaches making a drug successfully accessible to patients. Tailor-made approaches involve analyzing the unique characteristics of drugs, its indications, and different healthcare systems across countries. While it is difficult to identify clear trends, at least for costly one-time treatments, the direction is quite understandable combining both outcomes and annuities. The outcomes component guarantees that only effective treatments are reimbursed, and the annuity component limits the immediate budget impact. In the near future, it is not anticipated that new reimbursement schemes will be introduced that deviate significantly from the models described here. While Pfizer announced for the now withdrawn Beqvez® a warranty program that resembles earlier schemes, agreements for other ATMPs approved in 2024 were not (yet) disclosed in detail. For instance, Orchard Therapeutics (now subsidiary of Kyowa Kirin) Lenmeldy® / Libmeldy® explains that they are working on outcomes-based agreements with payors and governments but details remain unclear. Considering it being the most expensive drug to date with $4.25M, an outcome-based agreement can be considered appropriate. This of course is also applicable to all other costly ATMPs not discussed extensively here. [55]

Kymriah® and Yescarta®
It is important to consider all stakeholders in the process: payors, manufacturers as well as intermediaries / service providers. Hospitals can be relieved from high upfront purchasing costs by adjusting the billing scheme.

Xalkori® and Alunbrig®
In a competitive market, the better outcomes-based model can become a driver for success.

Epclusa® and Mavyret®
Population-based models can boost prescriptions and improve the patients' access but might limit the business opportunities for manufacturers while assuring a predictable cash flow.

Luxturna®
Using specific outcomes and measuring them in the short and long term offers transparency to all stakeholders, thus enhancing trust in pharma companies and healthcare systems.

Zolgensma®
Generating additional evidence and showing sustained effect is relevant for most one-off (curative) therapies in a rare disease setting; The comparison of standard lifetime therapy costs and the NPV calculation for annuity payments is crucial to assess the opportunity.

Entresto®
Hard endpoints from trials such as hospitalizations (significant financial burden for payors) can be a good baseline and starting point in RWE settings. In certain circumstances, even a genericized market can be conquered with innovation.

Repatha®
Defining the exact outcome is critical as it determines the risk distribution between the payor and manufacturer.

Zynteglo®
Even with a positive cost-effectiveness claim, there is no guarantee that payors and manufacturers reach an agreement. A drug lacking acknowledgment of adding value versus existent treatments can lead to access gaps and less innovation for patients.

Roctavian® and Beqvez®
Customized strategic approaches per market and flexibility lead to success in both market access and commercially, e.g. considering the duration of warranties.

Elevidys®
Companies do not want to follow a "one-size-fits-all approach" as some companies develop their own innovative pricing model strategies to reach their targets and achieve success. Sometimes, companies do neither pursue outcomes-based approaches nor financial-based models.

Casgevy® and Lyfgenia®
Even with highly innovative methods such as gene editing and with prices well above $1M, pricing decisions can become a building block of the competitive strategy.

Based on the case studies and their learnings, specific requirements can be derived that outcome measurements have to fulfill to be suitable for risk-sharing agreements (see Figure 13). Outcomes have to be:

- meaningful to patients and have an impact on their life (e.g. number of strokes and heart attacks on Repatha® treatment in hyperlipidemia)
- specific to the disease and attributable to the drug not being confounded by other factors such as age (e.g. need for blood transfusions in hemophilia)
- measurable in the real-world setting (e.g. achievement of motor milestones in SMA during regular check-ups)
- find the right timing sufficient for the drug to show an effect but also not be too far in the future to remain predictable (e.g. survival with Kymriah® and Yescarta® in ALL)
- Economically impactful and the outcome assessment should not outweigh potential benefits (e.g. hospitalizations as used in Entresto®)

FIGURE 13: SUCCESS PARAMETERS OF OUTCOME MEASUREMENTS IN IPOMS

Despite their current and increased use, IOPMs might still develop further. Crucial for the models' success is and will be:

1. to identify measurable outcomes and tie them to reimbursement
2. to adapt the models depending on the research and development focus in the future
3. to further develop the regulatory environment which will shape the models and vice versa

OUTCOMES OUTLOOK

As mentioned earlier, the defined outcome in innovative pricing models determines the risk allocation between the contracting parties. When it comes to what is being measured as clinical trial outcomes or in real-life settings, the worldwide shift towards digital data generation is on everyone's lips. Use cases such as electronic drug prescriptions, electronic health records, or digital health applications will transform the way health systems assess the benefits of interventions

or allocate resources. On a population level, e.g., health services research can be improved through anonymous datasets from studies or patient records and thus identify changes in public health, or unmet needs and contribute to finding solutions. While generating new data is most important for outcomes-based agreements, already existing but underutilized data as well as routine data should not be neglected. Pioneers like the German platform Honic® aim to democratize healthcare data and research in a European data-privacy and data-security-compliant manner, a possible blueprint architecture for other European countries. Linking near-time real-world data from healthcare providers across silos (e.g. laboratory, GPs and specialists, hospitals, pharmacies) at scale could be promising fostering health services research and consequently improving public health and contain costs. Artificial intelligence should not be neglected considering analyzing datasets. Use cases for IOPMs could be e.g. finding patterns of biomarkers to decide upon their most appropriate combination to measure, for instance, treatment success. Not only established pharma players actively use AI across the value chain but also many large tech companies active in healthcare such as IBM, Google, Microsoft, and Amazon.

Especially on a patient level, digital applications can lead to better outcomes and satisfaction. Considering the case studies, passive as well as active assessments could add value. Wearables such as smart watches, smart rings, or even implants collect and process data and transfer them to e.g. the treating physician. In SMA, monitoring of physical activity can be an indicator of appropriate motor function development after being treated with Zolgensma®. As the drug is indicated for infants, passive monitoring offers the advantage and convenience to families of not needing the patient to perform certain assessments actively. Another example could be Entresto® where not only the aforementioned hospitalizations could be taken into account, but also other parameters related to heart failure such as shortness of breath, sleep disturbances, or pulse irregularities. Here again, AI could help to identify patterns and to some extent, mobile health providers such as Apple, Samsung, and Oura can already contribute to monitoring user health. Wide application in e.g. rare diseases is, however, not yet achieved.

When it comes to active monitoring, the level of monitoring-innovation highly depends on the kind of measurement. A simple translation of questionnaires (patient-reported outcomes, PRO) from the analog to the digital sphere would be at the bottom end of innovation. For instance, patients could report on their quality of life and with it their functioning and improvements on a regular basis. Furthermore, caregivers could provide their impression of the patient's well-being through so-called Home Reported Outcomes (HRO). On the other end of the spectrum is the combination of apps and devices. For instance, standardized tests in a home setting such as measuring the handgrip strength of Duchenne patients with a vigorimeter could be combined with passive measurements or questionnaires as described above.

Using approaches like the ones explained could not only facilitate assessing the drug's effect, whether it achieves what it promises, and the resulting reimbursement implications. It could also transform care being more patient-centered, support the patient to stay compliant, or bridge between two doctor's appointments.

INDICATIONS OUTLOOK

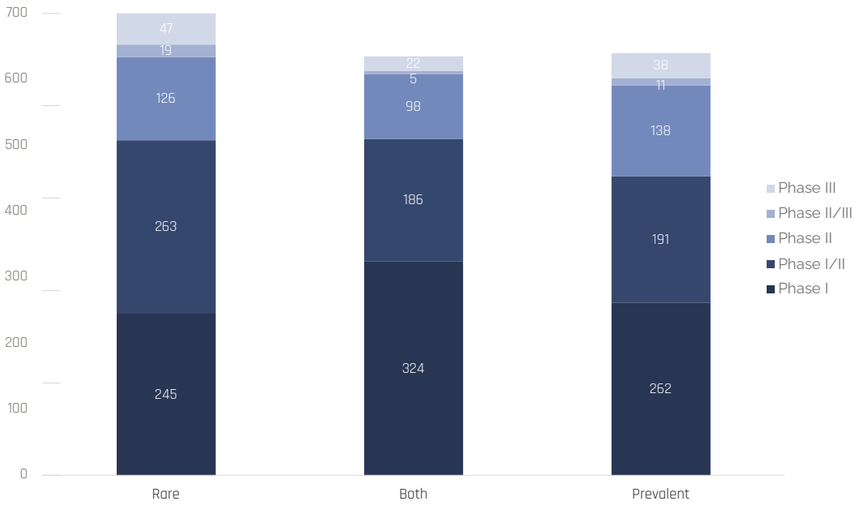
While currently approved ATMPs are primarily indicated for rare diseases – often justifying high prices due to small patient populations – recent trends in research and development suggest a notable shift. Historically focused on rare conditions such as retinitis pigmentosa or thalassemia, the gene and cell therapy pipeline is now expanding toward more prevalent diseases (see Figure 14). [48]

Although oncological therapies continue to dominate the pipeline, the scope of research is broadening significantly. New programs target metabolic disorders like diabetes, infectious diseases such as HIV, or musculoskeletal and connective tissue disorders including osteoarthritis. This diversification reflects a growing ambition to apply such therapies to conditions affecting much larger patient populations.

However, this shift also brings a set of specific challenges. Expanding the potential recipient base requires once again a fundamental rethinking of pricing and reimbursement strategies. Even if these therapies prove cost-effective by curing chronic diseases, their cumulative budget impact could overwhelm healthcare systems. Innovative payment models and long-term value assessments will be critical to ensure sustainable access.

Technologies such as CRISPR or small interfering RNA could also contribute to a further acceleration of the trend of disease root targeting including prevalent indications. Yet, these innovations come with their own set of hurdles. Manufacturing and distribution at scale remain complex and resource intensive. Moreover, the safety profile of these therapies must be exceptionally robust, especially

FIGURE 14: CURRENT CLINICAL TRIALS BY PHASE AND PREVALENCE



when administered to large and diverse patient populations. Past experiences have shown that some gene therapies have struggled to meet these safety expectations.

REGULATORY OUTLOOK

Regulators will also have a say in the future of non-standard reimbursement schemes. Potentially, more public-private partnerships might evolve so that pressing unmet needs in e.g. rare diseases or financially non-viable therapeutic areas would be further targeted. An example of this is the antibiotics strategy in the UK where the government implemented a subscription model uncoupling drug volumes from reimbursement to foster public health. In the case of antibiotic resistance, stockkeeping alone would be reimbursed as sparse use of antibiotics is being promoted. [9, 37]

Additional attention should be given to the European HTA regulation which became effective in 2025 for oncological products and ATMPs, will be followed by orphan drugs in 2028, and the remainder in 2030. This mandatory centralized benefit assessment process aims to contribute to less bureaucratic efforts for manufacturers, standardize appraisals, and facilitate market access. Indirectly, it will also have an impact on national pricing and reimbursement all over Europe – the ultimate decisions and negotiations will, however, remain national. To achieve regulatory and subsequently commercial success, manufacturers must implement early feedback cycles with regulatory authorities. This encompasses evidence generation of, e.g. pivotal trials and finding the right outcome, real-world evidence expectations, as well as health economic analyses. [25, 51]

Given the similarities and differences between all different reimbursement models, one can conclude that the optimum can be achieved as a compromise between manufacturers and payors and that the process should be developed and planned strategically. Ideally, considerations of potential reimbursement strategies should already start early in the trial program. For instance, choosing the right outcome measures in phase II is crucial to building upon in pivotal trials – right outcome in the sense of achieving regulatory approval but also satisfying payors. For the latter, outcomes should also be measurable in a real-world context and attributable to the respective drug. Under certain circumstances, companion diagnostics might facilitate this, however, also potentially increase the regulatory hurdle and the market adoption. [52]

To assess the approach best suited for a product, the above-mentioned case studies offer valuable learnings. Those learnings can be translated into successful market access and commercial strategies.

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ABOUT STRADOO®

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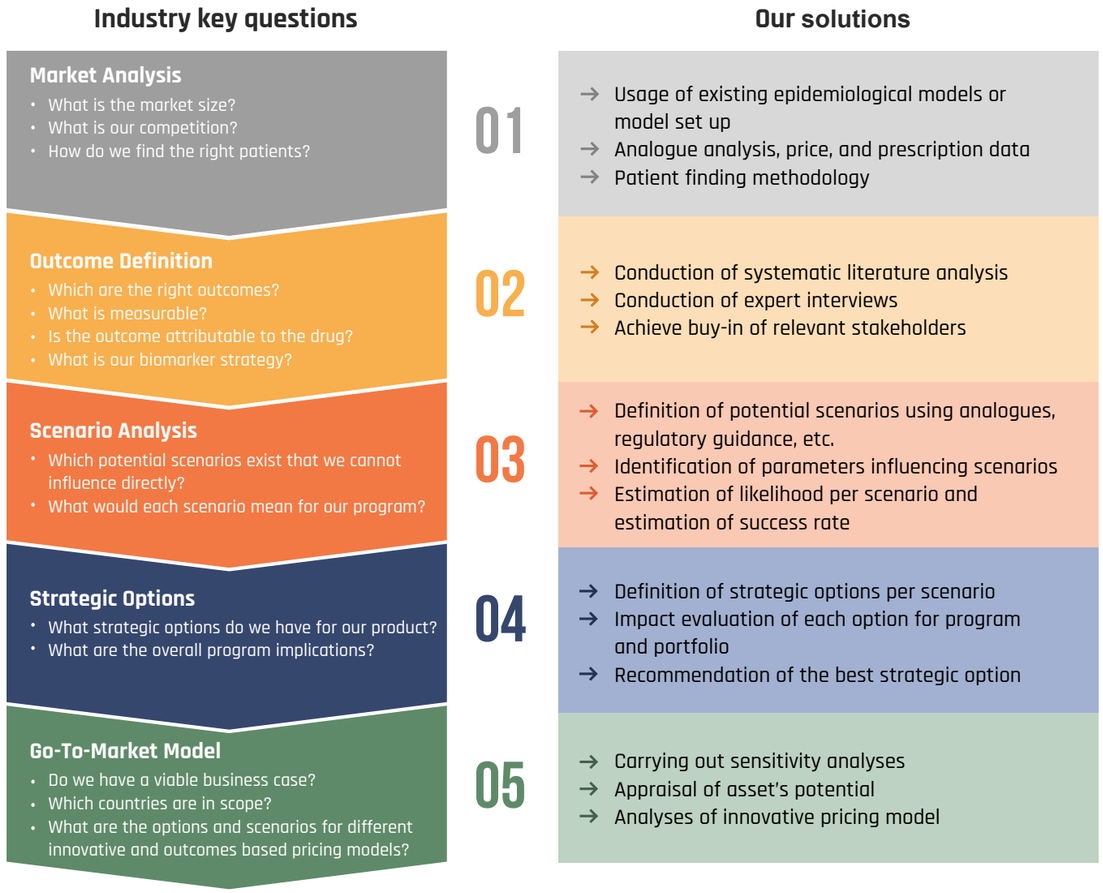
stradoo® is a globally acting strategy consulting and advisory firm focused exclusively on the life sciences industry. Several years ago, we set out to create innovative management tools that would transform the way organizations define and execute their strategies. Today, our tools are being used by most of the world's leading healthcare companies and institutions to solve their problems and enhance their competitiveness. Having worked in all major markets in diverse indications and knowing the client's needs, we can help when it comes to strategic work for innovative pharmaceuticals.

For IOPM-related topics, different questions must be raised and can be answered using various methodologies and their solutions as displayed in Figure 15.

FIGURE 15: FROM MARKET TO MODEL: METHODOLOGICAL APPROACH OF IOPMS.



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