DEMONSTRATING THE VALUE OF INNOVATION

Meeting the Needs of FDA, Payers, Providers, Consumers

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Who Defines Value from Innovation?

To Capture Value from Innovation, Manufacturers Must Meet the Evidentiary and Economic Needs of Four Key Stakeholders

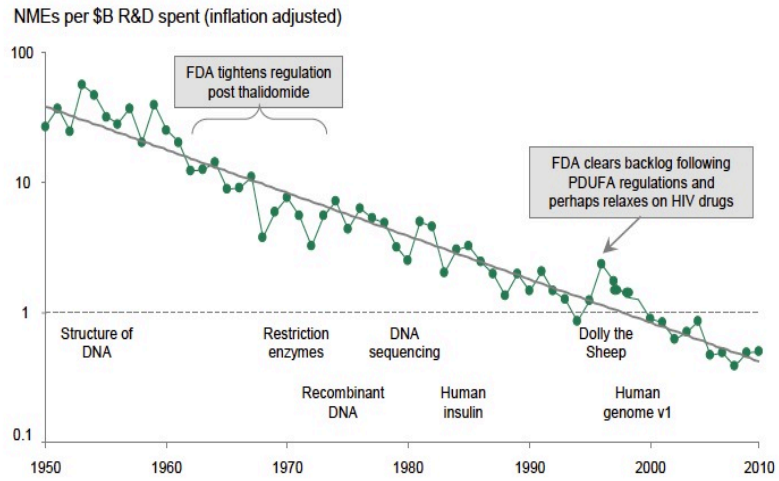
FDA	Market Authorization and Post-Market Surveillance
Insurers	Coverage, reimbursement, and pricing
Providers	Physician prescription and hospital budgets
Consumers	Cost sharing, engagement, adherence

There is an important feedback loop from market authorization, access, and adoption to incentivize further investment in research and development

FDA

Regulatory

Market Access



Note: R&D costs are estimated from PhRMA annual survey 2009; NMEs are the total number of small molecule and biologic approvals by the FDA
Source: Bernstein Research "The Long View – R&D Productivity" (September 30, 2010)

The Reverse of Moore's Law: An Exponential Decrease in New Drug Launches per $Billion Spent on R&D

Value as Defined by the FDA

- FDA interprets product value as efficacy when used in ideal research settings and safety relative to unmet need
- It recognizes that social value will depend on clinical performance and cost under real world conditions but wants to allow products passing its threshold to prove themselves to payers, physicians, and patients
- Evidence required to demonstrate (this concept of) value traditionally consisted of randomized trials and clinical endpoints, with a lower bar for follow-on products (generics, biosimilars, substantially equivalent devices)
- In each case, FDA weighs the value of additional data against the burden of time delay, cost, rapid product cycles

Lowering the Bar to Market Authorization

- In recent years FDA has made a dramatic shift towards reducing evidentiary demands in order to accelerate approval and reduce regulatory costs
- Promising drugs (esp. oncology, orphan) receive special consideration/advice, priority review, approval for special designs (e.g., one-arm trials, surrogate endpoints)
- This makes it easier to get on the market. It is being combined with requirements making it more difficult to stay on the market: post-launch follow-on studies (if used surrogate endpoints), studies using real world evidence (RWE) over the product life cycle, safe use requirements (REMS), and site of care (COE) restrictions

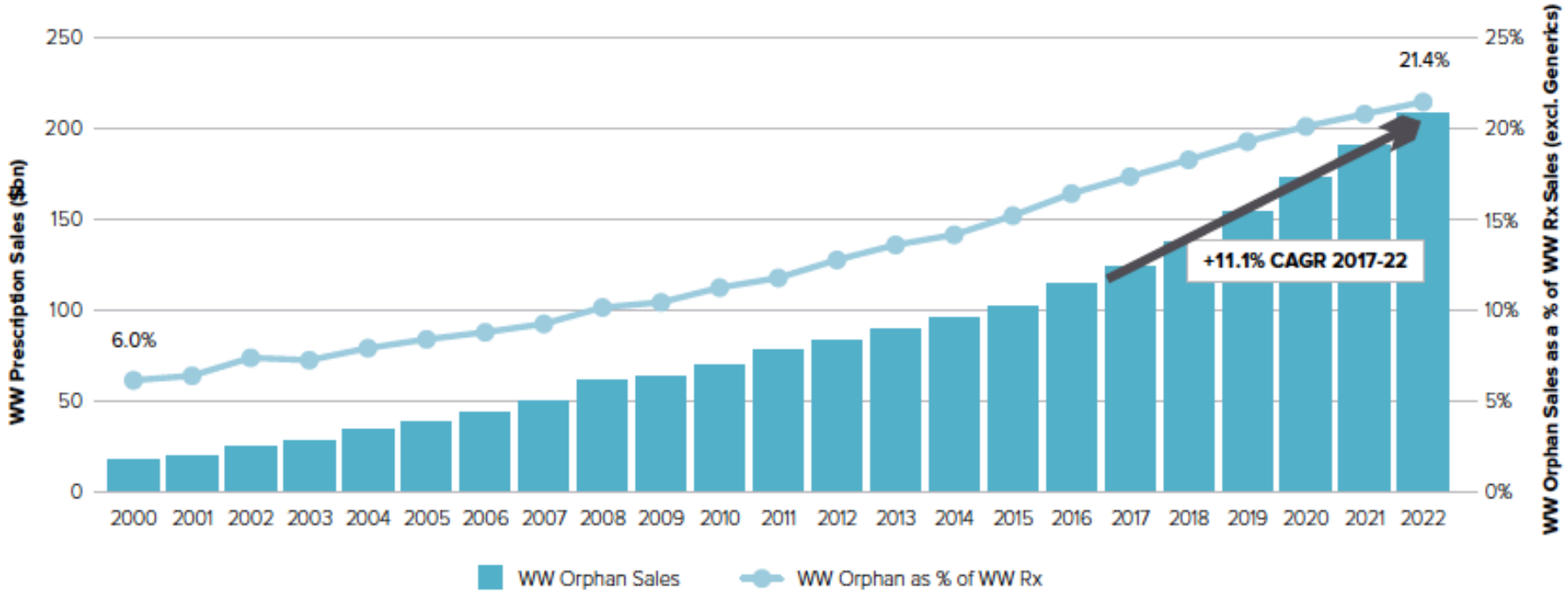
Which Roles for Real World Evidence?

- The 21st Century Cures Act enabled/exhorted the FDA to increase its use of RWE, but challenges include:
  - There is no gold standard of RWE data quality across EMR, insurance claims, patient surveys, sensors on wearables or in the home, etc.
  - These data sources typically are not integrated with one another
  - Machine learning methods are sifting thru them to find patterns, but users feel uncomfortable about inferences when they cannot understand the algorithms and feel confident about causality
- Most immediately, RWE can be used for:
  - Control arm for trials where randomization not possible due to small patient populations, ethical limits on assigning patients as controls, etc.
  - Insurance claims post-adoption can document complications, changes in utilization and costs, etc. across diverse patient sub-groups
  - Patient experience data provides endpoints supporting claims of safety/efficacy where hard clinical endpoints are not available

Example: Orphan Drugs Benefit from Research Grants, Tax Credits, Smaller Trials with Surrogate Endpoints, Extended Regulatory Exclusivity

Worldwide Orphan Drug Sales & Share of Prescription Drug Market (2000-2022)

Source: EvaluatePharma® February 2017



Payer
Coverage and Pricing

"You don't know how lucky you are! A quarter of an inch either way, and it would have been outside the area of reimbursable coverage!"

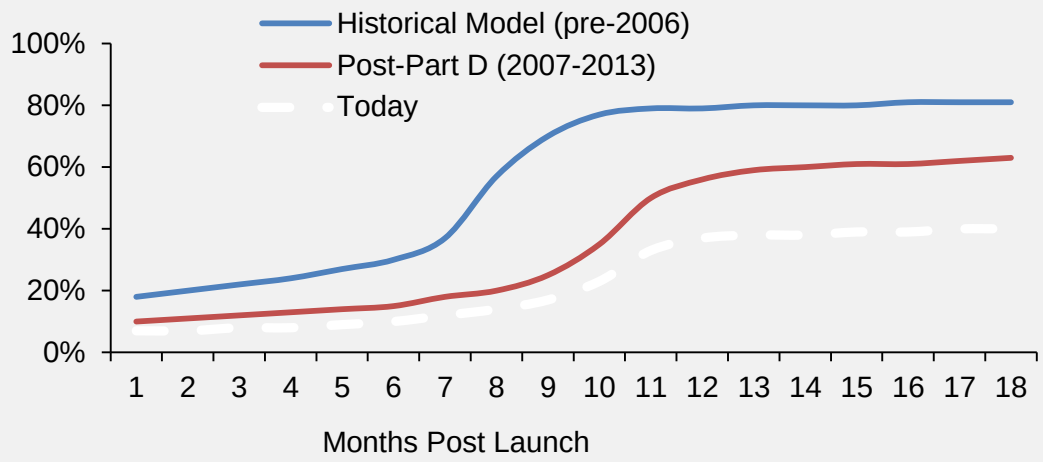
Value as Defined by Payers

Insurers and employers traditionally were under pressure to approve all technologies that improve outcomes, no matter how small, regardless of cost, no matter how large. Evidence demands were minimal (beyond FDA authorization)

- Now payers are defining value in terms of comparative clinical and cost effectiveness
- They are tightening coverage (formulary inclusion, prior authorization, step therapy), provider payment incentives, and consumer cost sharing as means to obtain reductions in price and utilization
- These tools are effective.

More Intense Prior Authorization and Cost Sharing Are Slowing Drug Adoption Relative to Projections

Percent of Potential Post-Launch Adoption Actually Achieved, With Changing Intensity of Payer Management



‡ *Source: QuintilesIMS,* Payer and Managed Care Insights, *Novartis*

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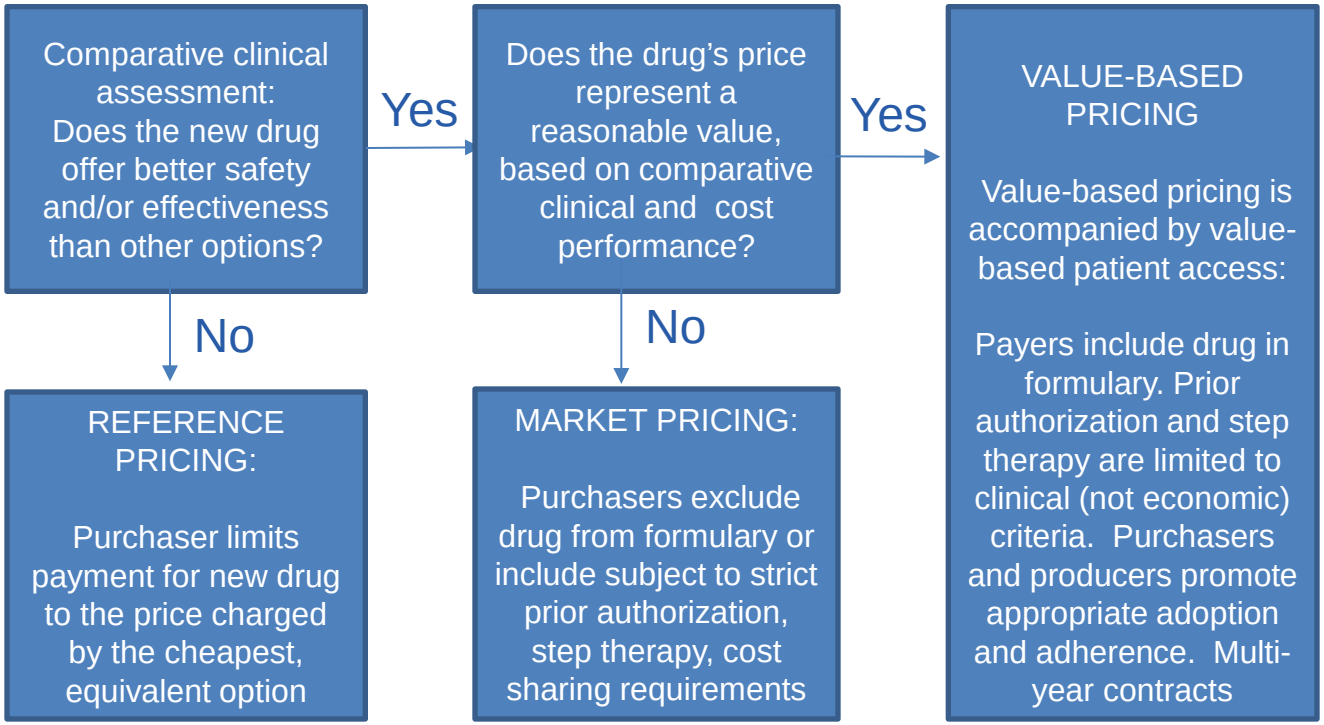
The Emerging Logic of Value-Based Pricing and Patient Access Criteria



Example: Manufacturer Reduces Price to ICER ‘Value-based’ Benchmark in Exchange for Lighter Prior Authorization and Cost Sharing

BUSINESS | HEALTH CARE

Regeneron and Sanofi Plan to Cut Cholesterol Drug Price in Exchange for Wider Coverage

They seek to offer rebates and discounts for Praluent and want insurers to ease restrictions on some patients

A cost-effectiveness analysis by an independent group incorporated new clinical trial data showing that Praluent reduced the risk of death. PHOTO: SANOFI AND REGENERON PHARMACEUTICALS/ASSOCIATED PRESS

By Joseph Walker

March 10, 2018 9:00 a.m. ET

Provider
Prescription and Purchasing

"Geez Louise—I left the price tag on."

Value as Defined by the Hospital and Physician

- In the ‘medical arms race,’ hospitals competed for physician affiliations and admissions via adoption of state-of-the-art technology, regardless of cost
- In the new context of bundled payment and shared savings, hospitals are developing new strategies with respect to technology assessment, purchasing, and use
- Hospitals, and physicians aligned with hospitals, interpret value as quality, measured by short-term outcomes, and cost, measured by impact on the hospital budget and physician gain-sharing
- They do not focus on cost and benefit to society

Alignment, Assessment, and Purchasing

- Physician alignment & incentives
  - Hospital employment of physicians; joint ventures and co-management for ambulatory infusion, imaging and surgery centers; physician payment linked to organizational performance with gain-sharing bonus for reducing hospital costs; limits on ties with manufacturers (‘conflicts of interest’)
- Technology assessment: ‘value committees’
  - Major new clinical equipment and supplies need to be approved by committee dominated by physicians, based on evidence of performance and cost to the hospital budget. Committees also serve a cultural function: physicians begin to think of value as including cost (to the hospital)

Capital Equipment and Supplies

- High-value capital equipment (e.g., radiotherapies)
  - Major capital purchases have always been subject to financial review to a greater extent that consumable 'physician preference items', but the bar is rising as payers consider 'Center of Excellence' contracting to obtain better prices (and perhaps better outcomes) by contracting with more limited numbers of facilities. COE contracting also potentially helps payers counter the consolidation of local markets. This makes hospitals more aware of clinical equipment as either a path towards COE or an unreimbursed cost burden if COE status is not achieved
- High-value supplies (e.g., implantable devices)
  - Increasing reliance on formal RFP and external benchmarking; reduce number of suppliers to simplify supply chain and maximize discounts; physician alignment supports creditable threat to switch suppliers

Example: Bundled Episode Payment for Device-Intensive Procedures

- Medicare CCJR initiative was mandatory in 67 markets, combining Part A, B payments. Alternative models combine post-discharge readmissions and subacute services in bundle. Was to expand to cardiac, spine procedures. Trump administration switched from mandatory to voluntary and halted expansion to cardiac.
- Strategy: create incentives for physicians to make clinical choices aligned with hospital concept of value
- Peer-reviewed evaluations report:
  - Reduction in discharges to post-acute
  - Small decline in costs
  - No decline in quality, patient mix

Source: AM Ryan. JAMA 2018; 320(9):877-879

Consumer
Engagement & Adherence

"The gentleman at the other register would like to cover your co-pay."

Value as Defined by the Patient

Patients often have lacked the information and incentives to demand high-value health care

"You're responding beautifully. Let's go ahead and see what happens if we increase your deductible."

They now increasingly have the incentive, but still need information and support to make value-based choices

Decision Support

Company	Target Population	Product Offering
Online Transparency Tool castlight HEALTH	• Patients with significant cost sharing requirements facing choice among providers with significant price and quality differences	• Information on price, quality, location of alternatives • Titrated to individual's network and benefit design • Employers offered analytics
AIM SpecialtyHealth™	• Patients prescribed high cost radiology or infused drug	• AIM staff phone patients once receive referral info through prior authorization. Suggest lower priced sites of care
Sutter Health	• Patients with multiple ED visits, inpatient admissions, unplanned readmissions, diagnosis of CHF, COPD, three or more chronic conditions	• Complex case management program
Aetna® Healthy Actions Program	• Patients benefitting from screening & preventive services, chronic disease management, maternity ('beginning right')	• Employer contributes to HSA, reduces deductible, offers gift cards if patient completes health risk assessment and indicated preventive and/or management programs
OPTUM™ Decision Support	• Patients facing complex treatment alternatives	• Nurses counsel members on treatment alternatives, low-cost site of care, medication choices and adherence, lifestyle change

Digital Technologies to Support Consumer Engagement: Effectiveness to be Demonstrated

Bottom Line: Innovators Need to Prove Value to All Stakeholders, According to Each Definition

FDA

- Regulators are making it easier to get on the market, but also easier to get pulled off the market: demanding life cycle RWE

Insurers and employers

- Payers are using HTA evidence (informally) when assessing value and seeking price-volume contracts that protect budgets

Physicians and hospitals

- Physicians and hospitals increasingly are budget-holding purchasers, focused on cost (to them) as well as performance

Consumers and patients

- Patients increasingly are engaged and price-sensitive consumers; care experience and out-of-pocket cost are key

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