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Principled Drug Pricing Centered on Innovation and Choice: Part 1

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Principled Drug Pricing Centered on Innovation and Choice: Part 1 Synopsis (1/2)

- **The US drug pricing debate is one of the most important contemporary societal issues**. However, this debate has been severely handicapped not only by its extreme complexity and concomitant lack of understanding of the totality of the drug pricing ecosystem, but also by the dearth and non-transparency of the key facts. Within our report we have utilized a data-driven approach (much of it proprietary), combined with in-depth analysis of global drug pricing systems, to identify the underlying fundamental and structural issues of the unique US drug pricing ecosystem. This approach has allowed us to suggest a set of putative interlinked changes that would address the ecosystem's underlying flaws.

- **In our view, the US drug pricing ecosystem will inevitably undergo significant changes** - these changes are likely to occur rapidly, resulting in a dramatically different pricing ecosystem. In other words, the debate is not just near-term (election induced) noise. The US drug pricing ecosystem has evolved (it was not built by design) in a direction that, if left unchecked, will shortly turn into a fundamentally broken system. A significant risk for the key constituents of the drug pricing ecosystem (i.e. patients, biopharma innovators and payers) are government measures, meaning new legislation that is unlikely to rapidly address the fundamental underlying causes of the problems but rather attempt to deal with the most prevailing symptoms and side-effects.

- **In order to prevent this outcome, we advocate a coordinated approach** from the biopharma manufacturers and payers to drive course-correcting efforts, since this is likely the most effective and efficient path forward for both society and industry (although we do think legislative change may be a necessary part of the cure). In an efficacious drug pricing ecosystem, revenues from marketed branded drugs should reward innovative value, and more so motivate future innovative value to the multiple players in the drug ecosystem, in a fashion proportional to their direct contribution of value. The paramount risk of failure to address the current flaws in the system is the lessening of future innovation and advancement in therapeutics.

- **Within the report we provide data, analyses and arguments** to support our view that, although prices of branded drugs are significantly higher in the US than in the comparative developed world, in totality how much the US heathcare system spends on drugs (currently) is not the problem. Rather the fundamental problem is with three central, and intimately linked, elements that have evolved in the last 10 years within the US drug pricing ecosystem, specifically: (1) non-value driven drug pricing, (2) low transparency across multiple parts of the ecosystem, and (3) high frictional costs.

- **Within our report we show that individual net and list drug prices do not necessarily reflect the value** (i.e. cost/benefit) to the system due to a combination of non-value based pricing at launch, elevated and frequent price increases that are non-cost/benefit driven, and increasingly high drug rebates that fail to be fully passed through to the ultimate consumer (patients). The high price increases and much publicized "bad actors" in the US ecosystem are a symptom rather than a cause of the core problems. We also show that the "gatekeeper" job of the cost/benefit assessment has fallen onto PBMs. PBMs have a fundamental conflict of interest in asserting cost/benefit measures, due to the rebate/access conundrum. . This conundrum results in excessively high frictional costs, as well as frequent financial incentivization that result in favoring drugs with subpar cost/benefit ratio. These three central problems are further compounded and enabled by the lack of transparency and choice across multiple parts of the ecosystem.

Source: MTS analysis

Principled Drug Pricing Centered on Innovation and Choice: Part 1 Synopsis (2/2)

- **Our suggested solution is the "all hands on deck" approach**, where biopharma manufacturers and payers work together to bring about drug pricing reform. A coordinated effort, if enacted with vigor and determination by the industries, could lead to a relatively fast and effective change to the current pricing ecosystem. The free market and consumerism based principles of drug pricing are unique to the US ecosystem, as all other countries have effectively socialized medicine. Whilst free markets principles are the right fundamental structure for pricing drugs and motivating further innovation, the current system has exploited the extremes resulting in a near broken system.

- **With regards to the biopharma industry**, we advocate a move towards uniform and principled value (cost/benefit) bias for drug pricing and moving away from the current approach by pricing drugs based on "what the ecosystem can handle right now." The key hurdle for success is how to accurately define value – which we broadly describe as either delivering a clinical benefit in a completely unmet medical need or significant increase in benefit/efficacy in comparison to marketed products. Value pricing already exists in many regions of the comparative developed world, and we believe the US healthcare system should move from a laggard to a leader position on value based pricing.

- **For the payer side of the industry**, we advocate for increased transparency and choice in the prescription Rx element of insurance. Specifically, we propose a system, a consumer chosen Rx benefit, where the Rx element is broken out of the overall medical benefit and the consumer is empowered to make a selection out of a number of different bands of Rx coverage. Within each band of Rx coverage, the cost is directly proportional to level and breadth of Rx coverage. Under this system, rebates and the resultant conflict of interest, can be significantly reduced or eliminated.

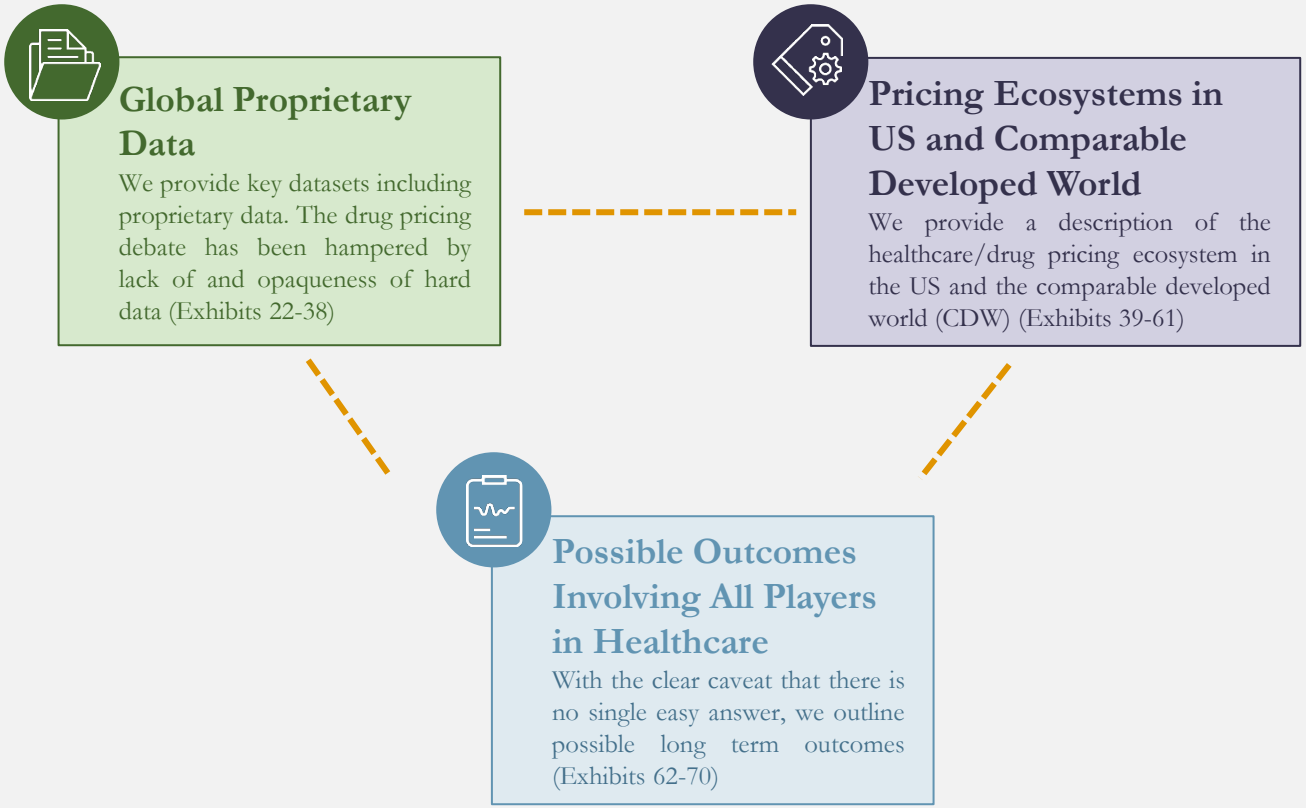
- **Through combining the above suggested measures**, the cost/benefit requirement of an effective drug pricing ecosystem moves primarily to the manufacturers, and frictional costs are reduced, and the "check" in the system is the consumer choice of the level of Rx cover.

- We hope you find the report informative and thought-provoking. We further highlight that the report's purpose is to act as a forum for continued debate. We welcome comments and questions to the coordinating author, Ravi Mehrotra (mehrotra@mtspartners.com) and/or to any of the Partners at MTS.

Source: MTS analysis

This Report Acts as a Forum of Continued Debate on Drug Pricing by Providing Proprietary Data, Description of Pricing Ecosystems & Possible Outcomes

US drug pricing debate is one of the most important contemporary societal issues. However, this debate has been severely handicapped not only by its extreme complexity and concomitant lack of understanding of the totality of the drug pricing ecosystem, but also by the dearth and non-transparency of the key facts.



We welcome comments and questions: mehrotra@mtspartners.com

Source: MTS analysis

Organization of Our Report

1	Summary Slides: Principled Drug Pricing Centered on Innovation and Choice: Part 1 (Exhibits 6-23)
2	Key Data on Healthcare and Drug Spend, and Pricing (Exhibits 24-40)
3	Healthcare and Drug Pricing Ecosystems: US vs. Comparable Developed World (Exhibits 41-63)
4	Possible Outcomes for US Drug Pricing Ecosystem (Exhibits 64-72)
5	Appendix (Exhibits 73-88)
6	MTS Health Partners (Exhibits 89-90)

Source: MTS analysis

1. Summary Slides: Principled Drug Pricing Centered on Innovation and Choice

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MTS View on the US Drug Pricing Ecosystem

A successful and efficient drug pricing ecosystem is of key importance to society – drugs increase the quality of life, save lives and lower total healthcare costs.

Revenues from drugs should reward "innovative value" and motivate future innovation value to the multiple players in the drug pricing ecosystem, proportional to the contribution of value.

The current US drug pricing ecosystem (which was not created by design) has evolved into **a system that is not efficiently rewarding, and is at risk of not optimally encouraging future, innovative value.**

A critical mass of "trip wires" has been hit: (1) increased visibility/focus on the rebate system, (2) irrational price rises, (3) savings from patent cliffs of small molecules have gone to price rises of established drugs, (4) publicity of how much higher specific drugs are in the US vs comparable developed world (e.g. diabetes), (5) publicity of "bad actors".
These trip wires are all symptoms rather than the underlying cause.

The US drug pricing ecosystem will undergo significant changes that are likely to occur rapidly, resulting in a dramatically different pricing ecosystem. To deliver the optimal principled drug pricing ecosystem, changes should occur within all system participants driven by biopharma manufacturers and payer intermediates.

Source: MTS analysis

The Key Take-Homes from Our Analysis of the US Drug Pricing Ecosystem

Data

Totality of $1,052/capita of US drug spend (~1.9% GDP or ~10% healthcare spend), or even the average US/comparable developed world drug price premium (~2.1x) is NOT the problem

Ecosystem

The evolutionary direction of the totality of the current **drug pricing ecosystem is the problem** – it fails to efficiently and proportionally reward innovative value

Non-value driven drug pricing	**Low transparency** across multiple parts of the ecosystem		**High frictional costs** not proportionally rewarding contributors of value
Cost/Benefit ≠ Value	Low transparency of net drug prices	Differential contributions/ benefit for insurance with little/no choice	~14% of drug's list price is attributed to ecosystem frictional cost; Conflicts of interests are being masked as frictional costs at multiple points in the ecosystem

Possible outcomes

The emphasis is on the Biopharma industry to base drug pricing to a value- (cost/benefit) and outcomes-based principal, moving away from the current free market "what the ecosystem can bear" system. Drug price rises are not the cause of the problem but rather a symptom. True value based pricing could still lead to dynamic prices after launch (both up and down) based on post-launch changes in benefit assessment.

Differential and non-transparent **rebate levels are now a headwind rather than a tailwind to drive appropriate cost/benefit value**.

The rebate system needs a dramatic overhaul via coordinated efforts of all parties involved.

Introduction of choice, of level of contribution, and consequent transparent level of benefit for the Rx element of insurance cover. Change driven by insurers/PBMs and central governing bodies.

Frictional costs across all parts of the ecosystem should be reduced to a minimum. The largest frictional cost is the insurance based intermediator cost, which is in turn principally driven by the rebate system. **Value based pricing and transparent net-pricing can reduce/eliminate the rebate system**. Other (non-direct) frictional costs include level and content of **S&M/OTC spend by manufacturers.**

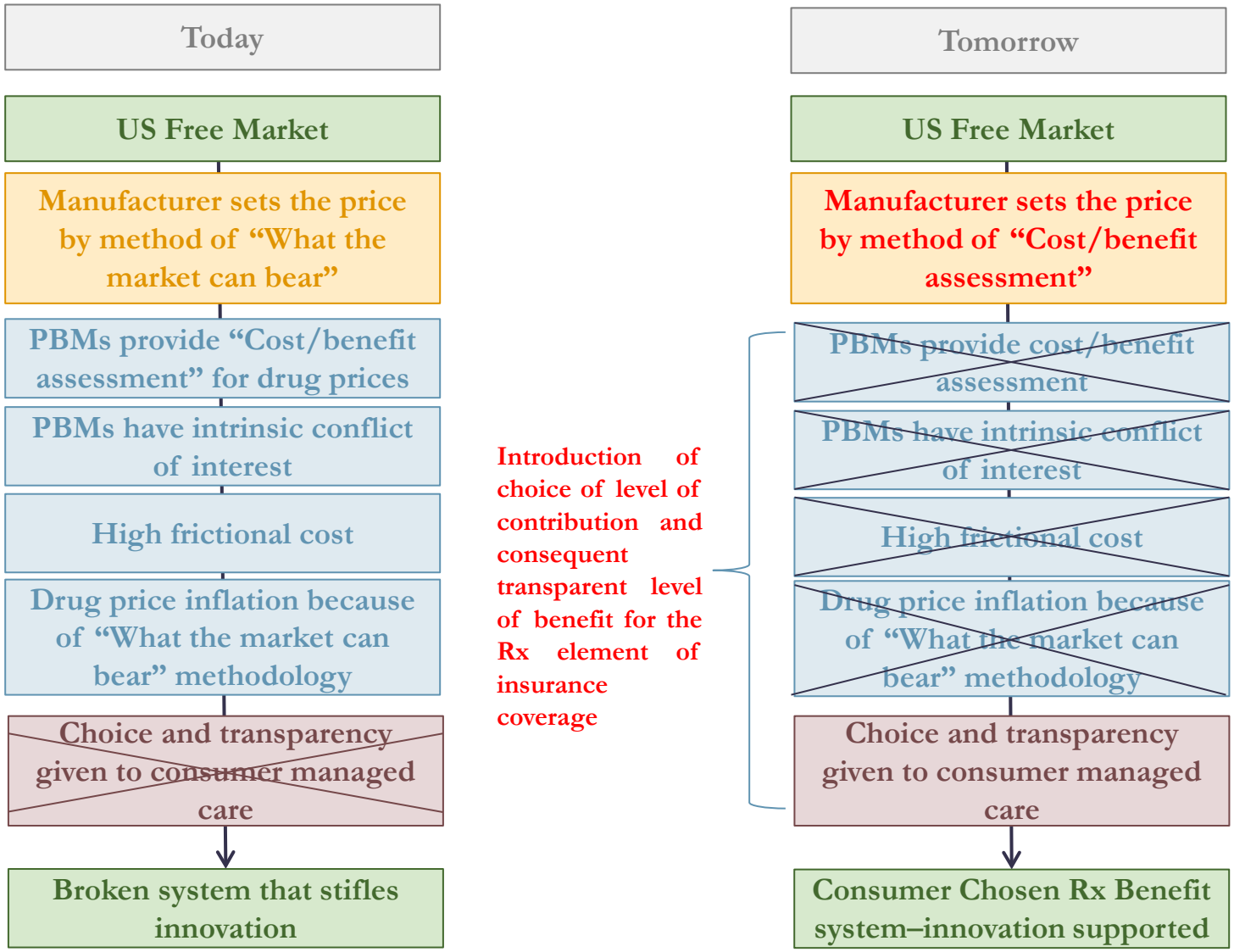
Two key actionables:

(1) Biopharma industry should move uniformly to an innovative value based drug pricing

(2) Increase in transparency and choice in the Rx element of the insurance system

Source: MTS analysis

The Effect of the Proposed Actionables on the US Drug Pricing Ecosystem

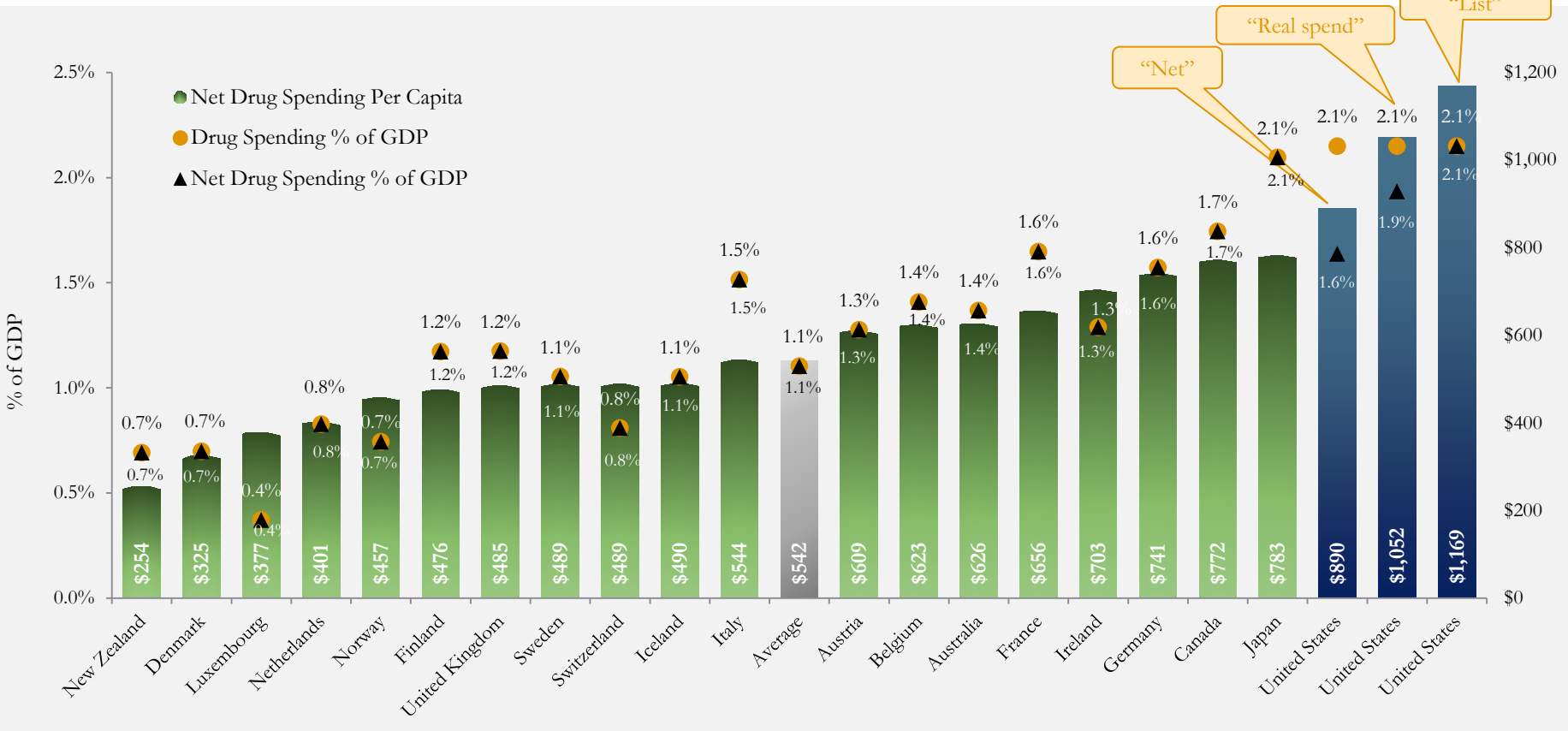


Source: MTS analysis

Total "List," "Real," and "Net" Drug Spend in the US and Across Comparable Developed Countries

US spends more on drugs than other countries, but not that much more when discounts (rebates and coupons) are considered

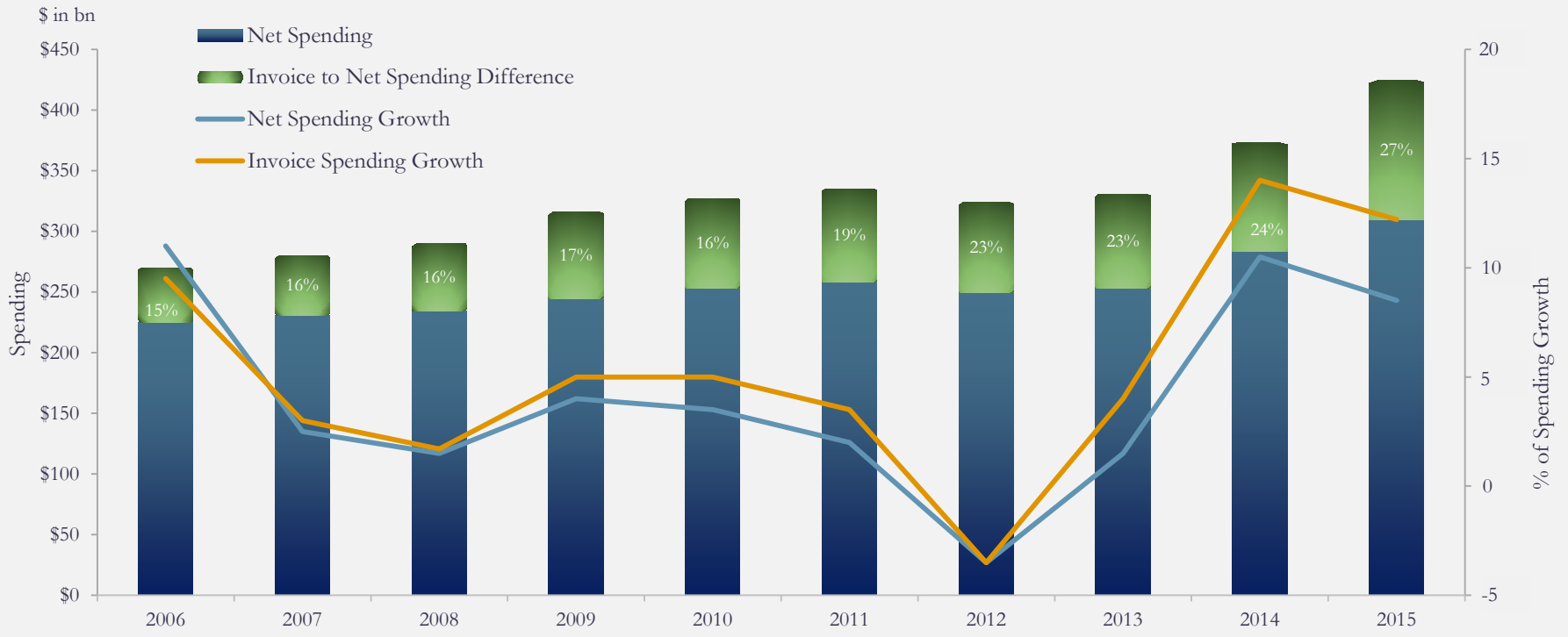
"List" (aka the "Gross" or "Invoice") = Sticker price which is not realized at all in the current US ecosystem, but is frequently quoted in data sources, media and what public perceives as the true cost of drugs
"Real spend" = The actual cost to the ecosystem calculated by MTS – details of our analysis are in the next section
"Net" = $ amounts captured in totality by drug manufacturers



Source: OECD, Disposable Income Per Capita: 2013 Data; 2014: United States, Australia, Netherlands, Finland; 2012: New Zealand; 2009: Japan, Total drug spend, Drug spend per capita: 2014 Data, 2013: Australia, Japan; 2007: New Zealand; https://data.oecd.org/healthres/pharmaceutical-spending.htm; MTS analysis

Total List (Gross) and Net US Drug Spending Over Last 10 Years

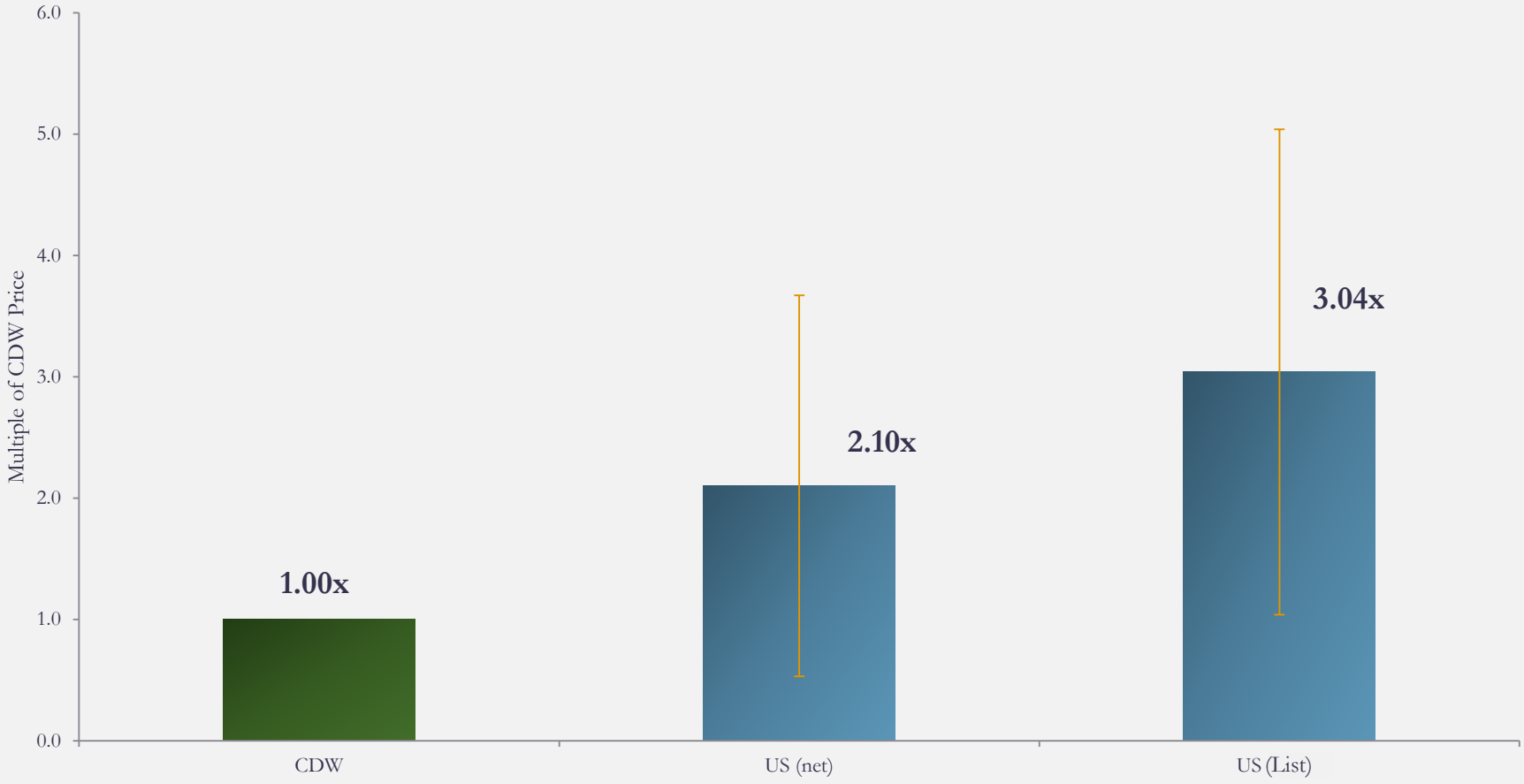
High Rebates, which are unique to the US ecosystem, are responsible for List (Gross) to Net but also drive high frictional system costs. Rebate levels have increased notably over the last 10 years.



Source: IMS Health, MTS analysis

List vs. Net Price of Top 20 Drugs in the US vs. Comparable Developed World (CDW)

US premium is on average 3x than comparable developed world (CDW), but with discounts it is reduced to 2.1x (for Top 20 Drugs). US has an average 27% list to net discount and there is between 20-800% US price premium vs. CDW for individual drugs.



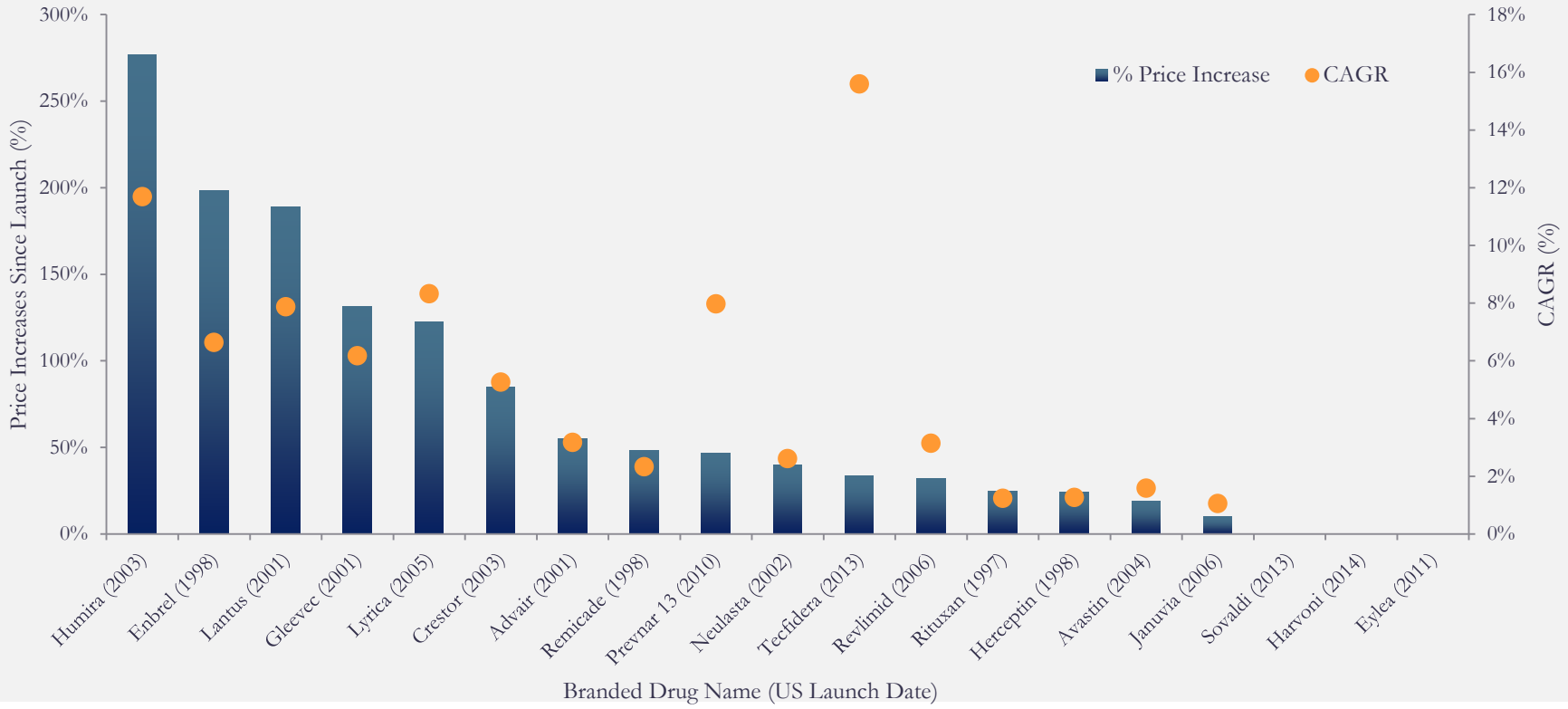
Source: PriceRx, MTS analysis, CDW = Netherlands, Spain, UK, and Switzerland

Percent Increase of List Price Since US Launch for the Top 20 US Drugs

Significant drug price increases are unique to the US "free-market" based pricing ecosystem.

Price increases in the US, since launch to current prices of the top 20 drugs vary greatly.

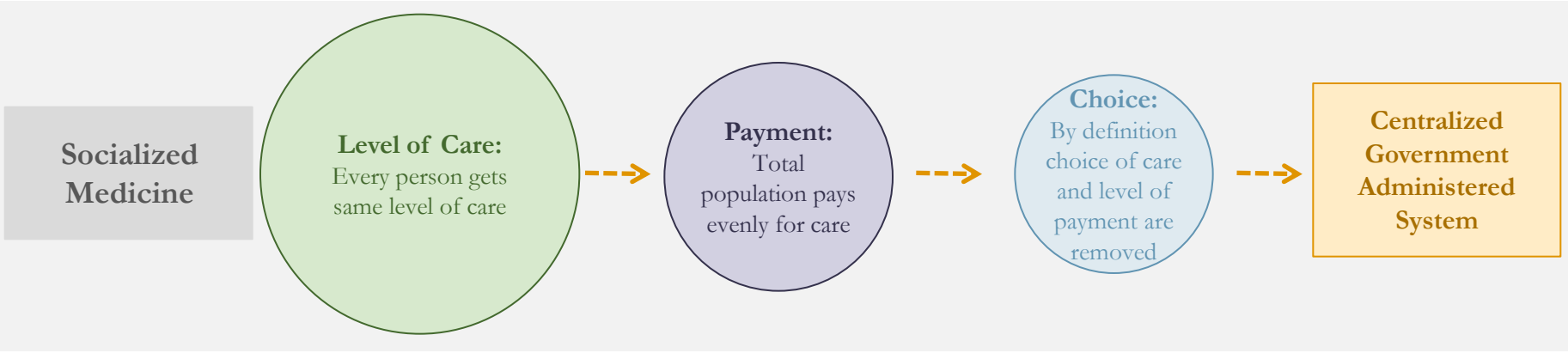
There is no "fundamental" basis for the price increases – they happen because the US ecosystem simply allows them to happen.



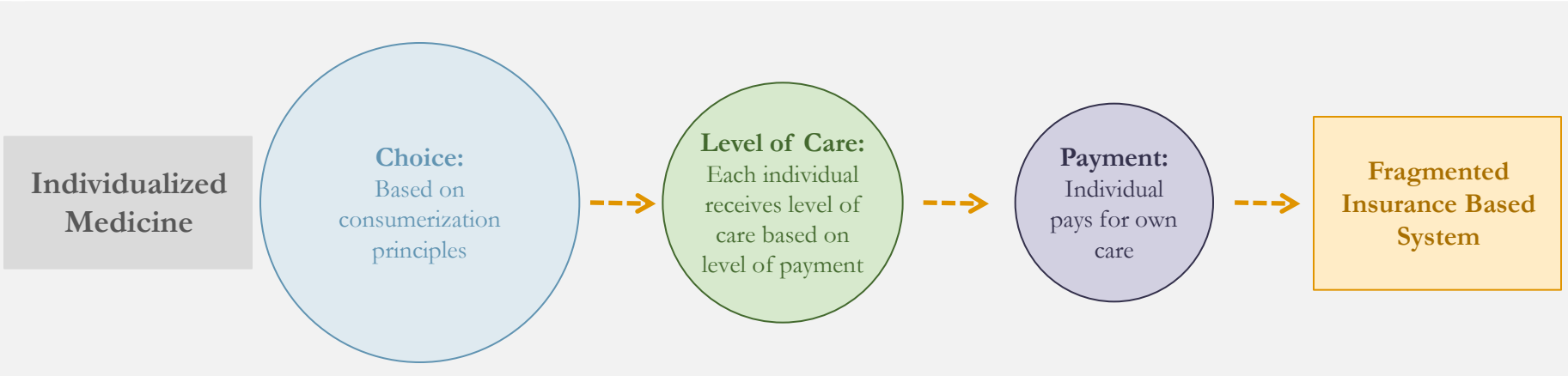
Source: PriceRx, MTS analysis

The Core Principles of Socialized Medicine in Comparable Developed World (CDW) vs. Individualized Medicine in the US

The healthcare system in most countries in the comparable developed world (CDW)



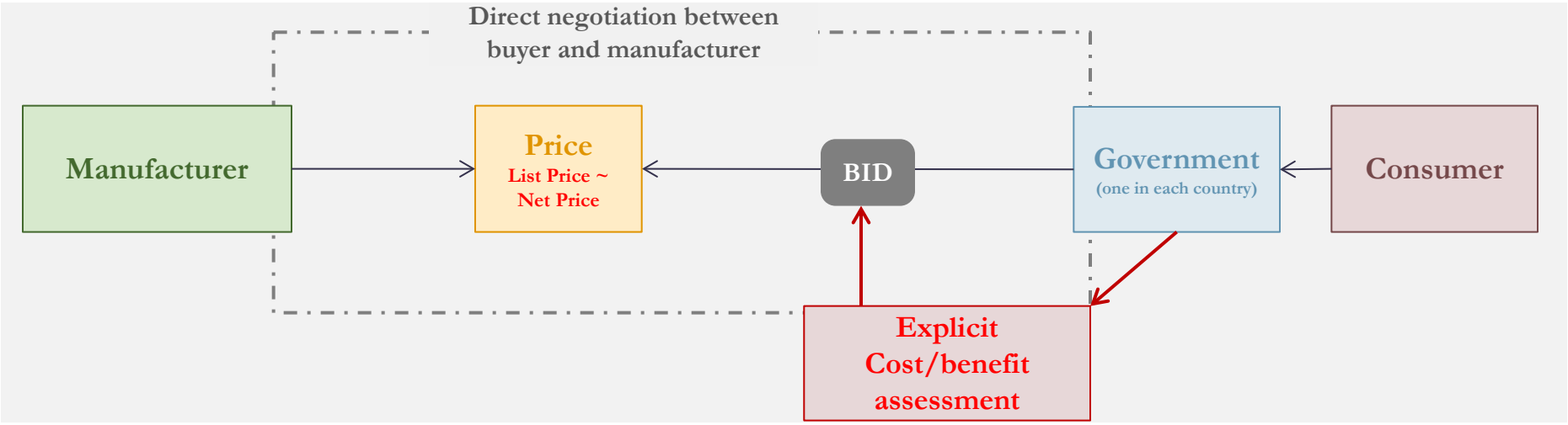
The US healthcare system is unique and is fundamentally based on an individualized system, but lack of choice, transparency & concomitant lack of direct cost-benefit leads to a concept we coined as "Pseudo-consumerism"



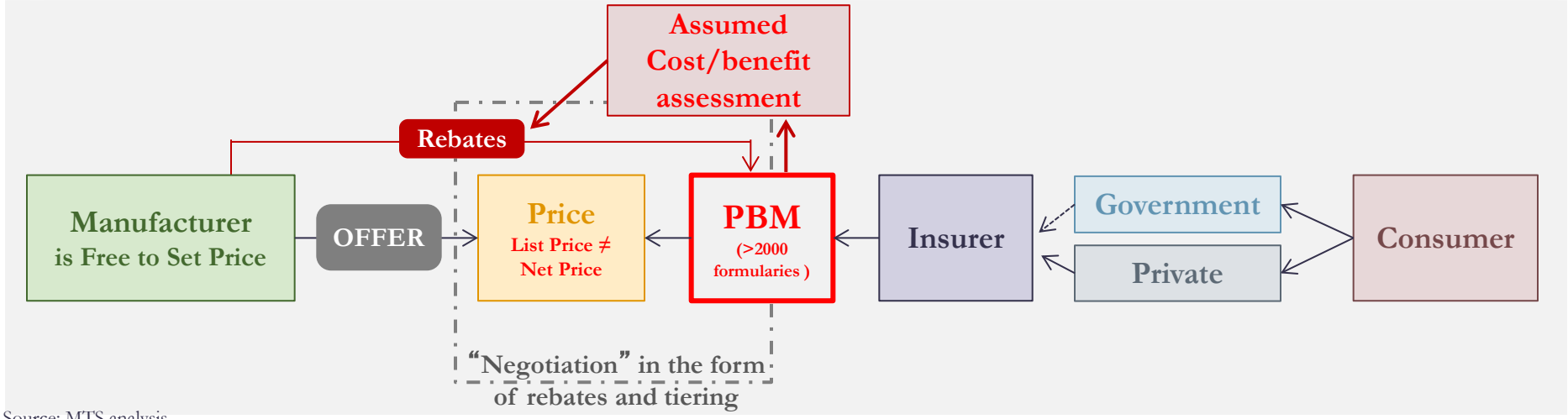
Source: MTS analysis

The Extremely Complex "OFFER" Drug Pricing Ecosystem in the US vs. the Relatively Simple "BID" Drug Pricing Ecosystem in the CDW

Comparable Developed World (CDW) = "BID" System, transparent prices and low frictional cost

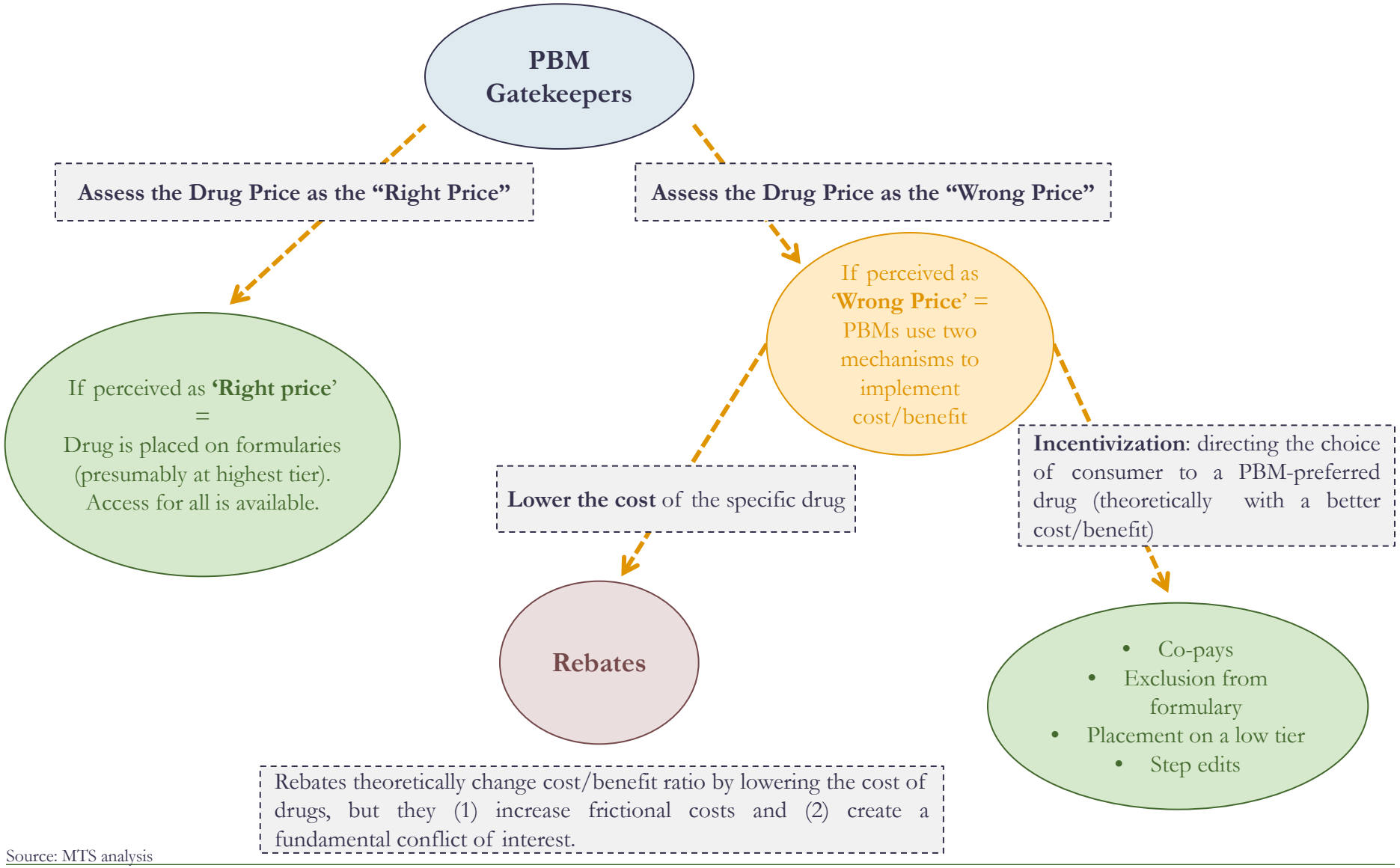


US = "OFFER" System, non-transparent prices and high frictional cost



Source: MTS analysis

PBMs Theoretically Drive Cost/Benefit in the US Drug Pricing Ecosystem via Lowering Costs or Incentivization



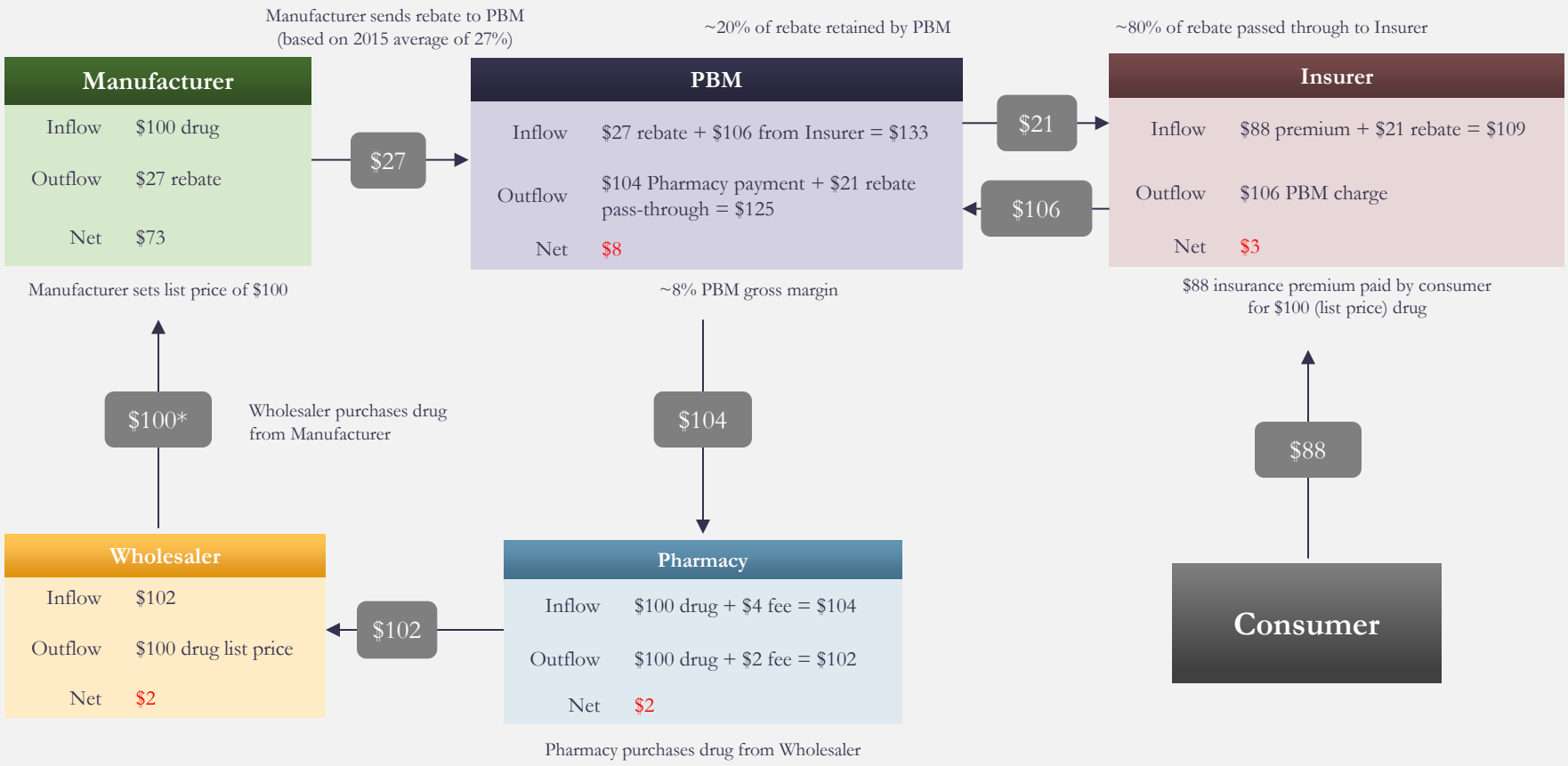
Source: MTS analysis

MTS Calculated Money Flows in Totality (Using a Nominal $100) Within the US Drug Pricing Ecosystem

In the "totality" of the ecosystem for every $100 of list price drug sales, manufacturers receive $73 net dollars, Wholesalers and Pharmacy $4, PBM's $8 and Insurers $3. Direct frictional costs are marked in red

The effective pass through price for the consumer (for $100 list price drug) is $88, paid via insurance premiums

PBM-based Healthcare System



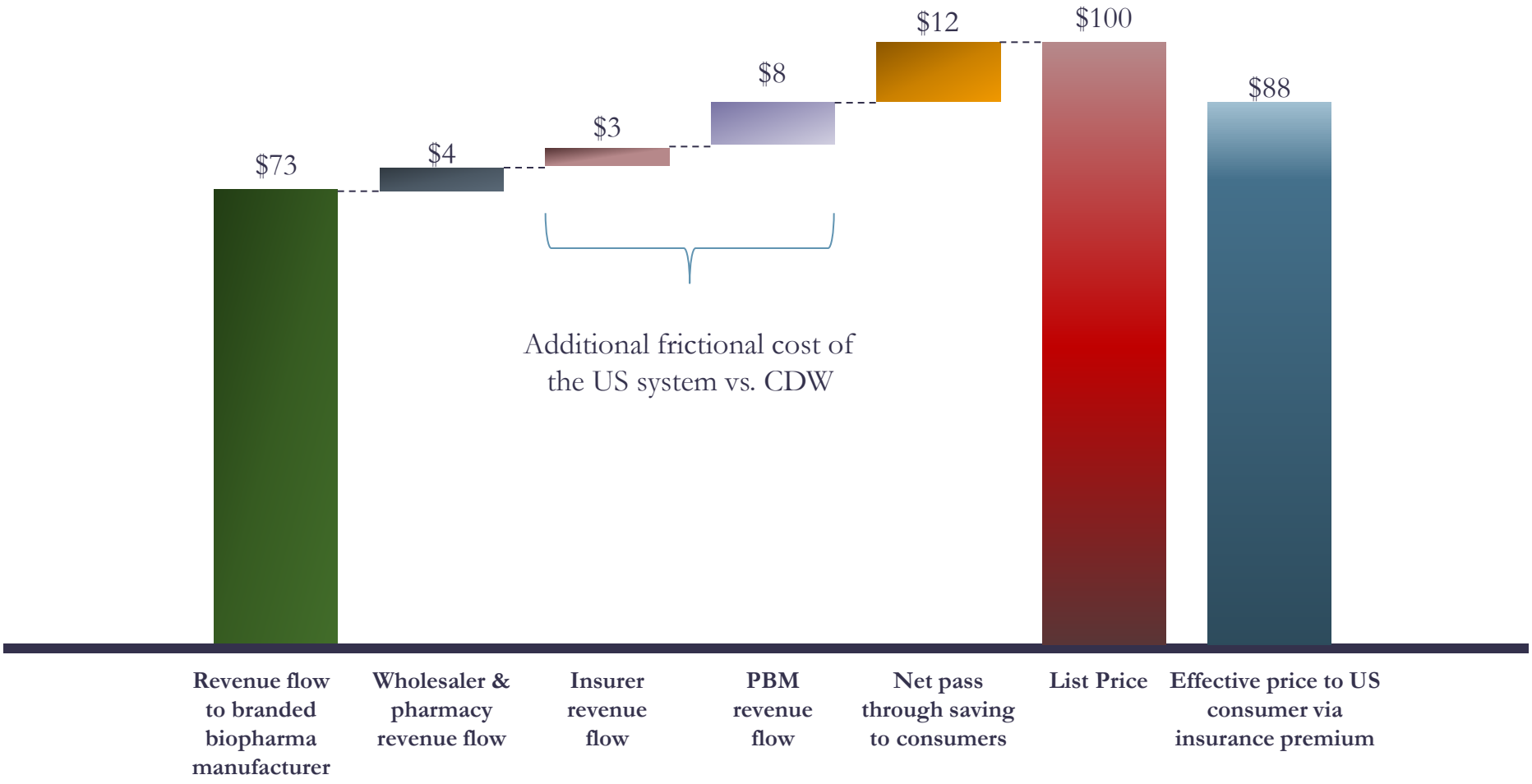
(*) In reality, the Wholesaler negotiates a small discount to the list price from the Manufacturer, further driving down the effective price of the drug.

Source: MTS analysis

Overview of MTS' Estimated Frictional Costs for (a Nominal $100) List Price Branded Drug in the US Drug Pricing Ecosystem

For an average $100 list price branded drug, the effective cost to the end-user is $88, $15 are absorbed in frictional costs and the biopharma manufacturer receives $73

The "intermediator" insurance/PBM system is unique to US drug pricing ecosystem and drives a 23% savings from the list price, of which around half flows to the end-user



Source: MTS analysis

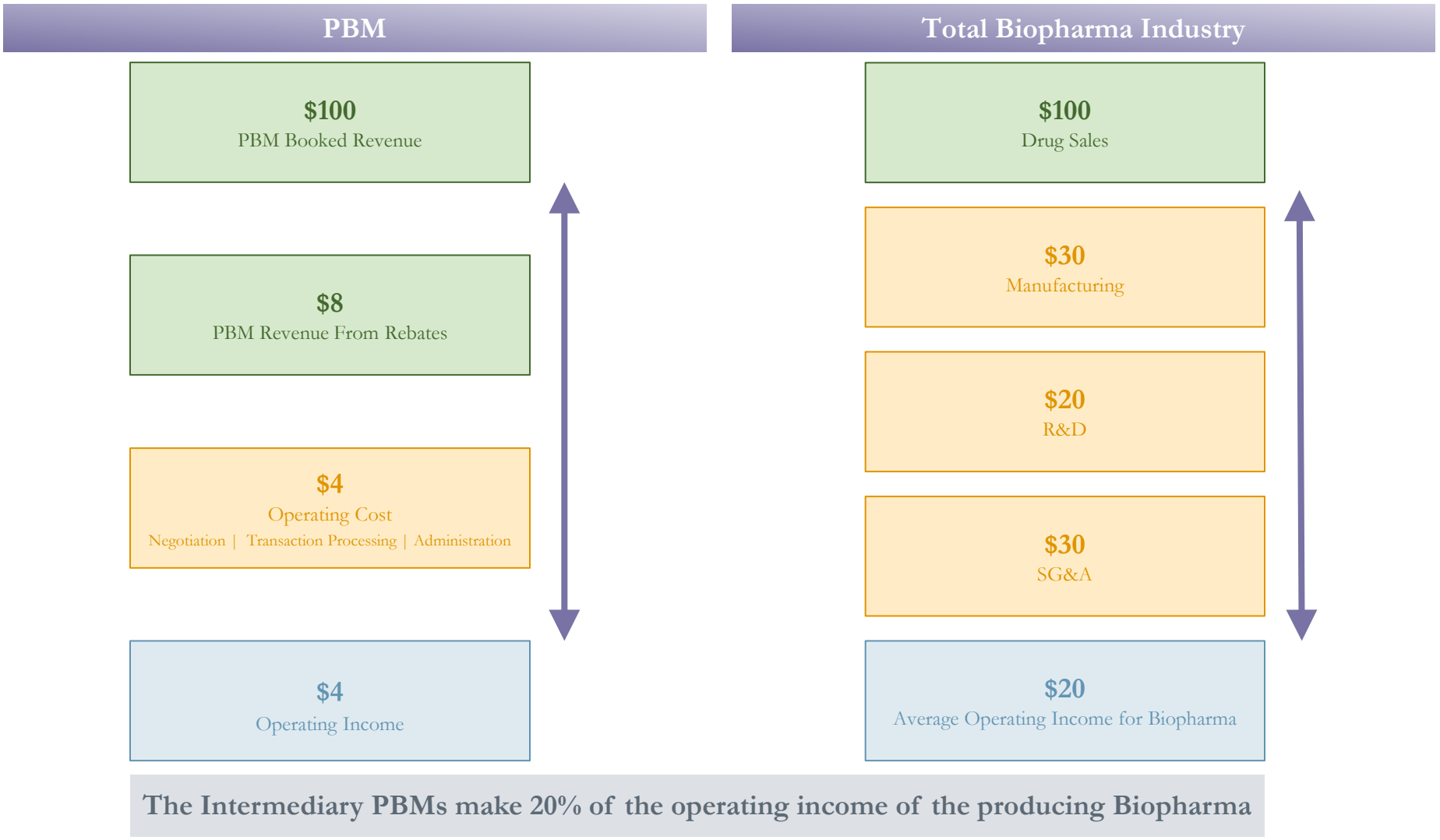
Solution for the List Price/Net Price/Rebate Conundrum: List Price = Net Price = Less Frictional Costs and Conflicts of Interest

For an individual drug, higher rebates flow through to the PBM and obviously increase frictional costs to the system. Higher drug prices and rebates benefit both the manufacturers and PBMs but increase frictional costs. Net price = List price results in the lowest frictional costs.

	List Price	Rebate	Net Price	% Fric. Cost
Higher Rebate (Fixed List Price) = Increased Frictional Costs; Incentive to the PBM	$100	$27	$73	27%
	$100	$36	$64	36%
	$100	$48	$52	48%
Higher List Price (Fixed Net Price) = Increased Frictional Costs; Incentive to the PBM	$100	$27	$73	27%
	$150	$74	$76	49%
	$200	$124	$76	62%
Today: Higher List Price, Higher Rebate, Higher Net Price = Increased Frictional Costs; Incentive to the Manufacturer and PBM	$100	$27	$73	27%
	$150	$48	$102	32%
	$200	$72	$128	48%
Future (?) : List Price = Net Price; Both Manufacturer and PBM are incentivized to make drug choice based on true cost/benefit	**$73**	**$0**	**$73**	**0%**

Sources: MTS analysis

Quantifying the Profitability of Drugs and Rebates in the US Drug Pricing Ecosystem: PBMs vs. Biopharma - Does the Work Justify the Margins?



Disclaimer: The drug operating costs are for the totality of the whole industry
Source: MTS analysis

MTS' Views on the Three Key Issues That Should be Addressed in the US Drug Pricing Ecosystem and Our Proposed Actionables

(1) US drug prices are not principally based on cost/benefit

The emphasis is on the Biopharma industry to base drug pricing on a cost/benefit assessment and outcomes based principals.

- Move away from the current free market, i.e. "what the ecosystem can bear" system.
- Drug price rises are not the cause of the problem but rather a symptom.
- Value based pricing could still lead to dynamic prices after launch (both up and down) based on post launch changes in benefit assessment.
- Most likely a concentrated effort with regulatory bodies will be necessary.

(2) Lack of transparency and choice across multiple parts of the ecosystem

Low transparency of net drug prices.

- Differential and non-transparent rebate levels are currently a headwind rather than tailwind driving value based on cost/benefit assessment.
- The rebate system (which is responsible for non-transparency of drug prices) needs a dramatic overhaul via coordinated efforts of manufacturers, regulators and payers.

Differential contributions/benefit for insurance are not visible and there is little/no choice.

- Choice and transparency of level of contribution and concomitant level of Rx coverage should be introduced and driven by insurers/PBMs, as well as central governing bodies.

(3) High frictional costs are driving conflicts of interests and not proportionally rewarding contributors of value

Frictional costs are ~14% of list drug price.

- PBM's frictional costs are masking major conflicts of interest.
- The largest frictional costs are the insurance based intermediator costs, which are principally driven by the rebate system.
- Rebates to PBMs are one of the key drivers underlying price increases in the last decade.
- Value based pricing and transparent net-pricing can reduce/eliminate the rebate system.
- Other (non-direct) frictional costs include level and content of S&M/OTC spending by manufacturers.

Two key actionables:

(1) Biopharma industry should move uniformly to an innovative value based drug pricing,

(2) Increase in transparency and choice in the Rx element of the insurance system

Source: MTS analysis

Key Actionable #1 – Biopharma Industry Should Move Uniformly to an Innovative Value Based Drug Pricing

Many players in the Biopharma industry would argue that US drug prices are already value based.

- **We would argue that this is only loosely correct and certainly not uniform across the Biopharma industry – e.g. high drug price inflation without changes in benefit by definition is not value-based pricing.**
- **The key hurdle is how to define value, which is a whole topic in itself, but regardless, a basis of value pricing already exists in many regions of the comparable developed world.**
- **We define "innovative value" as:**

Innovative Value

Delivering a clinical benefit in a completely unmet medical need

or

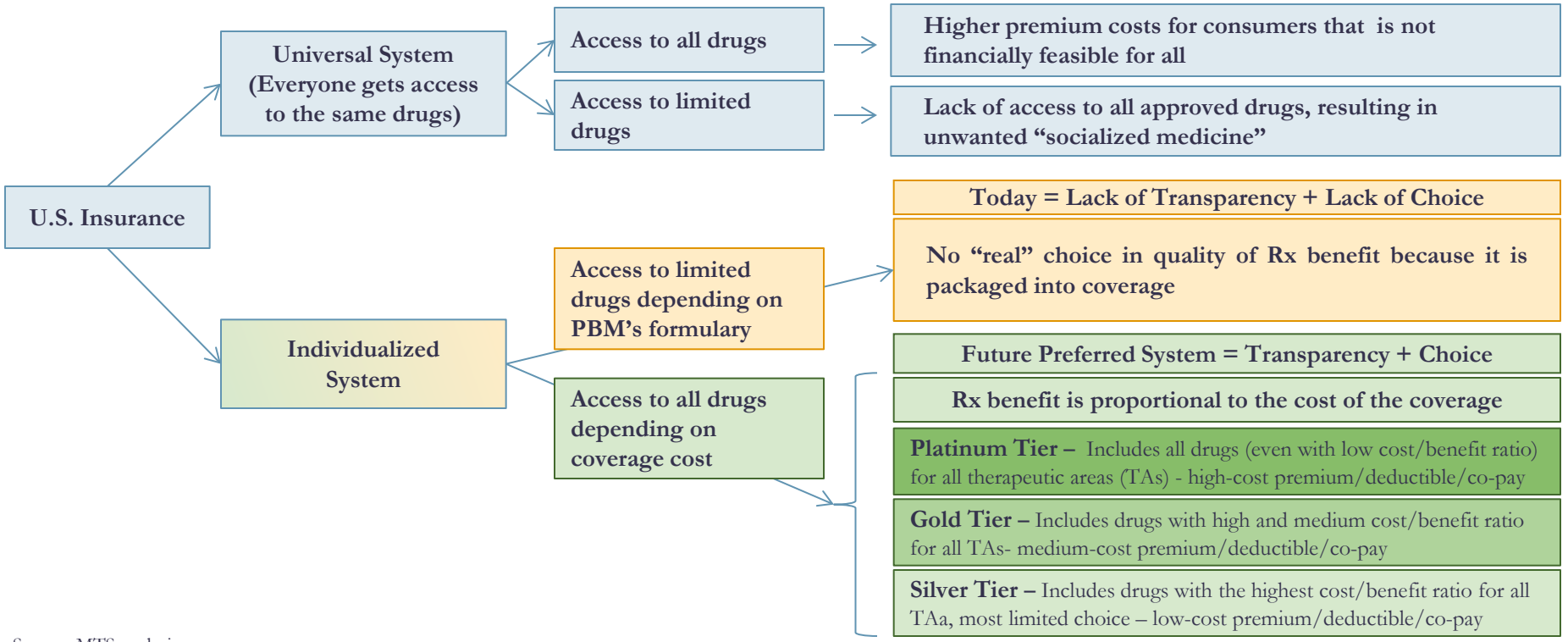
Significant increase in benefit/efficacy in comparison to marketed products in a therapeutic area

- Innovative value drugs should provide benefit to the healthcare system, as well as have societal value
- An innovative value drug doesn't necessarily need to have a novel mechanism of action, but should be by the above definition in either the area of an unmet medical need or provide significant increase in efficacy/benefit in comparison to currently available treatments
- A "me-too" drug with no material improvement in benefit/efficacy does not provide innovative value (obviously!)
- Innovative drugs with marginal improvement should be premium priced at marginal levels
- Innovative value drug pricing should be based on the clinical trial data that is reflective of the real world setting
- The cost/benefit measurement of a drug should be reassessed if the real world setting appears to be substantially different from the clinical trial results

Source: MTS analysis

Key Actionable #2 – Increase in Transparency and Choice in the Rx Element of the Insurance System

1. The US is unlikely to move to a socialized healthcare system, rather it will remain a predominantly insurance based system
2. The cost of insurance is simply the (amortized) cost of the benefit garnered
3. The "Alice in Wonderland" insurance system is access to all drugs for all citizens, that is simply not financially feasible for the system (and is also "unlimited socialized medicine", which exists nowhere in the world!)
4. A basic (consumer) principal of insurance is differential coverage for differential cost
5. The differential coverage for differential cost system already exists in the US! The two key problems with current system are:
   (a) the end-consumer has little/no choice in selection of the Rx benefit,
   (b) there is little transparency in the cost/level of coverage
6. We propose a Consumer Chosen Rx Benefit system, where Rx benefit is directly proportional to the cost/level of insurance coverage with full transparency and choice



Source: MTS analysis

2. Key Data On Healthcare and Drug Spend and Pricing

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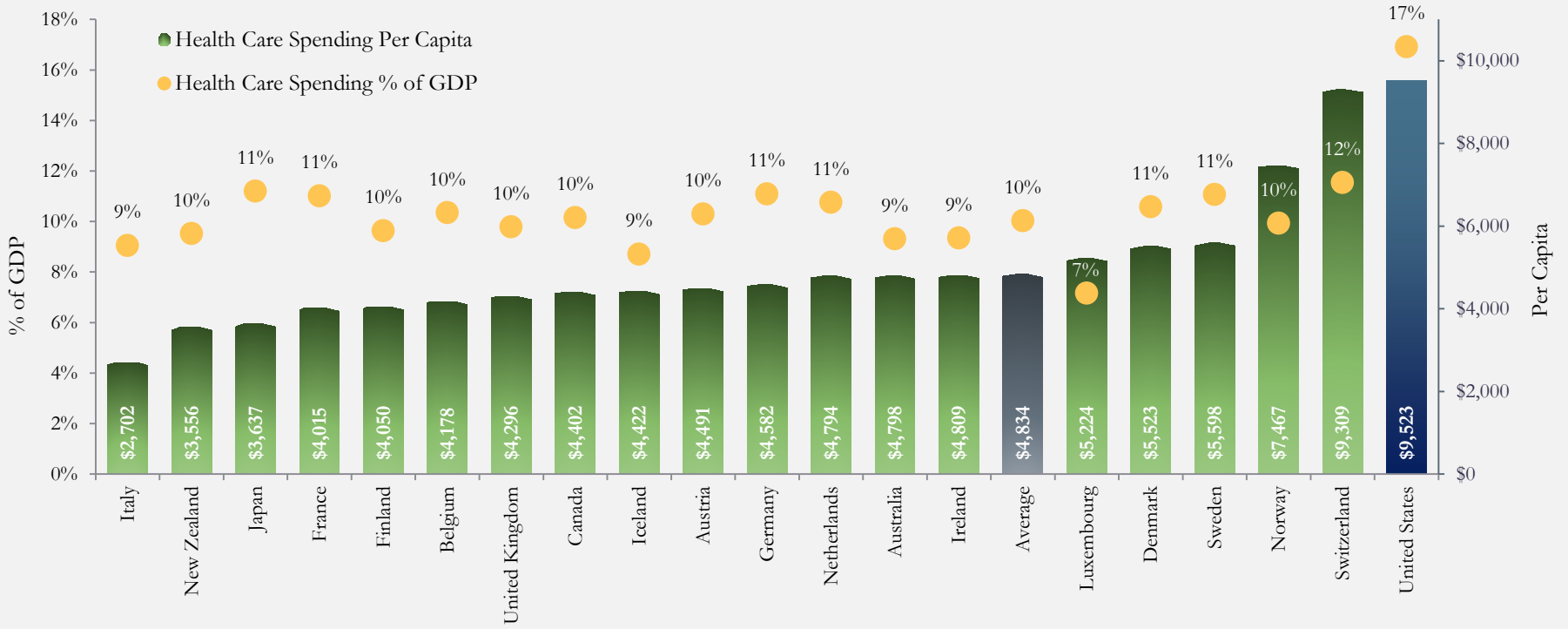
Total Healthcare Spend Across Select Comparable Developed Countries

The US Spends the Most on Overall Healthcare Spend in Comparison to Other OECD Countries

- Per capita, the US spends around twice as much (absolute and % of GDP) as the average of the comparable developed countries
- The average US GDP/capita is $56k vs. $49k for comparable developed countries

Healthcare Spending of 20 Select OECD Countries



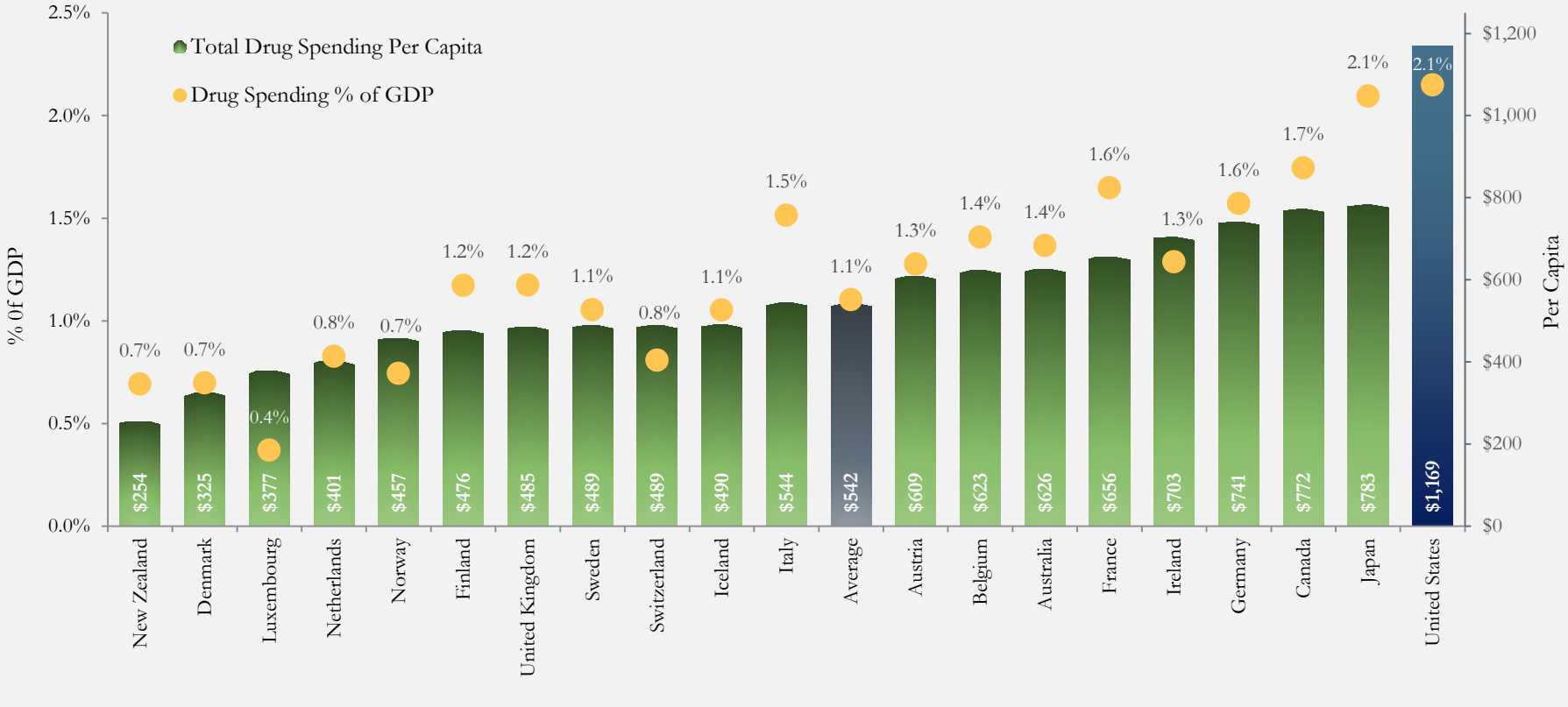
Source: OECD, Disposable Income Per Capita: 2013 Data; 2014: United States, Australia, Netherlands, Finland; 2012: New Zealand; 2009: Japan, Total Hospital Spending, Hospital Spending Per Capita: 2014 estimated data; 2013: Australia, Japan, and Norway; 2007 New Zealand, Total drug spend, Drug spend per capita: 2014 Data, 2013: Australia, Japan; 2007: New Zealand;
Source: https://data.oecd.org/healthres/pharmaceutical-spending.htm; MTS analysis

Total "List" Drug Spend Across Select Comparable Developed Countries

The US Spends the Most But It s Not An Apples-to-Apples Measure

Most analysis of drug spend in the media uses "list" price datasets

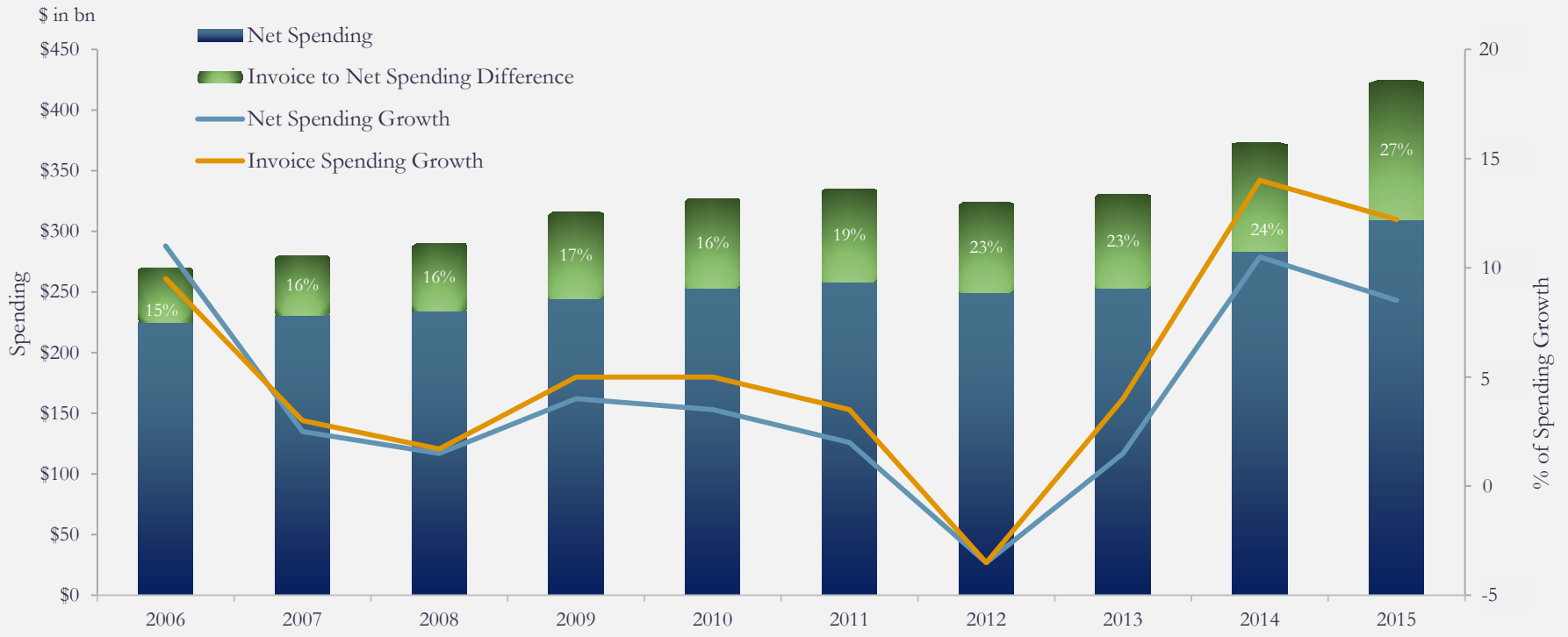
As we describe later within this report "list" drug pricing for the US is not an accurate apples-to-apples measure when comparing to comparable developed countries



Source: OECD,, Disposable Income Per Capita: 2013 Data; 2014: United States, Australia, Netherlands, Finland; 2012: New Zealand; 2009: Japan, Total drug spend, Drug spend per capita: 2014 Data, 2013: Australia, Japan; 2007: New Zealand; https://data.oecd.org/healthres/pharmaceutical-spending.html; MTS analysis

Granularity Underlying Drug Spending in the US: Total List (Gross) And Net US Drug Spending Over Last 10 Years

High rebates, which are unique to the US ecosystem, are responsible for List (Gross) to Net but also drive high-frictional system costs. Rebate levels have increased notably over the last 10 years.



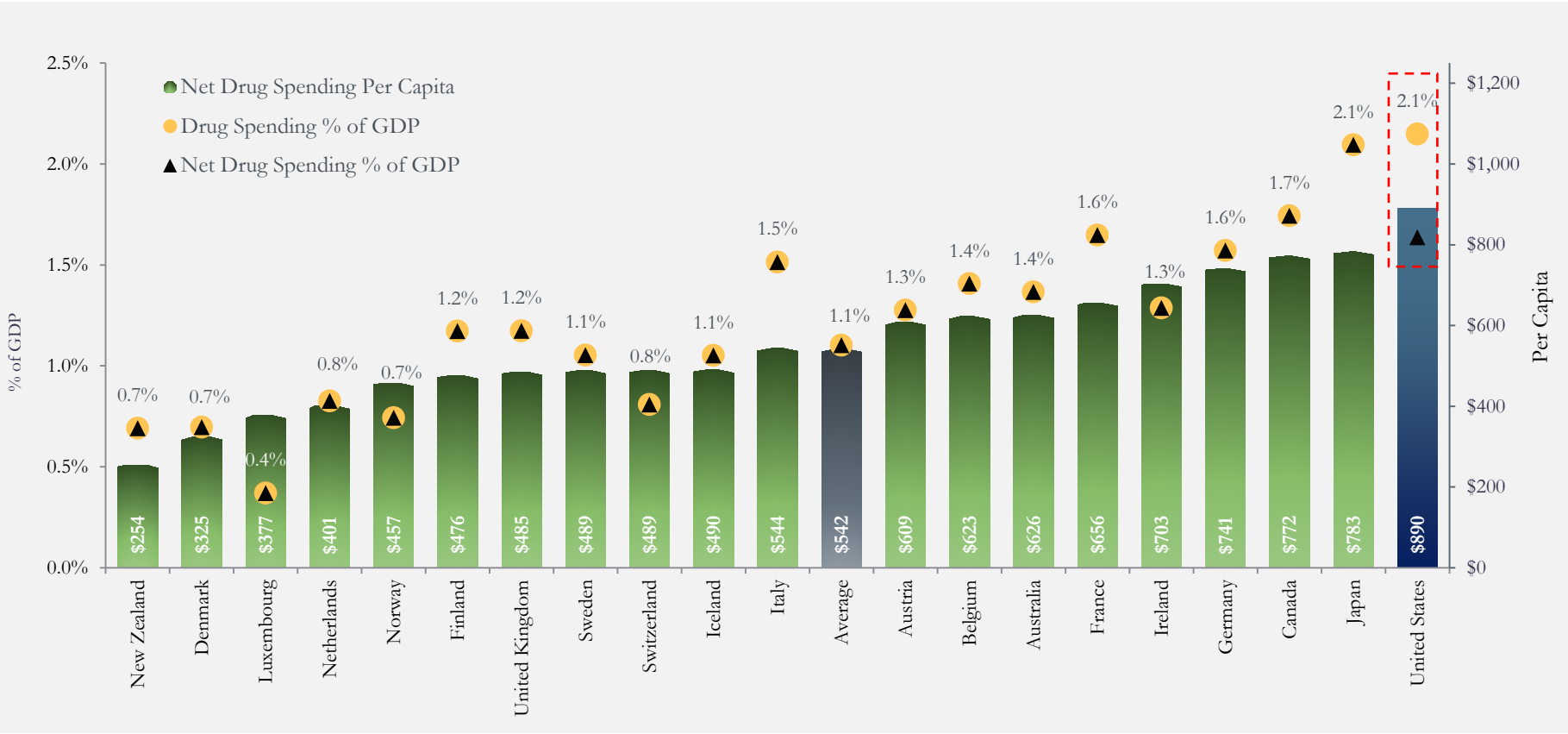
Sources: IMS Health, MTS analysis

Adjusted Drug Spend Across Select Comparable Developed Countries:

Based on Net Pricing US Still Spends More On Drugs But Not That Much More

"Invoice" = Sticker price which is not realized at all in the ecosystem

"Net" = Amount captured in totality by drug manufacturers

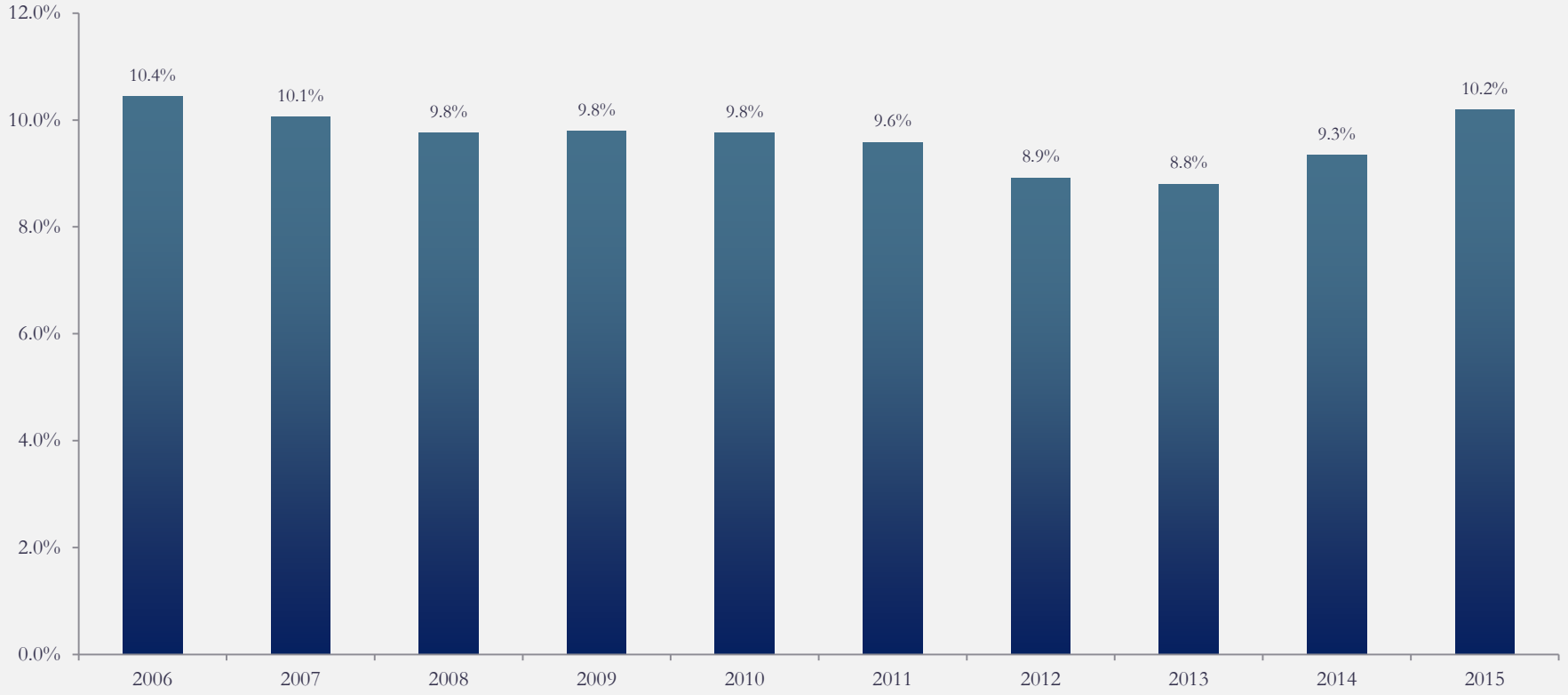


Source: OECD, Disposable Income Per Capita: 2013 Data; 2014: United States, Australia, Netherlands, Finland; 2012: New Zealand; 2009: Japan, Total drug spend, Drug spend per capita: 2014 Data, 2013: Australia, Japan; 2007: New Zealand; https://data.oecd.org/healthres/pharmaceutical-spending.htm; MTS analysis

Drug Spend as Percent of Healthcare Expenditures Across the US Over the Last 10 Years based on "Net" Drug Prices

- Using "Net" drug revenues captured in totality by drug manufacturers
- The proportion of healthcare spend on drugs has been around 10% for the last 10 years

Drug Spend as a % of Total Health Expenditures



Sources: IMS Health, OECD, Disposable Income Per Capita: 2013 Data; 2014: United States, Australia, Netherlands, Finland; 2012: New Zealand; 2009: Japan, Total drug spend, Drug spend per capita: 2014 Data, 2013: Australia, Japan; 2007: New Zealand; https://data.oecd.org/healthres/pharmaceutical-spending.htm; MTS analysis

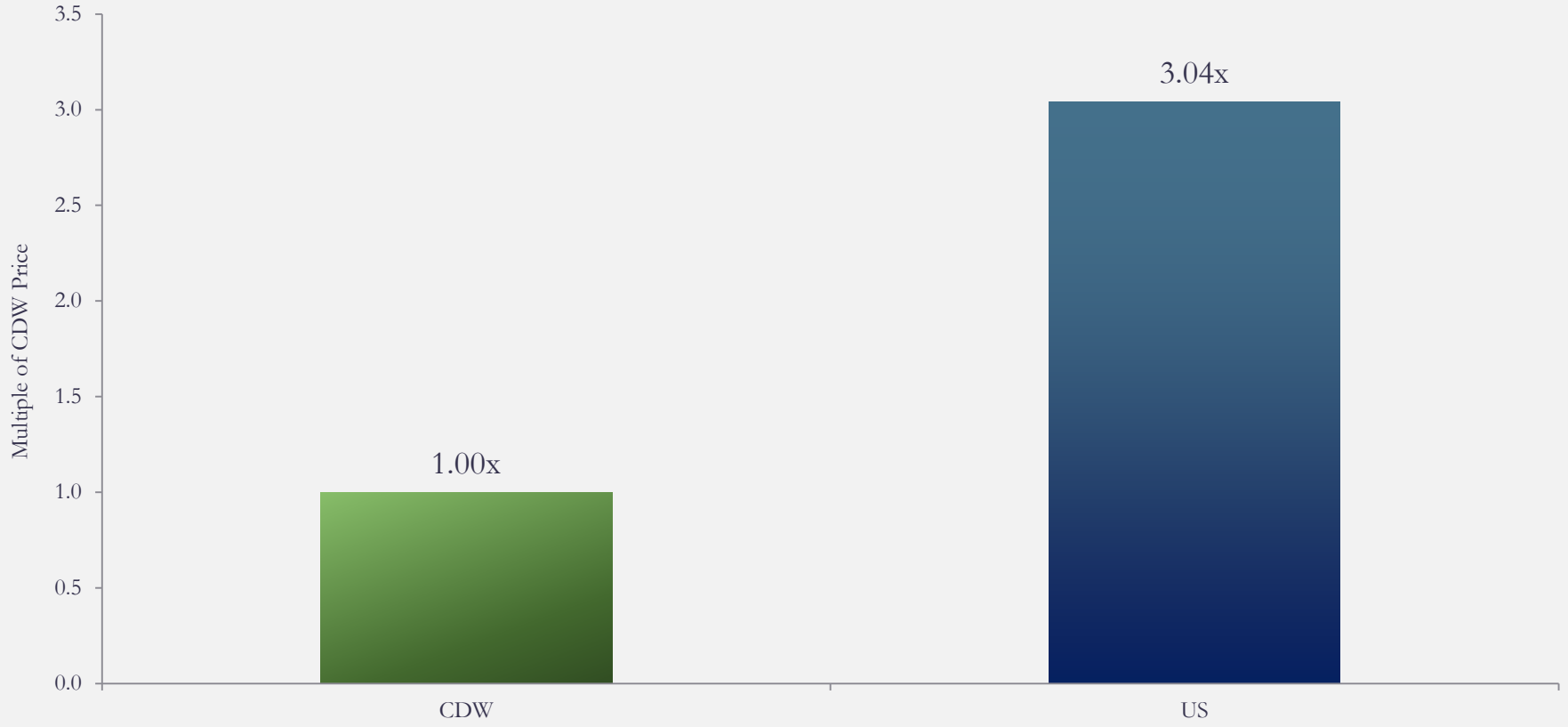
General Methodology for Getting "Real Data" on US Drug Prices vs. Comparable Developed World

- Pricing analysis was performed for top 20 grossing drugs based on US sales revenue in 2015
- Using iFHP2013 report we pulled pricing for a number of selective drugs across various countries including UK and calculated the average pricing of drugs in rest of the comparable developed world (CDW) vs. US
- Using various databases (PriceRx, Evaluate and IMS) we pulled historical pricing, increases in the pricing over the years, as well as net prices
- Net prices in the US are based on reported revenues and prescription data available via IMS
- For the launch prices, we used UK prices and compared them to US prices

Source: MTS analysis

List Price of Top 20 Drugs in the US vs. Comparable Developed World (CDW)

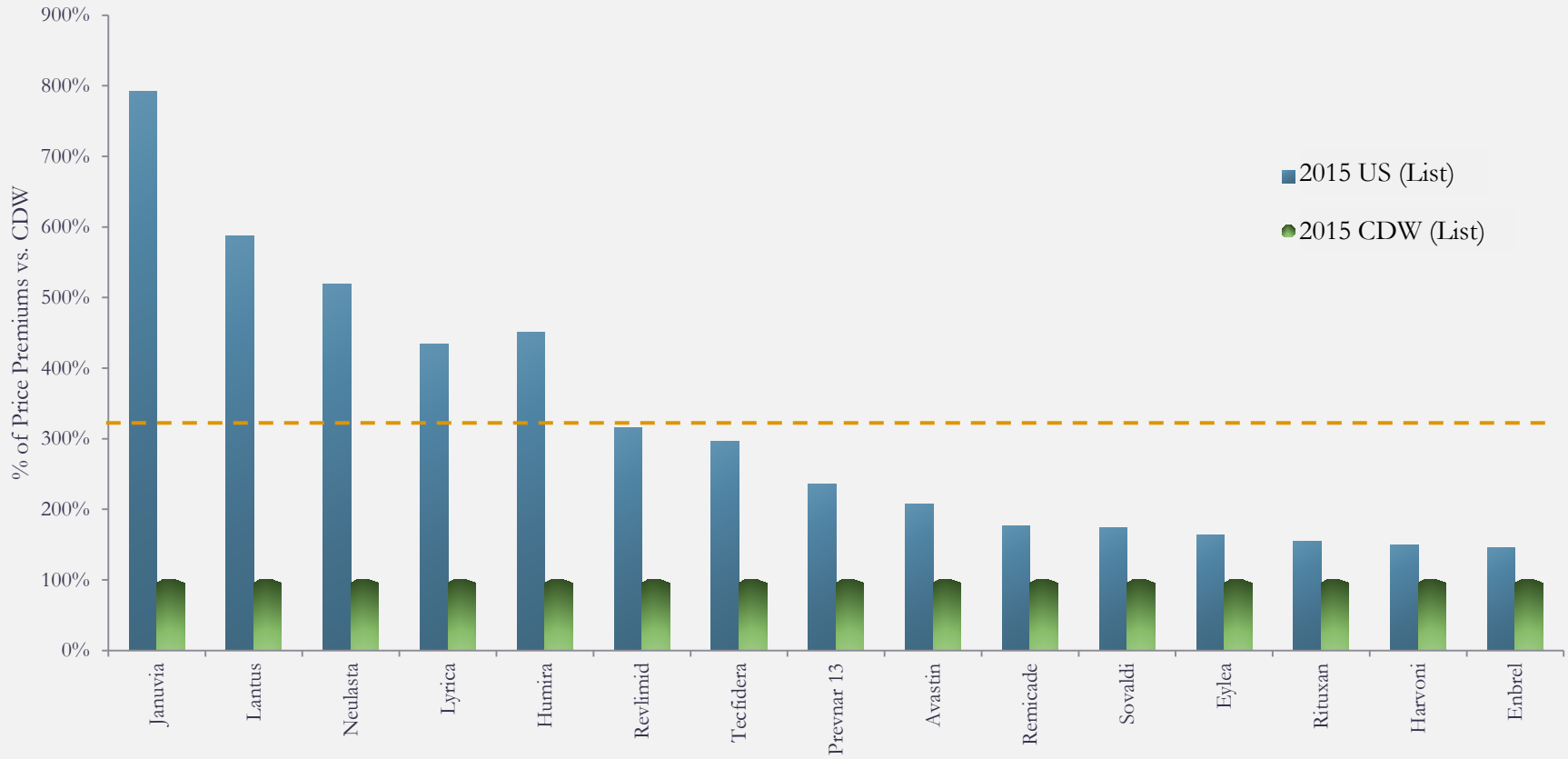
The List (Gross) price is on average 3.04x higher in the US vs. CDW



Sources: PriceRx, MTS analysis

High Variability of List Prices Between the US and Comparable Developed World (CDW)

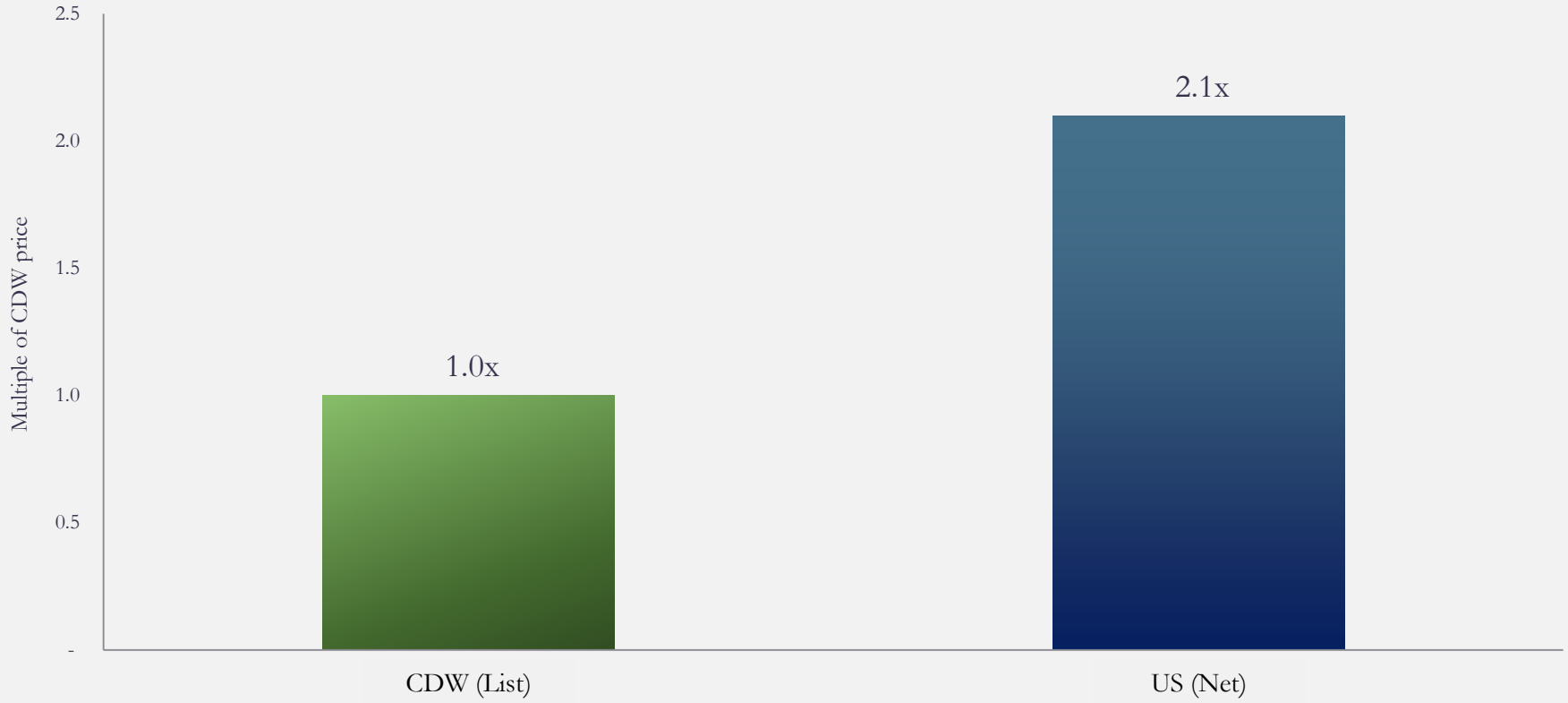
But there is large variability in the list price premiums of US vs. CDW



Sources: PriceRx, MTS analysis

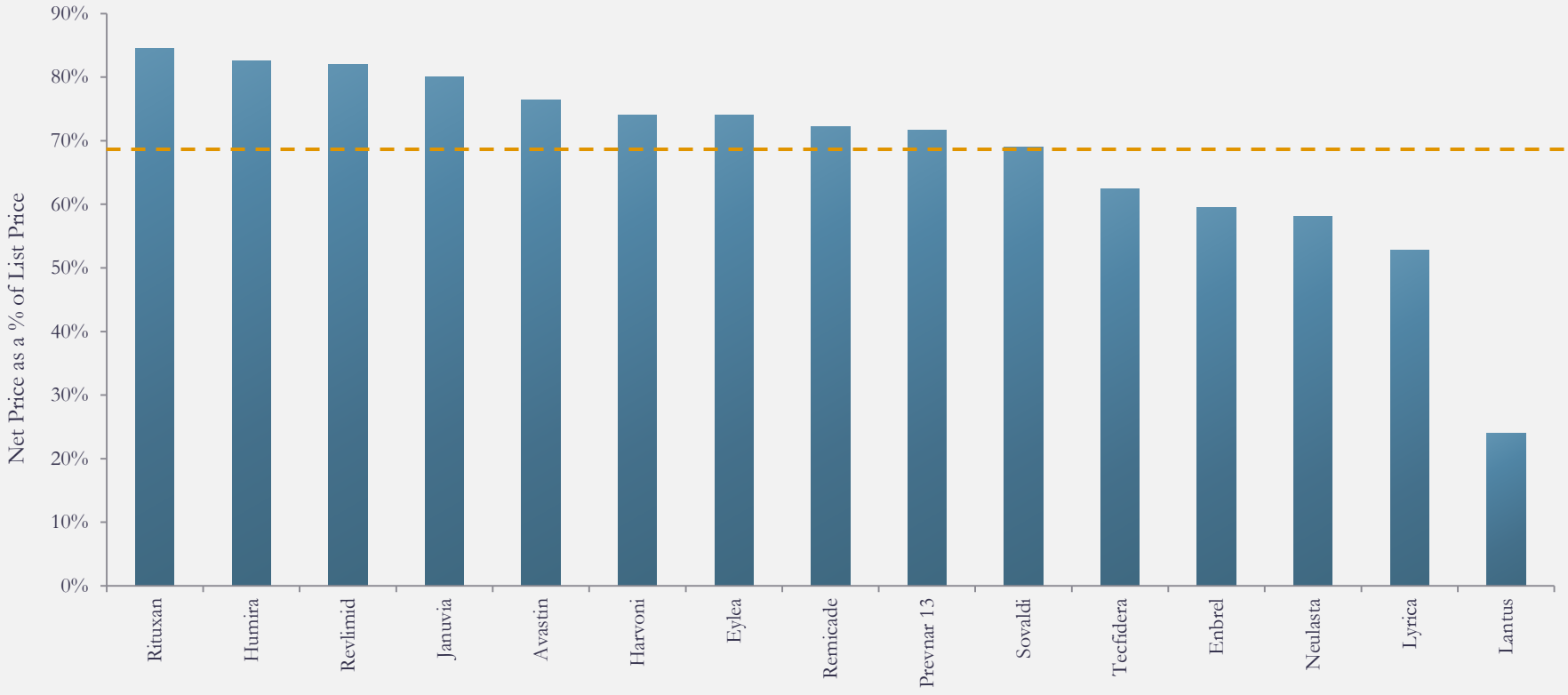
Net Price Of Top 20 Drugs in the US vs. Comparable Developed World (CDW)

The "Net" price (i.e. that received by the manufacturer) is on average 2.1x higher in the US vs. CDW



Sources: PriceRx, MTS analysis

High Variability of List to Net Drug Price Discount in the US

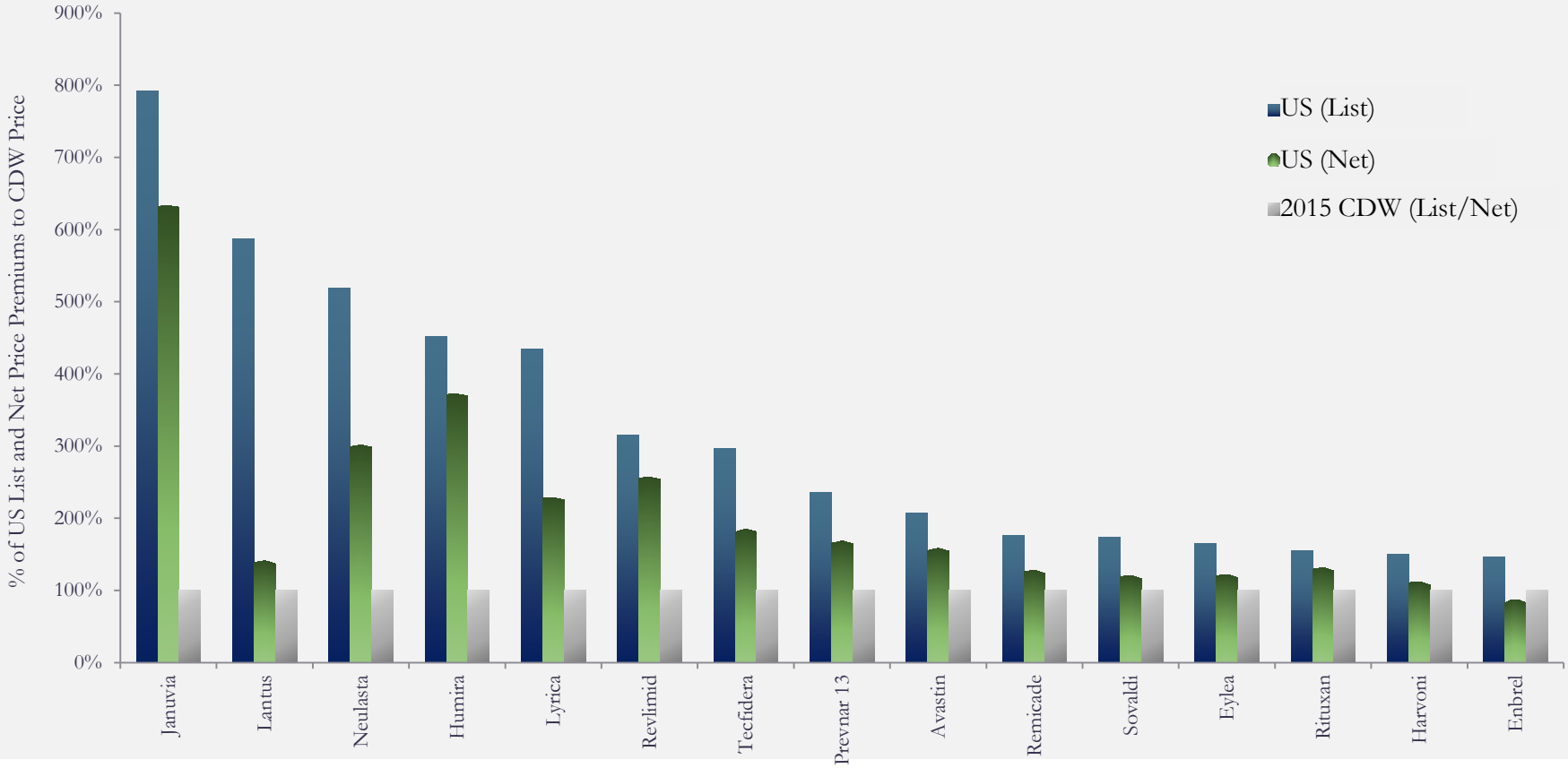


Sources: PriceRx, MTS analysis

Both List Prices (>3.04x) and Net Prices (>2.10x) Remained Higher in the US than CDW for Top 10 Drugs in 2015

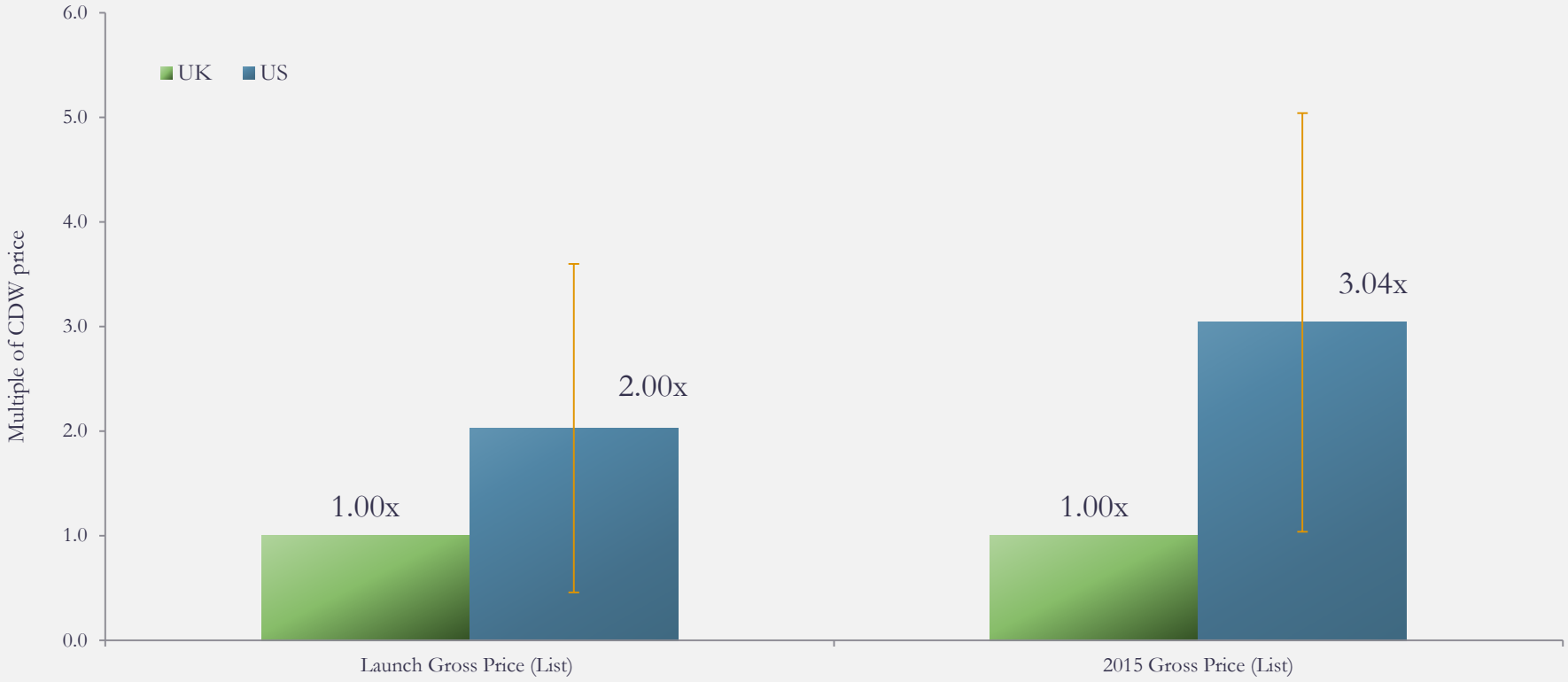
The drug manufacturers pay rebates and discounts to Medicare, Medicaid, United Health Care, Aetna and PBMs. These discounts make up net price.

Even after rebates/discounts which are ~35% on average, the cost of drugs remain significantly higher in the US vs. UK.



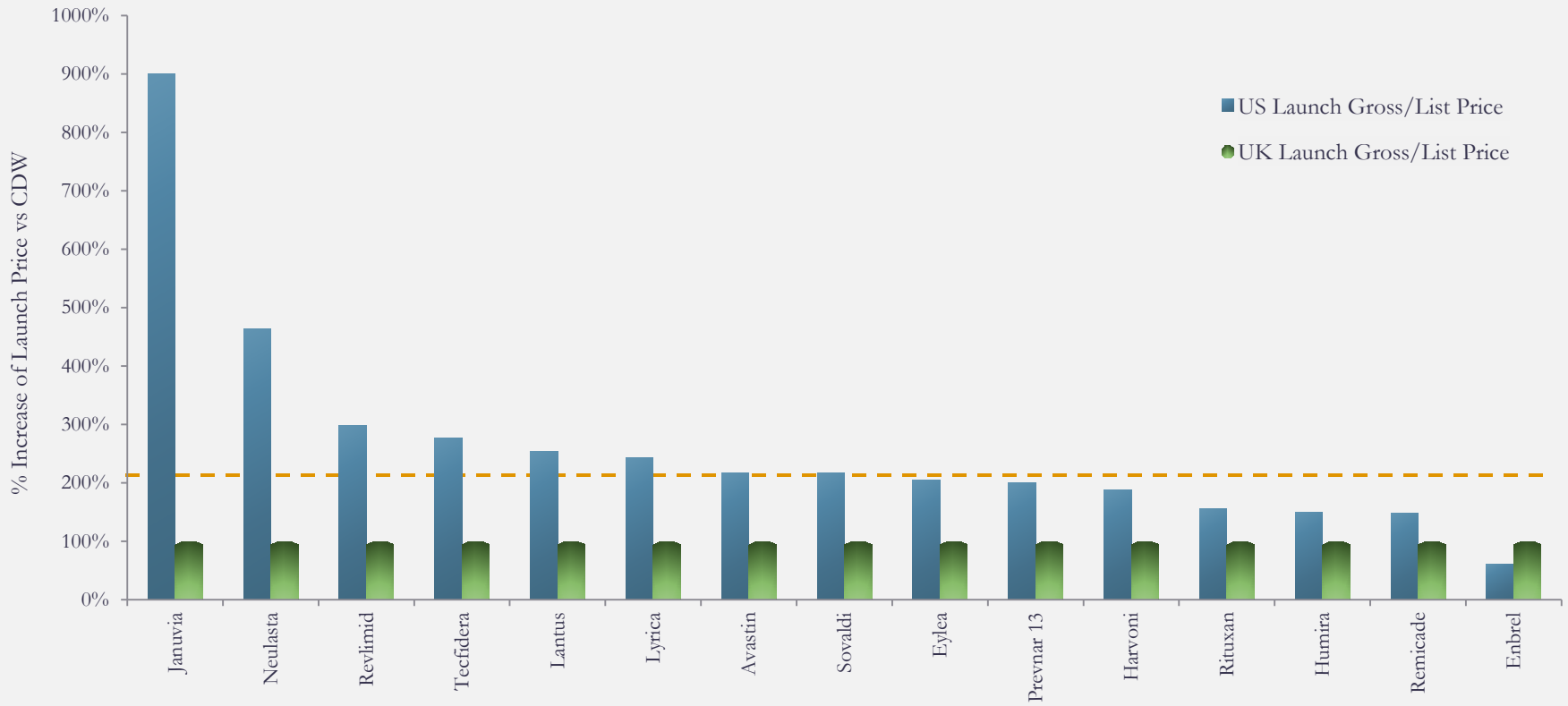
Sources: PriceRx, MTS analysis

Drugs in the US are Launched at a Higher Price and Then are Subject to Price Rises



Sources: PriceRx, MTS analysis

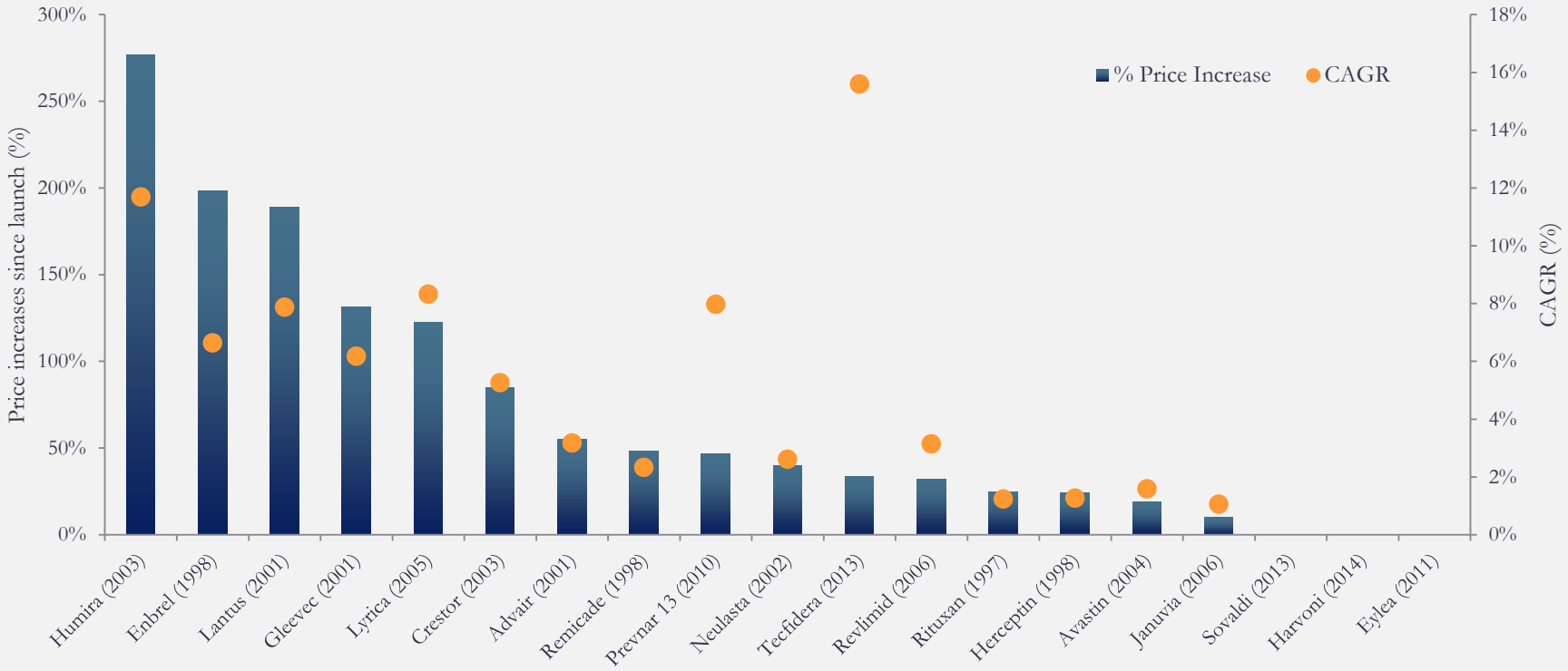
Top 15 Drugs based on WW Sales in 2015 were Launched on Average at Double the Price in the US than UK



Sources: PriceRx, MTS analysis

Percent Increase of List Price Since Launch For the Top 20 US Drugs

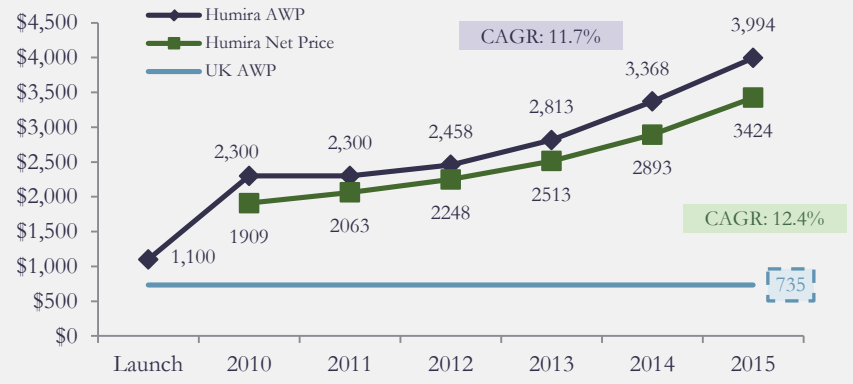
- Significant drug price rises are unique to the US "free-market" based pricing ecosystem
- Price increases in the US, since launch to current prices of the top 20 drugs vary greatly
- There is no "fundamental" basis for the price rises – they happen because the US ecosystem simply allows them to happen



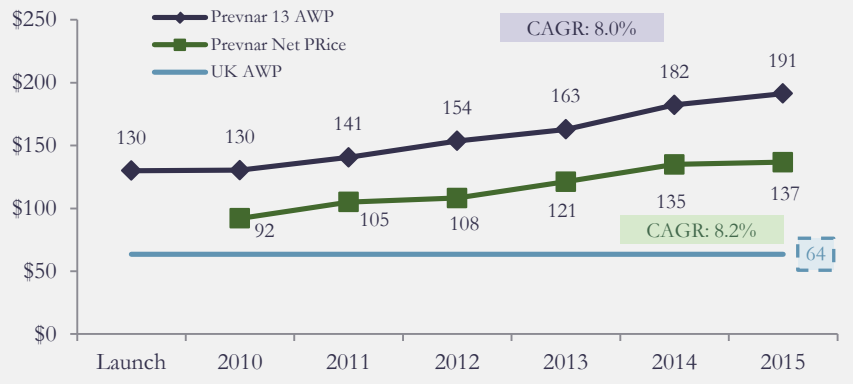
Sources: PriceRx, MTS analysis

Higher Launch Price and Steady Price Increases Lead to Increased Differential Price of Drugs in the US vs. UK

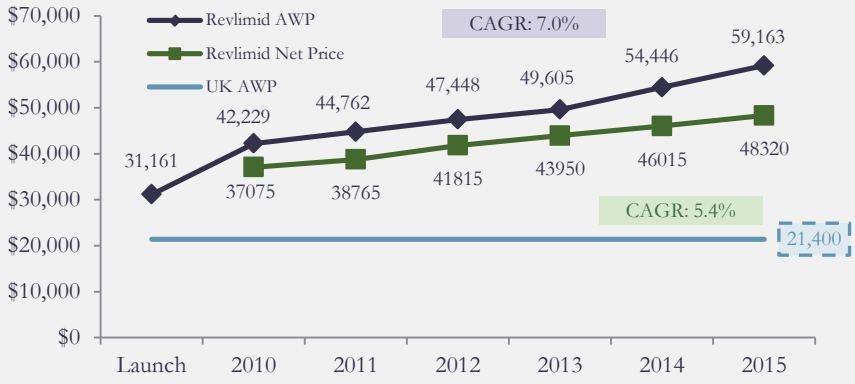
Humira



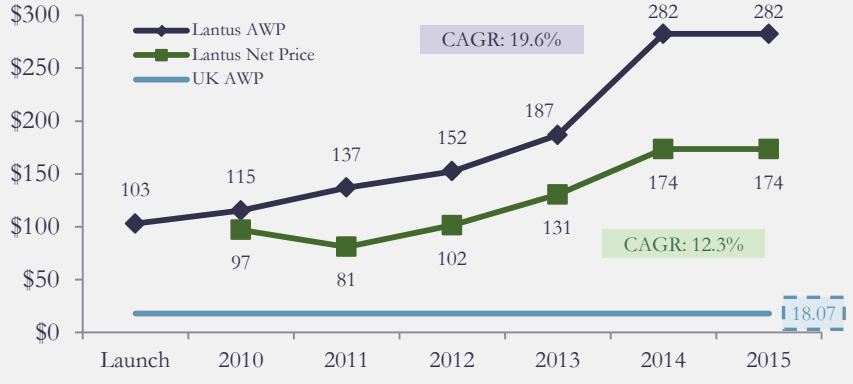
Prevnar



Revlimid

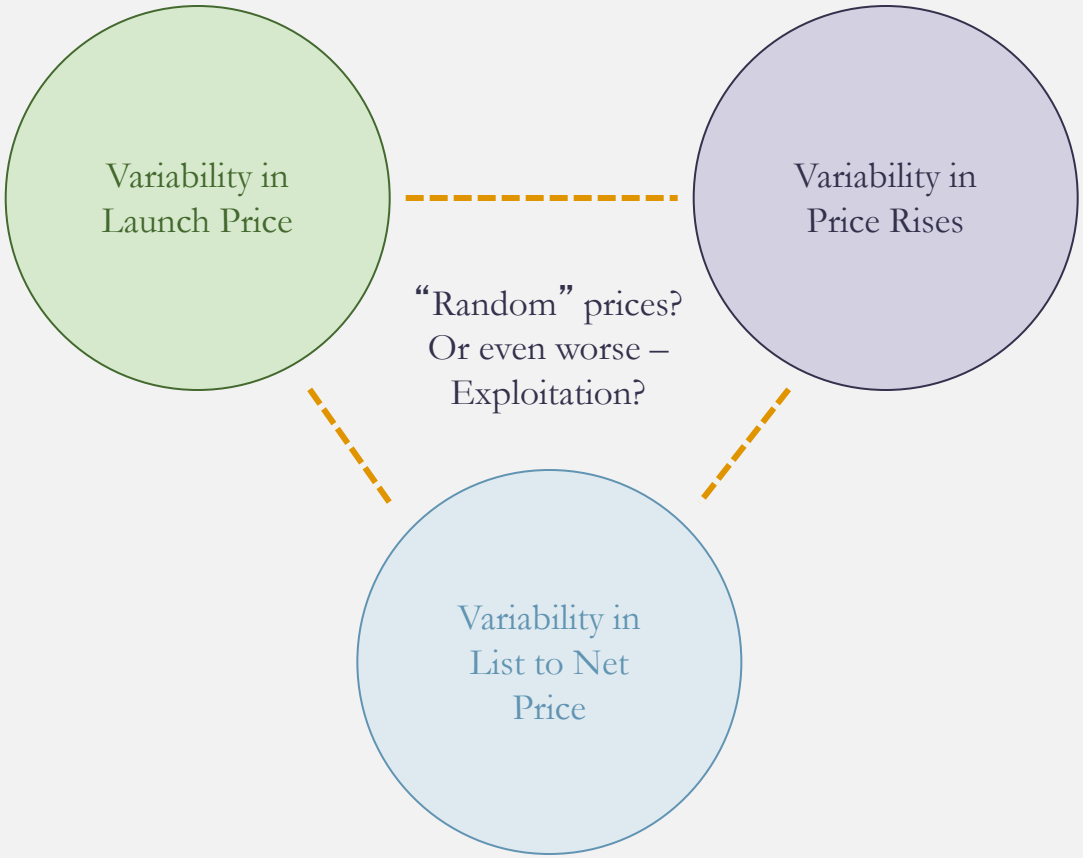


Lantus



Sources: PriceRx data, MTS analysis

So Why do Consumers Think Drug Prices are "Random"?



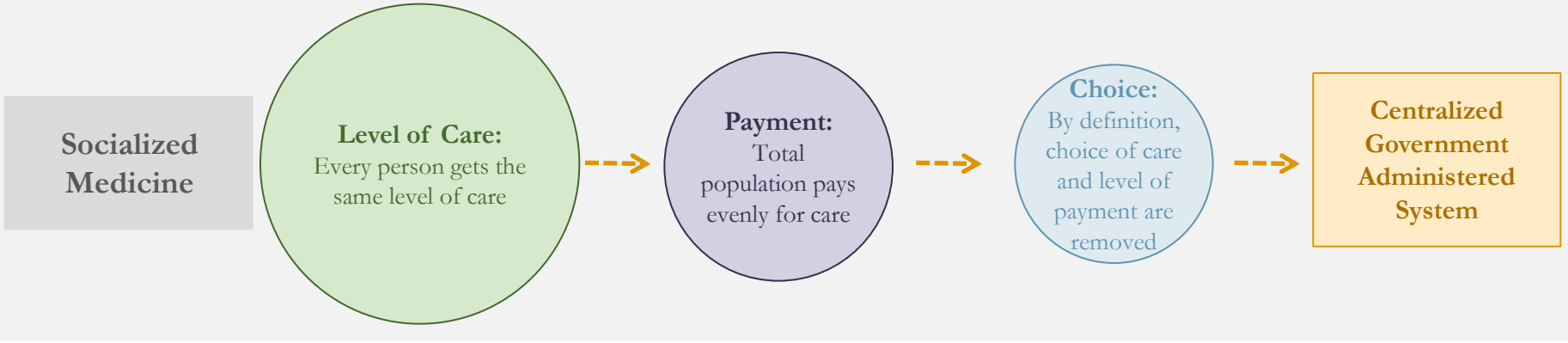
Source: MTS analysis

3. Healthcare and Drug Pricing Ecosystems: US vs. Comparable Developed World

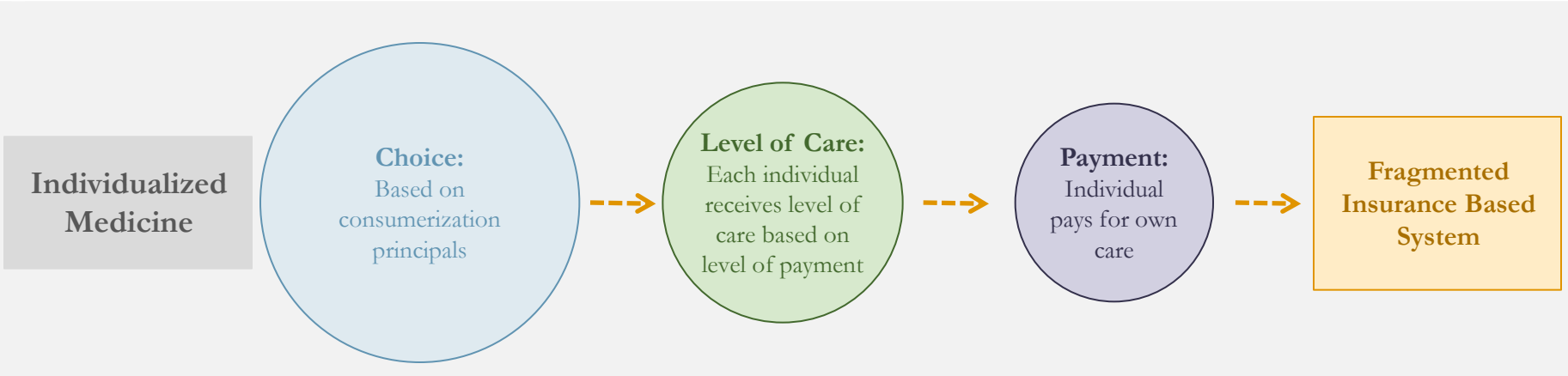
MTS | HEALTH PARTNERS

The Core Principles of Socialized Medicine in the Comparable Developed World vs. Individualized Medicine in the US

The healthcare system in most countries of the comparable developed world (CDW)

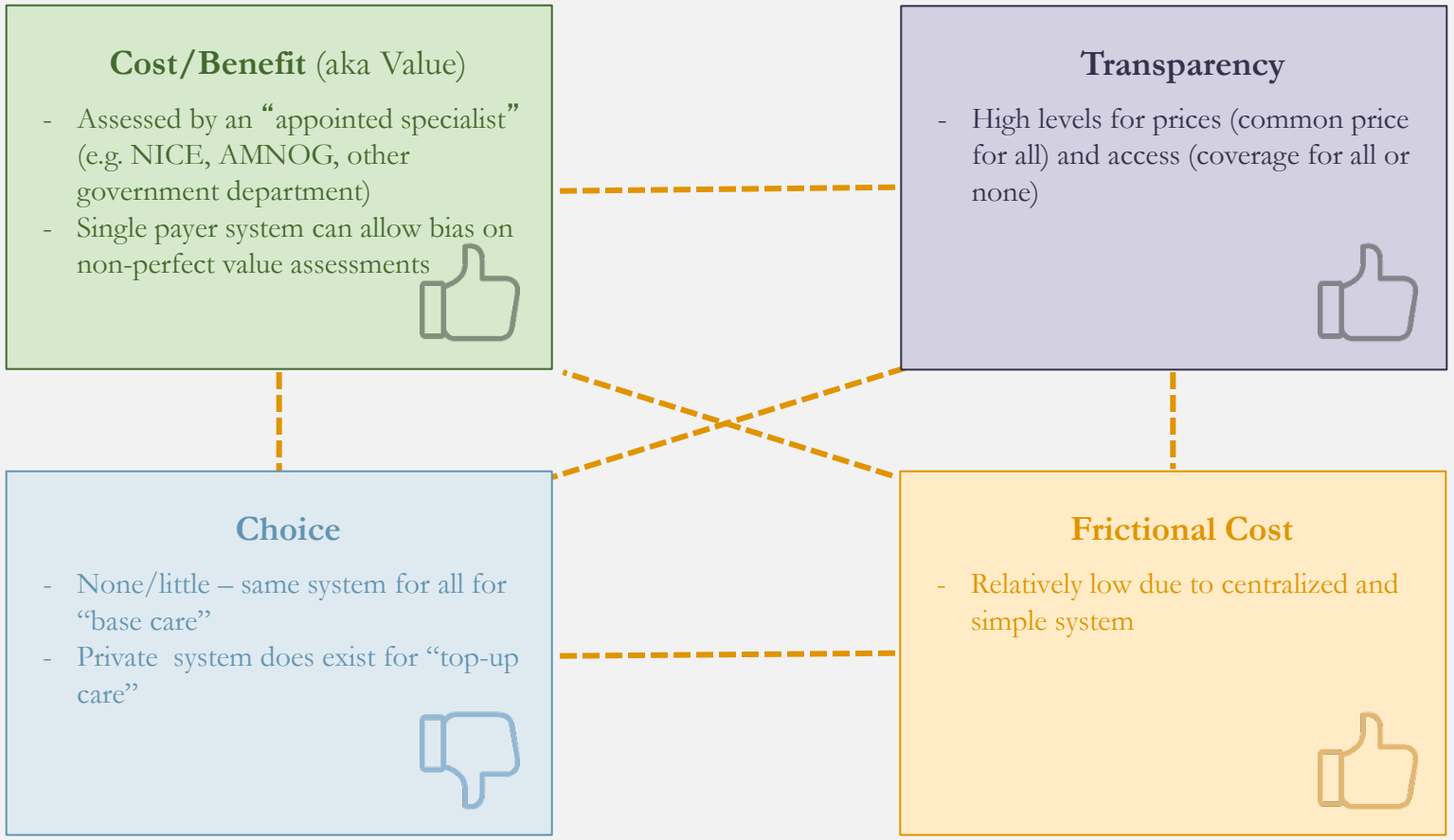


The US healthcare system is unique and is fundamentally based on an individualized system, but lack of choice, transparency & concomitant lack of direct cost-benefit leads to a concept we coined as "Pseudo-consumerism"



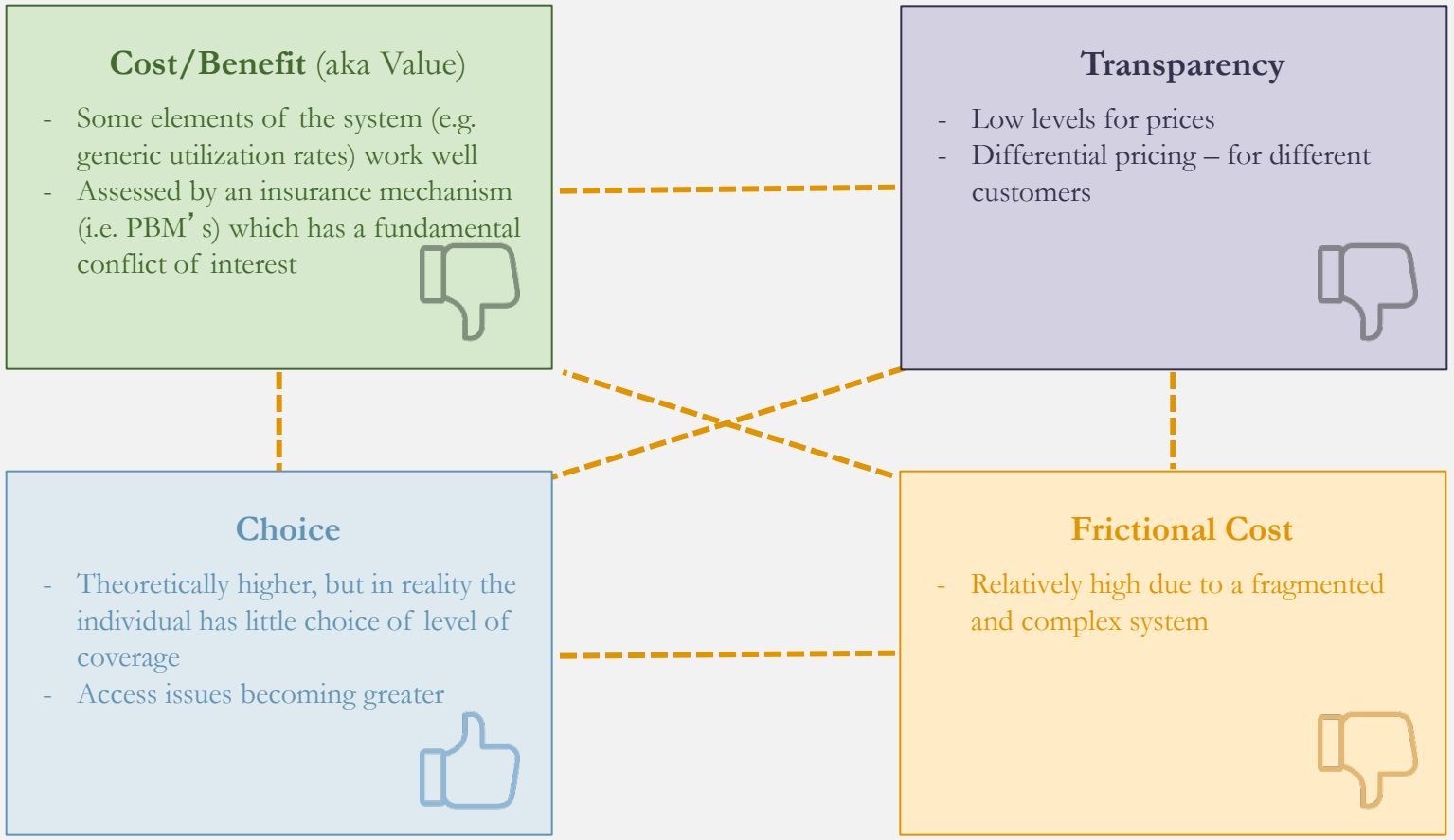
Source: MTS analysis

The Four Pillars of Drug Pricing – Under Comparable Developed World Socialized Based Healthcare Systems



Source: MTS analysis

The Four Pillars Of Drug Pricing – Under US Free-Market Based Healthcare Systems



Source: MTS analysis

The Unique US Healthcare System is based on the Principles of Individualized Medicine and 3rd Party Payment System

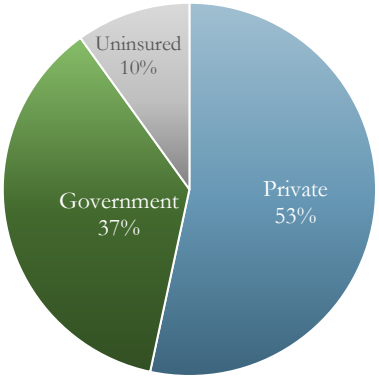
US

"Free market and consumerization based system where differential care is paid for by individuals with differential contribution"

CDW

"Socialized medicine is universal care for all administered by the government"

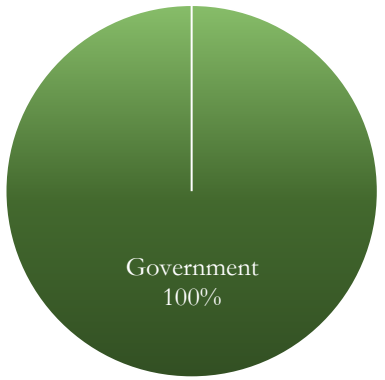
Lives Covered



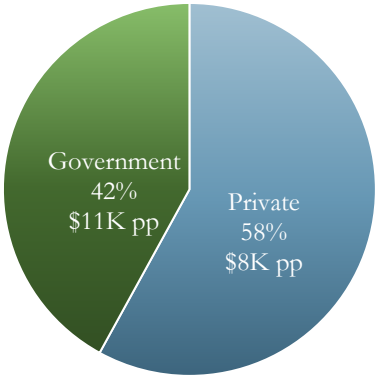
Most uninsured people are in low-income working families. 48% cite "too expensive" for the main reason they remain uninsured.

Medicare: 40%
Medicaid: 51%
CHIP: 4.4%
VA: 5.6%

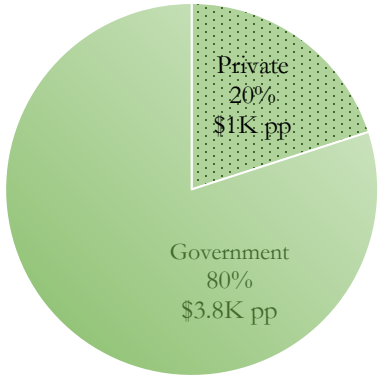
Employee Sponsored: 88%
Other: 12%



Spending



Multi Payer System



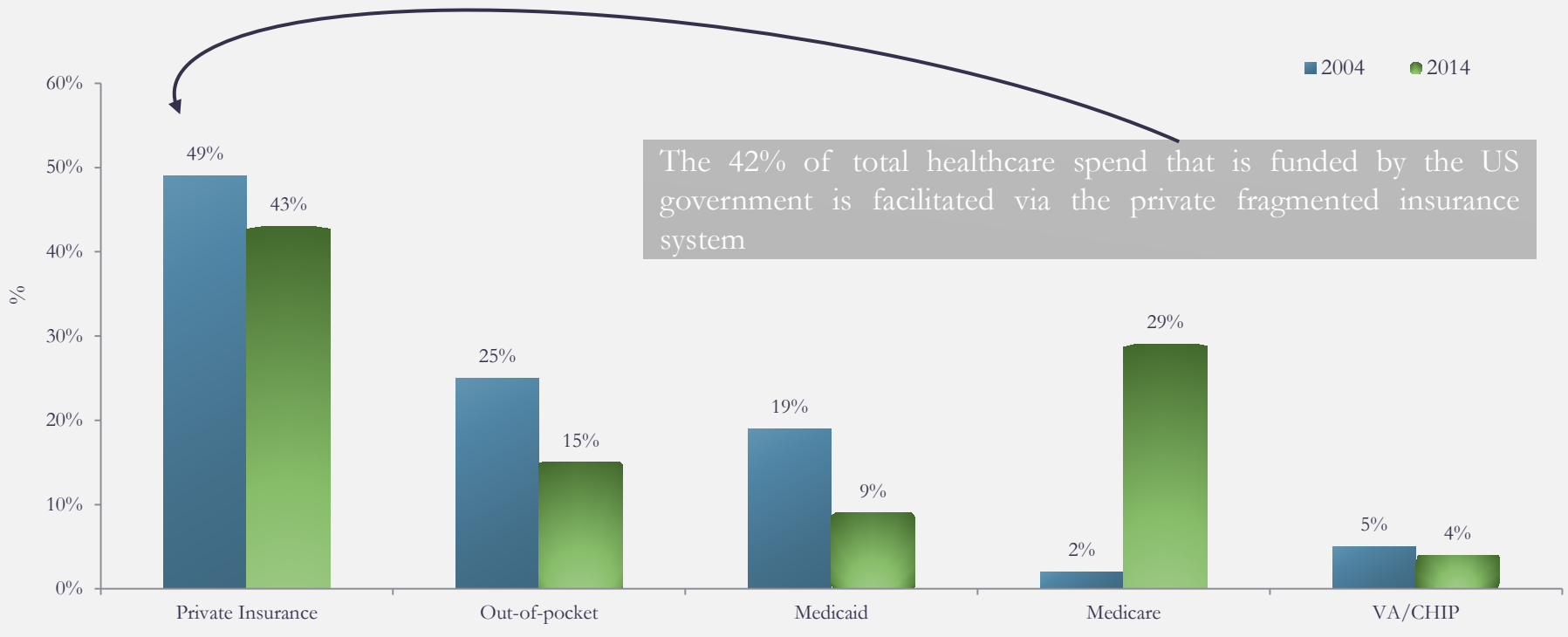
20% "Top-up" for faster care and choice care

Single Payer System

Sources: MTS analysis, CMS

US Government (Medicare) is Rapidly Becoming Major Payer for Prescription Drugs but is Effectively Just Another Arm of the Private Insurance System

Distribution of Total National Health Expenditures on Retail Prescription Drugs by Payer

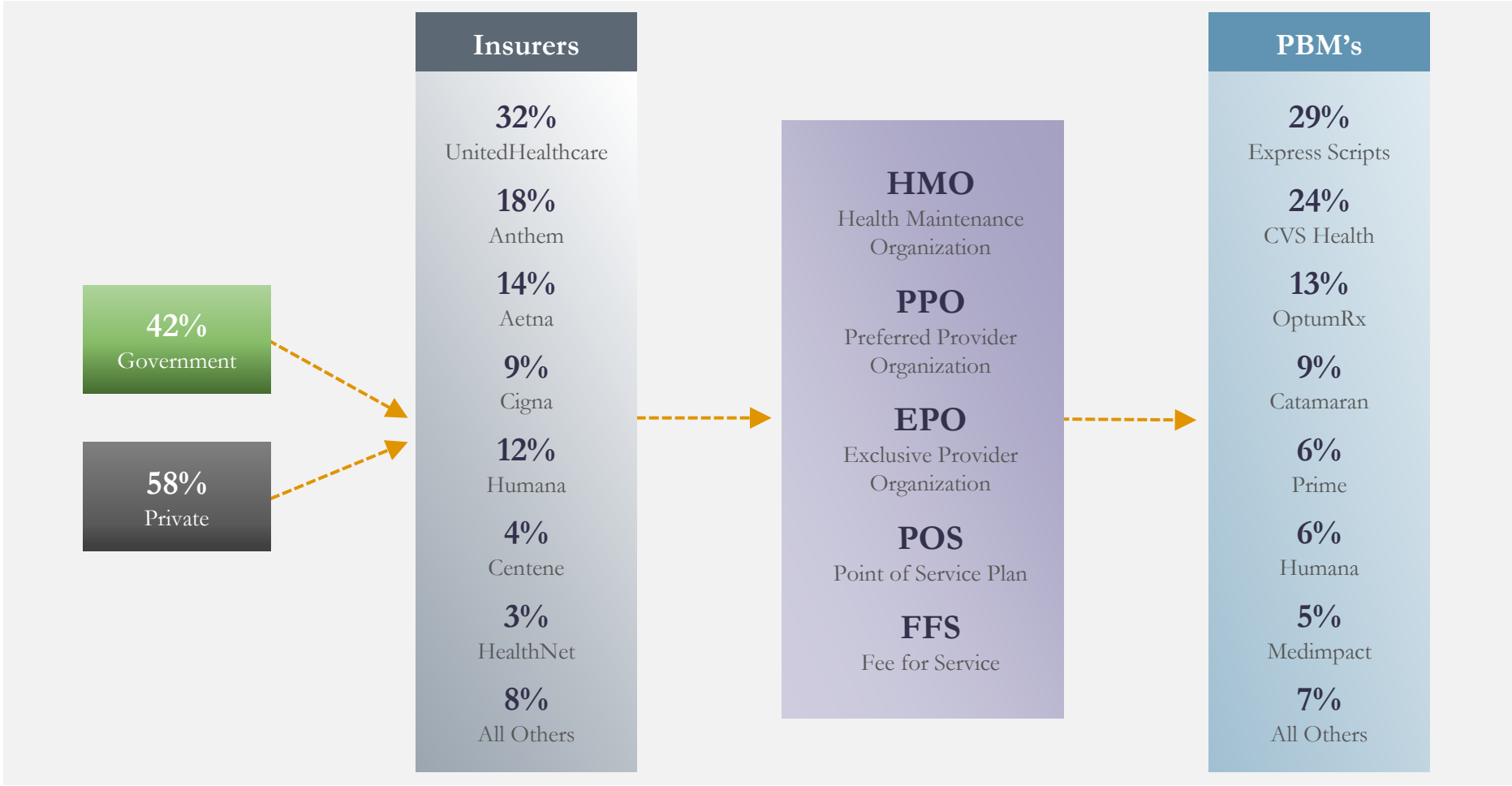


Source: National Health Expenditure (NHE) data from Centers for Medicare and Medicaid Services; MTS analysis

In the "Bundled" US Insurance-based System Rx Drug Benefits are Actually Administered By PBMs

There are 5 main types of insurance mechanisms for medical expenses (e.g. doctor visits, hospital stays, procedures, etc.)

Essentially all insurers "sub-contract" the prescription drug administration to PBMs (approximately 10% of total premiums)



Source: National Health Expenditure (NHE) data from Centers for Medicare and Medicaid Services; MTS analysis

What are Pharmacy Benefit Managers (PBMs)? They have 3 Key Roles in the US Drug Pricing Ecosystem

Administration

- Act as the administrator of Rx benefit of insurance plans

What is a PBM?

- PBM's administers, or handles, the prescription drug benefit component of employer's health plans. PBMs process and pay for prescription drug claims and are responsible for assisting employers with managing their prescription benefits.
- They serve as an intermediary between the payor and everyone else in the healthcare system.

How do they make money?

- PBMs earn profits through "spread pricing" – by paying one price to pharmacies and charging employers or unions at higher prices PBMs keep the difference.
- Health plans are unaware of the spread because it is not transparent.
- On top of the spread price, PBMs earn "administration fees", as well as "rebates" and "discounts".

Cost/benefit implementation

- Assessment via P&T committee
- Facilitation via formularies and **access**

Assessment of cost benefit

- PBMs decide on formularies using Pharmacy and Therapeutics (P&T) Committees, which consists of Clinical Review Committees (CRC) and Value Assessment Committees (VAC) – these process are not transparent.
- CRCs provide evaluations and make clinical recommendations for each product and pass these recommendations to the VAC.
- VACs provide reviews of the financial components and make final tier placement decisions for drugs.

Formulary

- A formulary is a list of the pharmaceuticals an insurer covers.
- Types of formularies: open (a relatively unrestrictive list of prescription drug choices available through an insurer) and closed (a specific list of covered prescription drugs).
- PBMs often reshuffle their formularies due to drugs losing their patent protection. Primary incentive for reshuffling is to continue to obtain rebates from manufacturers.
- After the P&T review – drugs are placed on a tiered benefit plan design according to clinical and cost data. Insurers often offer plans with 3 or more tiers.

Lower costs of drugs

- Consolidate buying power
- Capture rebates

Consolidate buying power for smaller companies

- Conceptually, PBMs consolidate multiple smaller companies and provide "numbers" for negotiation purposes.

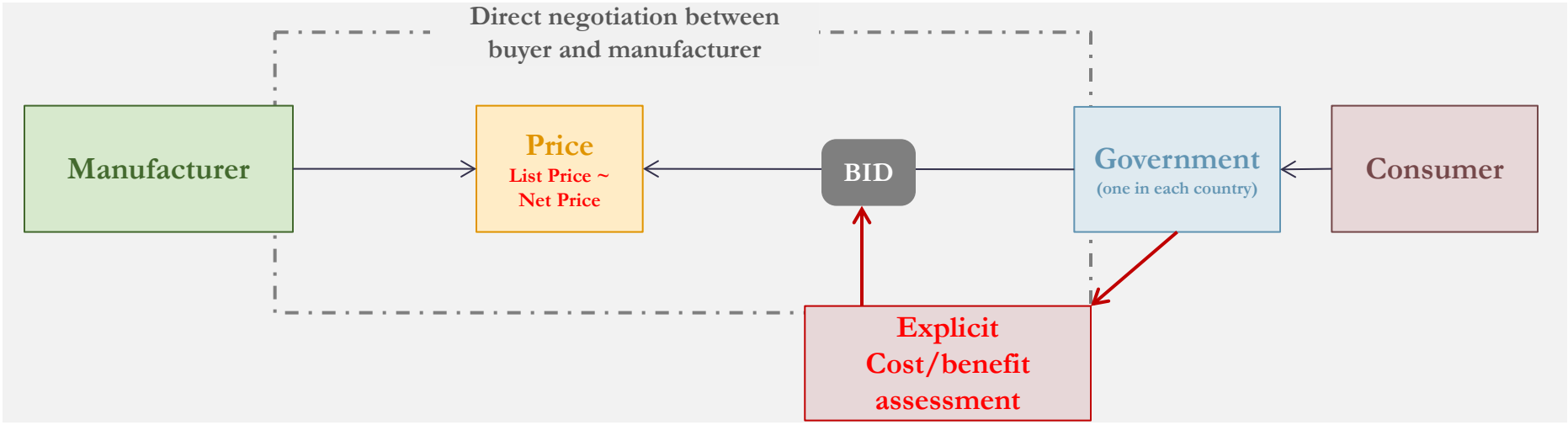
Rebates

- Drug manufacturers pay rebates to PBMs, essentially only to the party responsible for adjudicating the pharmacy claim. Only PBMs can demonstrate to the manufacturer an adequate ability to control and manage utilization rates.
- Various types of rebates:
  - ✓ Flat/access discounts – a rebate typically offered for formulary positioning
  - ✓ Performance discounts (adjusting) – a rebate typically affiliated and compared to quarterly national market share figures
  - ✓ Performance discounts (fixed) – a rebate typically affiliated and compared to a fixed-non-adjusting market share
  - ✓ Combination discounts – a rebate combination of flat/access discounts and performance discounts.

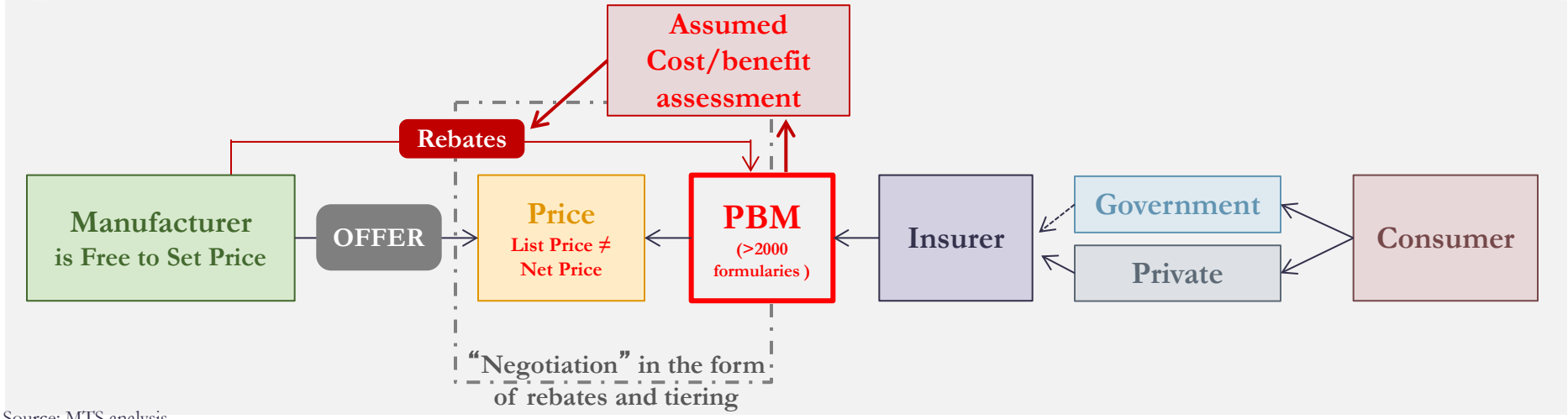
Source: National Health Expenditure (NHE) data from Centers for Medicare and Medicaid Services; MTS analysis

The Extremely Complex "OFFER" Drug Pricing Ecosystem in the US vs. the Relatively Simple "BID" Drug Pricing Ecosystem in the CDW

Comparable Developed World (CDW) = "BID" System, transparent prices and low frictional cost

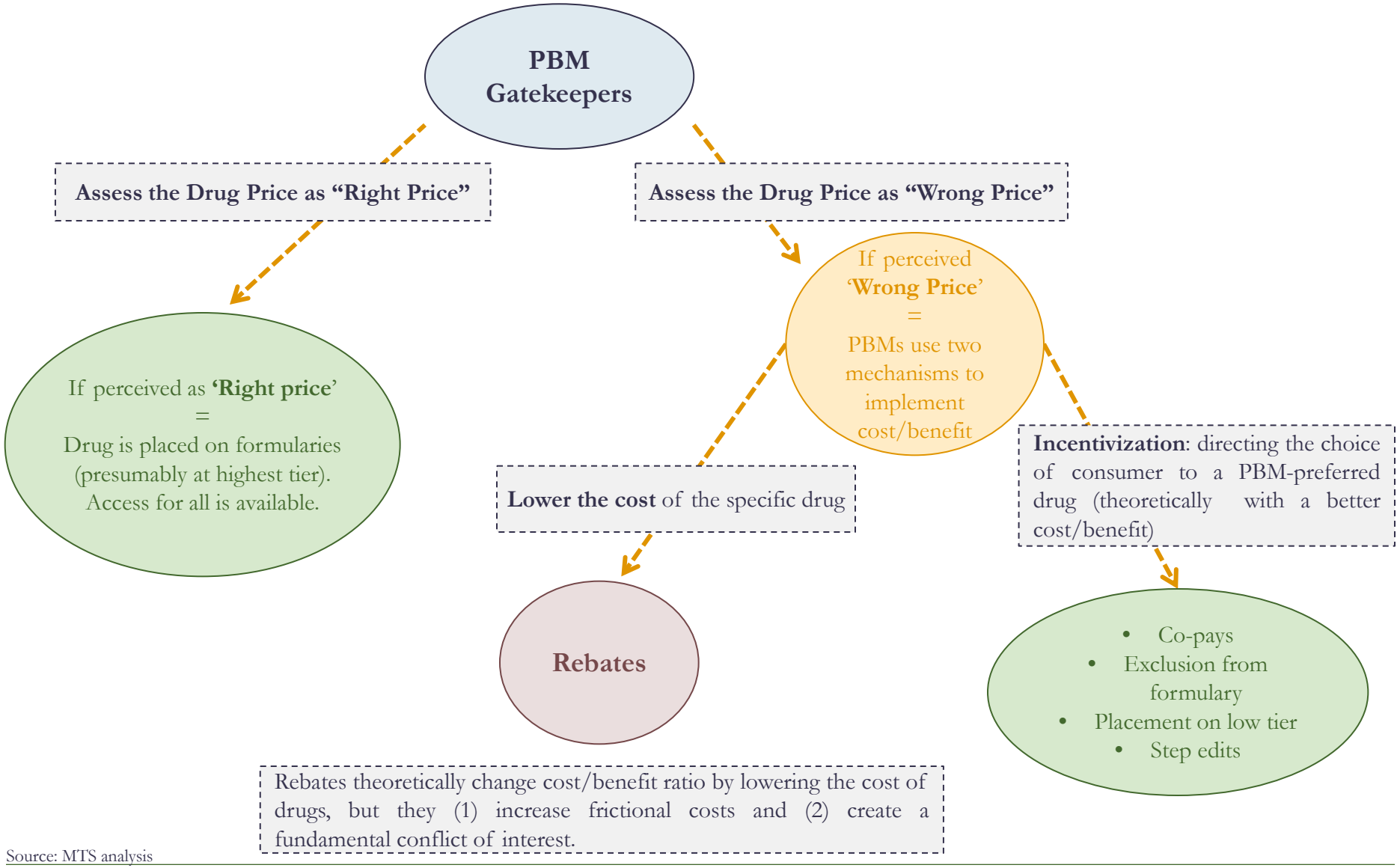


US = "OFFER" System, non-transparent prices and high frictional cost



Source: MTS analysis

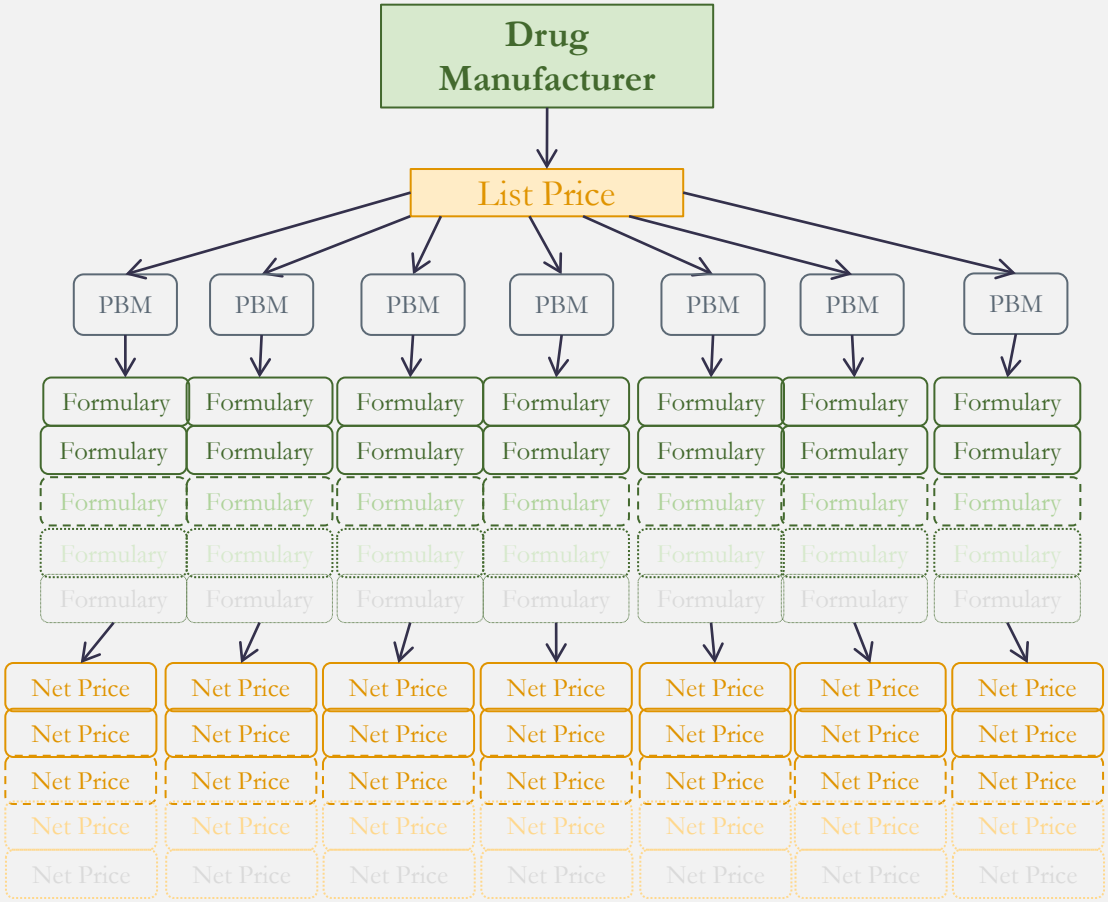
PBMs Theoretically Drive Cost/Benefit in the US Drug Pricing Ecosystem via Lowering Costs or Incentivization



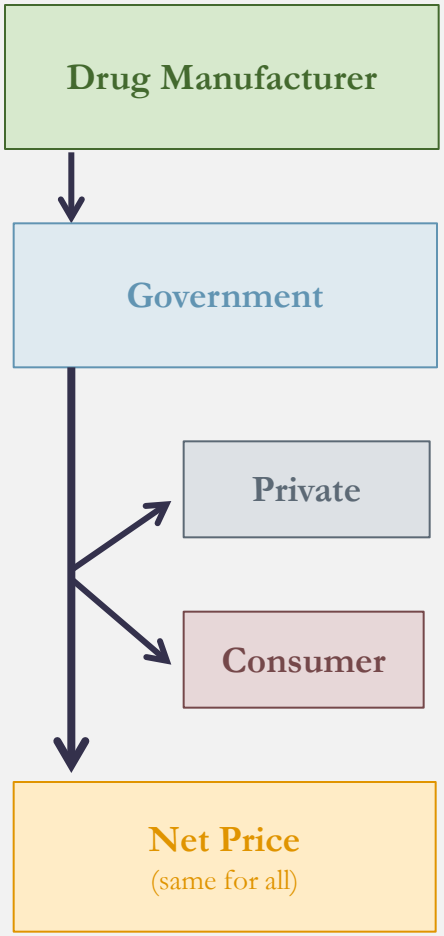
Source: MTS analysis

Comparable Developed World = One Payer = One Transparent Price; US = >7 Payers, >2000 formularies = Multiple, Non-Transparent Prices

U.S.



CDW



Source: MTS analysis

Drug Pricing Mechanisms Under Government Insurance Programs

Medicare Part D: structural challenges to discount negotiation

- Reports estimate that the US could save up to $16bn if Medicare Part D prices were negotiated
- Medicare Part D program cannot directly negotiate rebates with branded manufacturers due to non-interference clause

Veterans' Benefit Association: multiple cost reduction mechanisms

- VBA pays for brand-name drugs at an average retail price of 60% of that paid by Medicare Part D
- The VBA's actively managed formulary selects one of four mechanisms that offers the best price on a drug-by-drug basis

Medicaid and CHIP: steeper discounts achieved in part because Medicaid discounts are set by law whereas Medicare prices are negotiated by private insurers and drug companies

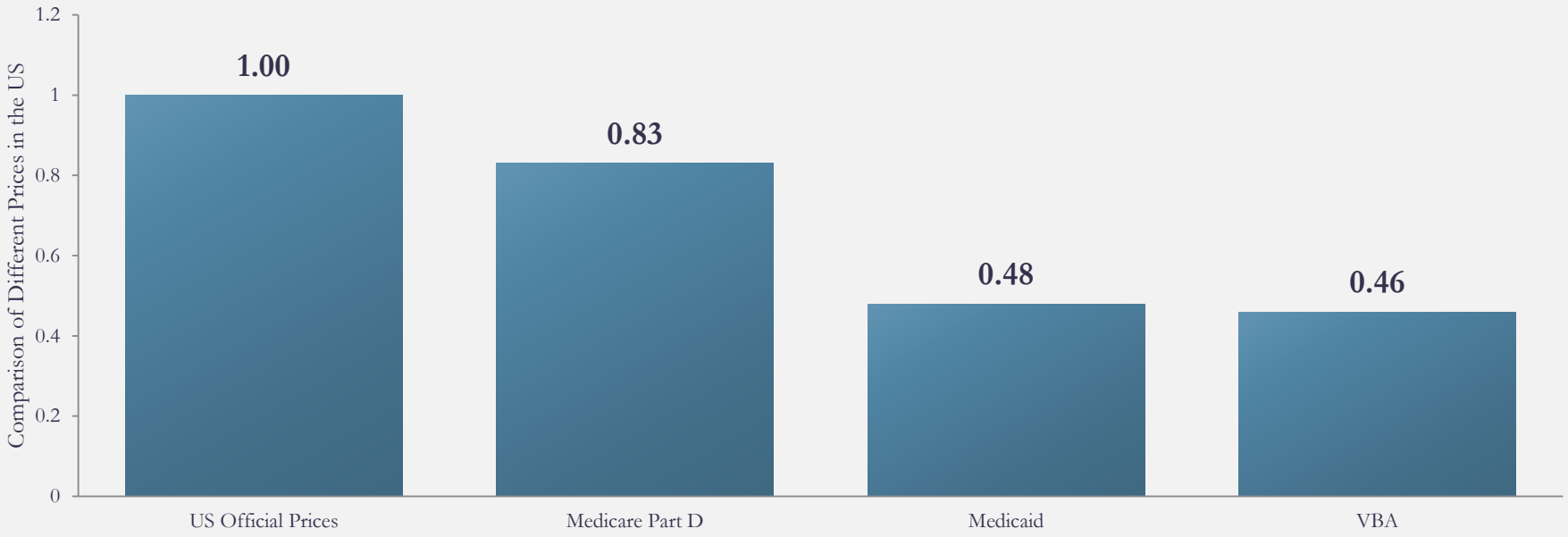
Program (% US prescription drug spend)	Discount / rebate based on average price paid by other purchasers	Discount / rebate equal to lowest price offered to other purchasers	Discount / rebate if Rx price grows faster than inflation	Negotiated Pricing
Medicaid & 340B (9%)	-23.1%	✔	✔	**Medicaid:** State-level **340B:** Via "prime vendor"
VA & DOD (4%)	-24.0%	✔	✔	National-level
Medicare (29%)	**Part D (Pharmacy drug coverage)** ▪ Plans negotiate prices in private markets ▪ On average, 33% higher prices than Medicaid **Part B (Hospital drug coverage)** ▪ Typically pays average sales price of drug plus 6% fee ▪ Proposed changes, to be tested in late 2016, include: reduction to 2.5% fee on Average Sales Price (ASP), plus flat $16.80 payment per drug ▪ Additional new value-based pricing strategies to be rolled out in early 2017			

Sources: CMS Website, Commonwealth Fund; MTS analysis

Net Drug Pricing Under Government Insurance Programs

Lack of ability to directly negotiate effetely puts Medicare Rx prices at approximately the same net prices levels as commercial plans

Comparison of Average Drug Prices Paid to Brand Name Rx Manufacturers (US Official List Price = 1)



Sources: CMS Website, Commonwealth Fund; MTS analysis

The #1 Feedback from Biopharma Manufacturers: PBMs Have Major Conflict of Interest When it Comes to Gatekeeping the Rx Budget

Conflicts of Interest:

PBMs promote drugs that yield the highest dollars in rebates – not necessarily the ones that are in patients' best interest.

"Rebate pumping" is achieved by creating a formulary that replaces "lower" cost drugs with "higher" cost that offer larger rebates. "Rebate pumping" results in higher costs to health plans and consumers that feeds into higher spreads and more PBM profits.

BioPharma Dive | 10/4/2016

NCPA Wants Congress To Examine PBM Role

Fierce Pharma | 10/11/2016

Insulin Prices Are Way Up, But Drug-Makers Say PBMs Are Collecting The Loot.

The Hill | 9/29/2016

The Man Behind The Curtain In Drug Price Increases.

Seeking Alpha | 10/4/2016

CVS Health – PBM Scrutiny Overhangs Industry

WSJ | 10/3/2016

Drug-Makers Point Fingers At Middlemen For Rising Drug Prices

Ian Read | Jefferies 2016
CEO Pfizer

"…the absence of rebates would be healthy for the system."

Heather Bresch | 8/24/2016
CEO Mylan

"They (PBMs) need to be at the table because this system needs to be fixed."

Mike Rulis | 11/4/2016
SVP Novo Nordisk

"In order to get on the lists, we need to offer rebates. Those rebates have increased over the years."

Source: MTS analysis

Estimating The Net Rebate that PBM Retains

($ in bn)	2015	2014	2013	2012	2011	2010
PBM Segment						
PBM Product Revenues						
Network revenues	$56.5	$58.5	$63.2	$57.8	$30.0	$30.1
Home delivery and specialty revenues	40.8	38.6	37.6	33.0	14.5	13.4
Total PBM Product Revenues	97.3	97.1	100.8	90.8	44.6	43.5
PBM Service revenues	1.7	1.3	1.0	0.8	0.3	0.3
Total PBM Revenues	**99.0**	**98.4**	**101.8**	**91.6**	**44.8**	**43.8**
Cost of PBM services	90.8	90.6	93.8	84.5	41.7	40.9
PBM Gross Profit	**8.2**	**7.7**	**8.0**	**7.1**	**3.2**	**2.9**
Segment Gross Margin %	*8.3%*	*7.9%*	*7.8%*	*7.8%*	*7.0%*	*6.7%*
SG&A	3.9	4.2	4.5	4.3	0.9	0.8
PBM Operating Income	**$4.3**	**$3.5**	**$3.5**	**$2.8**	**$2.3**	**$2.1**

ExpressScripts is the only publically listed stand alone PBM – It has around 30% market share of total drug spend (in 2014 – Gross $373bn, Net $283bn). ESRX PBM Segment "Product Revenues" of $97bn correlates with this.

The difference between "Product Revenues" and "Costs of PBM Services" is the delta of monetary flow retained by the PBM (i.e. gross profit) of the revenue received for drugs and the payments of drugs net of rebates and administration fees. Accounts for rebates and administrative fees earned for the administration of this program, performed in conjunction with claims processing and home delivery services provided to clients, are recorded as a reduction of cost of revenues and the portion of the rebate and administrative fees payable to customers is treated as a reduction of revenues.

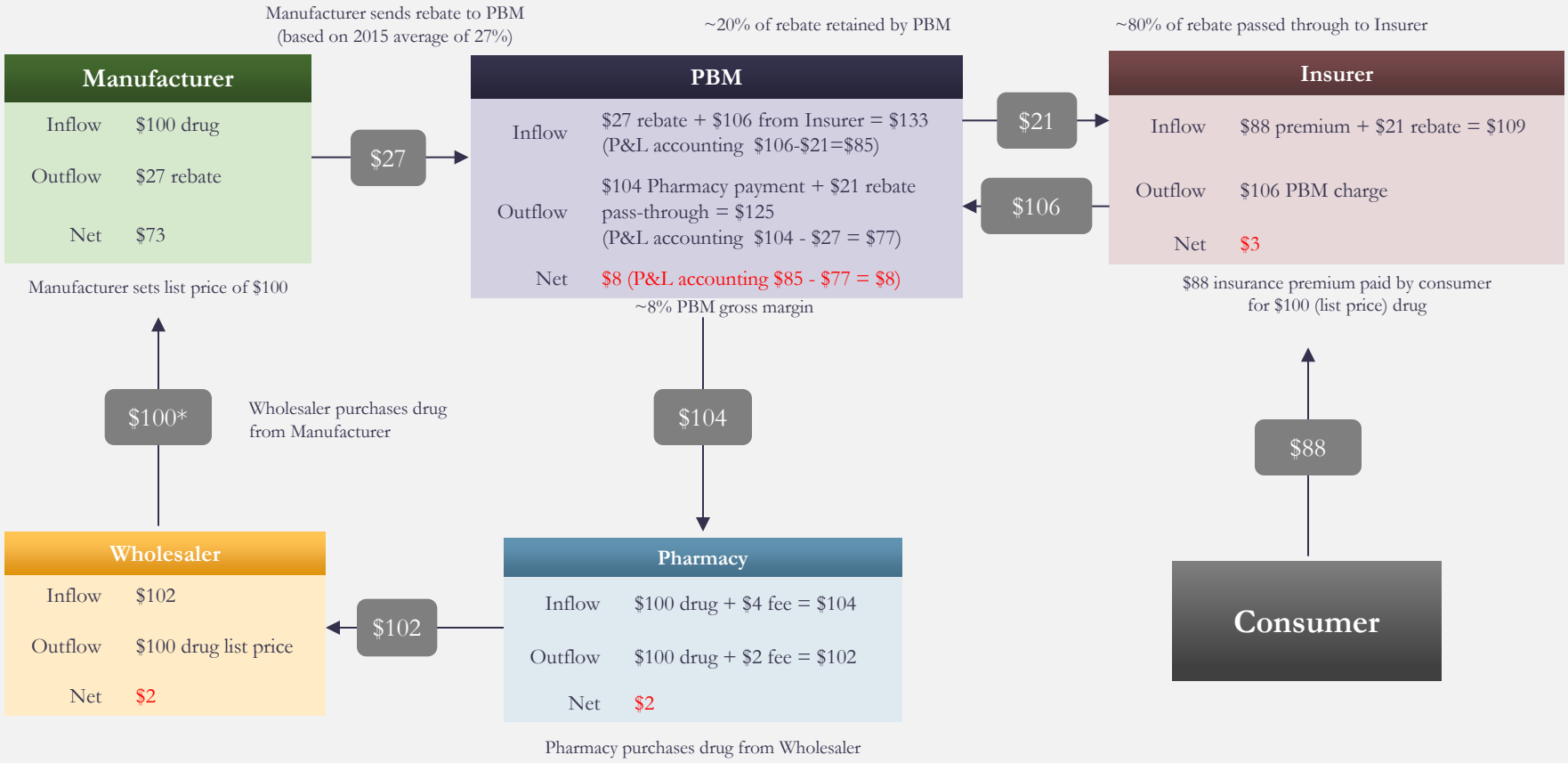
Sources: ExpressScripts, MTS analysis

MTS Calculated Money Flows in the Totality (Using a Nominal $100) Within the US Drug Pricing Ecosystem

In the "totality" of the ecosystem, for every $100 of list price drug sales, manufacturers receive $73 net dollars, Wholesalers and Pharmacy $4, PBM's $8 and Insurers $3. Direct frictional costs are marked in red

The effective pass-through price for the consumer (for $100 list price drug) is $88, paid via insurance premiums

PBM-based Healthcare System



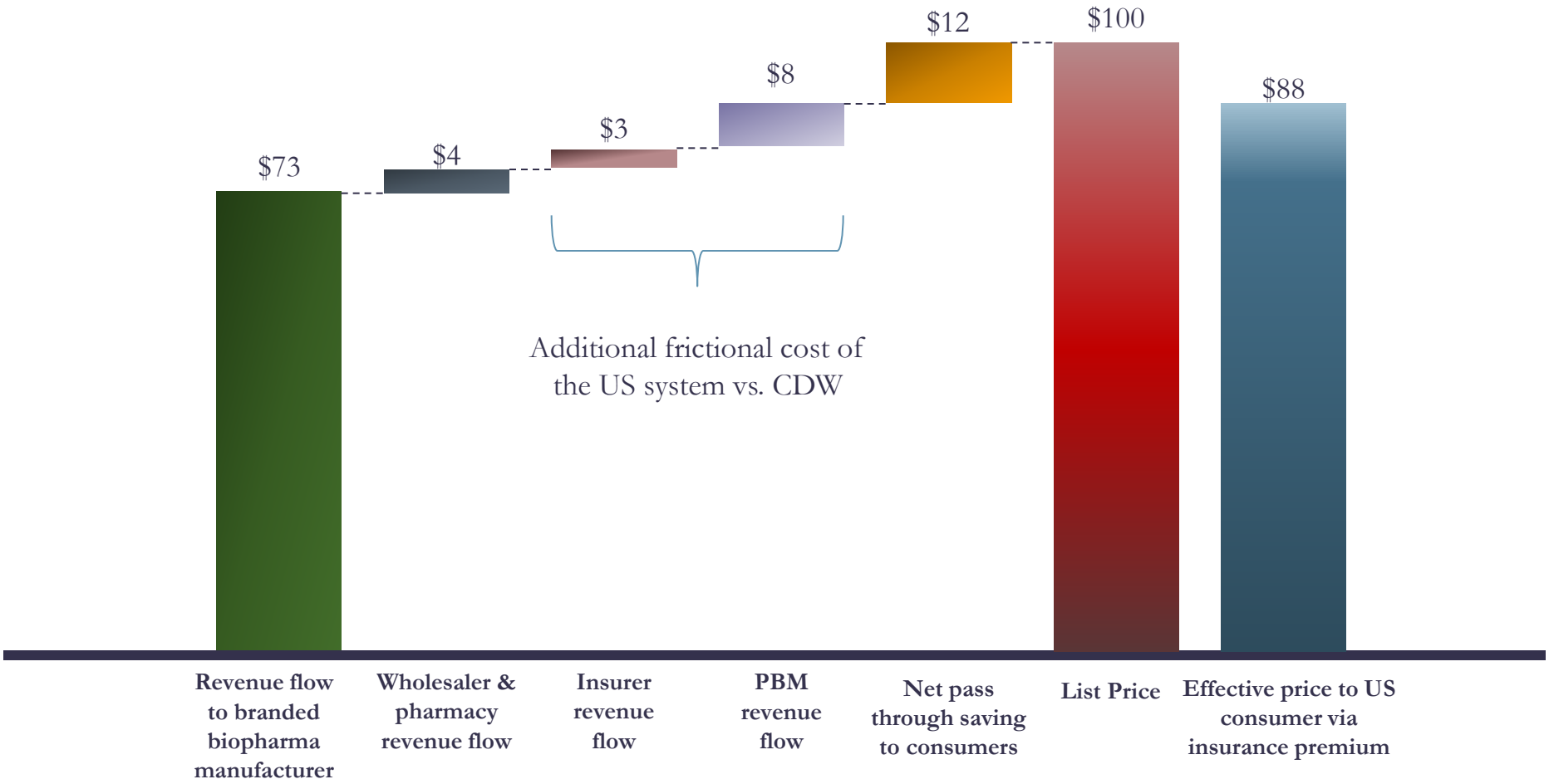
(*) In reality, the Wholesaler negotiates a small discount to the list price from the Manufacturer, further driving down the effective price of the drug.

Source: MTS analysis

Overview of MTS Estimated Frictional Costs for (a Nominal $100) List Price Branded Drug in the US Drug Pricing Ecosystem

For an average $100 list price branded drug, the effective cost to its end-user is $88, $15 are absorbed in frictional costs and the biopharma manufacturer receives $73

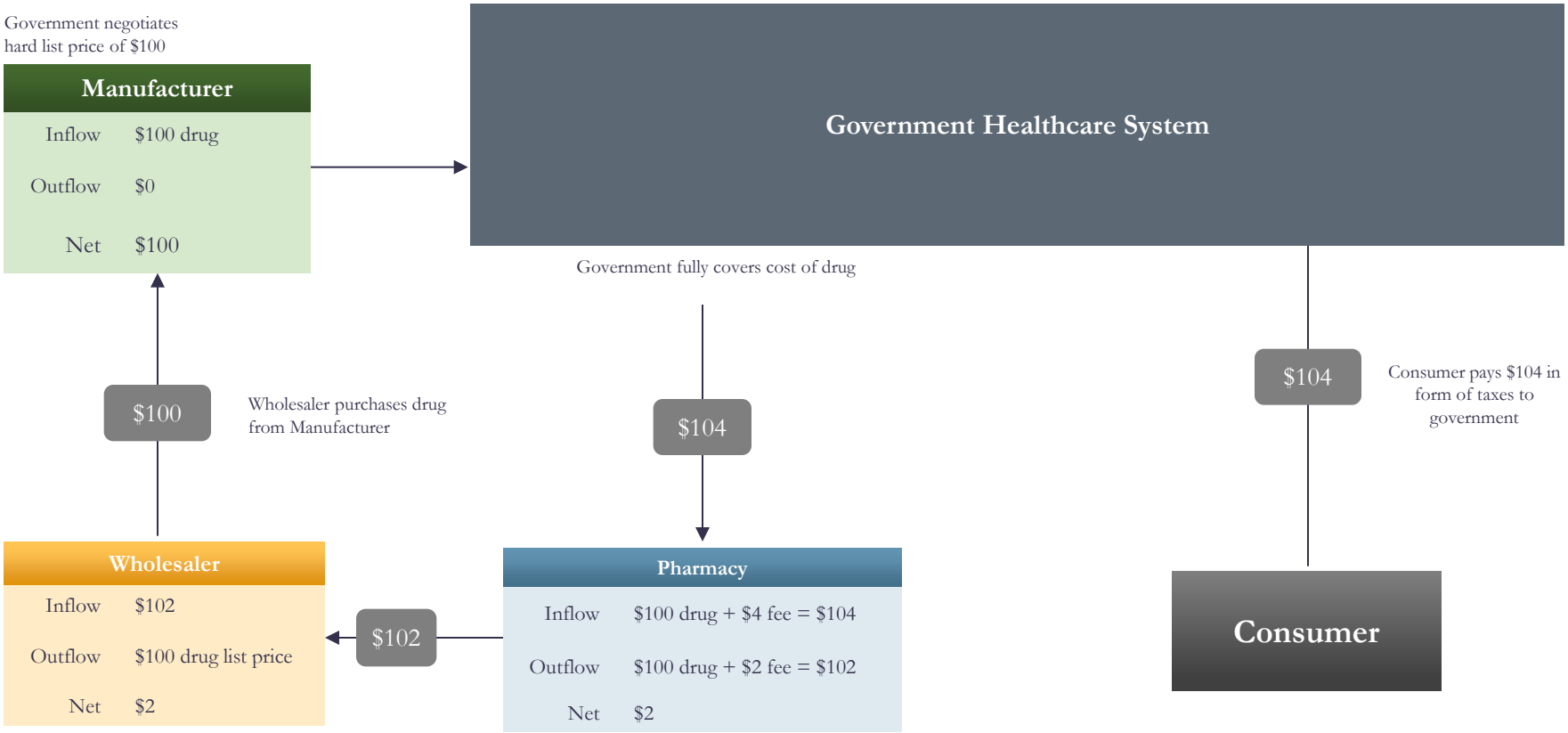
The "intermediator" insurance/PBM system is unique to US drug pricing ecosystem and drives a 27% savings from list price, of which around half flows to the end-user



Source: MTS analysis

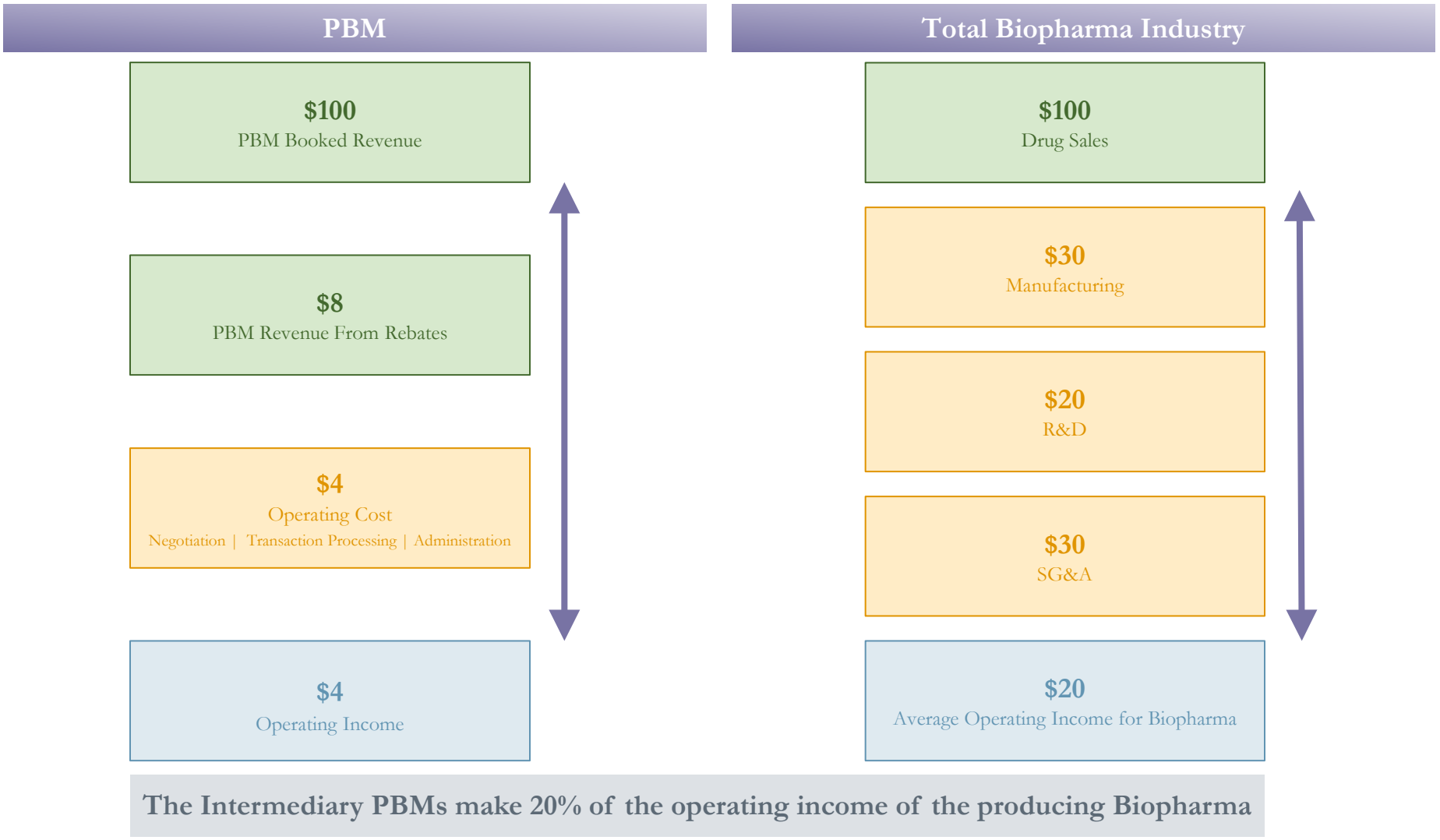
MTS Calculated Money Flows in Totality (Using a Nominal $100) Within the Comparable Developed World Pricing Ecosystem

- Government is the sole insurer and performs all the tasks of a PBM
- Government negotiates price of a drug, as does the PBM by negotiating rebates in a non-government healthcare system
- All consumers' taxes subsidize fees related to drug processing and drug cost, which the government pays in full



Source: MTS analysis

Quantifying the Profitability of Drugs and Rebates in the US Drug Pricing Ecosystem: PBMs vs. Biopharma - Does the Work Justify the Margins?



The Intermediary PBMs make 20% of the operating income of the producing Biopharma

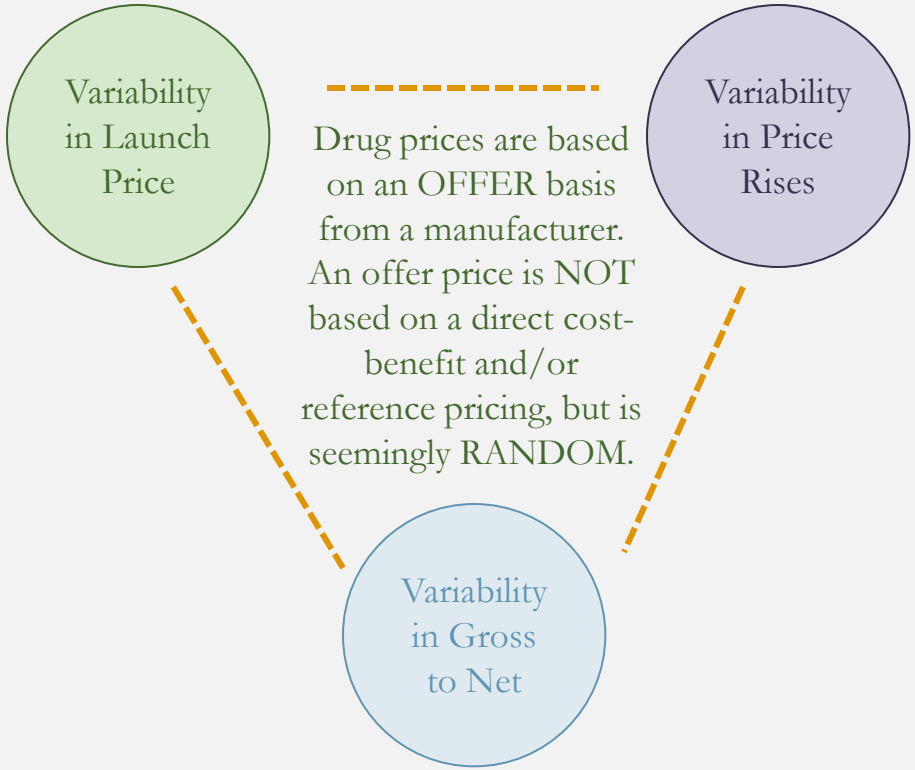
Disclaimer: The drug operating costs are for the totality of the whole industry
Source: MTS analysis

Randomness of Prices Leads to Perception of Consumer Exploitation in US Pricing System

CDW

Drug prices are based on a BID basis from a single payer. A bid price is based on a direct cost-benefit and/or reference pricing.

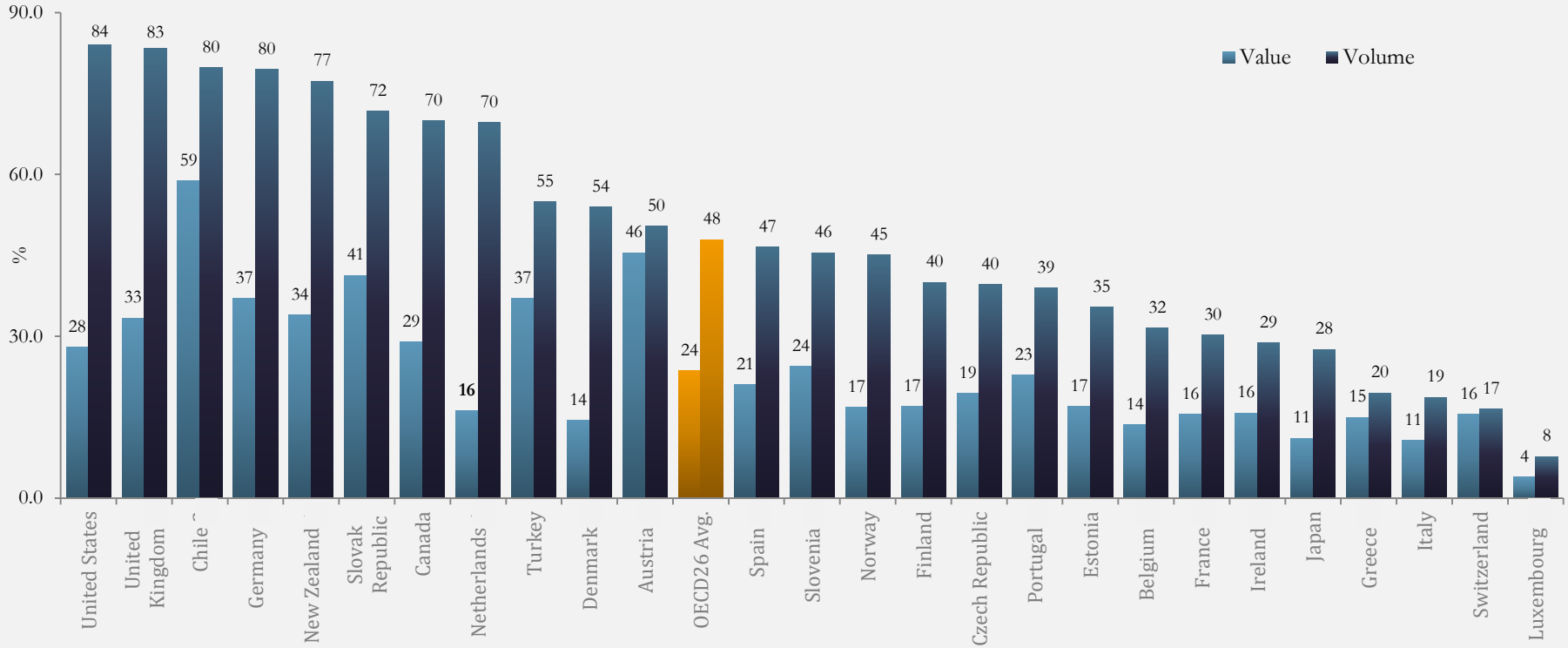
US



Source: MTS analysis

Access can be Logical in Controlling Costs…
US has Highest Generic Utilization Rates due to PBM Access Control Points

Share of generics in the total pharmaceutical market (2013 or nearest year)

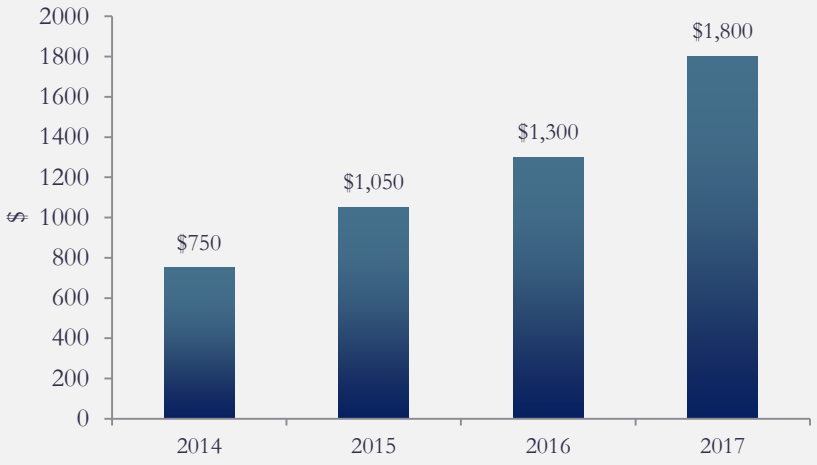


Sources: OECD, MTS analysis

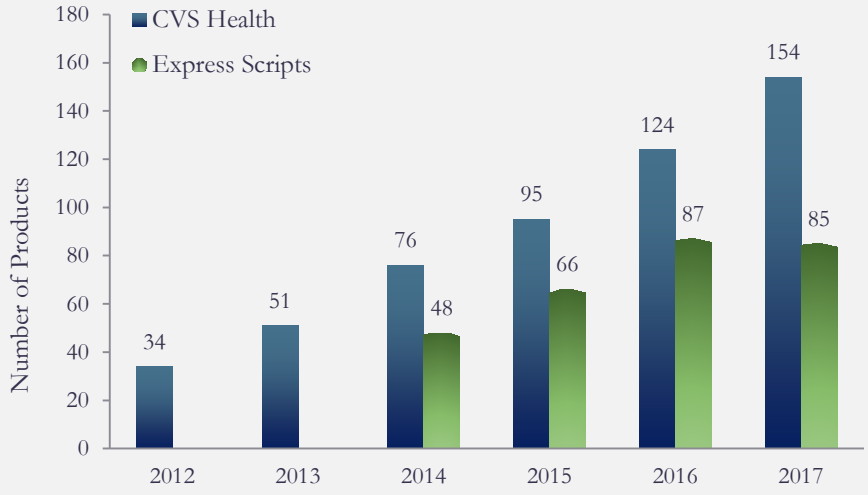
PBM Formulary Exclusions (aka Restriction of Access) Increasingly Being Used to Control Costs

- Express Scripts argues that formulary exclusions will save plan sponsors ~$1.8bn in 2017, compared to $1.3bn in 2016
- The number of products on exclusion lists has dramatically increased since 2012
- Both of the two largest PBMs, CVS and Express Scripts, have been adding to the list of formulary exclusions, albeit CVS at a significantly higher rate

Express Scripts Exclusion Value, 2014-2017



Number of Products on PBM Formulary Exclusion Lists, 2012-2017



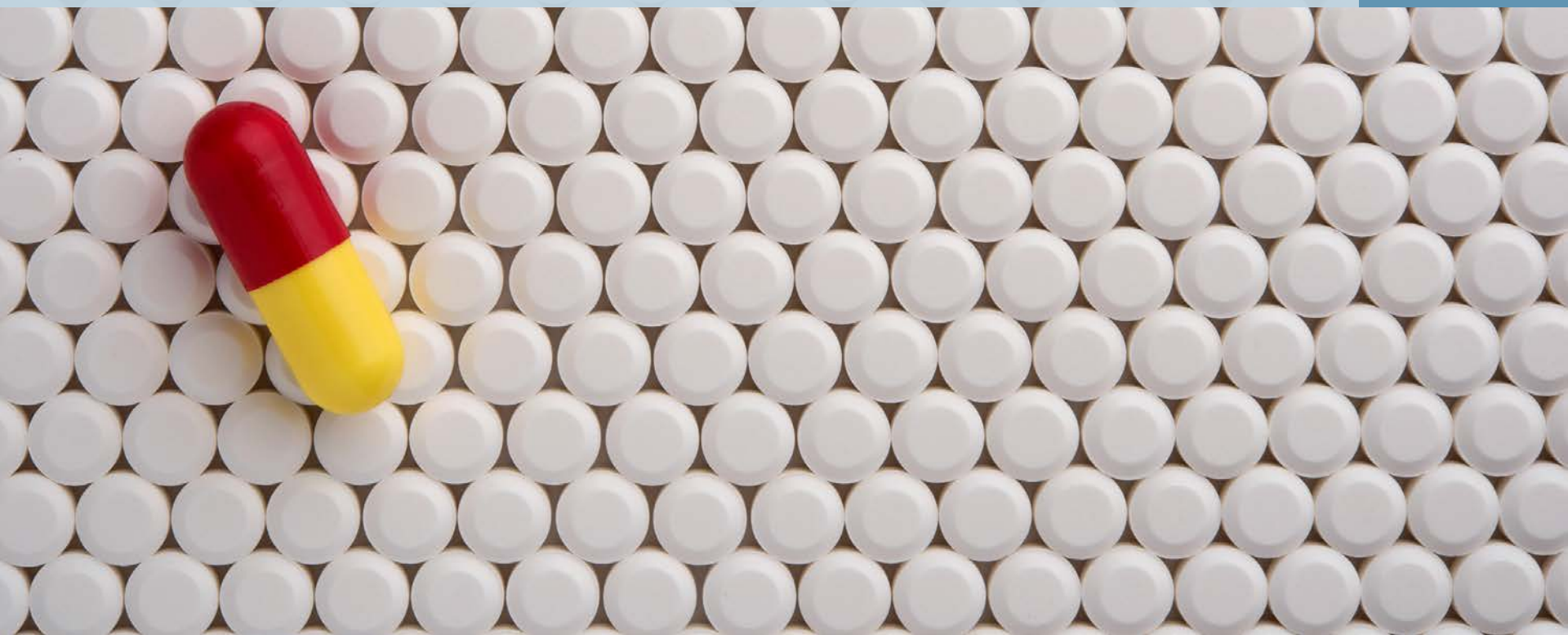
Sources: MTS analysis, ExpressScripts, CVS Health

Summary Comparison of the US vs. a Comparable Developed World Healthcare System Across Key Variables

	US	CDW
Payer Fragmentation	High: Indirect and multiple payers (Insurance)	Low: Direct and single payer (Government)
Economics of pricing	Offer to bid system	Bid to offer system
Basis of initial pricing	Set by manufacturer based on what market will bear (indirectly and loosely based on value and reference pricing)	Direct value- or reference-based set by the single buyer
Basis of subsequent price rises	Seller determined (still "offer" based system) Ultimately, what the fragmented market will bear	Formulary and generally limited to modest CPI calculation
Net pricing variance	Highly differential pricing to different segments	Uniform price (as there is a single buyer)
Transparency of pricing	Non – transparent	Transparent
Discounts on list price	Large (on average 27%) and viable via manufacturer rebates to PBMs, discounts and other price concessions	Little/no rebates as prices openly negotiated with single seller and buyer (most countries have some value discounts)
Access	Controlled via formulary tiering, exclusions, step edits (resulting in access that essentially becomes the "indirect pricing negotiation")	If pricing is in agreement (and treatment guidelines met) there are few access barriers. If no agreement on pricing then essentially all of the population does not have access

Sources: IFHP 2013, MTS analysis

4. Possible Outcomes for the US Drug Pricing Ecosystem



Will There Be Change?
Yes. But Who is Leading the Change is Key!

I	**Will there be change? Yes** a critical mass of "trip wires" have been hit: (a) increased visibility/focus on the rebate system; (b) structural/fundamental headwinds on winding down of the small molecule patent cliff; (c) next-gen of innovative drugs will have "inherently" high prices (e.g. I-O combinations); (d) publicity of how much higher specific drugs are in the US vs comparable developed world (e.g. diabetes) and (e) non-rational price rises.
a.	**Current system continues in current format** • Medicare and Medicaid lives coverage increases by ~6% and there are essentially no uninsured people in the US • Overall, the healthcare system can afford current pricing due to PBMs increased control over drug pricing • The "status-quo" results in increased "power" of PBMs that in theory become gatekeepers of the budget. The frictional costs continue to mask major conflicts of interest that are rebates and cost/benefit assessment based on PBM profit • Poorly defined "cost/benefit" system leads to discouragement of innovation and investment in novel, expensive, and risky treatment development
b.	**Government intervenes** • Government changes the law to allow Medicare/Medicaid via CMS to negotiate the pricing • CMS adopts a "cost/benefit" system – most likely based on a formula with a discount that does not appreciate differentiated R&D, orphan status, or amount of investment needed to develop new treatments • One possibility would be that the government devises a method to work closely with the FDA, where the FDA can instruct manufacturers in designing proper clinical trials, as well as assist in putting together the pharmaco-economic documents that would be part of approval • This system could reward innovation but it is left up to government to do it correctly
c.	**Self-help from both the Biopharma (move to uniform cost-benefit) and payer (increase in transparency and choice in the Rx element) led by industry** • A type of "cost/benefit" is bound to enter our industry sooner than later • We argue that industry led efforts in setting the framework of what cost-benefit system should be and how it will look is crucial in ensuring that innovation will be awarded appropriately and not grouped in general discounts • Manufacturers need to focus on designing clinical trials that are targeted for specific patient population and not immediately seeking broad approval, they should run cost/benefit analyses prior to launch, and finally implement Phase IV trials that could either lead to increase in pricing and justifiable pricing inflations, or decrease in pricing

Source: MTS analysis

What is Right and Wrong with the US Drug Pricing Ecosystem

Let's not throw the baby out with the bath water.

Fundamentally Right	The Reality	What Should Be Changed?
A "free market" based pricing system - the high risk and capital intensive nature of the biopharma industry can only be supported, in the long run, by a free market based industry (vs. government).	The US pricing ecosystem is not a true free market based pricing system due to lack of choice as well as lack of transparency on costs/benefits.	(1) Introduce mechanisms to garner true transparency on cost/benefit and concomitant choice. (2) "Discounts" to CDW should be lowered.
Access: A system conceptually allows consumers access to the broadest number of drugs if they are willing to pay.	The US does have the broadest range of drugs available BUT there are (growing) access barriers in the US with insurers/PBMs acting as gatekeepers. As most individuals have little/no choice of insurer, they have little/no choice of Rx benefit.	Choice and transparency of differential cost for Rx coverage should drive differential access.
Efficient utilization of lower cost "alternative" drugs.	The US has the highest utilization rates for generic drugs demonstrating that selective elements of the system work. Conversely, there is too high a utilization of expensive "me-too" branded drugs.	Change in branded "me-too" pricing dynamics - i.e. minor improvements in clinical effect should command appropriate pricing differential.
Innovation encouraged.	The US tends to be the fastest adopter of new technologies/drugs. Concomitantly, the US leads clinical trials of innovative treatments.	There are arguments that innovative drugs are not priced appropriately (actually too low) due to the high costs of "me-too" drugs.

Source: MTS analysis

MTS' Views on the Three Key Issues That Should be Addressed in the US Drug Pricing Ecosystem and Our Proposed Actionables

(1) US drug prices are not principally based on cost/benefit

The emphasis is on the Biopharma industry to base drug pricing on a cost/benefit assessment and outcomes based principals.

- Move away from the current free market, i.e. "what the ecosystem can bear" system.
- Drug price rises are not the cause of the problem but rather a symptom.
- Value based pricing could still lead to dynamic prices after launch (both up and down) based on post launch changes in benefit assessment.
- Most likely a concentrated effort with regulatory bodies will be necessary.

(2) Lack of transparency and choice across multiple parts of the ecosystem

Low transparency of net drug prices.

- Differential and non-transparent rebate levels are currently a headwind rather than tailwind driving value based on cost/benefit assessment.
- The rebate system (which is responsible for non-transparency of drug prices) needs a dramatic overhaul via coordinated efforts of manufacturers, regulators and payers.

Differential contributions/benefit for insurance are not visible and there is little/no choice.

- Choice and transparency of level of contribution and concomitant level of Rx coverage should be introduced and driven by insurers/PBMs, as well as central governing bodies.

(3) High frictional costs are driving conflicts of interests and not proportionally rewarding contributors of value

Frictional costs are ~14% of list drug price.

- PBM's frictional costs are masking major conflicts of interest.
- The largest frictional costs are the insurance based intermediator costs, which are principally driven by the rebate system.
- Rebates to PBMs are one of the key drivers underlying price increases in the last decade.
- Value based pricing and transparent net-pricing can reduce/eliminate the rebate system.
- Other (non-direct) frictional costs include level and content of S&M/OTC spending by manufacturers.

Two key actionables:

(1) Biopharma industry should move uniformly to an innovative value based drug pricing

(2) Increase in transparency and choice in the Rx element of the insurance system

Source: MTS analysis

How are Drugs Priced Around the World Currently?

Supply and Demand	Direct Pharmaco-Economic	Relative Cost Benefit	External Reference Pricing	Profit Control
• This is essentially the pricing system upon which the US drug pricing ecosystem has historically been set.	• PE based pricing led by UK's National Institute for Health and Clinical Excellence (NICE) and Germany's Federal Joint Committee/Institute for Quality and Efficiency in Health Care (G-BA/IQWiG; Germany). • Evaluates the (proposed) cost of a drug relative to the benefit of the drug expressed in terms of monetary value, efficacy or enhanced quality of life. • A large criticism of PE is the accurate measure of the "QOL" benefits.	• A variation of PE measurements but when the incremental costs of a drug is compared to the incremental benefit vs. another drug for the same (or similar) indication.	• External Price Referencing or International Price Comparison/Benching is widely used by CDW countries. • Defined as the practice of using the prices of a medicine in one or several countries in order to derive a benchmark or reference price for the purposes of setting or negotiating the price in a given country. • It is used in 29 countries in the EU, as well as in Iceland, Norway, Switzerland and Turkey.	• Relatively rarely used. • UK's PPRS (Pharmaceutical Price Regulation Scheme) is the primary example: PPRS Describes a profit framework which is negotiated between the Department of Health and the pharmaceutical industry. Covers branded drugs irrespective of their patent or exclusivity status. Allows YoY growth rate Companies are allowed to make up to 50% in additional profit before making additional payments to the government for excessive profits. Price increases are allowed if profits have fallen below 50% of allowable profit. • There have been some moves in the US to look at the profit of particular drugs to companies.

Source: MTS analysis

A Number of Pricing Mechanisms are Already in Effect in the US

	Definition	Example
P4P (Pay for Performance)	Specific performance based pricing within a specific indication	▪ Introduced in 2015 ▪ Entresto (heart failure) - P4P options proposed by Novartis when launched in early 2015 ▪ Aetna, Prime, Harvard Pilgrim and Cigna accepts P4P (under confidential terms)
Indication-specific pricing	Differential pricing for different indications	▪ Possible in 2017 ▪ Not as yet implemented but some understandable logic especially for oncology indications ▪ Express Scripts and CVS Health Corp has been a leading proponent ▪ Lilly has also made comments in support of this for Erbitux
Annuity pricing	Set initial (upfront) cost for drug and then further annual payments if drug continues "to work"	▪ Possible beyond 2018 ▪ Not implemented yet ▪ Most likely relevant for gene therapy products
Free Trial Period to Identify Responders	Initial use of drug at no cost, responders then start paying	▪ Applicable only for select drugs that have a responder population that is not possible to predict until the drug is used
Price Caps (Inflation Caps)	Formulary approaches to price rises after launch	▪ Introduced in 2016 ▪ The extent of price caps in the US is hard to accurately assess for the overall drug market but given that the process has started the momentum is likely to increase ▪ CVS commented that 90% of its contracts include "price protection"
Utilization Caps	Limits the per-member -per-month (PMPM) expense for a drug	▪ Introduced in 2017 ▪ Applicable to HCV drugs and PCSK9s
Formulary Exclusions	Closed formularies with select drug specifically excluded	▪ Increased significantly over last 5 years ▪ Lower premiums returned for closed formularies ▪ First introduced by Express Scripts

Source: MTS analysis

Why We Think the US System will Move Towards a Relative Cost/Benefit System

Past	Reality	Future
Consumer: "I want the best drug available"	Drug prices increased exponentially	Consumer: "I want the cheapest drug that is good enough"
"Me-too" drugs with minimal increase in benefit generated significant market share and launched at disproportionately higher prices	Competition dynamics are leading to a decrease in drug pricing and lowering of costs	"Me-too" drugs launched at significantly lower price in order to gain market share and provide pressure on existing treatments
Launch prices and price inflations driven by manufacturers to accommodate for frictional cost	Drug manufacturers portrayed as the villains of industry due to high "sticker" prices, even though those prices are never booked	Setting "realistic" drug prices and providing transparency to the frictional cost/net pricing
PBMs acting as gatekeepers for budget on prescription drug costs	Highly conflicted interest of PBMs as they benefit from high list prices due to the higher rebates offered by manufacturers	Curtailing list prices by manufacturer themselves by providing cost-benefit rationale and full transparency to consumers and thus avoiding high frictional costs
Lack of cost/benefit analysis by manufacturers	Complete lack of understanding behind setting drug pricing, leading to uproar from both consumers and government	Manufacturers taking the initiative to perform cost-benefit analysis prior to FDA approval; developing drugs with truly innovative characteristics will lead to justification of prices and lack of backlash

Source: MTS analysis

Key Actionable #1 – Biopharma Industry Should Move Uniformly to an Innovative Value Based Drug Pricing

Many players in the biopharma industry would argue that US drug prices are already value based

- **We would argue that this is only loosely correct and certainly not uniform across the Biopharma industry – e.g. high drug price inflation without changes in benefit by definition is not value-based pricing**
- **The key hurdle is how to define value, which is a whole topic in itself, but regardless a basis of value pricing already exists in many regions of the Comparable Developed World**
- **We define "innovative value" as:**

Innovative Value

Delivering a clinical benefit in a completely unmet medical need

or

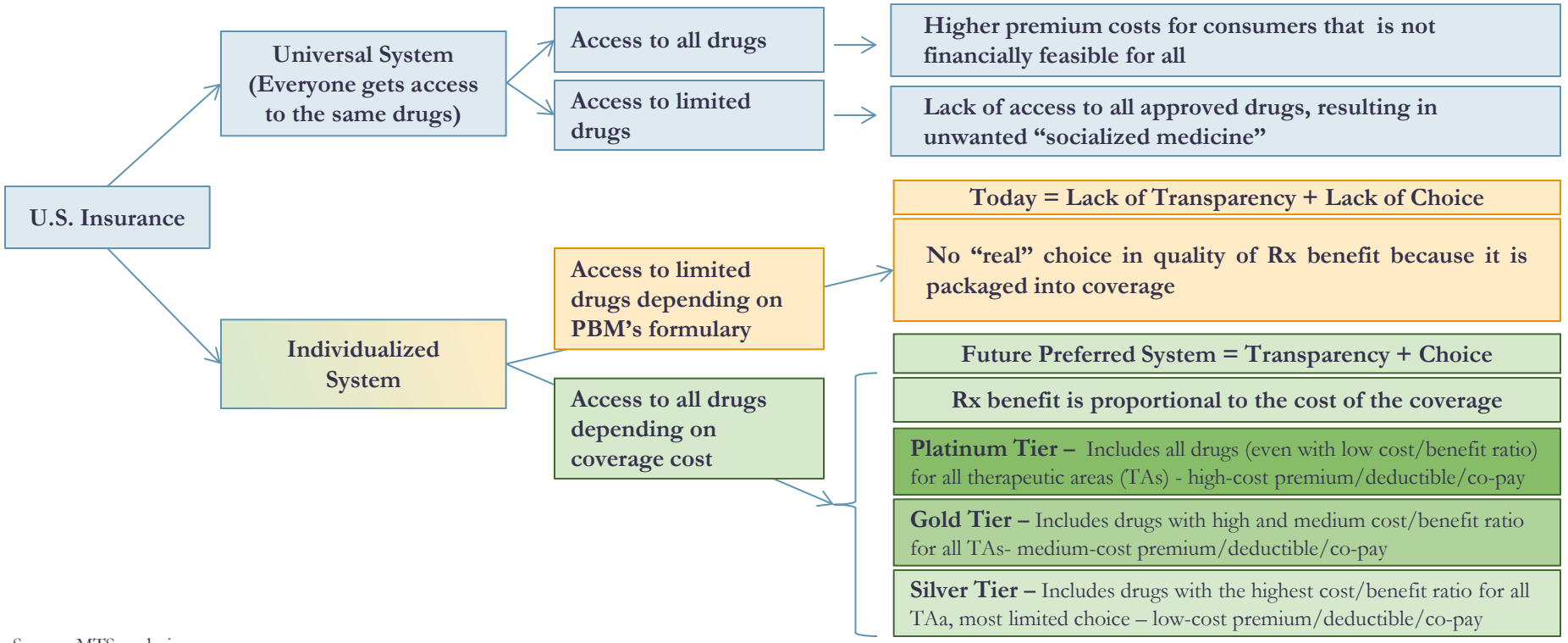
Significant increase in benefit/efficacy in comparison to marketed products in an therapeutic area

- Innovative value drugs should provide benefit to the healthcare system, as well as have societal value
- An innovative value drug doesn't necessarily need to have a novel mechanism of action, but should be by the above definition in either an unmet medical need or provide a significant increase in efficacy/benefit
- A "me-too" drug with no material improvement in benefit/efficacy does not provide innovative value (obviously!)
- Innovative drugs with marginal improvement should be premium priced at marginal levels
- Innovative value drug pricing should be based on the clinical trial data that is reflective of the real world setting
- The cost/benefit measurement of a drug should be reassessed if the real world setting appears to be substantially different from the clinical trial results

Source: MTS analysis

Key Actionable #2 – Increase in Transparency and Choice in the Rx Element of the Insurance System

1. The US is unlikely to move to a socialized healthcare system, rather it will remain a predominantly insurance based system
2. The cost of insurance is simply the (amortized) cost of the benefit garnered
3. The "Alice in Wonderland" insurance system is access to all drugs for all citizens, that is simply not financially feasible for the system (and is also "unlimited socialized medicine", which exists nowhere in the world!)
4. A basic (consumer) principal of insurance is differential coverage for differential cost
5. The differential coverage for differential cost system already exists in the US! The two key problems with current system are:
   (a) the end-consumer has little/no choice in selection of the Rx benefit,
   (b) there is little transparency in the cost/level of coverage
6. We propose a Consumer Chosen Rx Benefit system, where Rx benefit is directly proportional to the cost/level of insurance coverage with full transparency and choice



Source: MTS analysis

5. Appendix

MTS | HEALTH PARTNERS

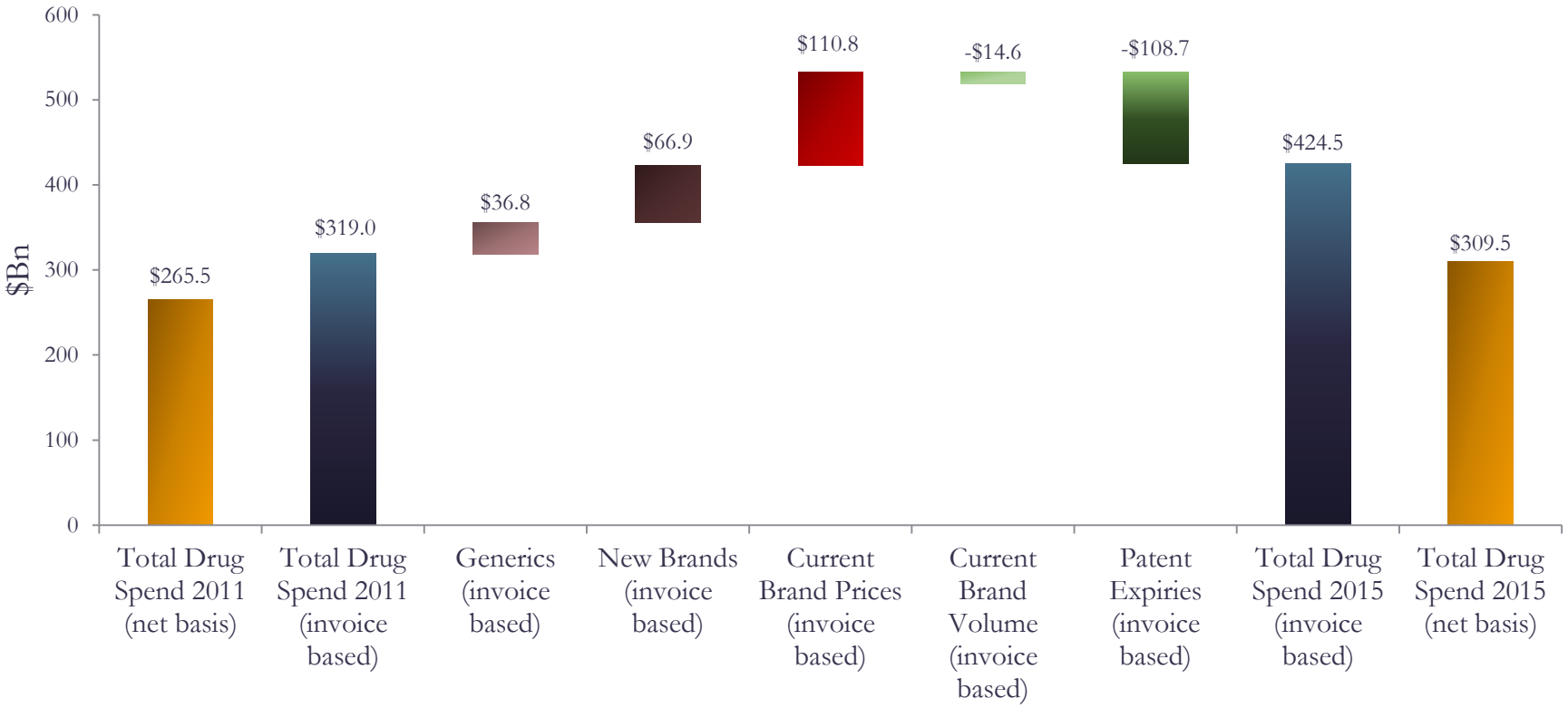
The Small Molecule Patent Cliff has Funded Historic Price Increases – Next Gen of Innovative Drugs will Require System Change

Patent Expiry Headroom Decreasing Going Forwards

- In 2016-2020 there is an estimated $178bn of patent savings, which is higher in absolute dollars, but lesser in percentage contribution than the past five years and no year will reach 2012 expiry levels

Next Generation Innovative Drugs Have "Inerrant" Higher Prices

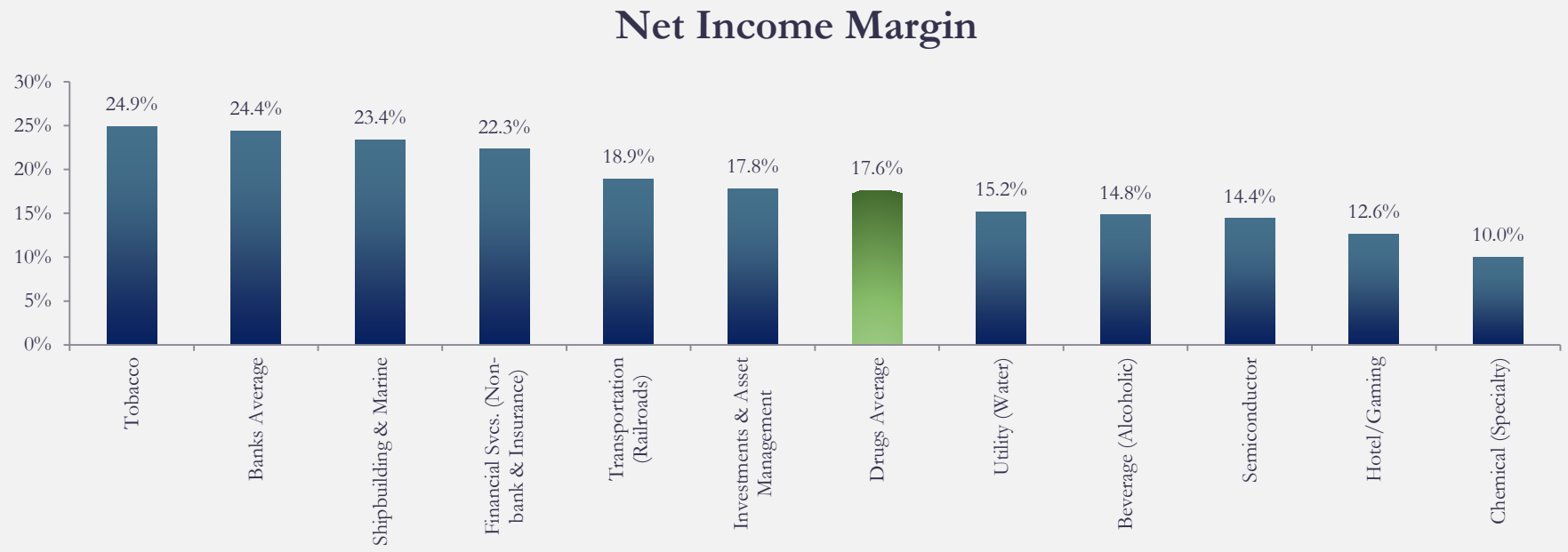
- Increased proportion of orphan drug launches
- Increased proportion of truly innovative and high cost combination therapies (e.g. I-O)



Sources: Kaiser Family Foundation. 1960-2014 based on National Health Expenditure and 2014-2024 Projected from CMS; MTS analysis

Current Biopharma Margins are Reasonable - Would be <5% if US Drug Prices Equaled CDW

- The graph below presents the cumulative net margins of all US public companies in a database compiled by an NYU Professor of Finance (many thanks!)
- Hence, the database takes all global revenues and costs (for a given year) for each sector
- Of the 648 biopharma companies in the database 17% are profitable and 83% are loss making (given that the vast majority of biotechnology companies are pre-revenue and focus on innovative R&D) - The biotech sector also has a large proportion of private companies (about 20x the number of public ones) which are essentially all loss making
- If US drug prices moved to CDW prices the Industry would have <5% net margins



(1) Aggregate of all companies within each sector with at least $0M market cap.

(2) Non bank or insurance.

Source: Aswath Damodoran, Professor of Finance at NYU (Damodaran.com); MTS analysis

We All Know Tech Heroes, What About Biotech Heroes Who Actually Contributed to Saving and Improving Quality of Life?

Tech Heroes

- **Sergei Brin and Larry Page** – founders of Google
- **Steve Case** – cofounder of America Online (AOL)
- **Jack Dorsey** – cofounder of Twitter
- **Bill Gates** – founder of Microsoft
- **Steve Jobs and Steve Wozniak – cofounders of Apple**
- **Pierre Omidyar** – founder of Ebay
- **Sean Parker** – creator of Napster and Facebook's first President
- **Peter Thiel and Elon Musk** – founders of PayPal (and Tesla)
- **Mark Zuckerberg** – founder of Facebook

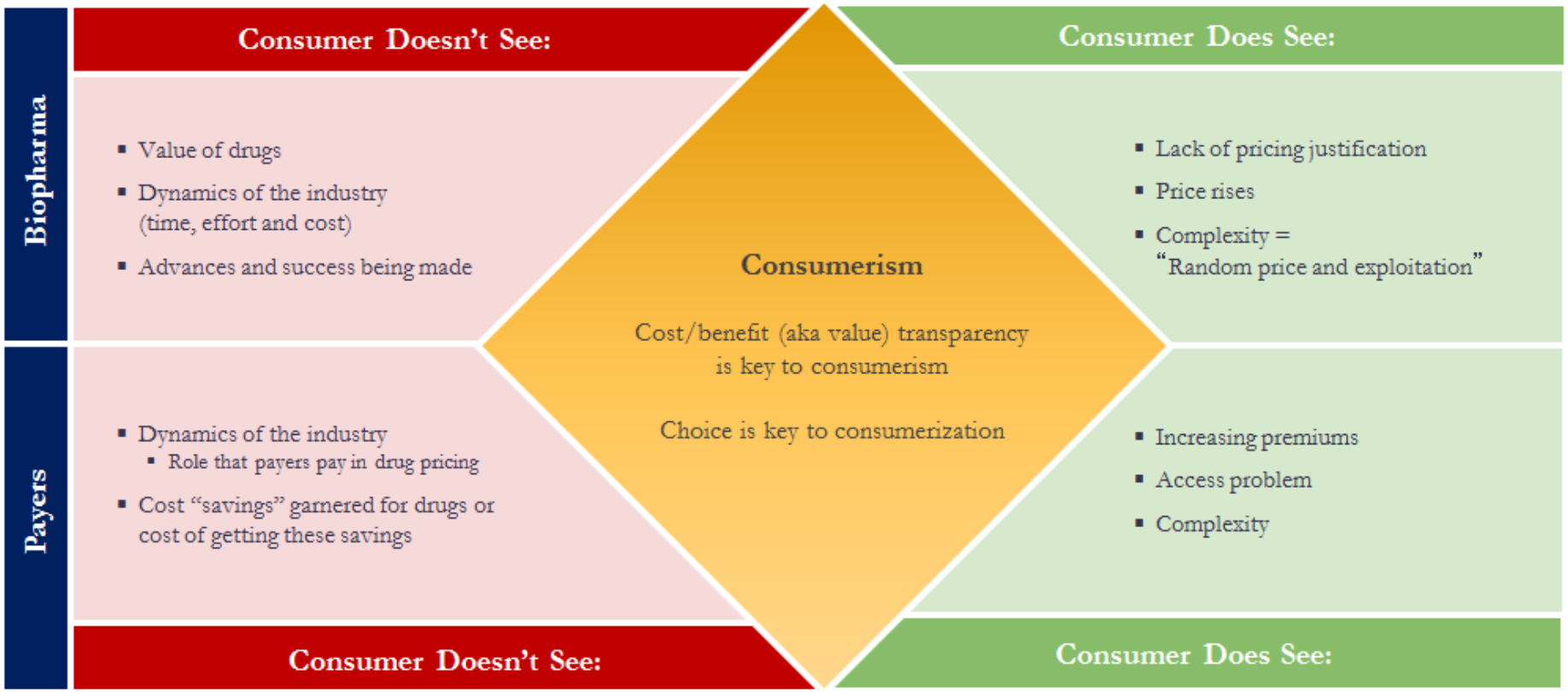
Biotech Heroes

- **Herbert Boyer & Staneley Cohen** - inventors of recombinant DNA technology, which launched biotechnology as we know it
- **Robert Langer** - MIT Professor - pioneer in tissue engineering and drug delivery and founder of numerous biotech companies
- **Arthur Levinson** – former CEO Genentech – accredited with turning around Genentech with launch of Rituxan and Herceptin
- **Stelios Papadopulos** - Chairman of Biogen, Exelixis, Regulus – scientist, analyst, "godfather" of biotech banking and mentor
- **William Rastetter** - as a CEO of IDEC he was instrumental in the company's decision to develop Rituxan
- **George Rathmann** - former CEO of Amgen - accredited with teaching the biotech industry how to raise money and direct R&D
- **Len Schleifer/George Yancopoulos** – CEO and CSO Regeneron – building a leading company on leading science
- **Robert Swanson –** cofounder of Genentech – VC who convinced Herbert Boyer that recombinant DNA had commercial value
- **Craig Venter** – founder of Celera Genomics – successfully led the first complete sequencing of the human genome

Source: MTS analysis

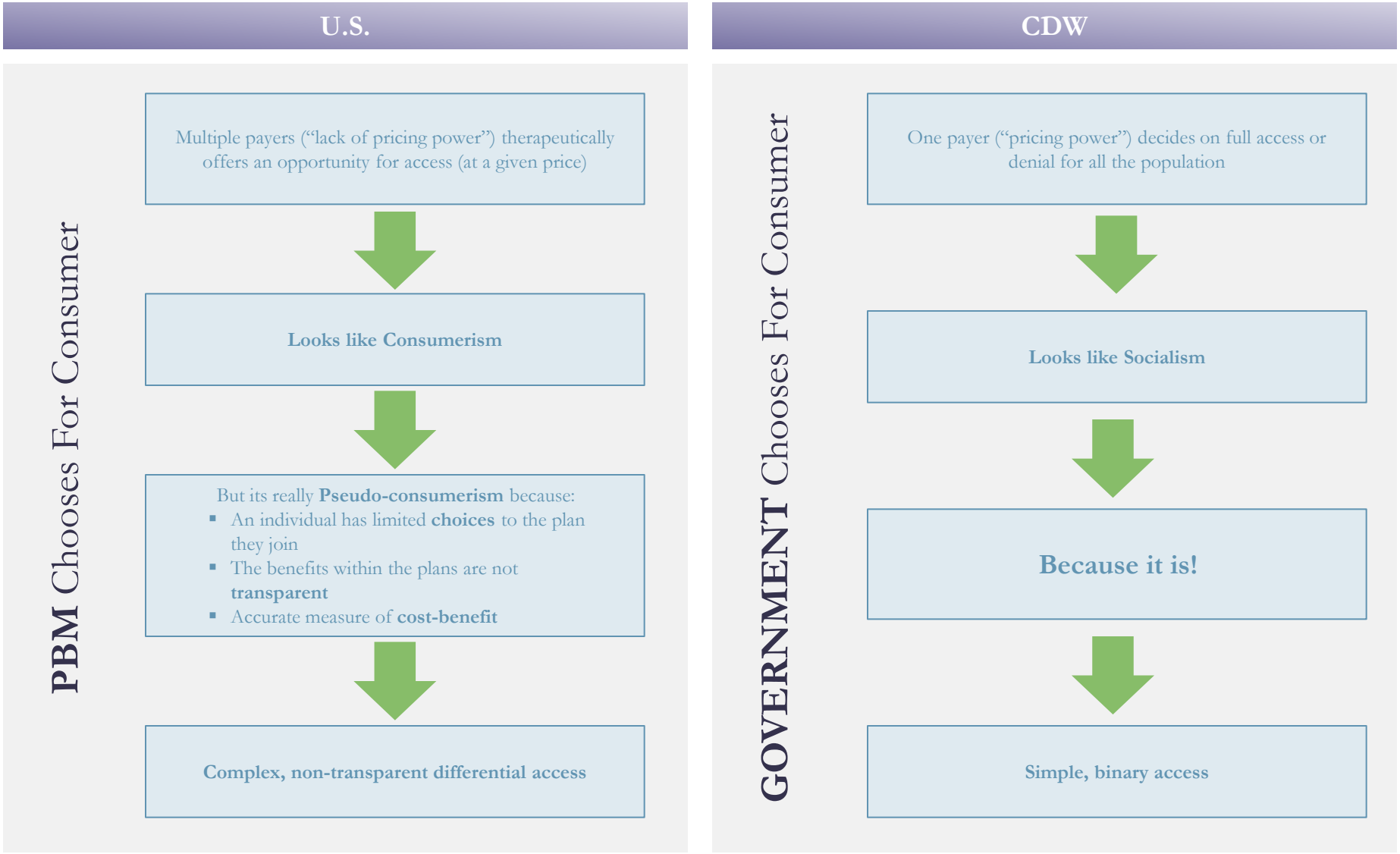
Consumerism is Central to the US Drug Pricing Debate

What Consumer Sees and Does Not See



Source: MTS analysis

CDW System = Socialism
The US system = Pseudo-Consumerism or Pseudo-Fragmented Dictatorship?



Source: MTS analysis

New Era of Innovation Will Drive Next Round of Drug Discovery

Why is now the right time to foster innovation?

Next Generation Technologies + New Therapeutic Agents

- New drug discovery technologies/tools include combinatorial chemistry, high-throughput screening, DNA sequencing and proteomics
- These technologies give more detailed understanding of human biology and disease mechanisms and provide avenues for drug design
- Drugs forms have expanded well beyond small molecules to now encompass antibodies, peptides, as well as DNA and RNA molecules

Transformational Clinical Benefit – Now focused on Achieving Cures

- New technology/knowledge has enabled companies to pursue treatments that address significant unmet medical needs and radically transform the lives of patients
- Examples: breakthrough HCV drugs, as well as the TKIs, which have allowed CML patients to achieve life expectancy in line with the general public

Value-based Pricing – A Mechanism that Rewards Innovation

- Value pricing, when adequately defined, eliminates the lack of transparency that currently plagues drug pricing in the US
- A 'valued priced' mechanism is consistent with current trends in healthcare services, like value-based insurance designs
- System will reward and incentivize those actors who pursue truly innovative treatments

Source: MTS analysis

Basic Concepts of Innovation in Free Markets – Where Do Drugs Fit Into This?

The extent of price caps in the US is hard to accurately assess for the overall drug market, but given that the process has started, the momentum is likely to increase	✗	New drugs in a therapeutic area tend to command a premium but older drugs simply catch up in price – e.g. MS and RA
To sustain "innovation pricing premium" constant improvements have to be made	✓	Despite very long life cycles in biopharma, we are in the era where relatively few rapid, improved follow-ons are approved and launched (e.g. Yervoy and Opdivo)
Innovation for innovation's sake does not work. Innovation needs to have utility	✓	Development of targeted and specialized therapies is much more important than if the novel therapy is a small molecule or mAbs
Innovation in big steps is great, but little steps which have real utility are equally valuable and needed	✓	New mechanism of action for unmet need gets rewarded, as does subsequent, improved safety
Innovation in many FMC goods have had to deal with costs approaching capital expenditure and cost of goods; this led to the respective industry adapting to novel pricing.	✗	Biopharma has been slow to adopt its pricing model. It will have to face changes in the near future (e.g. I-O)
Innovation must lead to drugs that will work in the majority of the population it's sold too	✗	Clinical trial settings do not reflect "real world" patient populations; currently, the system does not look or address drug effectiveness once the drug is on the market
Innovation tends to have high pricing transparency and costs which are more globally equilibrated	✗	Little pricing transparency (in the US) and global prices that are highly differentiated

Source: MTS analysis

Orphan Drugs are Unlikely to Stay Immune from the Drug Pricing Debate for Much Longer

There is unlikely to be any direct pharmacoeconomic or cost/benefit measure for most orphan drug prices…

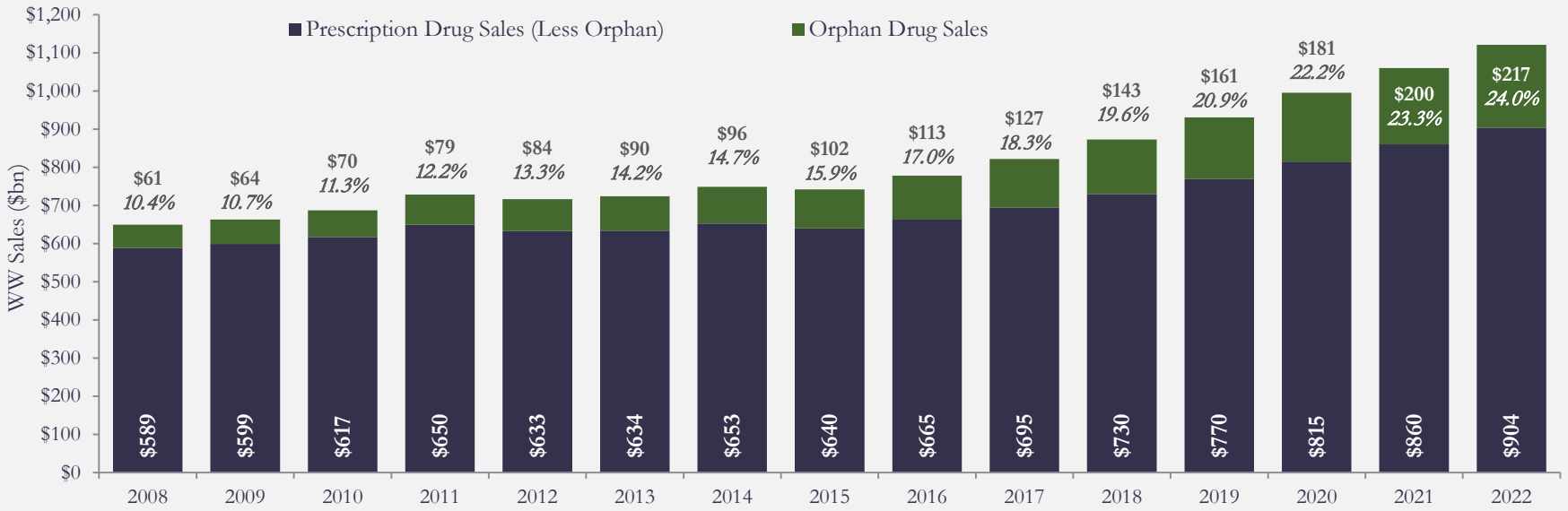
…But there are two key drivers for society in developing and appropriately pricing orphan drugs:

1. "Humanitarian insurance" – i.e. I am willing to give a small fraction of my healthcare costs for the few people with devastating diseases
2. Orphan drugs (and concomitant enabling technologies) frequently aid the development of drugs for much larger populations (e.g. gene therapy and RNAi)

…however there is a limit to the proportion of healthcare/drug costs that society will pay for orphan drugs in totality. Are we starting to reach this level?

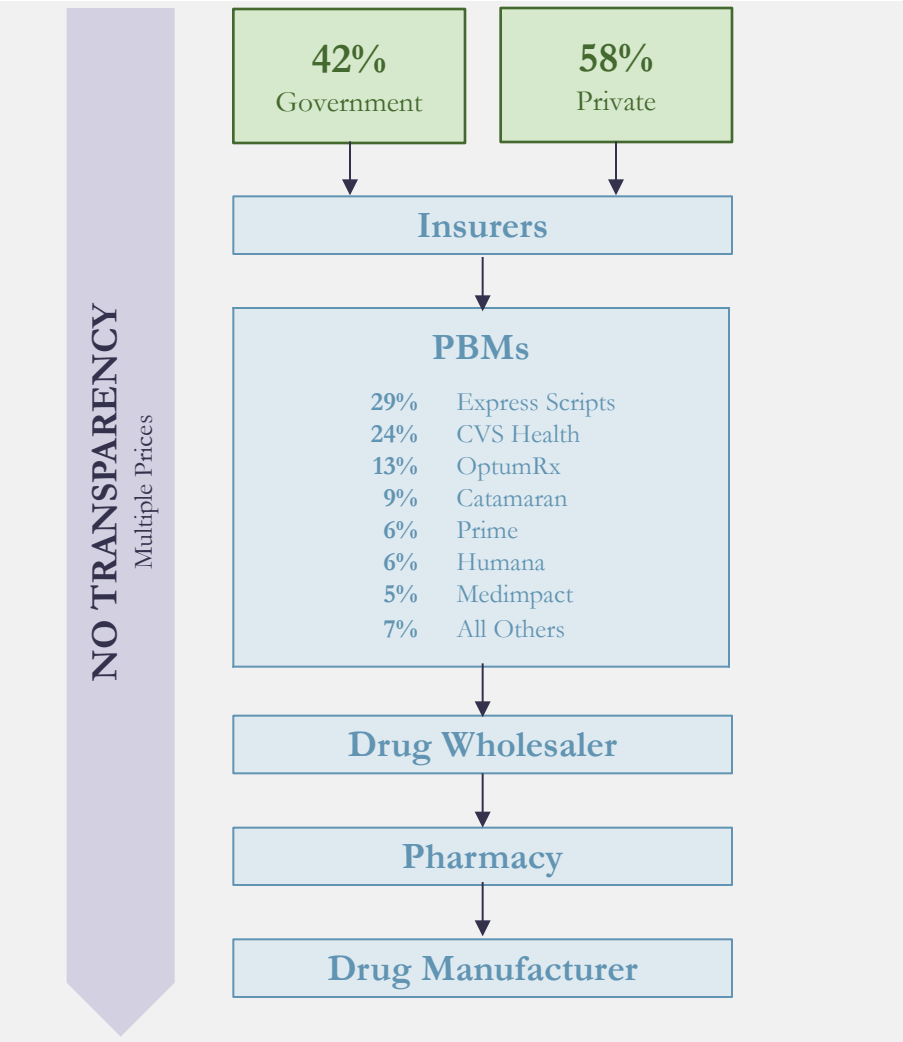
In 2008, ~10% drug costs were for orphan drugs. According to Evaluate Pharma projections this will rise to >20% by 2019

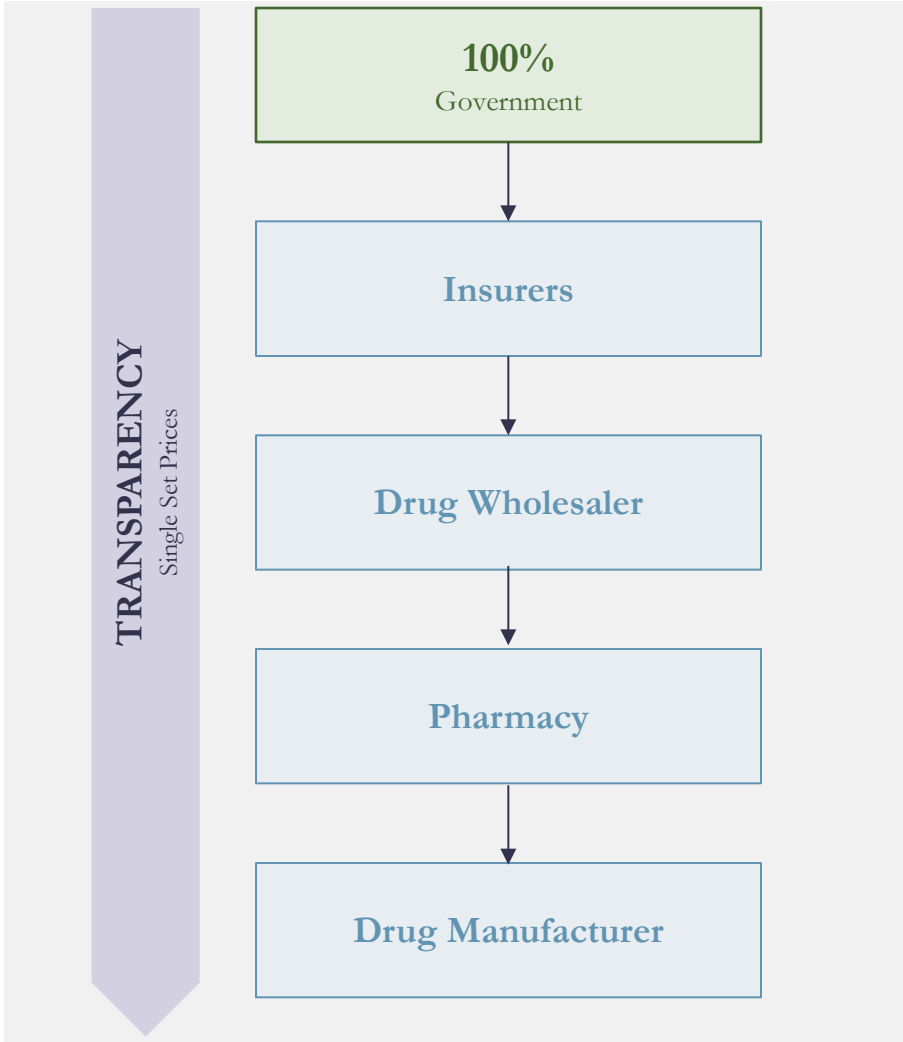
"Ballpark" cost/benefit will impact orphan drug prices and/or access (e.g. Anthem is not covering Exondys 51 (September 2016))



Source: EvaluatePharma as of 09/23/16; MTS analysis

PBMs are Unique to the US Drug Pricing System





Source: MTS analysis

The "Swings and Round-Abouts" of US Insurance System: Different Paying Structures with the Same Overall Cost

The US insurance system is comprised of various plans which offer consumers different fee structures

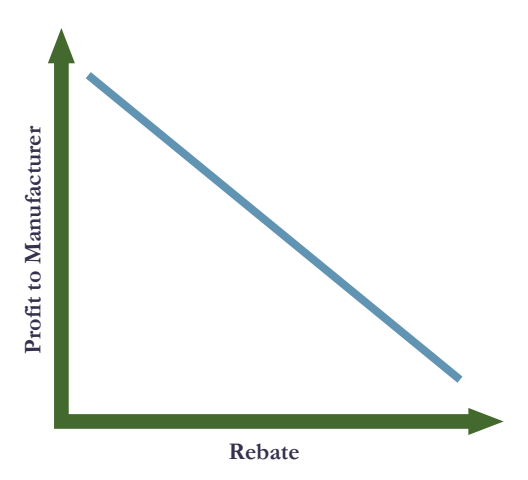
For example, plans with relatively high premiums are likely to have low coinsurance/copays, while plans with low premiums are more likely to have high coinsurance/copays

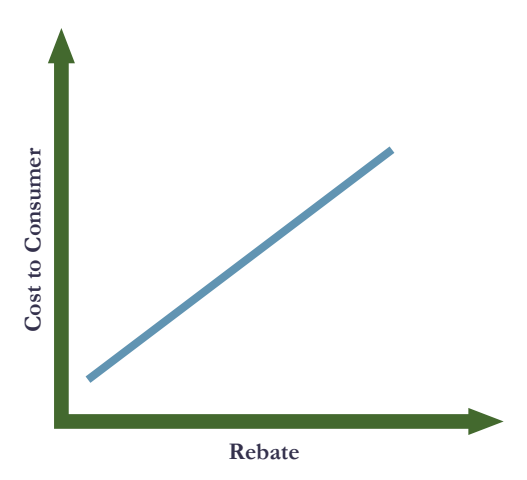
Ultimately, whichever fee structure is chosen, the overall cost always ends up to be the same

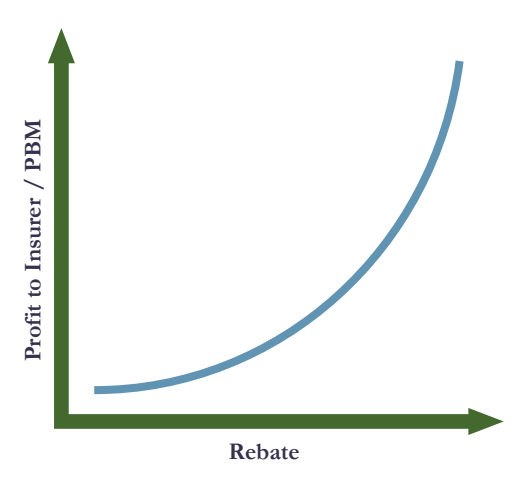
	Deductible	Coinsurance/Copay	Avg Spend
High Deductible; Low Coinsurance	$900	$100	$1000
Medium Deductible; Medium Coinsurance	$500	$500	$1000
Low Deductible; High Coinsurance	$100	$900	$1000

Source: MTS analysis

Insurers/PBMs Benefit from Larger Rebates and List Price Increases







Source: MTS analysis

Select Healthcare Systems' Macro Statistics

		Australia	Canada	UK	France	Germany	Japan
2013 Population	Total population (millions)	23.132	35.317	64.107	63.790	80.646	127.296
	% of population >65	14.4%	15.2%	17.1%	17.7%	21.1%	25.1%
Spending, 2013	% of GDP spent on health care	9.4%a	10.7%	8.8%	11.6%	11.2%	10.2%
	Health care spending per capita	$4,115a	$4,569	$3,364	$4,361	$4,920	$3,713
	Avg. annual growth rate of real health care spending per capita, 2009–13	2.42%b	0.22%	–0.88%	1.35%	1.95%	3.83%
	Out-of-pocket health care spending per capita	$771a	$623	$321	$277	$649	$503a
	Hospital spending per capita	$1,645a	$1,338	n/a	$1,600	$1,423	1,673a
	Pharmaceutical spending per capita	$590a	$761	n/a	$622	$678	$756a

Source: The Commonwealth Fund, International Profiles of Health Care Systems, 2015

[a] 2012

[b] 2009-12

[c] Adjusted for differences in the cost of living; MTS analysis

Select Healthcare Systems' Utilization Indicators

		Australia	Canada	UK	France	Germany	Japan
Hospital spending, utilization and capacity, 2013	Acute care hospital beds per/1000	3.36a	1.71a	2.28	3.35	5.34	7.92
	Hospital spending per discharge	$9,529a	$15,916a	n/a	$9,622	$5,641	$14,408b
	Hospital discharges per/ 1000	173a	83a	129	166	252	111b
	Avg. length of stay for curative care (days)	4.8a	7.6a	5.9	5.7	7.7	17.2
Public views of health system, 2013	Works well, minor changes needed	48%	42%	63%	40%	42%	n/a
	Fundamental changes needed	43%	50%	33%	49%	48%	n/a
	Needs to be completely rebuilt	9%	8%	4%	11%	10%	n/a

Source: The Commonwealth Fund, International Profiles of Health Care Systems, 2015

[a]2012

[b]2011

[c]Adjusted for differences in cost of living; MTS analysis

Select Healthcare Systems' Financing and Coverage

Healthcare System and Public and Private Insurance Role

	Government Role	Public System Financing	Private Insurance Role
Australia	Regionally administered, joint (national & state) public hospital funding; universal public medical insurance program (Medicare)	General tax revenue; earmarked income tax	~47.3% buy complementary (e.g., private hospital and dental care, optometry) and supplementary coverage (increased choice, faster access for nonemergency services, rebates for selected services)
Canada	Regionally administered universal public insurance program that plans and funds (mainly private) provision	Provincial/federal general tax revenue	~67% buy complementary coverage for non-covered benefits (e.g., private rooms in hospitals, drugs, dental care, optometry)
England	National Health Service (NHS)	General tax revenue (includes employment-related insurance contributions)	~11% buy supplementary coverage for more rapid and convenient access (including to elective treatment in private hospitals)
France	Statutory health insurance system (SHI), with all SHI insurers incorporated into a single national exchange	Employer/employee earmarked income and payroll tax; general tax revenue, earmarked taxes	~95% buy or receive government vouchers for complementary coverage (mainly cost-sharing, some non-covered benefits); limited supplementary insurance
Germany	Statutory Health Insurance system, with 124 competing SHI insurers (not-for-profit "sickness funds" in a national exchange); high income can opt out for private coverage	Employer/employee earmarked payroll tax; general tax revenue	~11% opt out from statutory insurance and buy substitutive coverage. Some complementary (minor benefit exclusions from statutory scheme, copayments) and supplementary coverage (improved amenities)
India	Divided between the central govt and the state. States are responsible for the delivery of health services. Central govt's responsibilities include policy making, developing regulatory framework and supporting the states' work	General tax revenue	Limited role (<5% of total expenditure) providing substitutive coverage for the upper class urban population
Japan	Statutory health insurance system, with >3,400 noncompeting public, quasi-public and employer-based insurers. National government sets provider fees, subsidizes local governments, insurers, and providers and supervises insurers and providers	General tax revenue; insurance contributions	Majority of population has coverage for cash benefits in case of sickness, usually together with life insurance. Limited role of complementary and supplementary insurance offered separately from life insurance

Source: The Commonwealth Fund, International Profiles of Health Care Systems, 2015; MTS analysis

Select Healthcare Systems' Provider Organization and Payment

	Provider Ownership		Provider Payment	
	Primary Care	Hospitals	Primary Care Payment	Hospital Payment
Australia	Private	Public (~65% of beds), private (~35%)	~95% FFS, ~5% incentive payments	Global budgets and case-based payment in public hospitals (includes physician costs); FFS in private hospitals
Canada	Private	Public/private mix (proportions vary by region), mostly not-for-profit	Mostly FFS (~45%–85%, depending on province), but some alternatives (e.g., capitation) for group practices	Mostly global budgets, case-based payment in some provinces (does not include physician costs)
England	Mainly private, limited number of NHS-owned practices with salaried physicians	Mostly public, some private	Mix capitation/FFS/P4P; salary payments for a minority (the salaried GPs are employees of private group practices, not of the NHS)	Mainly case-based payments (60%) plus budgets for mental health, education, and research and training. All include physician costs, drug costs, etc.
France	Private	Mostly public (67% of capacity), some private for-profit (25%) and private not-for-profit	Mix FFS/P4P/flat EUR40 [USD48] bonus per year per patient with chronic disease and regional agreements for salaried GPsa	Mainly case-based payments (includes physician costs in public hospitals but not in private) and non-activity-based grants for education, research, etc.
Germany	Private	Public (~50% of beds); private nonprofit (~33%); private for-profit (~17%)	FFS	Case-based payment (includes physician costs)
India	Mainly public, some private in urban areas	Private non- and for-profit (~63% of beds) and public	Salary for staff at public providers, FFS (paid OOP) for private providers	Global budgets for public hospitals
Japan	Mostly private	Mainly private nonprofit (~80% of beds), some public (~20%)	Most FFS, some per-case daily or monthly payments	Case-based per diem payments plus FFS, or FFS only (includes physician costs)

Source: The Commonwealth Fund, International Profiles of Health Care Systems, 2015 [bracketed] figure in USD was converted from local currency using the purchasing power parity conversion rate for GDP in 2014 reported by the Organisation for Economic Co-operation and Development (2015).; MTS analysis

6. MTS Health Partners, L.P.

MTS Health Partners, L.P. Overview*

Investment Banking

- Founded in 2000
- Privately owned, independent firm
- Aligned strategic and financial advisory services to healthcare companies of all sizes, from global corporations to venture-backed businesses
- Experience with a broad range of client and transaction types
  - Mergers and acquisitions, recapitalizations, restructurings, private placements, PIPEs, IPOs, structured debt financings, royalty monetizations and general strategic advice
- Senior partners all previously at bulge-bracket firms
- 34 closed transactions with total value of over $7.5bn since January 2015

Healthcare Services

- Managed Care
- Hospitals/Outsourced Services
- PBMs & Pharmacy Services
- Dialysis
- Home Healthcare/Hospice
- Post-Acute Facilities (SNF, IRF, LTACH, Hospice)
- HCIT
- Clinical Laboratories
- Healthcare Distribution/Supply
- Pharma Services

Life Sciences

- Pharma/Biotech
  - Large, Mid, Small Cap
- Specialty Pharma
- Generics
- Medical Devices
- Diagnostics
- Consumer Health
- Cell Therapy
- Outsourced Pharma Services

Advantages of a Partnership with MTS

Experienced	**Senior personnel –** decades of healthcare experience at top bulge-bracket investment banks
Attentive	**41 professionals –** larger size than most bulge-bracket healthcare teams ensures personal focus
Independent	**Stability** of execution, **unencumbered by balance sheet conflicts**
Trusted	**Long-term relationships** rather than short-term transactions, translating into **unbiased** advice
Aligned	Private equity mentality allowing for an **investor-focused perspective**
Healthcare – Focused	Unparalleled network provides **broadest reach** of any healthcare advisor

Source: MTS; * Securities offered through MTS Securities, LLC, an affiliated entity.