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 (JCA, 2025)

Single European Union (EU)-wide evaluation of the added clinical benefit of new therapies (oncology products and advanced therapy medicinal products (ATMPS) from 2025, orphan drugs from 2028, and all new products from 2030) versus the standard of care and directly informing national pricing and reimbursement decisions across all 27 member states. [1-3,9]

US Inflation Reduction Act (IRA, 2022)

United States (US) legislation enabled Medicare price negotiation for high-spend single-source drugs through IRA. Small molecules will be eligible beginning 7 years post-launch and biologics 11 years post-launch, with negotiated prices effective 2026 for first batch of negotiated drugs, making early lifecycle evidence planning essential.[4-5,13]

US Most Favored Nation (MFN) Pricing (Executive Order (EO) 14297, 2025)

US MFN benchmarks US drug prices to lowest eligible Organization for Economic Co-operation and Development (OECD) net prices via the Centers for Medicare and Medicaid Services (CMS) GENEROUS Model and is projected to reduce prices for high-cost branded therapies by 25-40%, tightly linking US reimbursement to international pricing.[6-8]

CORE POLICY INTERACTION: CONVERGING PRICING PRESSURES

Most EU drug pricing is based on external reference pricing (ERP).[3,9] The US MFN policy benchmarks Medicare and Medicaid prices against peer OECD and Group of Seven (G7) country prices.[6,8] Under the IRA, high-utilization Medicare drugs are subject to direct CMS price negotiation, with Maximum Fair Prices (MFP) effective from January 2026.[4-5,13] This means integrated multi-market price modelling is essential prior to launch, as national decisions carry global revenue consequences.[7]

27
EU member states subject to a single JCA scientific verdict for new oncology and ATMPs from Jan 2025[1]

7/11 years
To qualify for MFP negotiation: small-molecule/biologic post-approval [4-5]

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

$98.5 B
Congressional Budget Office (CBO) 10-year Medicare savings from IRA negotiations[13]

OBJECTIVES

Study Aims

- This research sought to develop an integrated global evidence generation and launch planning framework addressing US MFN and IRA, and EU JCA requirements.
- Additionally, it aimed to 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. Legislative texts, regulatory guidance documents, and official government communications were also reviewed.

RESULTS

- Primary sources included Regulation (EU) 2021/2282, P.L. 117-169, EO, dated May 12, 2025, HHS/CMS implementation guidance, and EUnetHTA methodologic14297al documents.[1,4,6,14]
- A four-phase strategic framework for addressing US MFN and IRA and EU JCA requirements was synthesized across the drug development lifecycle and is presented in Table 1.
- A three-domain recommendation on evidence strategy, pricing architecture, and execution/adaptation was developed and is presented in Figure 1.

RESULTS *continued*

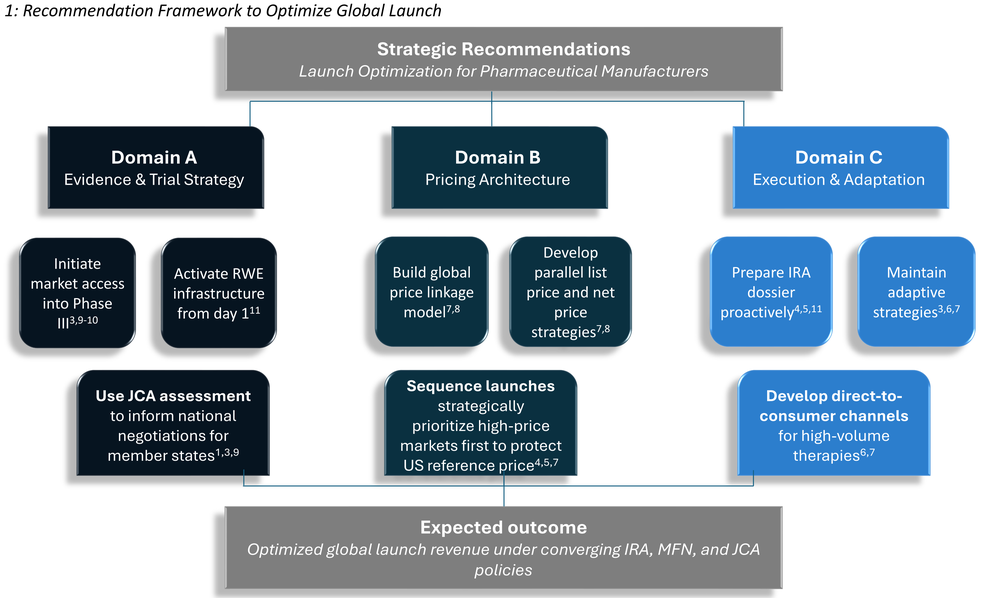
Table 1: Key Strategic Actions and Implications

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(s) and endpoints; power subgroup analyses; establish RWE infrastructure	Primary clinical endpoints; 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 (by individual member states separately)[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 any EU ERP cascade effects and potential US IRP exposure scenarios separately; model the IRA selection eligibility timeline based on Medicare spend and product age; Check OECD country prices for MFN; finalize launch sequencing	SLRs per JCA annex I: ITCs where no head-to-head RCT exists; early modelling of subpopulation value[1,9,10]	Low EU launch prices increase 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-approval (eligible for negotiation)*	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: CMS, Centers for Medicare and Medicaid Services; DTC, Direct-to-consumer; EMA, European Medicines Agency; ERP, External reference pricing; EU, European Union; G7, Group of Seven; IRA, Inflation Reduction Act; ITC, Indirect treatment comparison; IRP, Internal reference price; JCA, Joint Clinical Assessment; MEA, Managed entry agreement; MFN, Most Favored Nation; OECD, Organization for Economic Co-operation and Development; PICO, Population, intervention, comparison, and outcome; RCT, Randomized controlled trials; SLR, Systematic literature review; RWE, Real-world evidence; US, United States

* IRA price negotiation for **small molecules-** selection: 7 years, price applicability: 9 years; **biologics-** selection: 9 years, price applicability: 13 years

Figure 1: Recommendation Framework to Optimize Global Launch



CONCLUSION

Findings from the four-phase framework demonstrate that decisions made 3-5 years pre-launch including trial design, comparator selection, and subgroup planning directly influence JCA outcomes, EU pricing negotiations, and long-term revenue sustainability across both EU and US markets. Evidence gaps at submission, misaligned SLR/ITCs/value dossiers, weak price anchoring of OECD countries, or delayed negotiation readiness can constrain launch sequencing and compress global revenues. To address these risks, the framework identifies three core strategic domains: early integration of market access requirements into Phase III development and RWE activation at approval; implementation of global price linkage modelling and deliberate launch sequencing to manage reference pricing exposure; and sustained lifecycle execution through proactive negotiation preparation and adaptive commercialization strategies. Overall, coordinated evidence, pricing, and execution planning across the product lifecycle is critical to maintaining pricing flexibility and protecting global launch performance under converging policy reforms.

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