The synergy of AI and RWE: Developing integrated evidence plans for market access and IRA

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Our agenda today

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- Using RWD/E across the product lifecycle, as part of an integrated evidence plan
- Navigating regulatory guidance in a dynamic landscape
- Preparing for IRA requirements, leveraging AI-driven RWE
- Two case studies demonstrating how AI-enhanced RWE can address IRA needs
- The value of integrated evidence planning to transform asset development
- Q&A

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Level-setting on terminology: RWD/RWE 101

Data is collected along the patient journey:

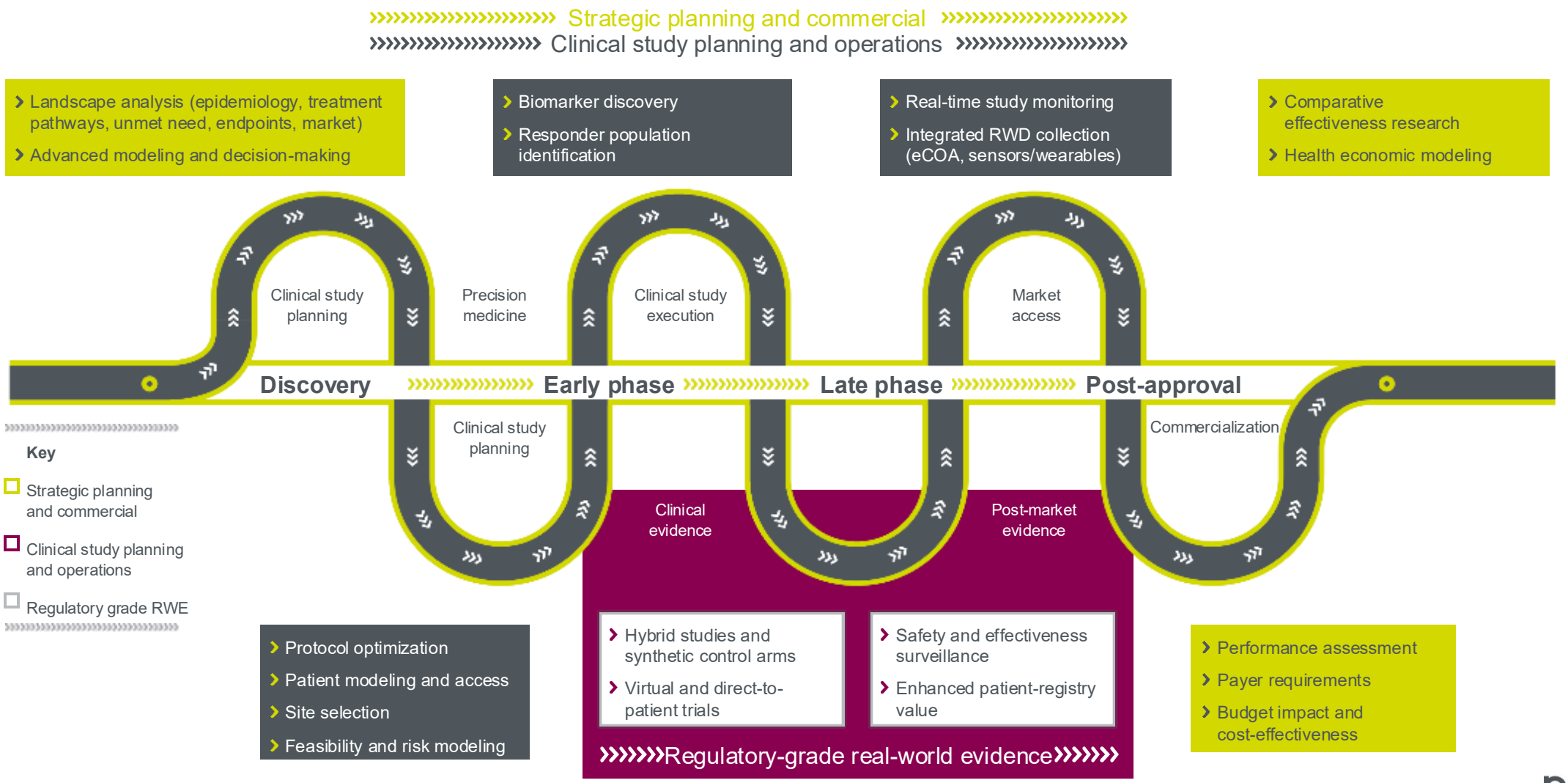
- Claims data
- Pharmacy data
- Disease registries
- Electronic health records
- Clinical trial data
- Social determinants of health
- Social listening
- Labs and biomarkers
- Wearables
- Hospital systems

Real World Evidence:
Information derived from analysis of Real World Data

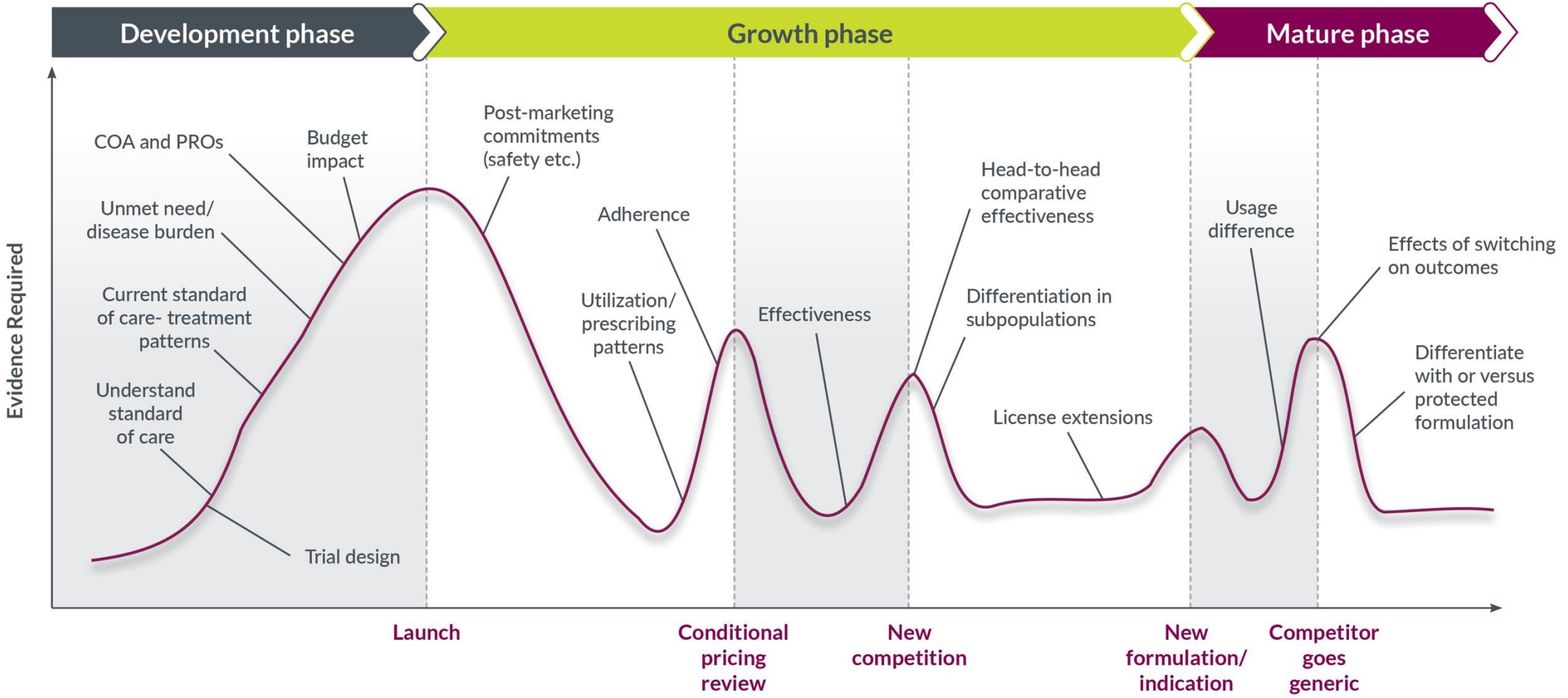
Real World Data:
Routinely collected data relating to patient health status or the delivery of health care from a variety of sources other than traditional clinical trials

- **Primary data**, which are collected specifically for research purposes (prospective e.g., low interventional, non-interventional study (NIS)
- **Secondary data**, which are collected for purposes other than the research question of focus
- **Hybrid data**, which are integrated primary and secondary data

Big data and RWE can be deployed across the clinical development and lifecycle management spectrum



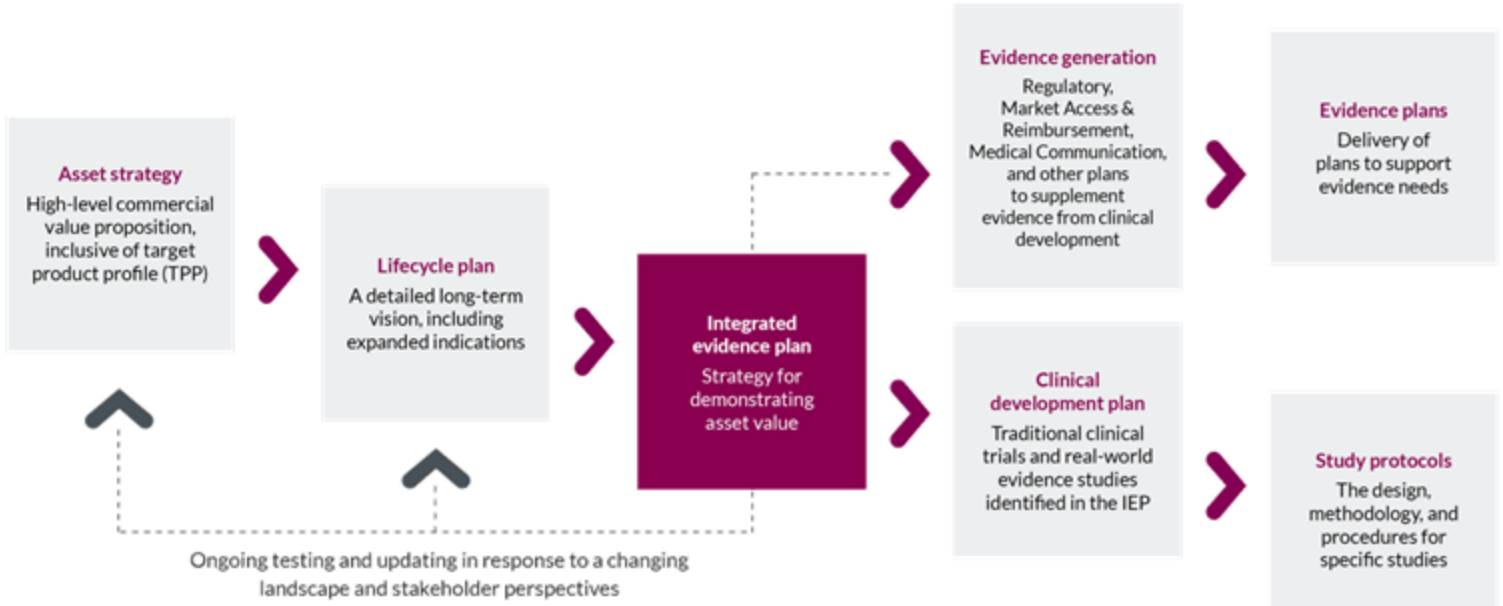
RWE is positioned to address specific value evidence and market access considerations



An integrated evidence plan (IEP) provides a cohesive framework to leverage RWE

The IEP as critical component of overall asset strategy and delivery

The IEP is a living resource, updated at key milestones as data is generated. It informs the clinical development and evidence generation plans and facilitates adjustments to the asset strategy and lifecycle plan based on emerging information.



Navigate RWE and AI guidance in a dynamic landscape

RWE regulatory guidance*

Design

- **Considerations for the design and conduct of externally controlled trials for drugs and biologic products** : Draft guidance for industry – Feb 2023
- **Real-world Evidence: Considerations regarding non-interventional studies for drugs and biologic products:** Draft guidance for industry – Mar 2024

Submissions

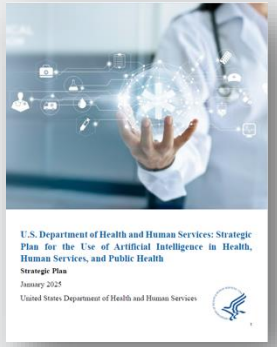
- **Data standards for drug and biologic submissions containing real-world data:** Draft guidance for industry – Oct 2021
- **Considerations for the use of RWD and RWE to support regulatory decision making for drug and biologic products:** Draft guidance for industry – Dec 2021

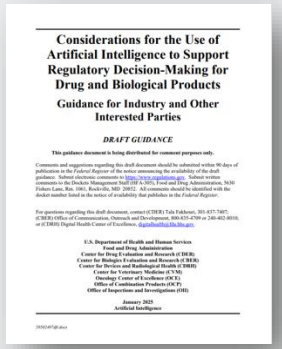
Data sources

- **Real-world Data: Assessing electronic health records and medical claims data to support regulatory decision making:** Draft guidance for industry – Sep 2021
- **Real-world Data: Assessing registries to support regulatory decision making:** Draft guidance for industry – Nov 2021

AI regulatory guidance*

- Regulatory and legislative compliance needs to be engineered into AI application development pipeline from the outset
- Regulatory agencies seem set to take a risk-based approach:
  - MHRA White Paper (Apr 2024)
  - EMA Reflection Paper (Sep 2024)
  - ICH M15 draft guidance on MIDD (Nov 2024)
  - FDA draft guidance (Jan 2025)
  - HHS AI Strategic Plan (Jan 2025)





Per MHRA:
"… the changes our customers make will not impact how we regulate."

There is a need to drive consensus on how we harness AI in RWE, with the right theoretical underpinning, in service of expediting patient access to much-needed drugs.

*Examples only, not an exhaustive list

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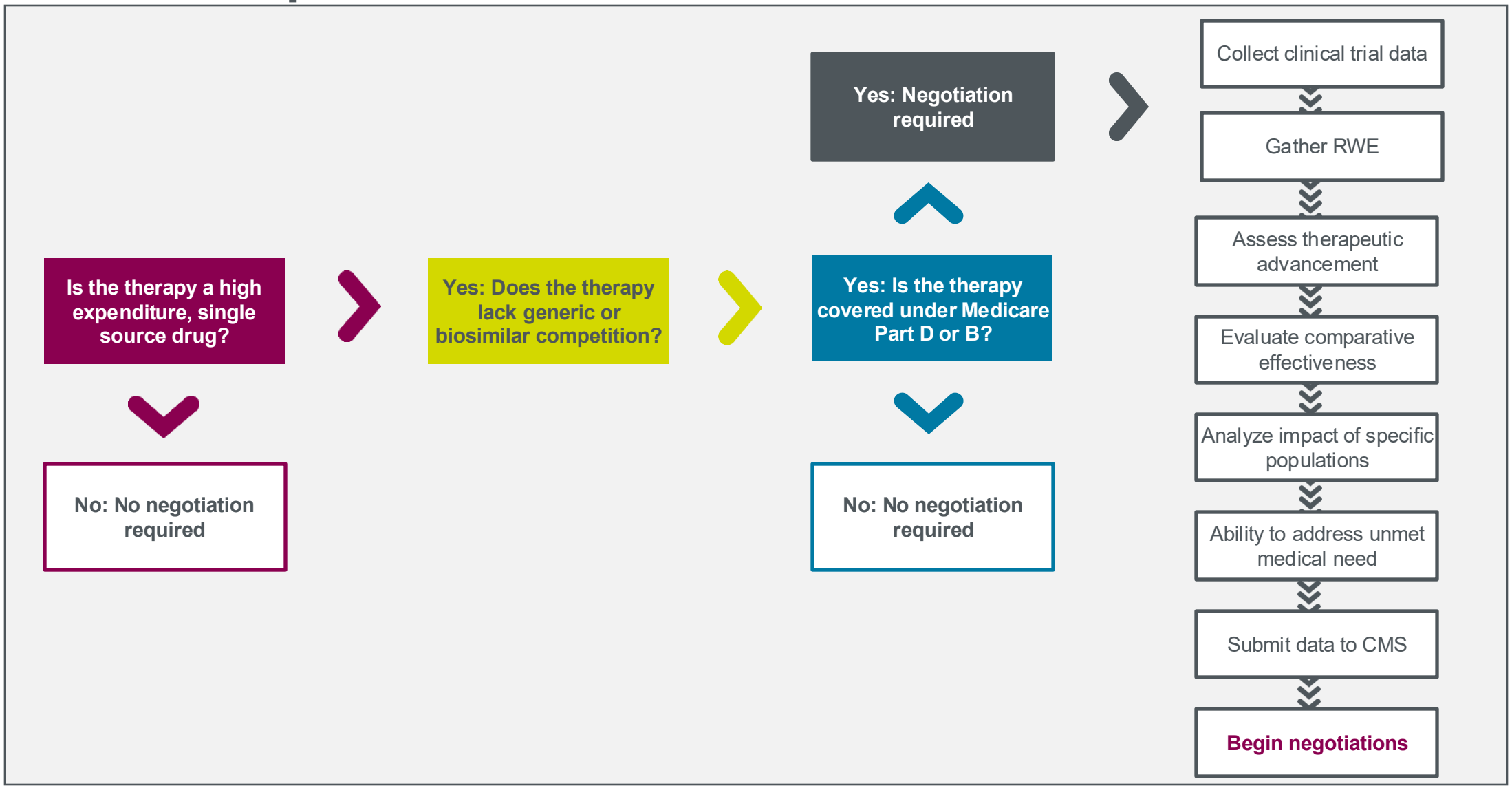
Leverage AI-driven RWE to navigate the impact of the Inflation Reduction Act (IRA) on US market access

- Under the IRA, Centers for Medicare & Medicaid Services (CMS) selects high-expenditure, single-source drugs that lack generic or biosimilar competition for price negotiations.
- The first cycle of negotiations began in 2023, with the negotiated prices set to take effect in 2026
- The Information Collection Request (ICR) process is a key component of the drug negotiation process established by the IRA

1. **Predict IRA requirements and plan ahead**
2. **Handle the ICR once an asset is on the list**
3. Provide evidence for value-based pricing

Understand the Medicare drug price negotiation process and the required documentation

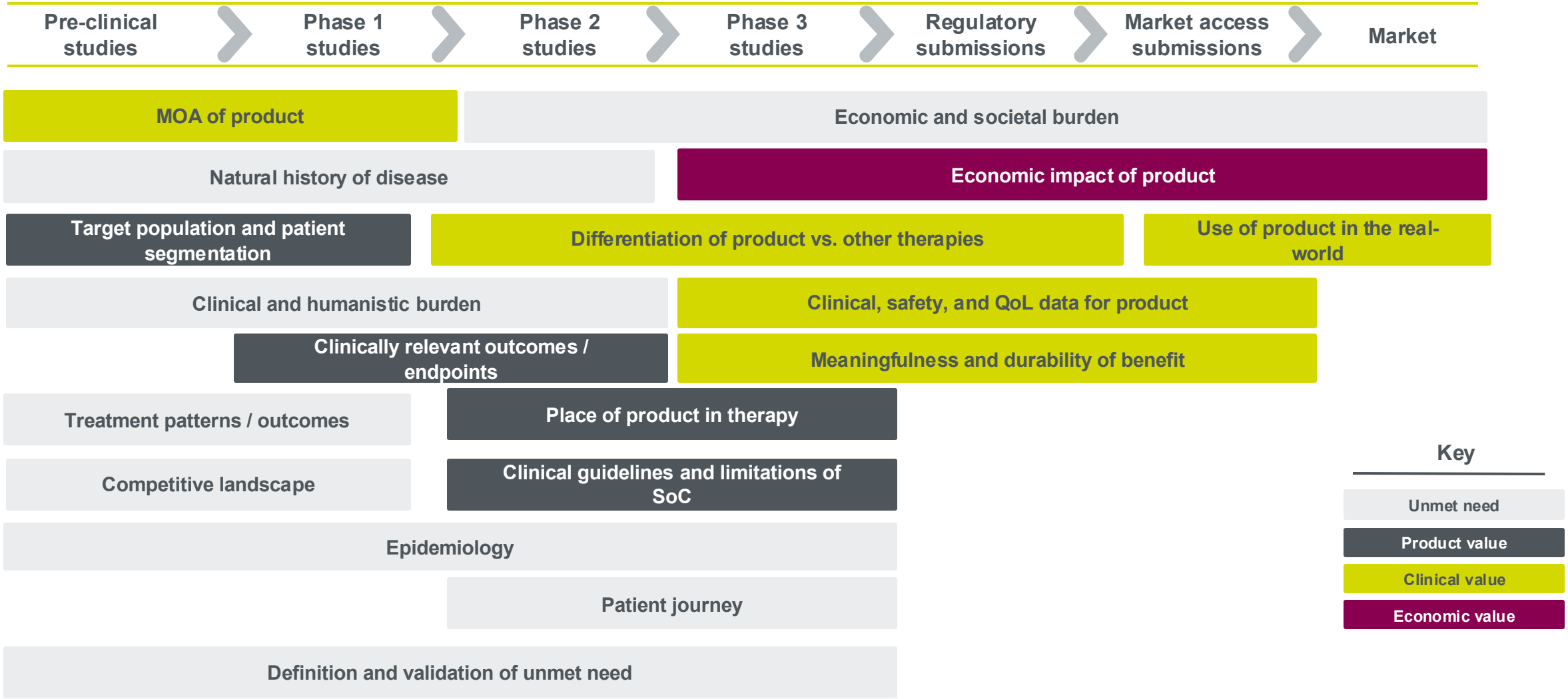


An IEP* can identify needs to meet ICR expectations

Unmet need	Product value	Clinical value	Economic value
Epidemiology, humanistic burden, societal burden, economic burden and treatment patterns	Breadth and number of FDA-approved indications, dosing flexibility and NCCN guideline recommendations	Key clinical trial data, comparative effectiveness evidence and RWE	Affordability (BI and reductions in HCRU), cost-effectiveness and societal value
Patient journey	Target population and patient segmentation	MOA of product	Economic impact of product
Natural history of disease	Clinically relevant outcomes / endpoints	Use of product in the real-world	
Clinical and humanistic burden	Place of product in therapy	Meaningfulness and durability of benefit	
Treatment patterns / outcomes	Clinical guidelines and limitations of SoC	Differentiation of product vs. other therapies	
Competitive landscape		Clinical, safety, and QoL data for product	
Epidemiology			
Economic and societal burden			
Definition and validation of unmet need			

*Illustrative example only

To generate cohesive evidence to meet ICR, actions should be planned throughout the product lifecycle



Harness AI to optimize IRA preparedness

Step 1:
Assessment of selection probability for IRA

- Therapy is single source
- Therapy lacks generic or biosimilar competition
- Therapy covered under Medicare part D or B
- Therapy is high annual expenditure

Step 2: AI-powered approaches streamline the creation of value-focused dossiers to meet CMS requirements.

Product value	Clinical value	Economic value	Unmet need
FDA-approved indications, dosing flexibility and guideline recommendations	Key clinical trial data, comparative effectiveness, RWE (treatment utilization, PRO & patient preference)	Affordability (BI and reductions in HCRU), cost-effectiveness, and societal value	Epidemiology, humanistic burden, societal burden, economic burden, and treatment patterns
AI Product research	AI SLRs & RWE	AI NMA & economic modeling	AI RWE & economic modeling

AI: Artificial Intelligence; IRA: Inflation Reduction Act; CMS: Centers for Medicare & Medicaid Services; FDA: U.S. Food and Drug Administration; RWE: Real World Evidence; PRO: Patient Reported Outcome; BI: Budget Impact; HCRU: Healthcare Resource Utilization; SLR: Systematic Literature Review; NMA: Network Meta-analysis

Key: Human review; AI-driven analysis

Case study: Development of a dossier summarizing the value of a product across multiple oncology indications

Issue

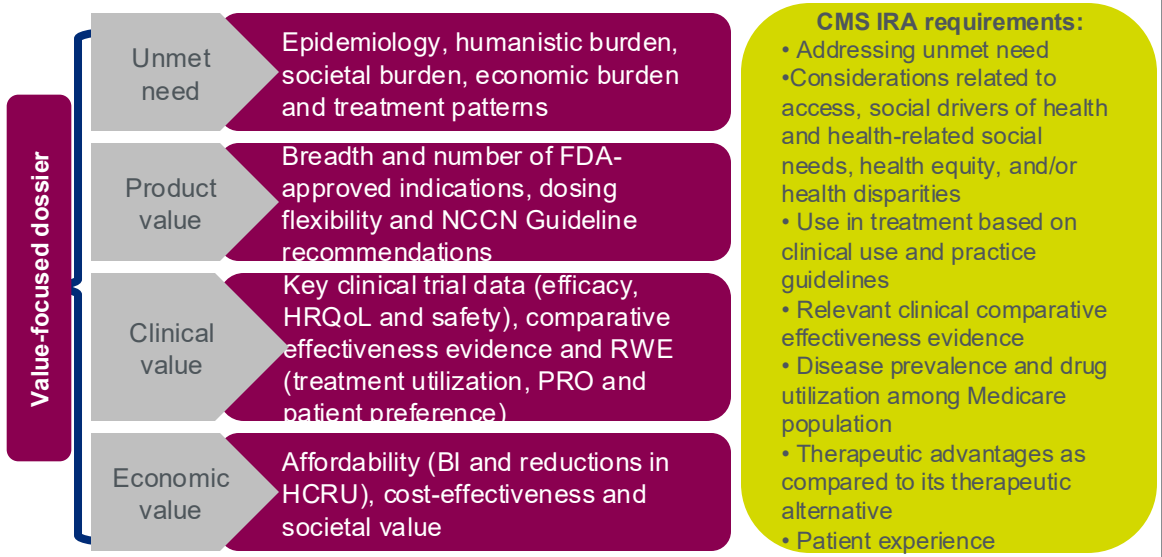
- Our client's product was **selected for US Inflation Reduction Act (IRA) price negotiations**, requiring a robust **evidence-based value justification** across all its approved indications aligned with CMS requirements

Solution

- We developed a comprehensive, **value-focused dossier based on CMS requirements** outlined in the Information Collection Request (ICR)
- The dossier consolidates the broad unmet needs, clinical, economic, and real-world evidence across all approved US indications incorporating comparative effectiveness data, budget impact models, and patient-centered outcomes

Outcome

- A fully integrated **value dossier**, aligned with **CMS ICR requirements**, that not only supports pricing negotiations and payer discussions under the US IRA framework, but also considered the broader brand portfolio strategy
- By taking a **holistic view** of the product's value across multiple indications, we provided insights into the **broader value implications** for the brand and portfolio, helping the client anticipate future market dynamics, pricing strategies, and potential impacts on access and reimbursement



Case study: Automation and AI to gain efficiencies while keeping quality and a human-in-the-loop

Situation and client challenge

- HEOR and Market Access face mounting pressure to increase efficiencies and deliver dossiers, SLR, economic models (CEM, e.g.), etc. faster while including more data.
- Hyperautomation and AI allow for improvements in time, cost, quality, and patient outcomes while requiring transparency, care, and oversight.

Parexel approach

1. Parexel developed nimble tools for each Hyperautomation and AI solution, first by growing from specific PoCs, then by ensuring human supervision and strict quality controls
2. Parexel tested each tool internally, according to pre-defined criteria of success and benchmarks of quality
3. Peer-reviewed publications are underway

Results and impact

- Increased efficiencies and value when tools are rolled out to our clients
- Unchanged superior quality-driven output

Client and geography

- All our clients will benefit from these tools, from Global to Local operations

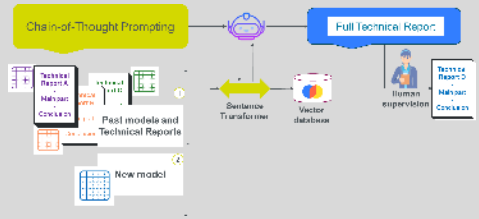
Parexel key value

- Expertise in Modelling, Access, Analytics, Evidence Review, …
- Established experience in HEOR Automation and AI

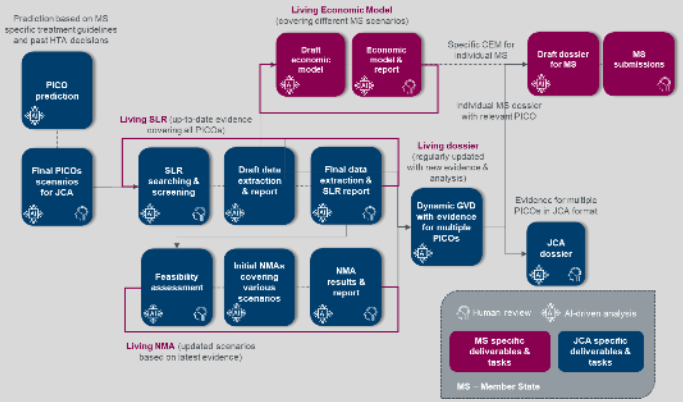
Example of Automation and AI tools

Modelling tools

- Draft Model Report Generator
- Model Structure Bootstrapper
- Model QC Helper
- Model Submission Trainer
- Model Adaptation Platform



End-to-end JCA integration tools



Analytics tools

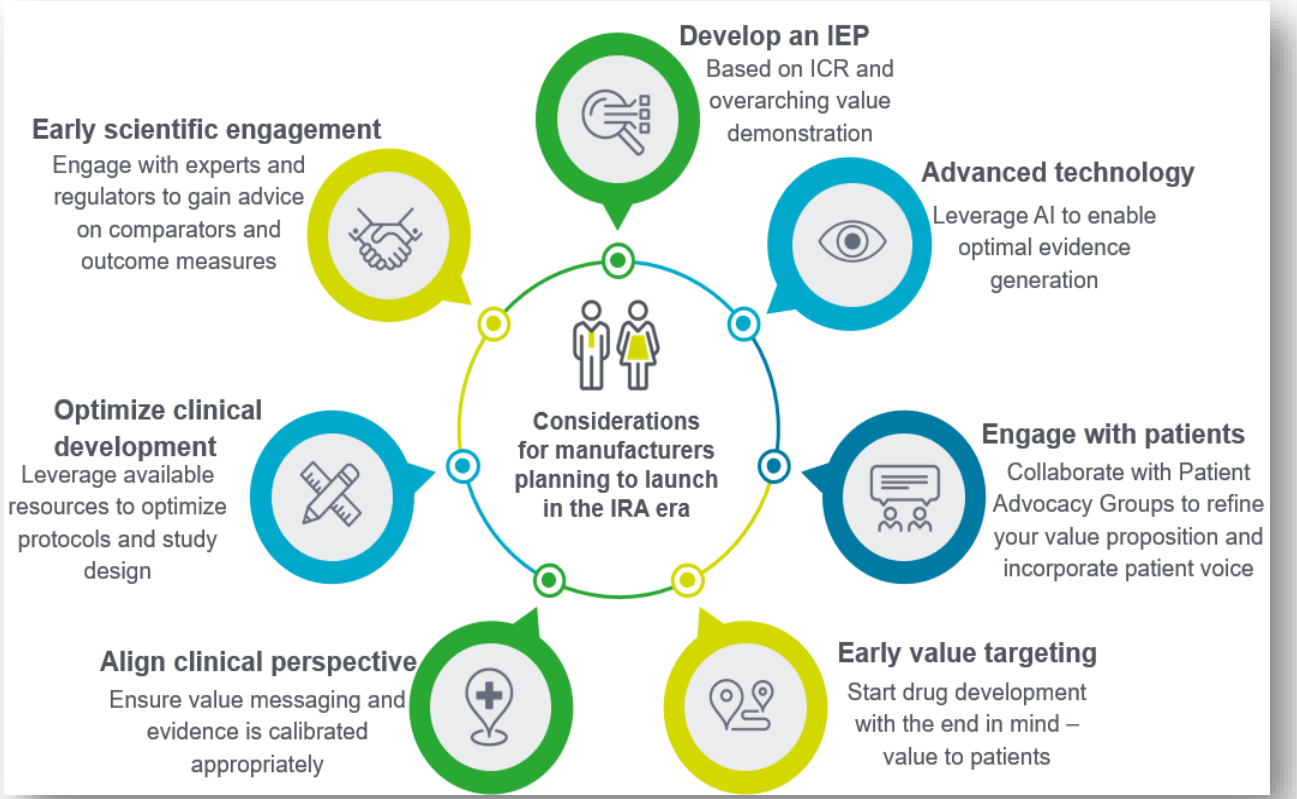
- NMA visualizer
- Feasibility assessment

CEM: Cost-Effectiveness Model; JCA: Joint Clinical Assessments; PoC: Proof-of-Concept; QQC: Quality Check; SLR: Systematic Literature Review

Early integrated evidence planning with AI-enabled RWE can transform asset development

- RWE continues to deliver critical patient insights, augmenting clinical trial data to underscore the value of medical devices and therapies
- AI-enabled RWE is positioned to transform asset development by allowing us to address complex questions efficiently and with first-time quality
- Preparing early, with integrated evidence plans, helps optimize evidence generation towards addressing regulatory, health technology assessment, and payer requirements

- IRA preparedness and meeting ICRs is a prime example



Questions?

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Visit Parexel at booth #1200

› **Learn more about Parexel's AI-powered solutions to optimize IRA preparedness**

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Appendix

Sample AI applications in HEOR

Overview of AI applications in HEOR and market access

Literature reviews and cost effectiveness modelling

- Accelerating systematic reviews
- Enhanced data extraction and quality assessment
- Natural language processing and social listening
- Endpoint analysis and surrogate outcomes assessment
- Quantifying uncertainties and evaluating scenarios

RWD and algorithm development

- Patient identification and optimizing protocol design
- Supporting clinical trial feasibility and recruitment
- Identifying patterns and trends in RWD
- Machine learning DNA deep learning techniques
- Accelerating analysis of big data/data lakes

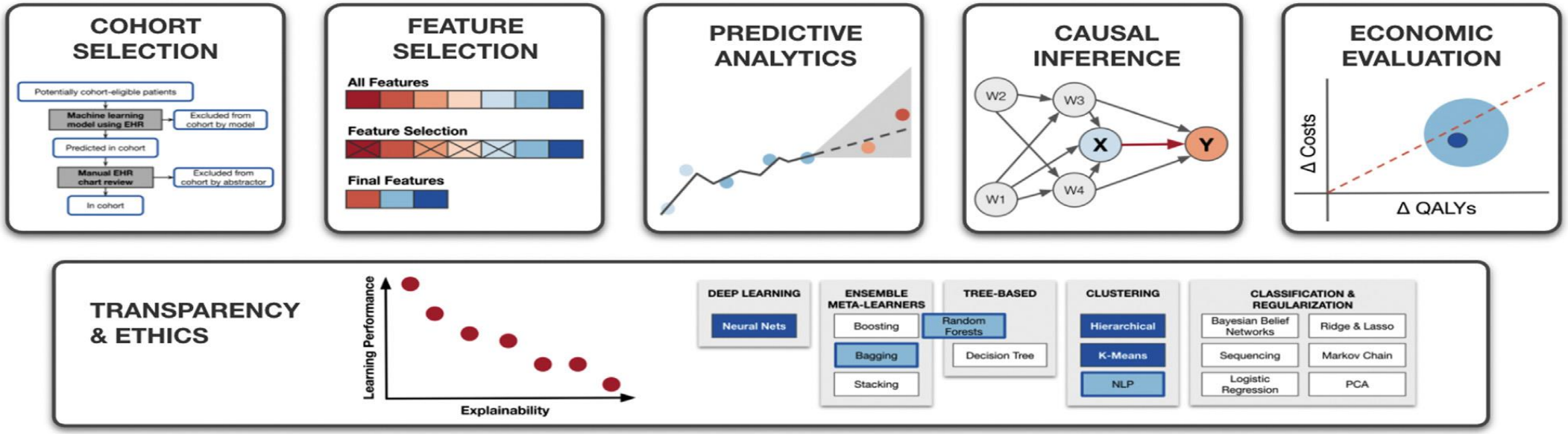
Reimbursement and pricing strategies

- Estimating the value of healthcare interventions
- Supporting value-based healthcare decision making
- Optimizing patient access to new therapies
- Enhancing affordability of healthcare services
- Supporting sustainable healthcare systems

Predictive analytics

- Predicting patient outcomes and treatment response
- AI in disease prevention and management
- Early detection and intervention
- Optimizing treatment pathways
- Supporting clinical decision-making

ISPOR Taskforce: Machine learning applications for HEOR



- **Cohort selection** for identifying samples with greater specificity with respect to inclusion criteria
- Identification of **independent predictors and covariates** of health outcomes
- **Predictive analytics** of health outcomes, including high cost or life- threatening situations
- **Causal inference** using targeted maximum likelihood estimation or double-debiased estimation – reliable evidence more quickly
- Development of **economic models** with reduce structural, parameter, and sampling uncertainty in cost-effectiveness analysis

Source: Padula WV, Kreif N, Vanness DJ, Adamson B, Rueda JD, Felizzi F, Jonsson P, IJzerman MJ, Butte A, Crown W. Machine Learning Methods in Health Economics and Outcomes Research-The PALISADE Checklist: A Good Practices Report of an ISPOR Task Force. Value Health. 2022 Jul;25(7):1063-1080. doi: 10.1016/j.jval.2022.03.022. PMID: 35779937.

Generally, leveraging algorithm development and predictive analytics helps answer a series of questions

Which set of prognostic factors/patient characteristics will accurately predict outcomes?

Can we use these predictors to estimate individual patient-level probabilities for single outcomes/multiple outcomes simultaneously?

Can we identify the variables that are most informative to collect for future patients?

How do we define optimal patient response profiles to flag those who may be at increased risk for adverse events or improved outcomes?

How can we combine the above information to facilitate clinical decision making?

Applying innovative methods to assess which prognostic factors best predict outcomes to inform patient identification and stratification

Patient level data including baseline characteristics (e.g., severity, comorbidities, demographics); HCP characteristics; etc.

Predictive model to assess individual probability of outcomes (e.g., clinical outcomes, treatment discontinuation, dose titration)

Rank most informative variables predicting outcomes

Define patient response profiles for respective treatment options

Individualized risk prediction can inform payer/policy decision making & guide clinical practice by clarifying value