Evidence Generation Recommendations to Support Global Pharmaceutical Launches Following Major Policy Changes in the US (Inflation Reduction Act and Most Favored Nation) and EU (Joint Clinical Assessments)

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BACKGROUND

EU Joint Clinical Assessment:
Single European Union (EU)-wide Joint Clinical Assessment (JCA) from 2025 that evaluates added clinical benefit of new therapies versus standard of care and directly informs national pricing and reimbursement decisions across all 27 member states.[1-3,9]

US Inflation Reduction Act (IRA, 2022):
The IRA enables Medicare price negotiation for high-spend single-source drugs beginning 7 years post-launch for small molecules and 11 years post-launch for biologics, with negotiated prices starting in 2026, making early lifecycle evidence planning essential.[4-5,13]

US Most Favored Nation (MFN) pricing (EO 14297, 2025):
MFN policy benchmarks US drug prices to the lowest eligible OECD net prices via the CMS GENEROUS Model and is projected to reduce prices for high-cost branded therapies by 25 to 40%, tightly linking US reimbursement to international pricing.[6-8]

CORE POLICY INTERACTION: CONVERGING PRICING PRESSURES:
Within the EU, most countries drug pricing is based on external reference pricing (ERP).[3,9] In the US, MFN benchmarks Medicare and Medicaid prices against peer Organisation for Economic Co-operation and Development (OECD) and G7 country prices.[6,8] Under the IRA, high-utilization Medicare drugs are subject to direct Centers for Medicare & Medicaid Services (CMS) price negotiation, with Maximum Fair Prices (MFP) effective from January 2026.[4-5,13] Together, these mechanisms mean every national pricing decision now carries global revenue consequences, making integrated multi-market price modelling essential before any launch price is set.[7]

27
EU member states subject to a single JCA scientific verdict Applies from Jan 2025[1]

7/11 years
Years until MFP takes effect: small-molecule / biologic post-approval [4-5]

25-40%
Estimated US list price reduction for high-cost therapies under MFN [7]

$ 98.5 B
CBO-projected 10-year Medicare savings from IRA negotiation program [13]

OBJECTIVES

Study Aim:

- Develop an integrated global evidence-generation and launch-planning framework addressing US MFN, IRA, and EU JCA requirements.
- Provide strategic recommendations for trial design, evidence planning, launch sequencing, and post-launch market access optimization.

METHODS

Study approach:

- A targeted literature review was conducted using MEDLINE to identify published literature on these policies. Additionally, legislative texts, regulatory guidance documents, and official government communications were reviewed.
- Primary sources included Regulation (EU) 2021/2282, P.L. 117-169, presidential action-executive order of May 12, 2025, HHS/CMS implementation guidance, and EUnetHTA methodological documents.[14-17]
- A four-phase strategic framework was synthesized across the drug development lifecycle.

RESULTS

The four phase framework for strategic actions addressing US MFN, IRA, and EU JCA requirements are explained in below *Table 1*.

Table 1: Key strategic actions and implications

Phase	Timeframe	Primary policy driver	Key strategic actions	Evidence focus	Pricing & Access Implications	Risk if neglected
I Trial design	3–5 yrs pre-launch	EU JCA [1,3,9]	Align Phase III PICO with JCA comparator and endpoints; power subgroup analyses; establish RWE infrastructure	Primary clinical endpoints (OS, validated PROs); JCA-defined comparator evidence, prospectively planned subgroups [3,9-10]	Determines JCA clinical value assessment informs pricing negotiations across all 27 EU states via ERP [3,9]	Non-quantifiable JCA verdict; pricing weakness across EU-27; RWE unavailable at IRA negotiation
II Evidence assembly	12–24 months pre-launch	EU JCA [9,10]+ US IRA[4,5]	Compile JCA dossier with SLR/ITCs; model EU ERP cascade effect and potential US IRP exposure scenario separately; model IRA selection eligibility timeline based on Medicare spend and product age; finalize launch sequencing	SLRs per JCA annex I: ITCs where no head-to-head RCT exists (lower uncertainty); early modelling of subpopulation value [1,9,10]	Low EU launch prices inflate MFN benchmark risk; poor evidence certainty weakens both JCA outcomes and future IRA negotiations [4,7,8]	Evidence gaps at submission; low ERP anchors and G7 MFN basket exposure; reactive IRA preparation
III Regulatory Submission & Market Access	At approval	EU JCA + IRA + MFN [6,7-8]	Parallel EMA/JCA submission; activate RWE from day one; prepare CMS value dossier; implement MEAs for ERP; develop net price strategy for IRA MFP, and GENEROUS MFN targeting Medicaid prices	Initiate structured post-launch RWE collection from day one; early effectiveness signals in routine care; aligned clinical and economic value narrative [1,7, 11]	Net-price exposure under GENEROUS MFN requires price governance beyond EU MEAs; JCA verdict indirectly informs national negotiations [7,8]	Delayed EU access; list price ERP exposure; GENEROUS net price benchmarking without complementary strategy
IV Lifecycle Evidence Generation	Years 1–7/11 years post	US IRA [4,11] + MFN [6,7]	Continuous RWE for subpopulation benefits; monitor Medicare utilization; leverage JCA verdict across EU-27; adapt to MFN evolution; explore DTC channels	Prospectively collected subgroup RWE demonstrating unmet need; utilization and spend tracking for IRA selection forecasting [4,11]	Strong subgroup RWE materially improves IRA negotiation position; early low-price launches may constrain global reference pricing ceilings via ERP and potential MFN-like mechanisms[4,7,8]	Weak IRA negotiation dossier; revenue compressed across EU and US without mature evidence defense

Keys:
CBO: Congressional Budget Office, CMS: Centers for Medicare & Medicaid Services, DTC: Direct-to-Consumer; EMA: European Medicines Agency, ERP: External Reference Pricing, EUnetHTA: European Network for Health Technology Assessment, GENEROUS: GENEROUS (GENErating cost Reductions fOr U.S. Medicaid); HHS: Health and Human Services, IRA: Inflation Reduction Act, ITC: Indirect Treatment Comparison, JCA: Joint Clinical Assessment, MEA: Managed Entry Agreements, MFN: Most Favored Nation, OS, Overall survival; PRO, Patient reported outcome, RWE: Real World Evidence, SLR: Systematic literature review;

RESULTS *continued..*

Figure 1: Strategic actions for pre and post launch

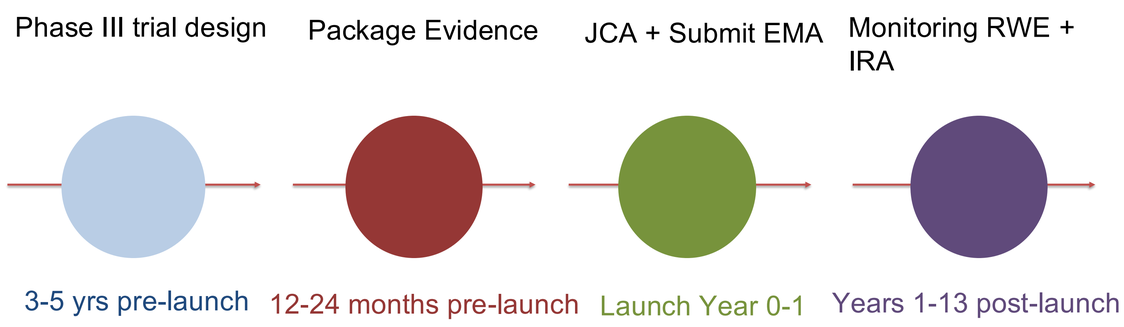
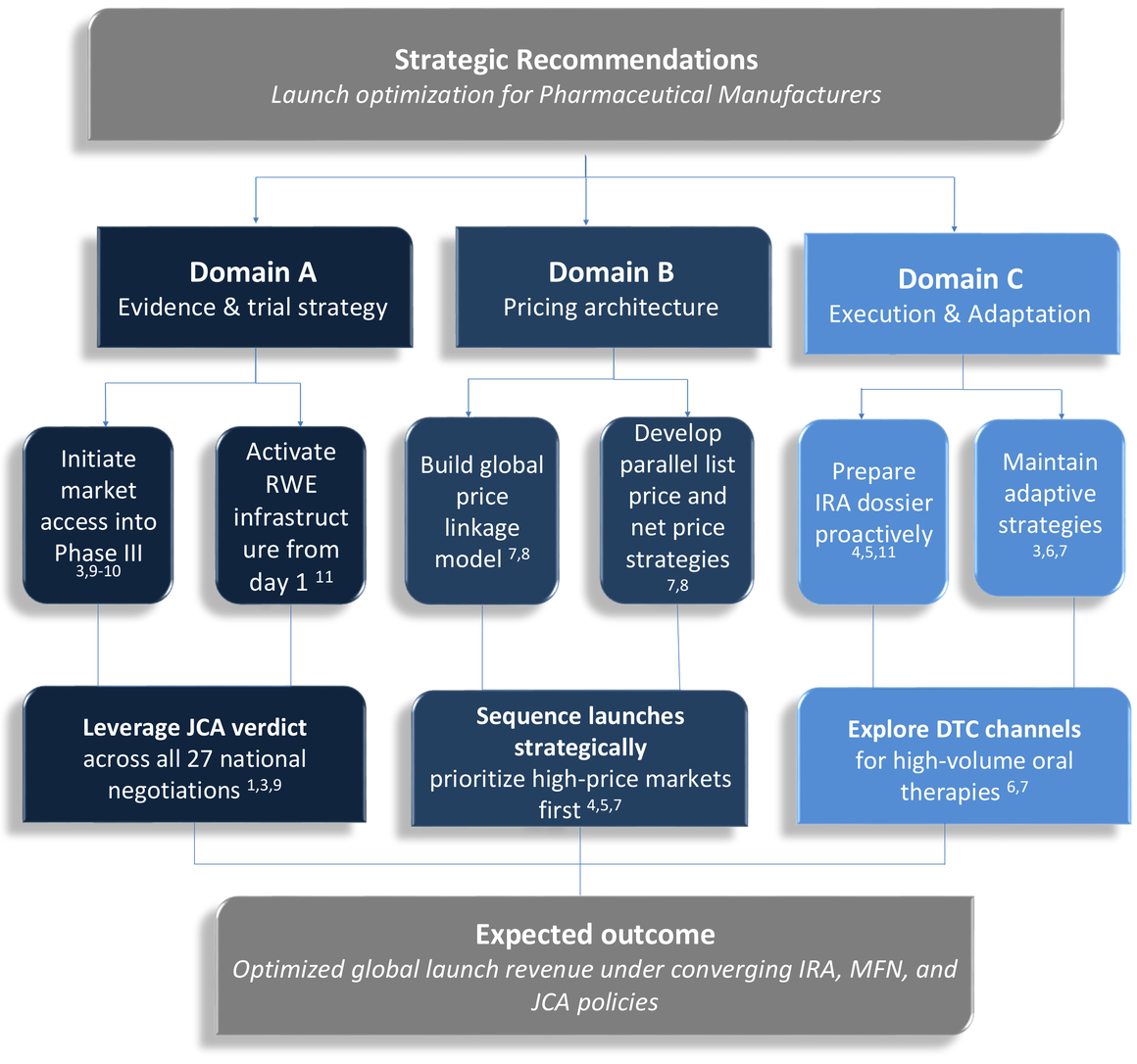


Figure 2: Recommendation framework to optimize global launch



CONCLUSION

Policies such as the IRA, the EU JCA, and international reference pricing approaches including the MFN are shifting value determination earlier in the pharmaceutical lifecycle and increasing interdependence across global pricing and access decisions. Early evidence generation, launch sequencing, and pricing choices now have durable global implications due to cross-country price referencing and Medicare negotiation frameworks. As a result, pharmaceutical manufacturers are transitioning from sequential, country-specific pricing approaches toward integrated, lifecycle-based global market access strategies. Organizations that align evidence and pricing planning early are better positioned to sustain market access and long-term revenue in an increasingly interconnected policy environment.

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