

DOLON

# The 'rituximab effect': the challenge of low-cost and off-label comparators in rare diseases

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*All opinions my own*

# The 'Rituximab effect'

95%

of rare diseases  
do not have an  
approved treatment<sup>1</sup>

67%

of rare disease patients  
have received medicine  
directly linked to  
their disease<sup>2</sup>

**Mainly low-cost off-label treatments?**

[1] Spotlight on rare diseases (2019) The Lancet; [2] RARE2030: Foresight in rare disease policy (2021) EURORDIS

# The 'Rituximab effect'

Non-exhaustive list of orphan indications for which rituximab is named in guidelines/studies<sup>1</sup>

Rituximab	gMG	ITP	PPMS
	wAIHA	Systemic vasculitis	IgA neuropathy
	NMOSD	SLE	Systemic sclerosis
Polydermato- myositis	1° Membranous nephropathy	Autoimmune pancreatitis	Autoimmune hepatitis
TTP	Eosinophilic granulomatosis	Dermatomyositis	Lupus nephritis
Necrotizing glomerulopathy	Multiple rituximab biosimilars available in Europe		~€5-10k (NMOSD)

[1] Shinde et al. (2020) Health Advances

**gMG**: Generalised myasthenia gravis; **IgA**: Immunoglobulin A; **ITP**: Immune thrombocytopenia; **NMOSD**: Neuromyelitis optica spectrum disorder; **PPMS**: Primary progressive multiple sclerosis; **SLE**: Systemic lupus erythematosus; **TTP**: Thrombotic thrombocytopenic purpura; **wAIHA**: warm hemolytic anemia

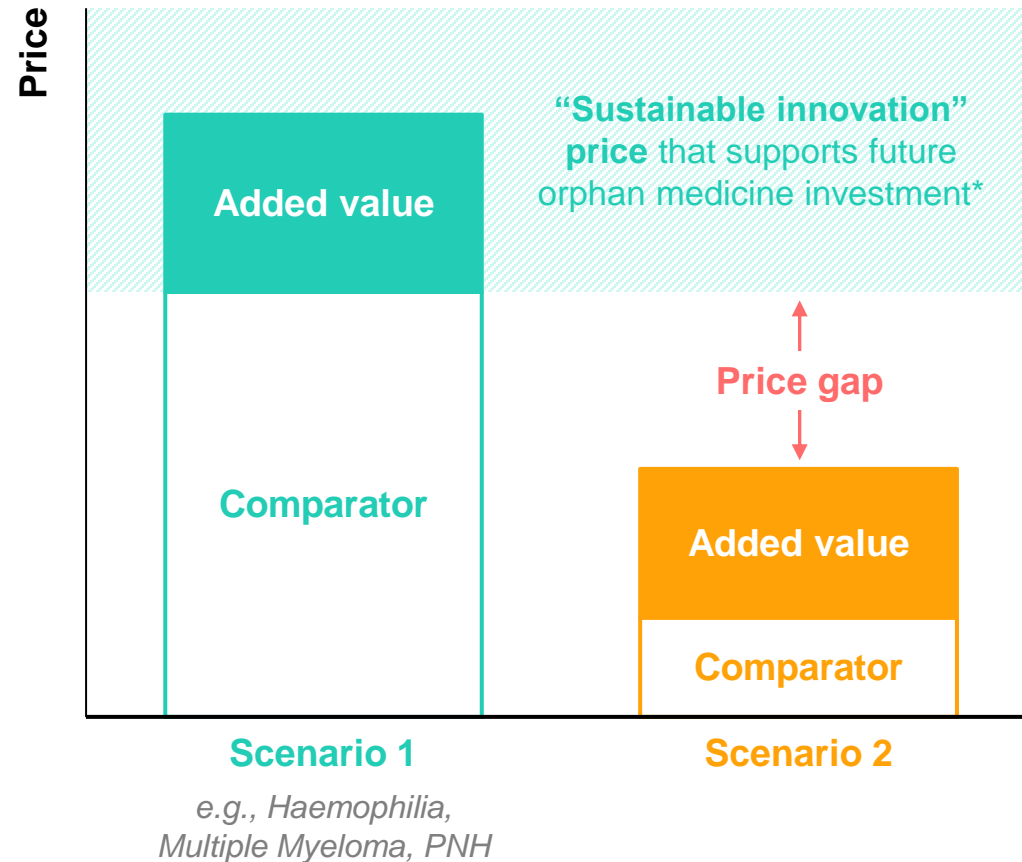
# The orphan pricing challenge with low-cost comparators

“

There was no room for manoeuvre in discussions [in France for Epidyolex] **because the comparators selected were essentially low-cost generics**

— Country Manager,  
Jazz Pharmaceuticals

APM News, Feb 2023



\*i.e., a return on investment that is broadly aligned with non-orphan medicine

# No agreed pricing framework to account for rarity



## Delays in reimbursement

~4 months

longer time to reimbursement than non-orphans<sup>1\*</sup>

## Limited patient access

37%

of orphan drugs available to patients in Europe (average)<sup>1\*</sup>

## Is economic return sufficient to justify early investment in orphan R&D programme?

Estimated % OMPs (2000-2020) economically viable in Europe<sup>2\*\*</sup>

17.2%

Estimated rNPV -€6.7 million



“

~50% orphan medicines have annual sales of €10 million or less in EU

— EU Technopolis Report 2019

\*EU average; \*\*Using revenues from Technopolis report. [1] EFPIA W.A.I.T Indicator 2021 survey (2021); [2] Dolon (2020). Available at: [www.dolon.com](http://www.dolon.com)  
 EU: European Union; OMPs: Orphan medicinal products; rNPV: Risk-adjusted net present value; US: United States

# Need a robust pricing strategy & rationale

- 1 Establish pricing principles / internal pricing framework
- 2 Triangulate a pricing corridor
- 3 Define pricing targets & rationale
- 4 Identify tactics to 'close the gap'
- 5 Instill confidence across the organization

## Why do we need an internal pricing framework?

1

To reflect **company ethos**; pricing must be aligned to corporate values

2

To allow companies to **explain** their pricing decisions

3

To ensure **consistency** of pricing decisions across portfolio and over time

4

So companies can **engage** in the ongoing debate about how P&R frameworks for orphan drugs should be structured

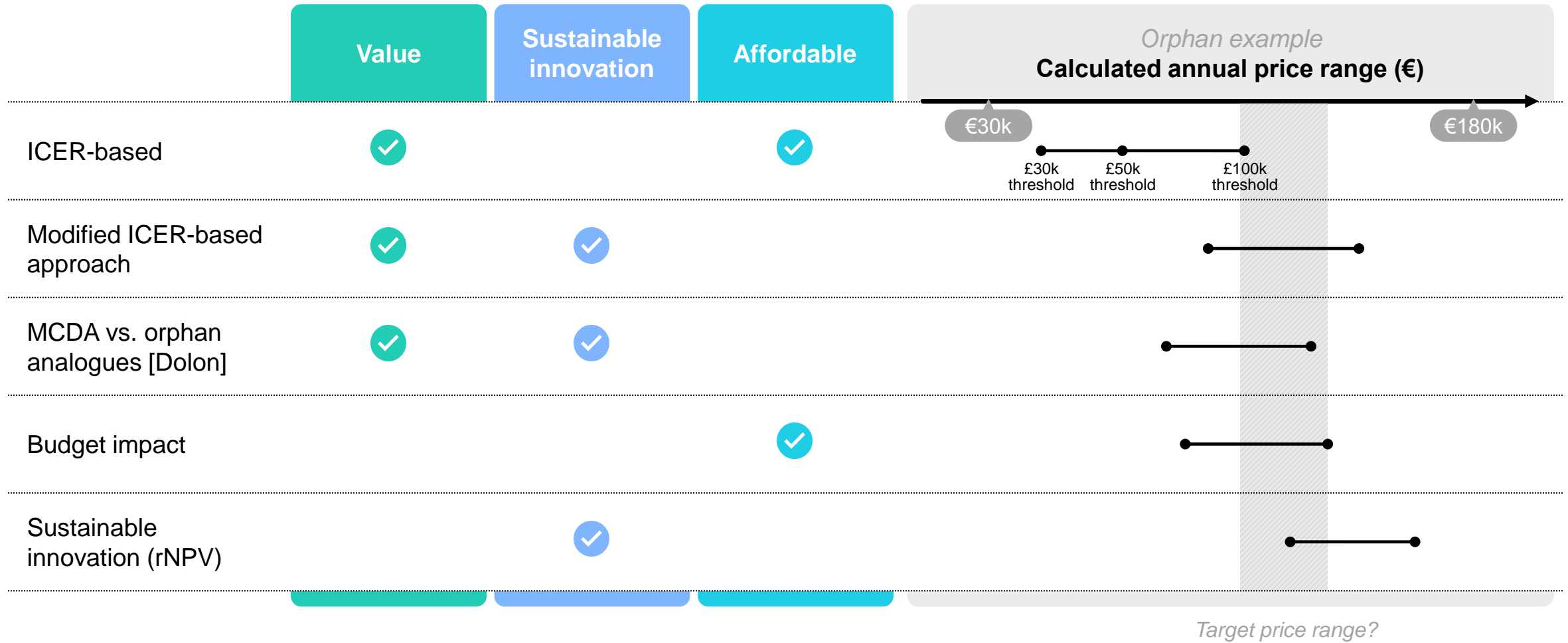
# Pricing principles often based on concepts of value, sustainable innovation and affordability

	Price should reflect <b>Value</b>	Price should ensure <b>Sustainable innovation</b>	Price should consider <b>Affordability</b>
<b>Biogen<sup>1</sup></b>	Value to patients, value to society, value-based framework	Innovation, shareholder value	Affordability
<b>BMS<sup>2</sup></b>	Value to patients, value to society	Innovation, investment in R&D, shareholder value	Affordability, sustainability
<b>Gilead<sup>3</sup></b>	Clinical value	Investment in R&D, cost of R&D	Differential pricing
<b>Sanofi<sup>4</sup></b>	Value to patients, value to society	Need to support ongoing trials, size of target population	Affordability
<b>Takeda<sup>5</sup></b>	Value to patients	Commitment to innovation	Affordability, sustainability
<b>Vertex<sup>6</sup></b>	Benefit to patients	Revenues fund ongoing research, scientific innovation	Access to all eligible patients

[1] Biogen. Available at: <https://www.biogen.com/responsibility/reporting-and-principles.html?accKey=Z>; [2] BMS. Available at: <https://www.bms.com/about-us/responsibility/position-on-key-issues/pricing.html>; [3] Gilead. Available at: <https://www.gilead.com/-/media/Files/pdfs/Policy-Perspectives/Product%20Pricing%20and%20Patient%20Access.pdf>; [4] Sanofi. Available at: [https://www.sanofi.us/-/media/Project/One-Sanofi-Web/Websites/North-America/Sanofi-US/Home/corporateresponsibility/Prescription\\_Medicine\\_Pricing\\_2019.pdf](https://www.sanofi.us/-/media/Project/One-Sanofi-Web/Websites/North-America/Sanofi-US/Home/corporateresponsibility/Prescription_Medicine_Pricing_2019.pdf); [5] Takeda. Available at: <https://assets-dam.takeda.com/raw/upload/v1675193360/legacy-dotcom/siteassets/system/who-we-are/companyinformation/positions-guidelines/takeda-position-on-global-pricing-eg.pdf>; [6] Vertex Available at: <https://www.vrtx.com/sites/global/files/Our-View-Drug-Pricing.pdf>. **R&D:** Research & development

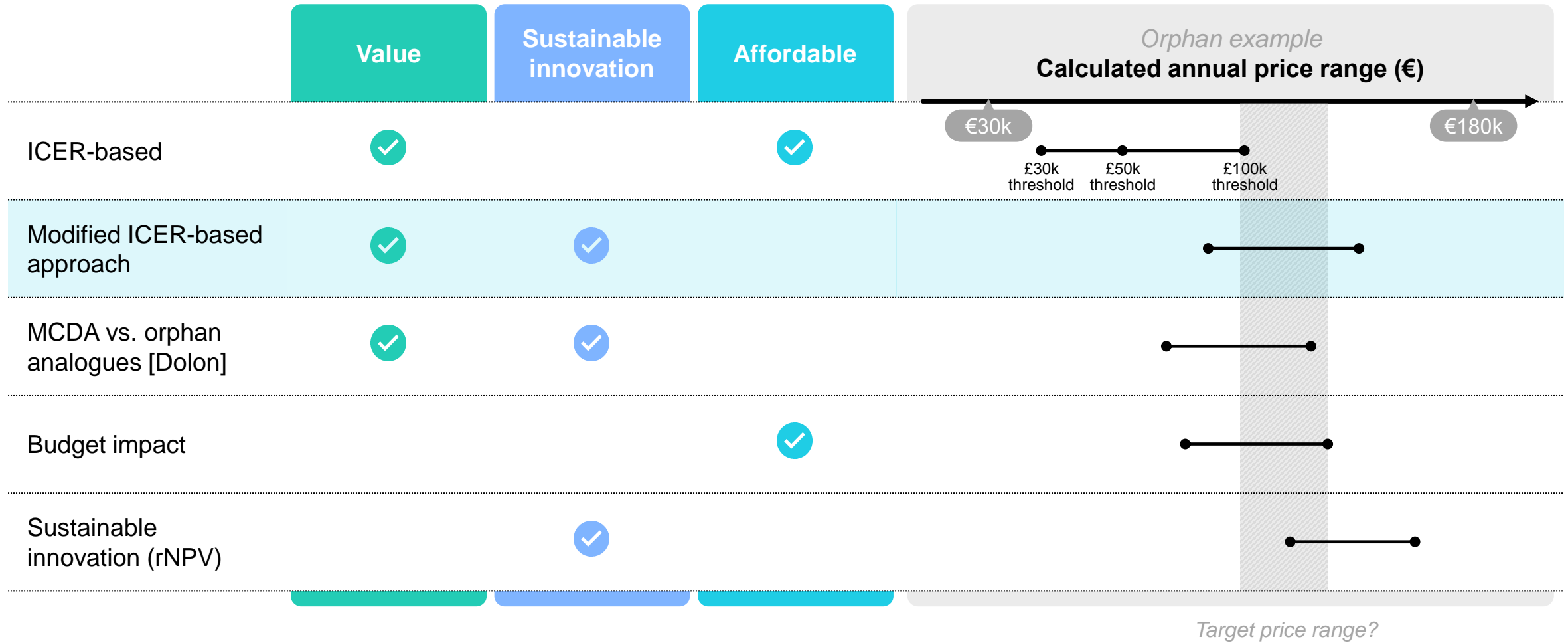


# Triangulating a price based on these concepts



ICER: Incremental cost-effectiveness ratio; MCDA: Multiple-criteria decision analysis; rNPV: Risk-adjusted net present value

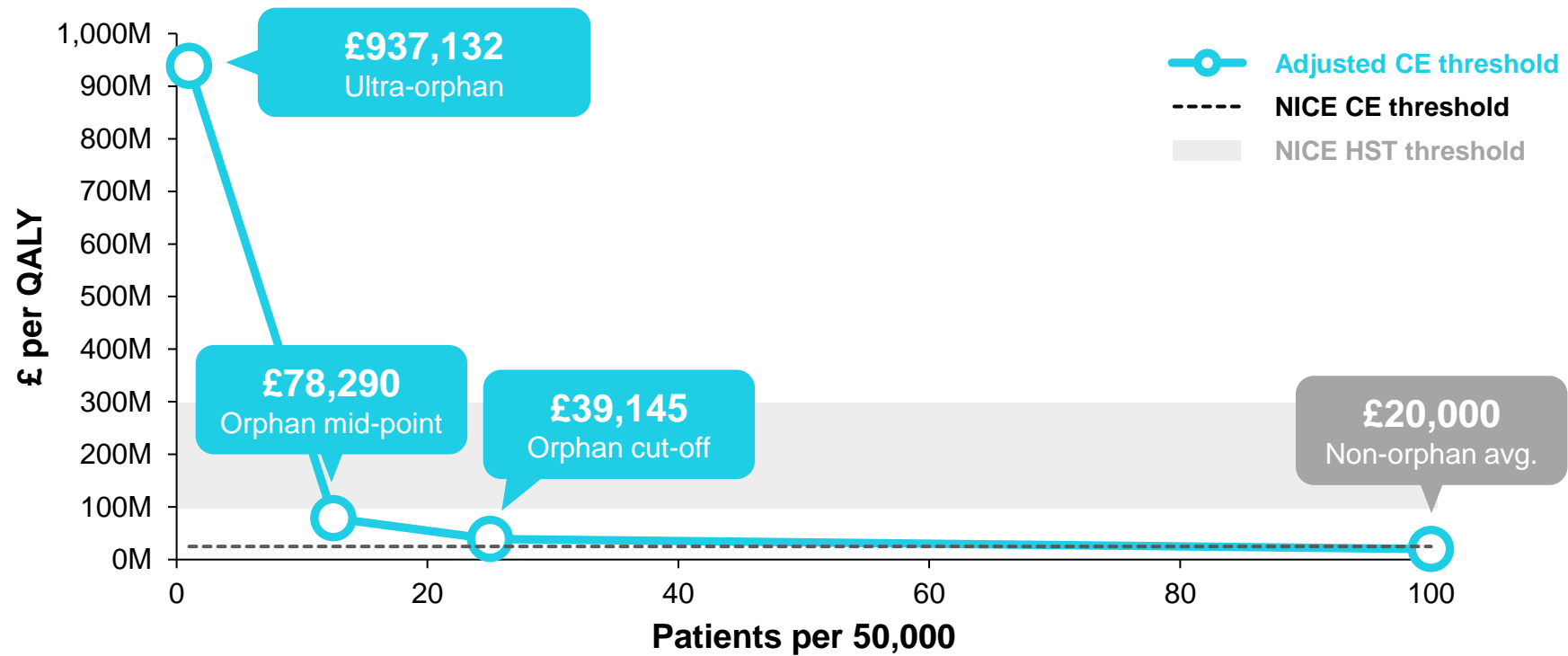
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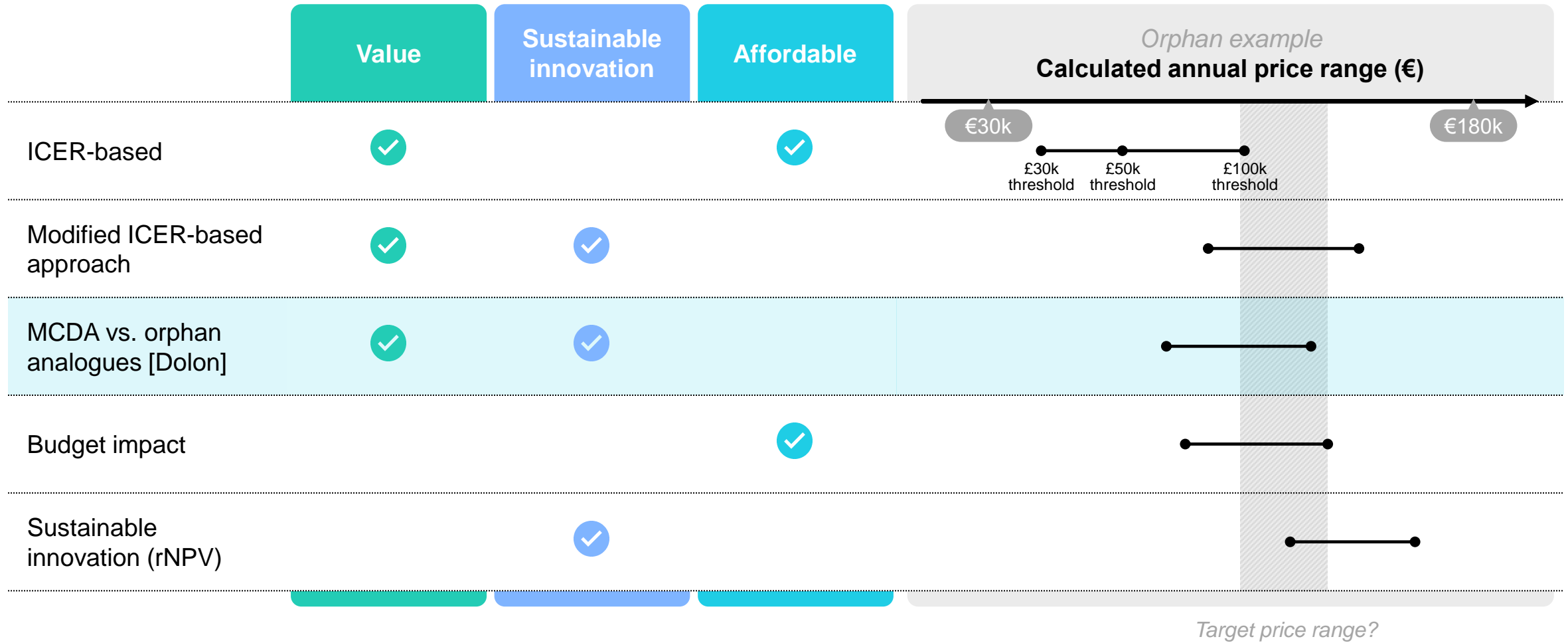
# Modified ICER approach that incorporates concept of sustainable innovation into the value calculation

## ICER thresholds that equalise R&D incentive between rare and non-rare diseases<sup>1</sup>



[1] Adapted from Berdud M. et al. (2020)  
 HST: Highly specialised technologies; ICER: Incremental cost-effectiveness ratio; QALY: Quality-adjusted life year; R&D: Research and development

# Triangulating a price based on these concepts

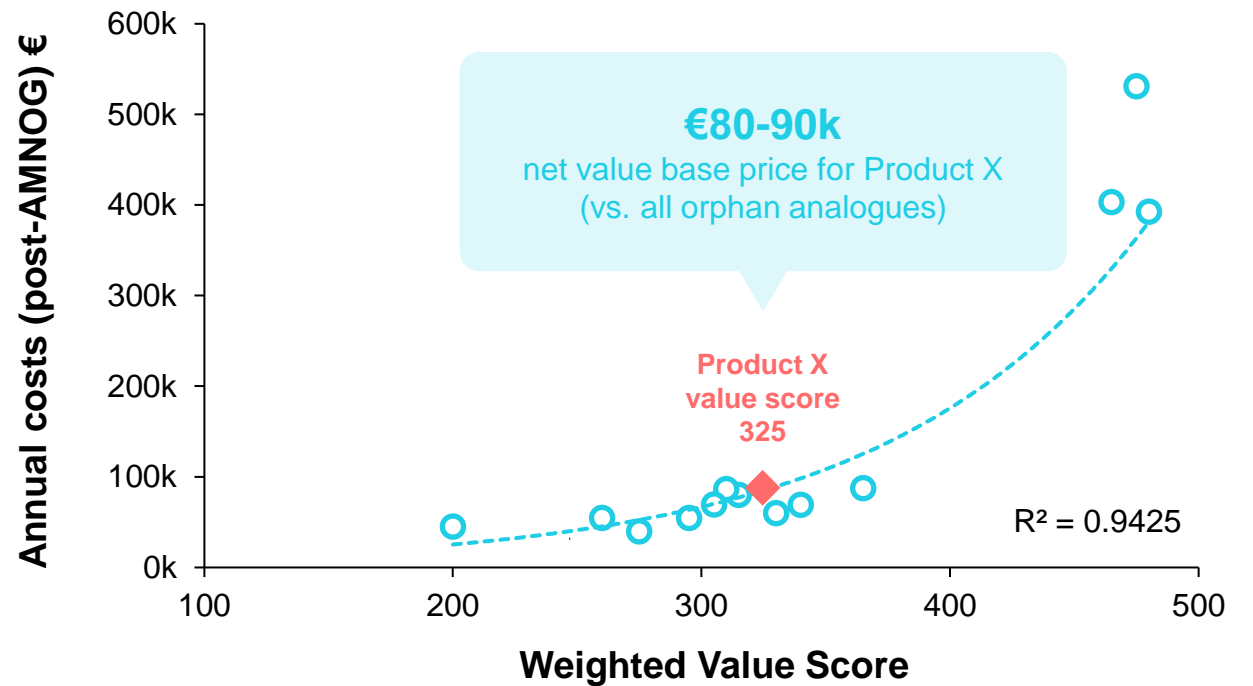


ICER: Incremental cost-effectiveness ratio; MCDA: Multiple-criteria decision analysis; rNPV: Risk-adjusted net present value

**MCDA approach: 'value-based' price relative to analogues from outside the indication**

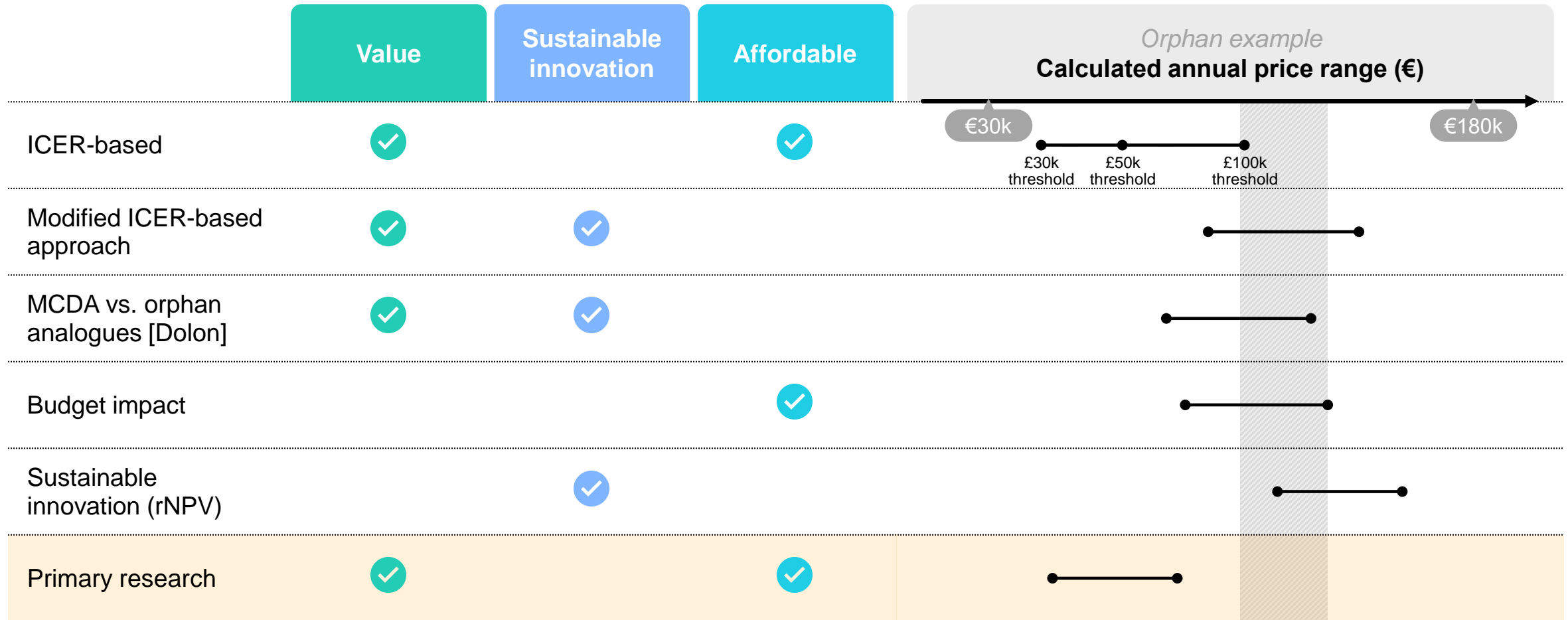
- 1 Identify relevant analogues
- 2 Determine value-based score
- 3 Adjust value score for prevalence
- 4 Calculate price for analogues
- 5 Plot value scores against annual price & trend line

**Annual cost (accounting for DoT) vs. weighted value score**  
Adjusted for prevalence



DoT: Duration of treatment; MCDA: Multiple-criteria decision analysis

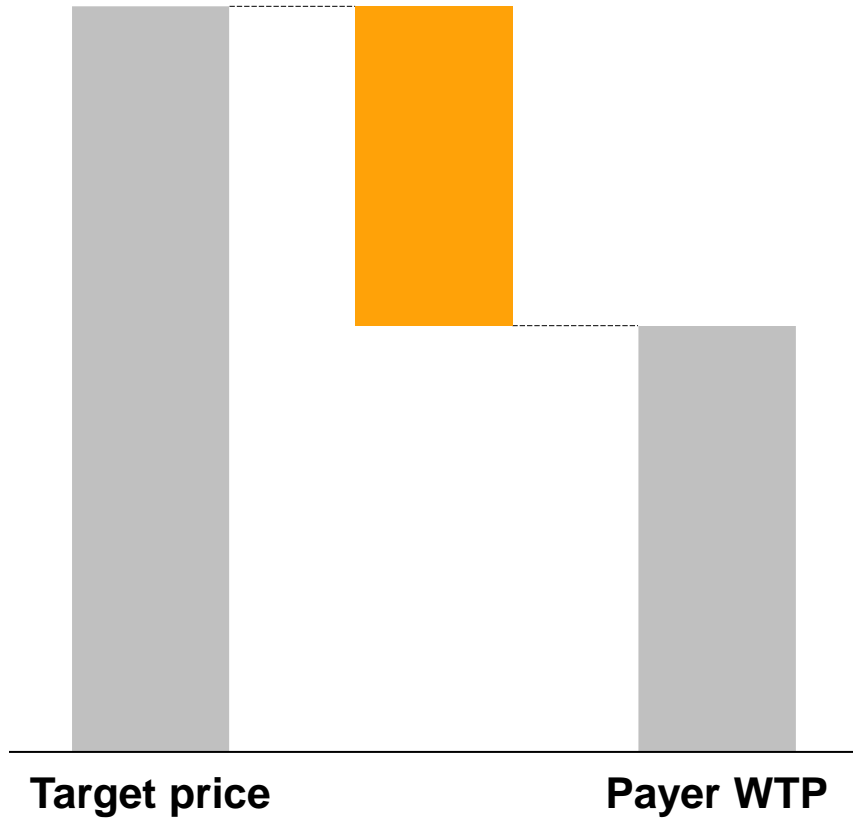
# Triangulating a price based on these concepts



Target price range?

ICER: Incremental cost-effectiveness ratio; MCDA: Multiple-criteria decision analysis; rNPV: Risk-adjusted net present value

# Approaches to closing the gap



**1**

**Within the existing P&R framework**

- Additional evidence
- MEAs / contracting
- Negotiation skills

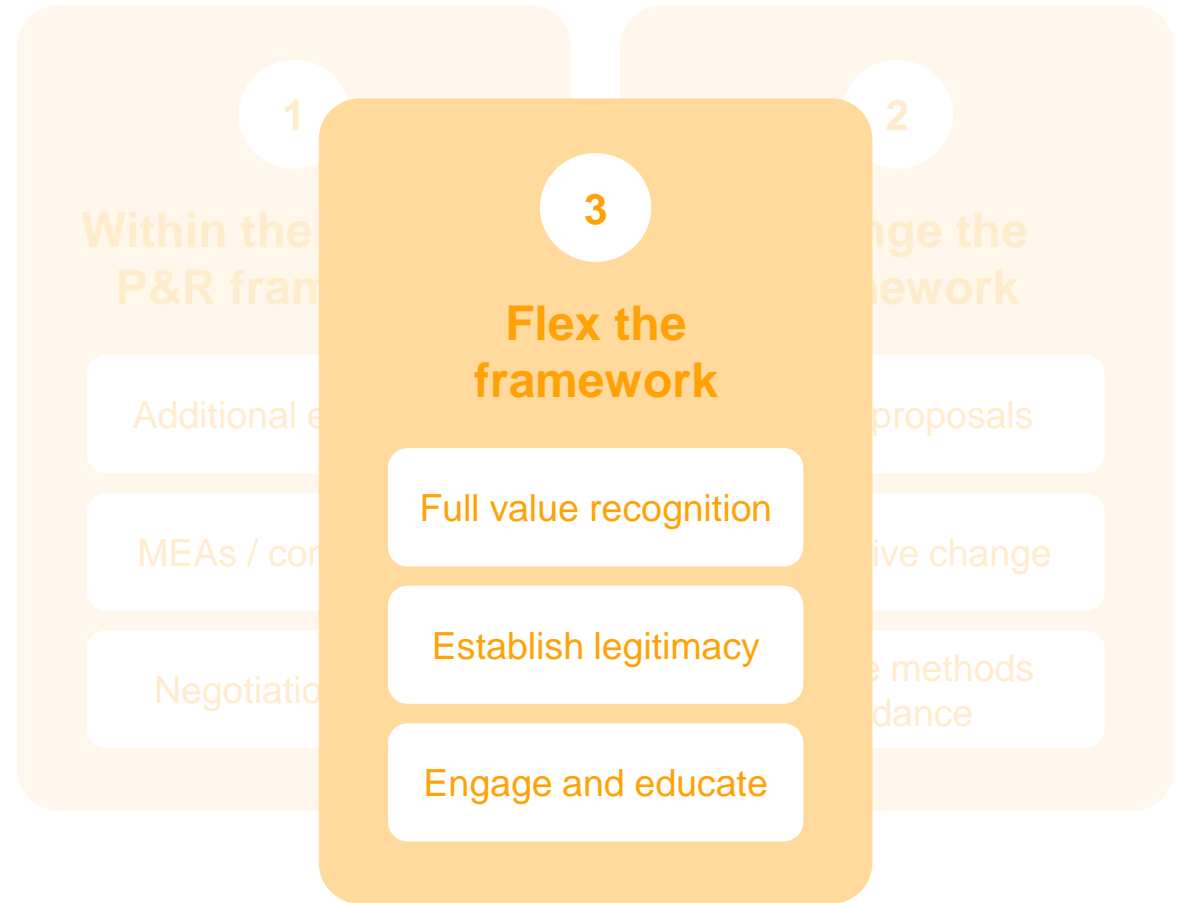
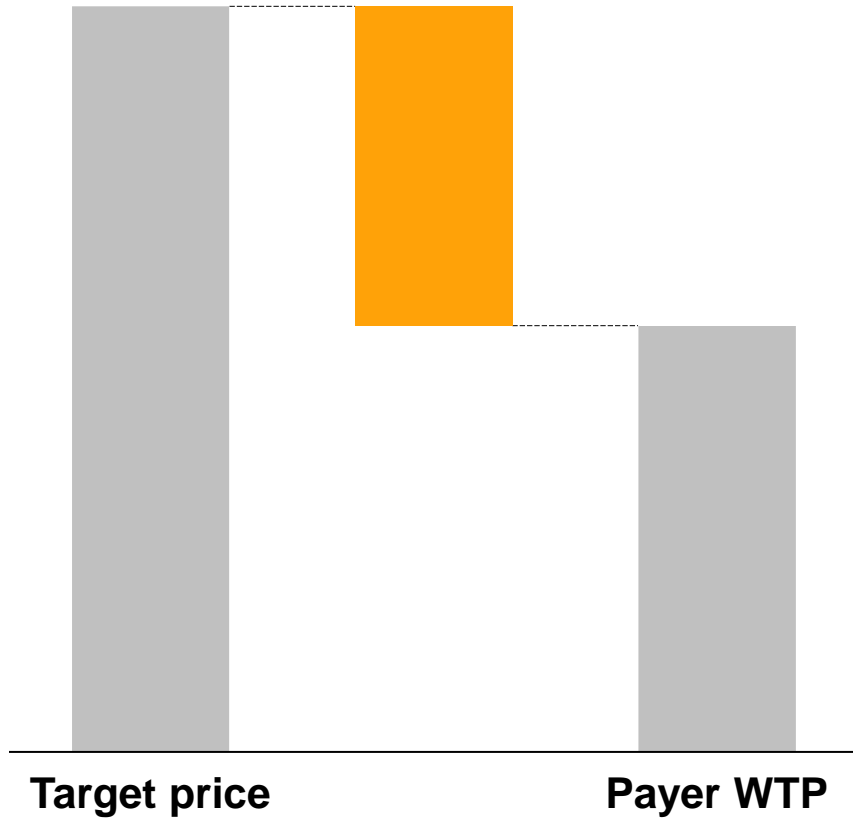
**2**

**Change the framework**

- Policy proposals
- Legislative change
- Update methods guidance

MEAs: Managed entry agreements; P&R: Pricing and reimbursement; WTP: Willingness to pay

# Approaches to closing the gap



WTP: Willingness to pay



# Ensuring **internal trust and confidence in the pricing strategy** is especially important in these cases...

## Key questions...

- 1 What are the **principles** that underpin your company pricing decisions?
- 2 What **process** was taken to define the pricing strategy?
- 3 What is the **rationale** for the price?  
(e.g., why price X and not Y?)

# Conclusions

Low-cost comparators can create a 'pricing gap' for orphan medicines

The lack of agreed rare disease pricing framework creates uncertainty and distrust between payers and manufacturers

A robust pricing strategy and process that is developed around principles of value, sustainable innovation and affordability is needed

In addition, need to advocate for European payer frameworks that balance value, affordability and orphan innovation economics