EE333

Quantifying The Societal Value Of Resmetirom For Metabolic Dysfunction Associated Steatohepatitis Using A Societal Value Modeling Approach

Thomas Flottemesch[1], Marlon Graf[1], Iris Brewer[1], Amal Jamaleddine[1], James Baumgardner[1], Jacki Chou[1], Yestle Kim[2], Nipun Atreja[2]
[1]Precision AQ, Bethesda, MD, United States, [2]Madrigal Pharmaceuticals, Inc., West Conshohocken, PA, United States

RESONANCE
Real-World Evidence of Resmetirom Advancing Outcomes, Natural History, Assessment, and Clinical Effectiveness

INTRODUCTION

- Metabolic dysfunction-associated steatohepatitis (MASH) is a progressive liver disease, associated with metabolic risk factors and contributing to significant morbidity, mortality, and healthcare costs.[1]
- Until recently, treatment was limited to lifestyle modification with modest effectiveness. Conditional approval of resmetirom, a thyroid hormone receptor-β agonist, represents the first pharmacologic therapy specifically indicated for MASH in the US and Europe.[2]
- While its efficacy has been evaluated in clinical trials, broader societal impacts remain underexplored. In this study, we quantify the societal value of resmetirom.

OBJECTIVES

- The objective of this study was to develop a societal value model (SVM) that combines disease progression, treatment uptake, pricing dynamics, and novel value elements to evaluate the long-term distribution of value generated by MASH treatment with resmetirom.

METHODS

Societal Value Model Framework

A SVM of resmetirom based on a 14-state, Markov cost-effectiveness analysis (CEA) with annual cycles was developed for the United States societal perspective.[3]

- Patients enter the model with F2 or F3 MASH that either remains stable, regresses, or progresses to F4, resulting in more advanced liver disease or death.
- For each year (2024-2054) of the analytic horizon, the SVM introduces a treatment-naive cohort whose forecasted size is based upon trends in the US population, MASH screening rates, and anticipated market growth.

The SVM estimates how societal value distributes across key stakeholders such as consumer, manufacturers, and a healthcare residual (other health system stakeholders).

- Monetized quality-adjusted life year (QALY) gains valued at $100,000 per QALY were used to estimate base case estimate of total societal value.
- Health improvements were supplemented with productivity effects, changes in caregiver burden, and innovation-related value elements.
- Future costs and benefits were discounted at an annual rate of 3%.

TABLE 1. Societal Value Model Parameters

PICOS	Description	
Population	**Retained from the adapted CEM**	• Male and female patients ≥18 years of age with MASH and liver fibrosis in alignment with the MAESTRO-NASH phase III trial, with fibrosis stages 2 or 3.*
	New elements for the SVM	• Each year, a resmetirom-naive cohort of patients with newly diagnosed F2 and F3 MASH will be introduced into the model • Cohort sizes will reflect observed and/or estimated resmetirom utilization during analytic timeframe
Intervention	• Blended arm of 80 mg and 100 mg resmetirom in a once-daily oral tablet (based on distribution of patient weights reported in the USPI)	
Comparator	• Standard of care: diet and exercise • At the time of model construction, there were no other existing approved therapies for MASH with significant fibrosis	
Outcomes	**Retained from the adapted CEM**	• MASH resolution • Fibrosis progression/regression, CC, DCC, HCC and LT • Liver mortality • Background mortality • Direct medical costs • QALYs accrued by the patients
	New elements for the SVM	• Total societal value • Societal surplus • Patient surplus/share • Manufacturer surplus/share
Setting	Base case analytic timeframe of 30 years	

**Note: the model population from the MAESTRO-NASH phase III trial includes 5% of patients with fibrosis stage F1B who were pooled with the patients with fibrosis stage F2*

Forecasted Model Inputs

- Annual treatment initiation estimates were derived from forecasts of U.S. adult population growth,[4] MASH prevalence and fibrosis-stage distribution,[5] disease detection and treatment eligibility,[6] and assumed market penetration.
- Treatment discontinuation rates were incorporated to estimate replacement demand and annual initiation cohorts over time.
- Treatment prices were projected across the product lifecycle, using annual revenues and sales figures from the manufacturer's annual reports and literature-based trends.[8]

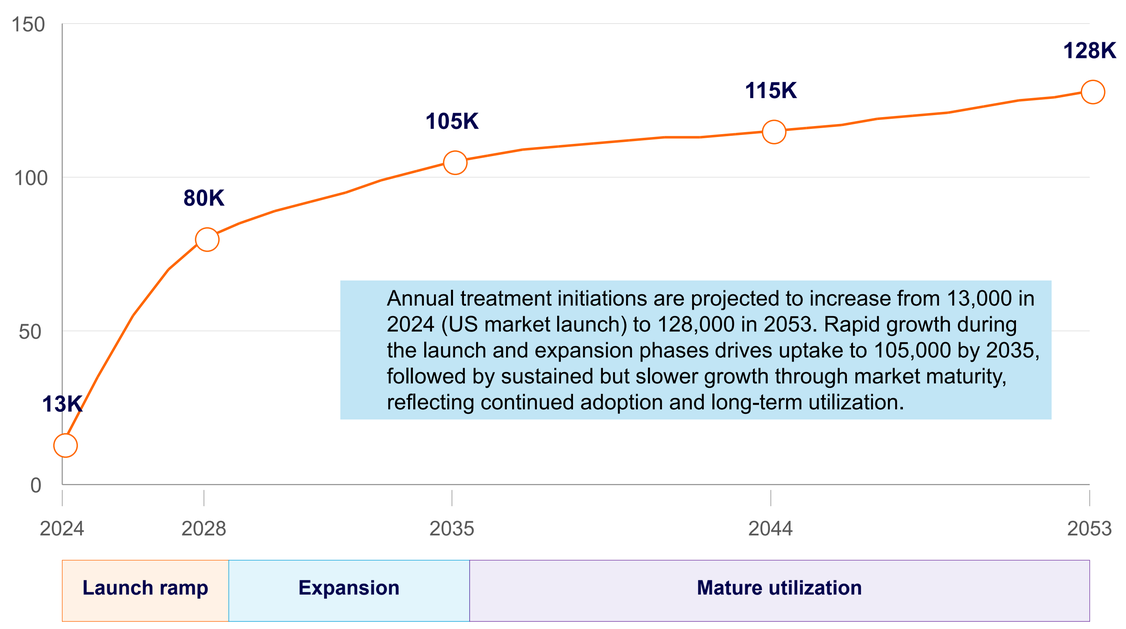
Novel Value Elements

- Productivity losses were estimated using baseline WPAI measures from patients with MASLD/MASH and scaled across fibrosis stages using published evidence demonstrating increasing economic burden with disease severity.[9,10]
- Caregiver burden was estimated using stage-specific non-medical costs and informal caregiving time.[1]
- Innovation-related value reflected the expected societal returns associated with reinvestment of manufacturer revenues into pharmaceutical research and development.
- One-way and scenario-based sensitivity analyses examined uncertainty related to treatment effectiveness, treatment uptake, pricing assumptions, discount rates, and valuation of health gains.

RESULTS

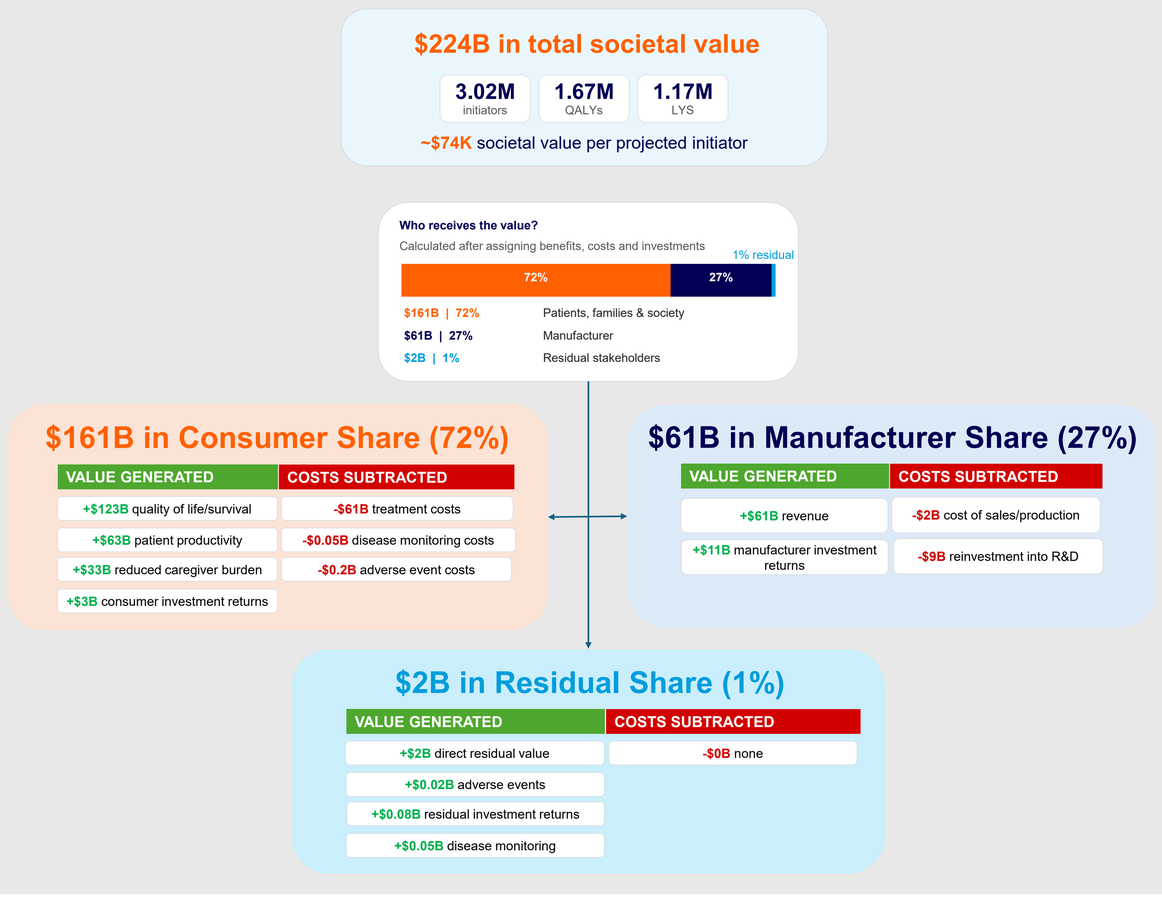
- Between 2024 and 2053, an estimated 3 million persons will initiate resmetirom, resulting in 1.7 million QALYs saved (QALYS).

FIGURE 1. Forecasted Resmetirom Treatment Initiation



- Over a 30-year lifecycle, resmetirom generates $224 billion in societal value:
  - $123 billion is generated from direct medical value of the estimated 1.2 million life years saved (LYS) and 1.7 million quality-adjusted life years saved (QALYS).
  - $96 billion is generated from indirect value in the form of combined increased patient productivity ($63 billion) and reduced caregiver burden ($33 billion).
  - $5 billion is from manufacturer reinvestment into R&D at a risk-neutral return.
- Sensitivity analyses indicated estimates were most sensitive to analytic time-frame (i.e., assumed duration of resmetirom's lifecycle), discount rates, and how QALYS are valued (i.e., underlying cost/QALY estimates).

Figure 2. Societal Value by Stakeholder



CONCLUSIONS

Treating a patient with MASH with moderate to advanced liver fibrosis with resmetirom provides substantial economic value to society beyond aspects that are captured by traditional cost-effectiveness analyses:

- **Over its lifecycle, resmetirom generates $224 billion in societal value or $74k per patient initiating treatment**
- **This vast societal value remains mostly with patients and society at large (72%) and a substantial share (45%) consists of broader (indirect) societal benefits such as increased productivity and reduced caregiver burden.**

Neglecting to account for these considerable benefits beyond monetized health gains bears the risk of systematically undervaluing innovative therapies and ultimately limiting access for patients.

ABBREVIATIONS

BMI: Body mass index; GIP: Glucose-dependent insulinotropic polypeptide; GLP-1: Glucagon-like peptide-1; IQR: Interquartile range; MASH: Metabolic dysfunction-associated steatohepatitis; MASLD: Metabolic dysfunction-associated steatotic liver disease; SC: Subcutaneous; SD: Standard deviation; T2D: Type 2 diabetes; WPAI: Work Productivity and Activity Impairment

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DISCLOSURES AND ACKNOWLEDGEMENTS

- TF, MG, IB, AJ, JB, and JC are all employees of Precision AQ
- YK and NA are employees of Madrigal Pharmaceuticals

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