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Interlinked cost-effectiveness analysis and forecast modelling as a tool to guide strategic clinical and commercial development

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SCAN ME

BACKGROUND/INTRODUCTION

- Health economics is intrinsically interlinked with net present value (NPV).
- In health economic models, potential costs and clinical outcomes of an asset are simulated and generate cost-effectiveness estimates and a value-based price.
- Various target product profile scenarios can be explored, including the severity of disease treated, potential comparators and short and long-term treatment effect.
- The health economic model generates a set of pricing corridors given a set of clinical assumptions along with the key drivers of economic value and evidence gaps.
- Model outputs (cost-effective price given a particular positioning and efficacy) can be used as inputs (price, patient numbers, cost of trials and evidence generation) for a forecast model, which generates estimates of NPV (with NPV>0 representing a return on investment and higher NPV representing higher returns).



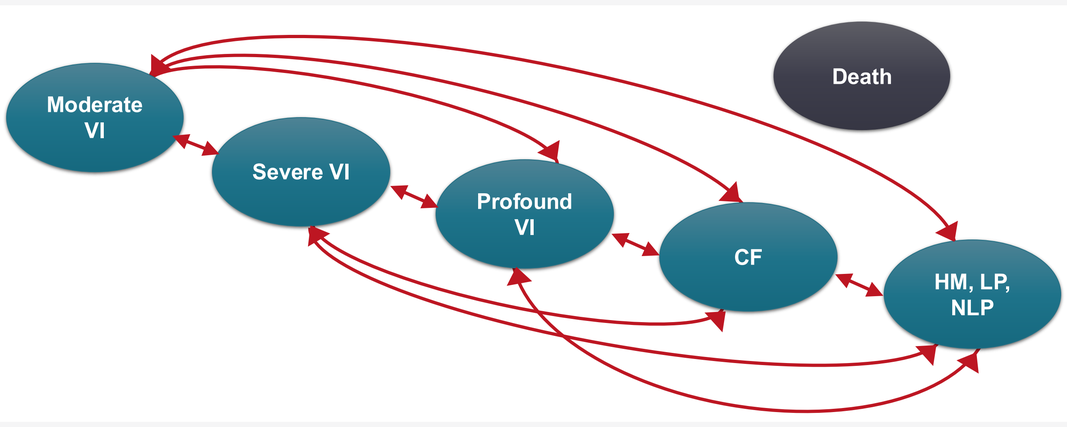
OBJECTIVE(S)

- Here we present a case study where we investigated value drivers of a potential gene therapy for the treatment of an inherited variant of retinitis pigmentosa (RP)

METHODS

- Two models were built in Microsoft Excel; one was a cost-effectiveness model (CEM) and the other a forecast model (FM).
- Due to the similarity of the diseases and the availability of published data to inform the model the CEM used the same structure as that used for reimbursement of the gene therapy Luxturna® in the UK (**Figure 2**), but with different assumptions for disease progression.
- The CEM considered a UK base case, but different markets were explored by proxy by considering different cost-effectiveness thresholds (e.g. 500,000 USD for the US vs. 30,000 GBP for the UK).
- The impact of assumptions including quality of life, progression rates, magnitude and duration of treatment effect on the cost-effective price of the treatment was explored through sensitivity and scenario analyses.
- The FM (**Table 1**) considered the US, UK, EU-4, Japan and China and included inputs for price, patient population, market share and development costs aligned with scenarios in the CEM. Inputs in both models were validated by interviews with clinical experts and payers.

Figure 1: Cost-effectiveness model structure



Abbreviations: CF, counting fingers; HM, hand motion; NLP, no light perception; VI visual impairment

Table 1: Forecast model inputs

			US	UK	France	Germany	Italy	Spain	Japan	China
1	Epidemiology	Prevalent cases per 100,000	25	25	27	27	25	25	25	26
		Prevalence	0.00025	0.00025	0.00027	0.00027	0.00025	0.00025	0.00025	0.00026
		Prevalent number (2025)	78,050	15,834	17,245	21,878	14,561	11,274	30,145	355,103
		Incident cases per 1,000,000	6	6	7.9	7.9	7.9	7.9	6	6
		Incidence	0.000006	0.000006	0.0000079	0.0000079	0.0000079	0.0000079	0.000006	0.000006
2	RP population	Diagnosis rate	Base case	50%	50%	50%	50%	50%	50%	50%	50%
		Inheritance pattern in diagnosed patients	Autosomal recessive	40%	40%	40%	40%	40%	40%	40%	40%
			Autosomal dominant	25%	25%	25%	25%	25%	25%	25%	25%
			X-linked	15%	15%	15%	15%	15%	15%	15%	15%
			Simplex	10%	10%	10%	10%	10%	10%	10%	10%
			Syndromic	10%	10%	10%	10%	10%	10%	10%	10%
3	TPP	Minimum age	5y+								
		Inheritance pattern	All non-syndromic cases								
		Minimum visual acuity required	20/200								
		Sufficient viable retinal cells	80%								
		Outcomes achieved	60%								
				US	UK	France	Germany	Italy	Spain	Japan	China
	Market share	Peak uptake of untreated patients achieved by gene therapy		20%	10%	10%	10%	10%	10%	10%	2%
		Uptake speed		Fast	Fast	Fast	Fast	Fast	Fast	Fast	Fast
4	Therapy	Launch year		2028	2030					2031	
		Maximum national capacity to treat		10000	10000	10000	10000	10000	10000	10000	10000
		List price (Per Patient)		$ 500,000	£ 360,000.00	€ 400,000.00	€ 400,000.00	€ 400,000.00	€ 400,000.00	$ 400,000	$ 400,000
		Discount		15%	45%	20%	20%	20%	20%	20%	50%

1 **Epidemiology**
Based on nationally recognised sources

2 **Retinitis Pigmentosa** population
Based on peer reviewed literature and NICE committee papers for Luxturna

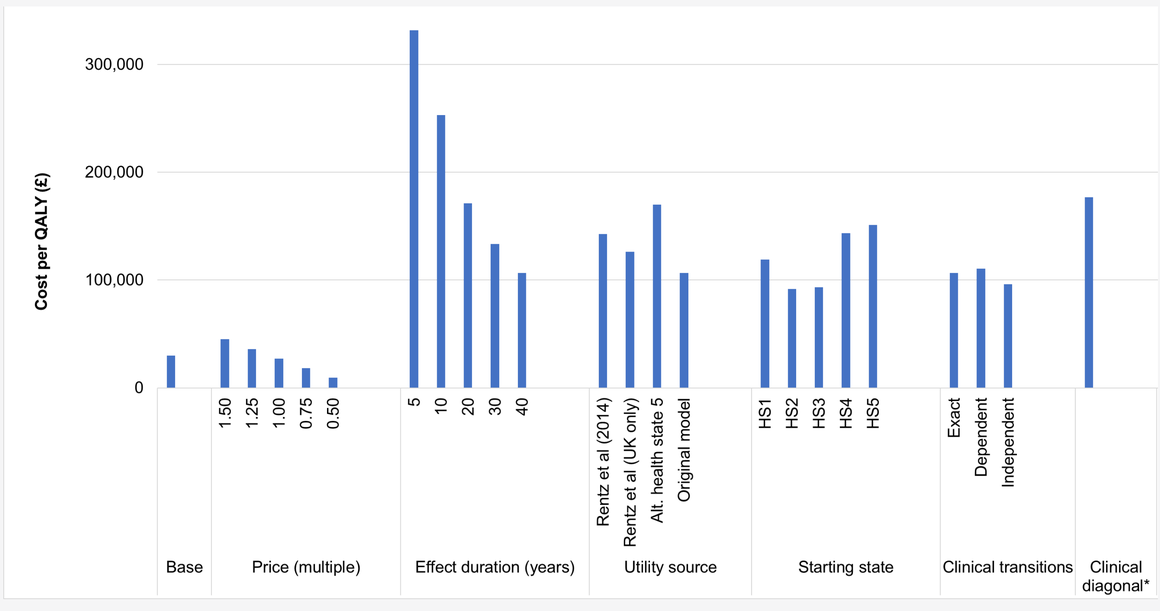
3 **Target Product Profile**
Based on information previously supplied by developer

4 **Market share**
Set at base case of with fast uptake – can be adjusted freely based on competitive market analysis

RESULTS

- Duration of treatment effect was critical and represented the largest uncertainty and driver of cost-effectiveness (**Figure 2**).
- Other important value drivers were treatment acquisition cost, quality of life (utility) associated with best and worst health states, and underlying disease progression.
- The CEM showed the potential value-based price range per eye to be between $120k – $180k, but contingent on assuming a 40-year duration of treatment effect (payers were willing to accept a shorter duration).
- This range was lower than the $250k per eye estimated via the payer research which was aligned with trends for pricing to be more constrained in markets undergoing cost-effectiveness assessments.
- A key concern was high budget impact, with outcomes-based agreements proposed as a potential mitigating approach.
- Using the CEM value-based price as an input into the FM translated into a forecast of around $2.7bn sales at peak (**Figure 3**).
- An NPV of ~$600m was predicted assuming a 25% discount rate and a risk-adjusted NPV of $50m.

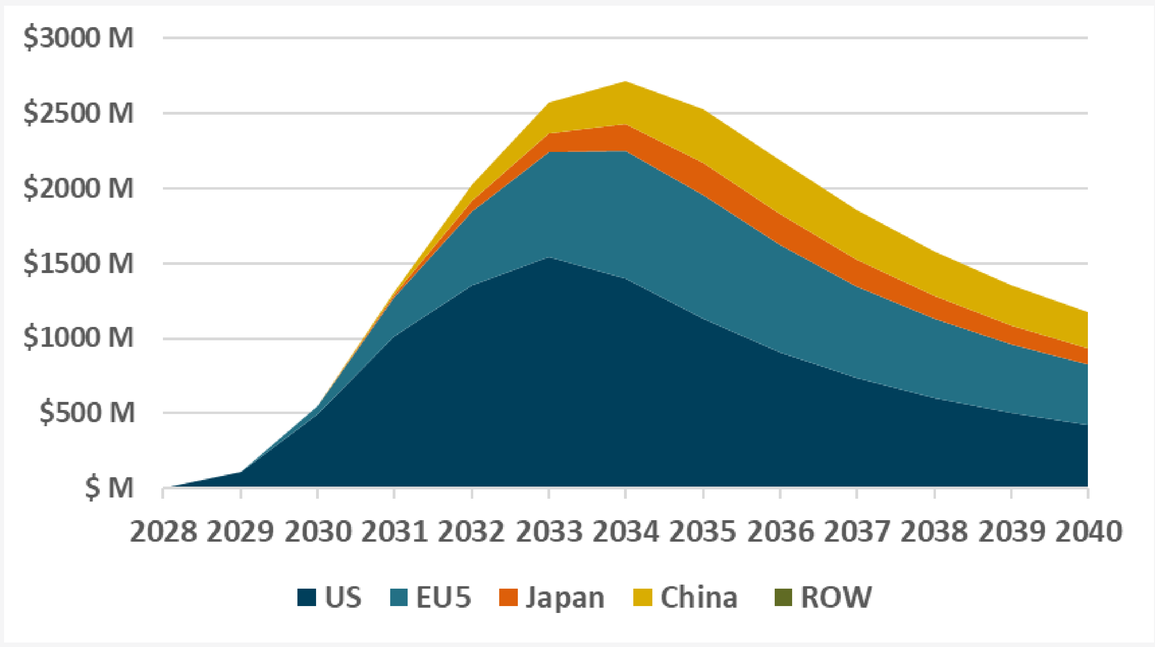
Figure 2: Most impactful inputs on cost-effectiveness



*Representing natural history progression

Abbreviations: HS,, health state; QALY, quality-adjusted life year

Figure 3: Gene therapy sales forecast



CONCLUSIONS & DISCUSSION

- The modelling concluded that evidence generation should focus on natural history and targeting rapid decliners as this subpopulation would better inform treatment effect of a product that stops decline while still generating high NPV due to potential for higher pricing.
- There is a trade-off between treating early and later, although as patients are younger, and vision loss is more severe, this is likely to be more easily addressed by adequate efficacy and safety evidence.
- A recent ICER evidence report for a RP gene therapy established a cost-effective price range between $33,500 and $135,200 per eye at willingness-to-pay thresholds of $50,000 to $200,000 per QALY[1]. This aligns well with our cost-effectiveness analysis and supports our approach.
- Interlinked cost-effectiveness analysis and forecast modelling represents an underused but powerful tool that can help guide strategic clinical and commercial development decision-making.

REFERENCES

1. Sonpiretigene Isteparvovec for Advanced Retinitis Pigmentosa: Effectiveness and Value. Evidence Report, March 26, 2025. Available from: https://icer.org/wp-content/uploads/2025/03/ICER_Retinitis-Pigmentosa_Evidence-Report_032625_For-Publication.pdf

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