

Prescription Drug Spending in the U.S.:
Is the Era of Slow Growth Over?
An Update of an Article with the Same Title
in the September 2016 issue of *Health Affairs*

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- The opinions and findings reported in this research are those of the authors, and are not necessarily those of the Research Sponsor or the institutions with whom the authors are affiliated. The authors accept responsibility for any mistakes and misrepresentations.
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Background

- US *invoice-based* spending on *retail* prescription pharmaceuticals increased by 14.2% in 2014 and 12.2% in 2015 – the largest increases since 2002
- Inclusive of *non-retail channels*, 2014 (2015) US invoice-based spending increased by 12.8% (11.8%) in real terms, much greater than average 1.8% growth 2005-2013.
- Is the recent era of slow price and spending growth over, and are we returning to a much earlier path of very rapidly increasing pharmaceutical prices and spending? This is our focus.
- The Rx drug market landscape is changing dramatically – buyer and PBM consolidation has increased, as has M&A activity among generic manufacturers; list prices are increasing along with negotiated rebates; following ACA, more folks are insured, but many with high deductible policies; innovations on supply side are increasing spending, but demand side efforts are focused on cost-saving
- How will these various potentially offsetting trends affect the growing “pharms” race?

Study Data and Methods: I

- We use QuintilesIMS' National Sales Perspective Data (NSP) that differ from CMS' published National Health Expenditure Accounts (NHEA) in two major ways:
- First, NSP tracks spending in both retail and institutional (e.g., provider hospitals, physicians, nursing homes, outpatient clinics) channels, not just retail channels monitored by NHEA that exclude rapidly growing specialty medicines (e.g., oncology and inflammation-related drugs)
- In 2014 these institutional/provider channel purchases accounted for about 21.9% of total NSP prescription drug spending – slightly larger in 2015, so very substantial and growing gap between NSP and NHEA
- NHEA data includes estimates of off-invoice rebates, whereas traditional NSP data have historically not included off-invoice rebates to insurers, providers, and pharmaceutical benefit management firms (PBMs)

Study Data and Methods: II

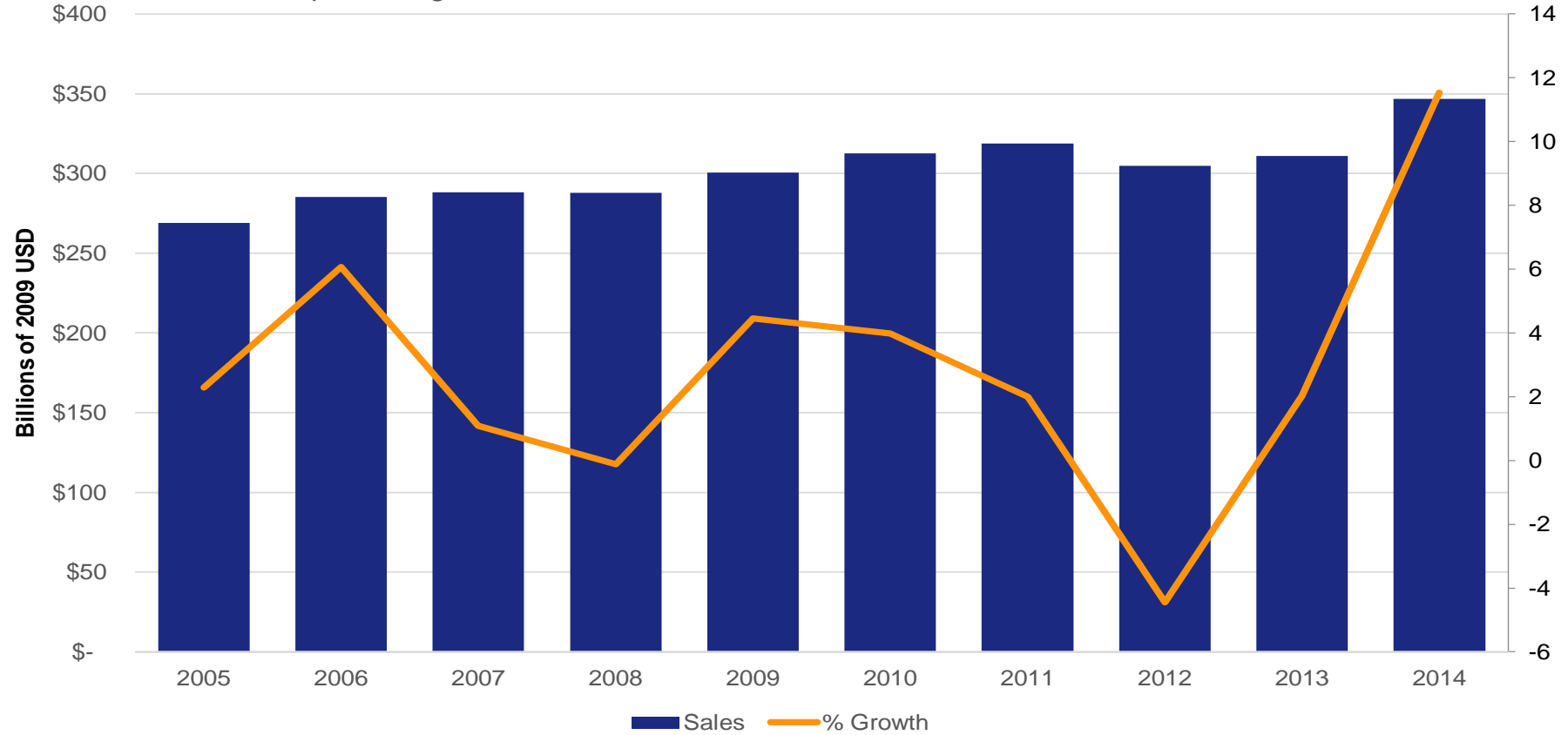
- Recently IMS has begun publishing aggregate estimates of off-invoice rebates, distinguishing “invoice sales” from “net sales” (*IMS Health, IMS Market Prognosis 2013-2017: North America-United States*, London, UK, September 2013; *Medicine Use and Spending in the US: A Review of 2015 and Outlook to 2020*, April 2016).
- IMS estimates aggregate average rebates by comparing NSP invoice data with net sales data disclosed for some brands in SEC 10K or 10Q filings and other public documents by manufacturer. The rebate share is computed as the percent difference between invoice and reported net sales; IMS projects average rebate share by therapeutic class when SEC and other public data are not available
- Related research has been reported in the 1 May 2015 publication by Credit Suisse, “*Global Pharma: Rising US Rebates Limit Margin Expansion*”. This reports estimated 2014 company-specific rebate data for 20 brand companies.

Study Results (Exhibit 1)

- 2006-2014 invoice spending for US prescription drugs, adjusted for inflation using the St. Louis Federal Reserve quarterly GDP price deflator, are presented in Exhibit 1
- Annual changes in real invoice spending have varied from a \$14.2 billion decline in 2012 to a \$35.8 billion increase in 2014
- In Exhibit 2 we decompose this growth into price and quantity components for brand and generic drugs, for new products launched in the prior two years, and for branded drugs that have lost exclusivity

Exhibit 1

Invoice Sales of Prescription Drugs



Note: Total sales of all prescription drugs, through all channels, but does not reflect off-invoice discounts and rebates. Spending is in 2009 dollars adjusted using the quarterly GDP deflator series provided by the St. Louis Fed.

Five Main Study Results: I (Exhibit 2)

- Between 2005 and 2013, growth of Rx pharmaceutical *real invoice* spending decelerated, from 6.1% in 2006 to a -4.5% in 2012.
- Second, in each year, increased *real invoice prices of incumbent brands* accounted for the largest share of overall spending growth, becoming particularly dominant in 2009.
- Note that while the number of innovative drugs approved by the FDA steadily increased in recent years, it is real invoice prices of *incumbent* brand drugs – not innovative new drugs – that fueled the overall real invoice price spending increases in years 2005-2013
- 2014 different in this way – increased spending on new blockbuster hepatitis C drugs a big factor affecting overall real invoice price spending

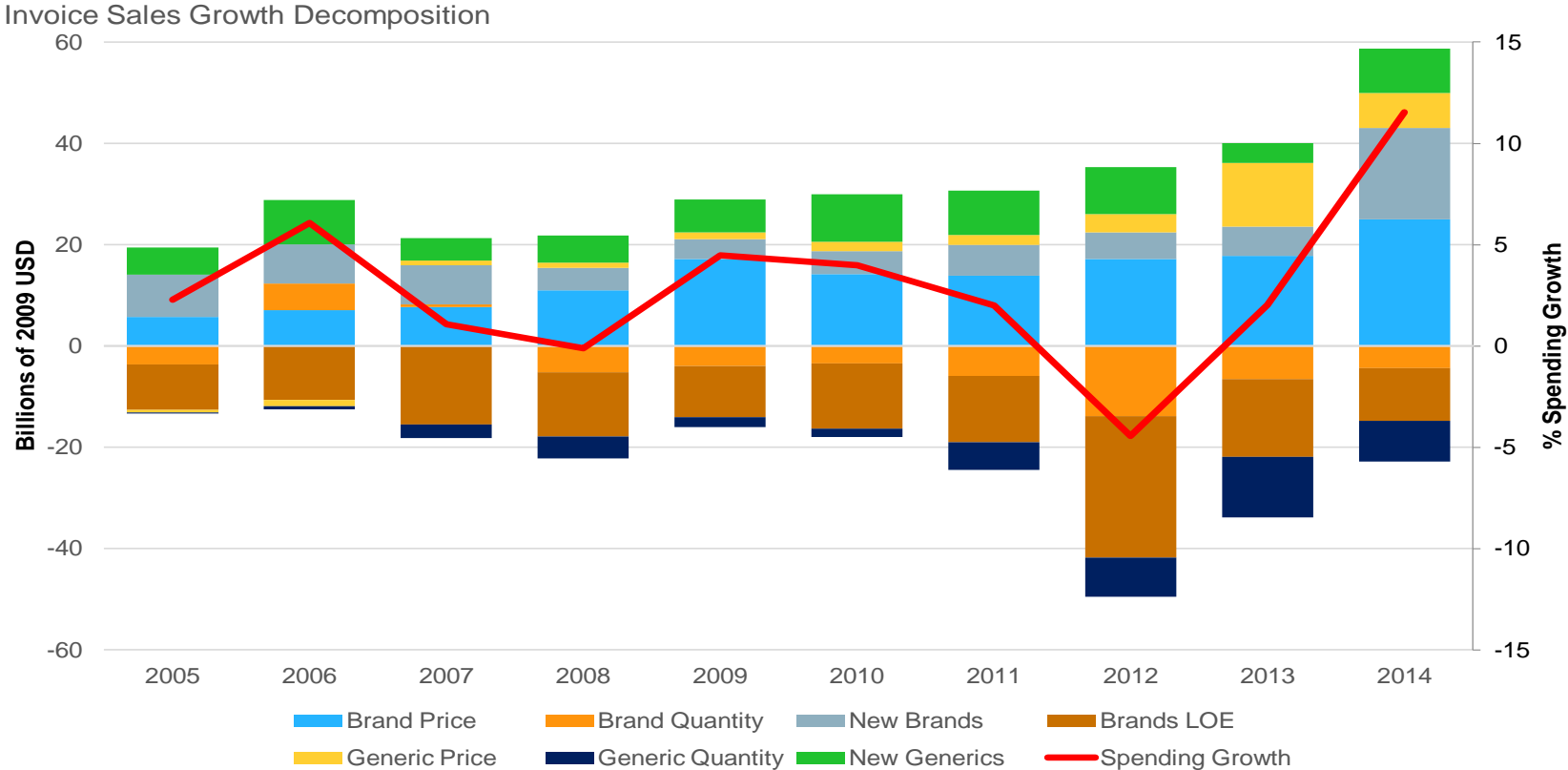
Main Study Results: II (Exhibit 2)

- Third, brand spending decreases resulting from loss of exclusivity (LOE) accounted for most of spending reductions, but this component was smallest in 2014, partially explaining the 2014 discontinuity
- LOE for incumbent brands was particularly large in 2012 when blockbuster drugs such as Lipitor™, Plavix™, Singulair™, Actos™ and Lexapro™ faced initial generic competition
- Products with LOE in 2012 accounted for \$49 billion in real invoice spending in 2011. By 2013, real invoice spending on those same brands and their generic counterparts had declined almost 80% to \$10.5 billion.

Main Study Results: III (Exhibit 2)

- Fourth, 2014 was the first year in the previous decade that spending increased significantly owing to the introduction of new *brand* drugs, especially the new generation of antiviral hepatitis C drugs Sovaldi™, Olysio™, Viekira Pak™ and Harvoni™.
- Other newly launched drugs treating cancers, multiple sclerosis, and diabetes also contributed to the 2014 growth in real invoice drug spending
- Finally, while prices of incumbent *generic* drugs have been increasing slightly since 2007, in 2013 and 2014 their increases were markedly greater and contributed more substantially to overall real invoice drug spending

Exhibit 2



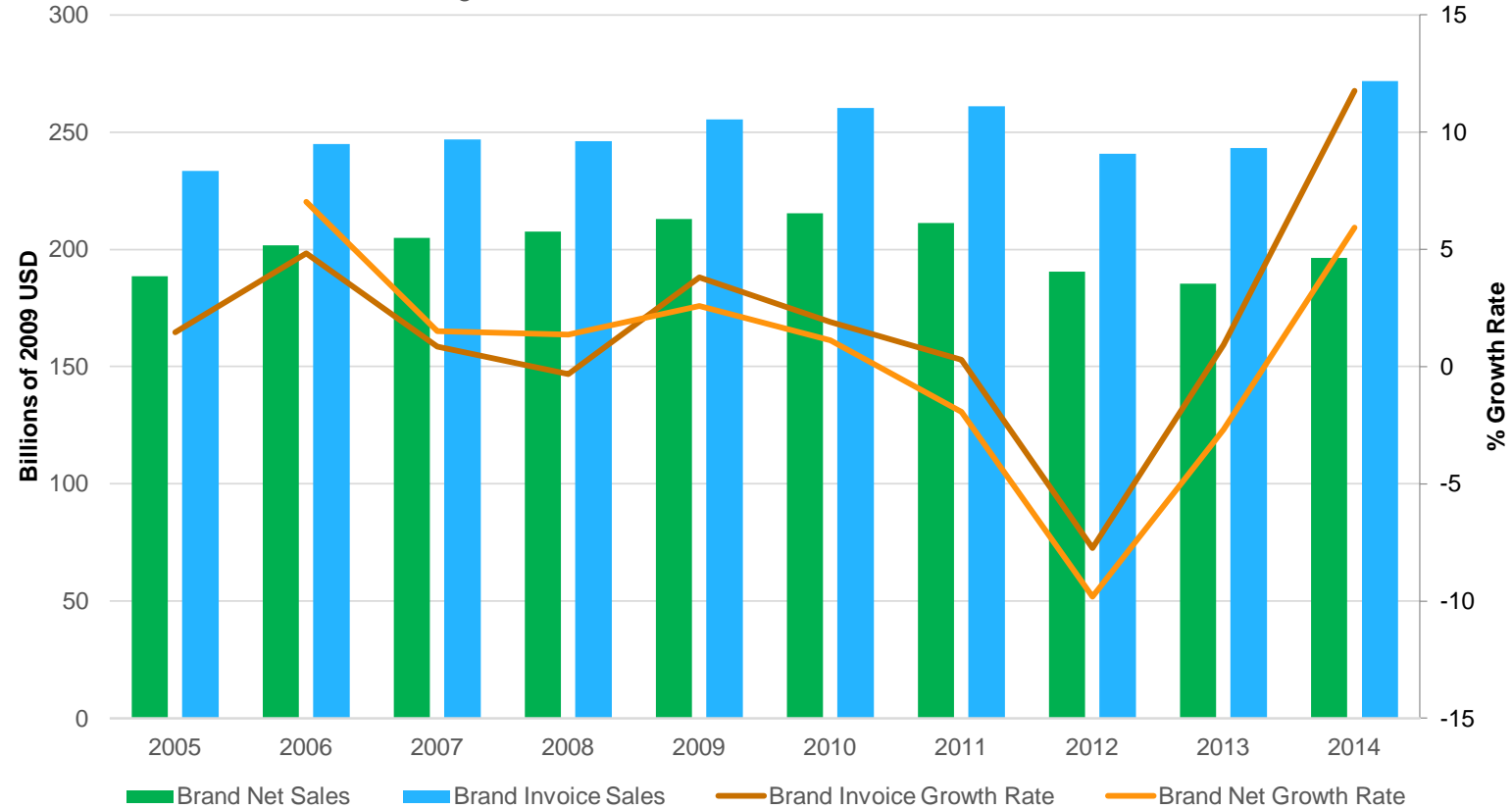
Note: Total sales of all prescription drugs, through all channels, but does not reflect off-invoice discounts and rebates. New segments are defined as new to the segment within 24 months, with membership assigned quarterly and aggregated to calendar years.

Gross and Net Sales, and Prices (Exhibit 3)

- Between 2005 and 2012 rebates reduced spending on brand products by approximately 18% each year (Exhibit 3 – relative height of blue and green bars). However, between 2010 and 2014 rebates increased from 18% to 28% of total brand spending – highlighting the importance of the distinct net and gross price trends
- The compounded 2005-2014 annual invoice real growth rate of prices was 6.4%, whereas net of rebates it was 5.4%, with most of the difference occurring after 2009. The total amount of rebates provided by brand manufacturers is almost \$280 billion.
- Since brand price increases are the largest component in overall Rx drug spending growth, this difference has a significant impact on total spending: Incorporating rebates decreases the growth rate of total brand plus generic real pharmaceutical spending from 2.0% to -0.3% in 2013 and from 11.5% to 7.4% in 2014.

Exhibit 3

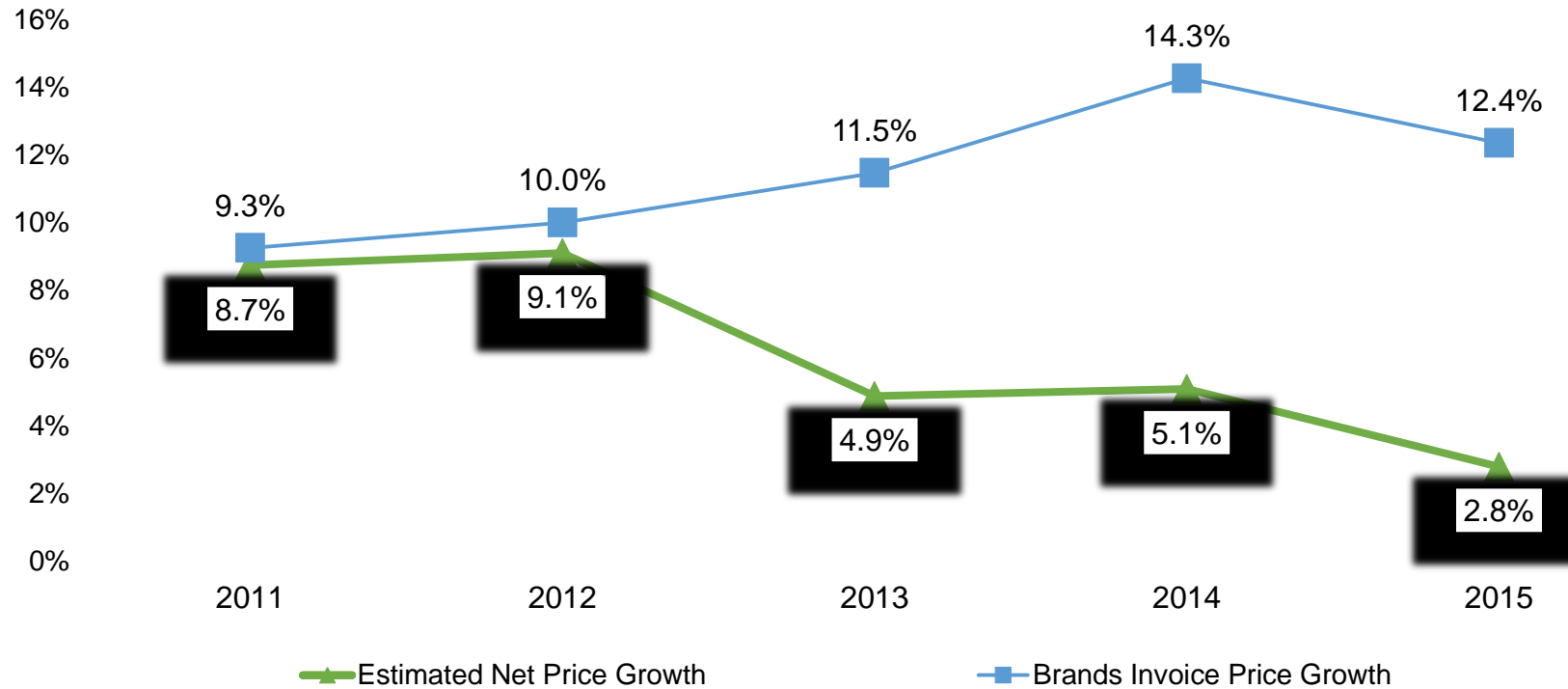
Invoice and Net Sales of Brand Drugs



Note: Total sales of branded prescription drugs, through all channels, reflecting sales net of off-invoice discounts and rebates where indicated

Net price growth slowed in 2015 to 2.8% as price concessions by manufacturers rose sharply

Protected Brand Invoice and Net Price Growth



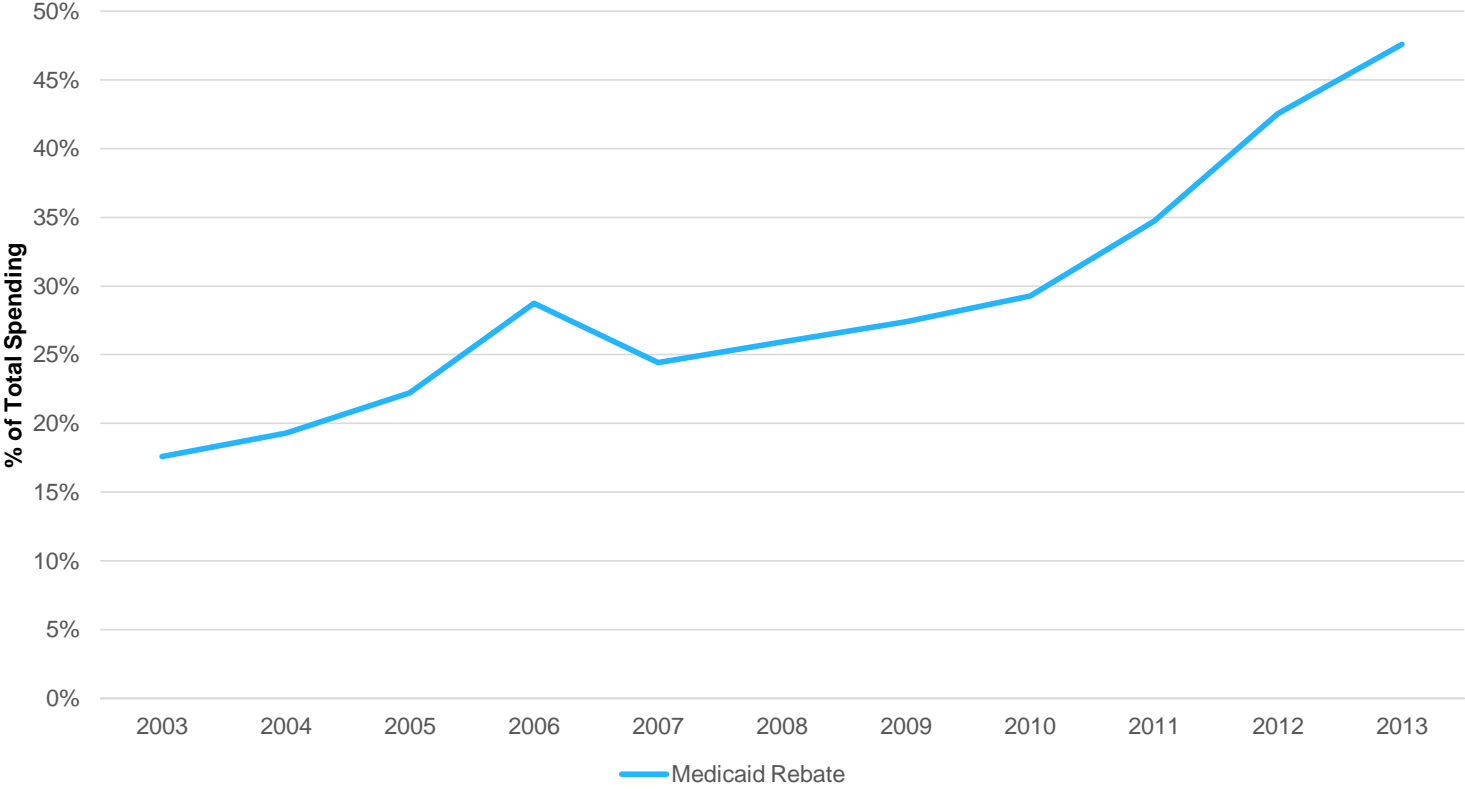
Source: IMS Health, National Sales Perspectives, IMS Institute for Healthcare Informatics, Mar 2016

The Importance of Medicaid Rebates (Exhibit 4)

- Rebates as a percent of gross Medicaid drug expenditures have increased dramatically 2003-2013 (no 2014 data available yet), from about 17.6% to 47.6%, reducing gross spending by almost a half.
- Most of the rebate increase occurred between 2010 and 2013, as provisions of the 2010 ACA legislation increased the minimal rebate from 15.3% to 23.1%.
- Due to the CPI kicker (that automatically increases the rebate percent on a one-for-one basis when growth in average manufacturer's price exceeds that of the CPI), the greater brand price increase in 2013-2014 discussed earlier formulaically triggered higher levels of brand rebates in the Medicaid program

Exhibit 4

Rebates to Medicaid Program



Medicare and Other Public Sector Rebates

- Medicare rebates have grown steadily, from 8.6% of total brand and generic drug costs (including the benefit portion of member premia) in 2006 to 12.9% in 2013 (no 2014 data available yet).
- In addition, the Medicare Coverage Gap Discount Program makes manufacturer discounts available to eligible Medicare beneficiaries receiving applicable covered Part D drugs while in the coverage gap, thereby reducing net prices.
- Manufacturers offer additional discounts to other federal (VA-DOD, Public Health Service), state (e.g., prison) and local (e.g., prison, family planning centers) government purchasers, as well as through the rapidly growing 340B program

Private Sector Manufacturers' Rebates: I

- Manufacturers also provide rebates to third party private payers, such as PBMs, hospitals and insurers. Much less is known about these rebates, but information gathered by IMS Health suggests that rebates tend to grow over the life cycle of brand drugs, peaking several years before LOE, but generally ceasing after LOE and generic entry.
- Considerable heterogeneity exists in the size of these rebates, both across firms (see the May 2015 Credit Suisse study) and across products within firms. Products in crowded therapeutic areas tend to have larger rebates. Discounts also differ across buyers, with larger buyers being able to extract greater rebates, particularly if they affect market share through formulary and utilization management policies.

Private Sector Manufacturers' Rebates: II

- In recent years, some PBMs have demanded and received multi-year inflation-protected contractual provisions incorporating automatic rebate increases whenever the list price is raised, leaving net prices unchanged
- The “pharms race” between new hepatitis C drug manufacturers and the PBMs has been highly publicized. In an earnings call to investors, Gilead announced that average discounts off list prices in 2013 on its hepatitis C drugs were about 22%, but by 2014 in the presence of several more competitors the average discounts off list prices increased to 46%.

Why the Simultaneous Increases in List Prices and Rebates?

- In context of Medicaid, simultaneity reflects formulaic policies
- High list prices combined with differential rebates appear to reflect the willingness and ability of brand manufacturers to charge distinct net prices to different sets of customers, i.e. the market power and practice of price discrimination. For this strategy to be feasible, purchasers must be heterogeneous in their willingness to pay, and arbitrage must be prohibited. In fact, arbitrage of this sort is mostly unlawful (e.g., hospitals can't sell to general public) or contractually prohibited in the US.
- Two recent market segmentation developments support increased price discrimination: Growth of PBMs, and expansion of the pool of individuals paying list price for pharmaceuticals. Let's look at each of them.

Recent US Market Segmentation Developments I: PBMs

- PBMs serve as intermediaries between manufacturers and insurers/payers, and between insurers/payers and network pharmacies, and occasionally also set up their own mail order and preferred network pharmacy operations.
- The three largest PBMs have increased their share of total commercial prescription volume from 42% in 2005 to 68% in 2015. This has increased their aggregated purchasing power and ability to extract rebates and discounts from manufacturers.

Recent US Market Segmentation

Developments II: More Cash-Paying Customers

- While the MMA and ACA reduced the number of uninsured individuals, the number of individuals enrolled in high deductible health plans (HDHPs), particularly those with health savings accounts (HSAs) has increased significantly – in 2015 24% of covered employees were enrolled in a HDHP, up six-fold from 4% in 2006.
- As more patients use these pharmacy and integrated HDHP accounts, and as deductibles increase, drug manufacturers are incentivized to increase their list prices to these cash-paying and less price-responsive consumers – for given thresholds, increased list prices means beneficiaries reach threshold more rapidly
- ACA also mandated a 50% discount on list prices for Medicare enrollees in the doughnut hole, creating incentives for manufacturers to raise list prices. Payer resistance can be meek, given a coinsurance rate of 25% and a rebate of 50%, payers only bear about 25% of list price (and of list price increases).

Recent US Market Segmentation Developments III: Muted Resistance to List Price Increases by PBMs, Others

- “Spreads” to wholesalers, PBMs and pharmacies are often a proportion of list prices
- Common practice by PBMs and wholesalers is to charge manufacturers a fixed fraction of list price to provide them with administrative and inventory services, increasing PBM/wholesaler revenues as list prices increase. Analogous indirect and direct intermediation remuneration (DIR) charges by PBMs to pharmacies participating in preferred narrow networks
- Example: Profit spread for PBMs and pharmacies is roughly the difference between prices reimbursed them by insurers and patients (say, list price minus 12%) and what they themselves pay for the drug (say, list price minus 15%), so as list prices increase, profit spread increases by $.03 * \Delta$ list price. This list price-dependent benefaction implies that PBMs, wholesalers and pharmacies face limited incentives to resist list price increases aggressively – though they still face competition

Generic Drug Prices - I: From Steady Decreases to Sharp Increases

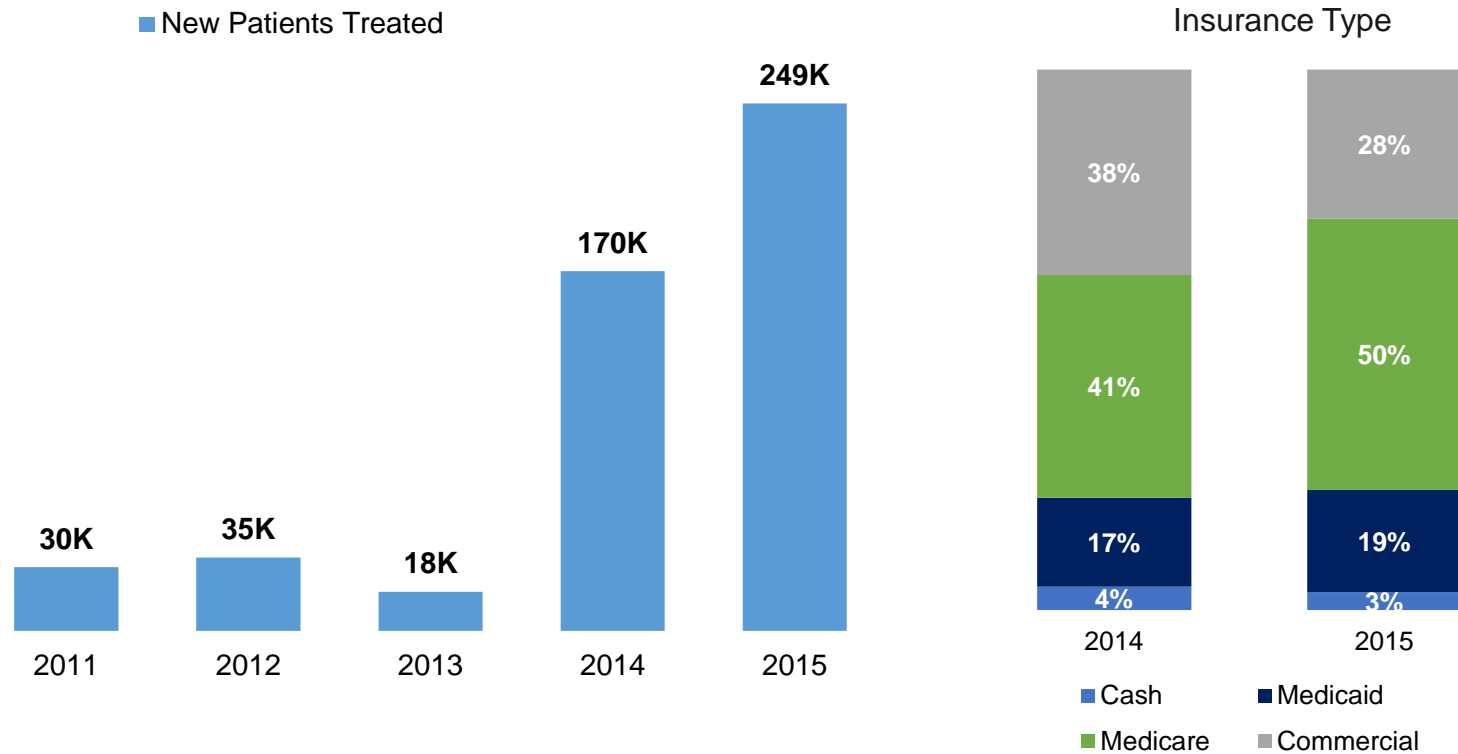
- Though their impacts have not been publicly quantified, much M&A activity by largest generic manufacturers has occurred recently (e.g., Teva, Sandoz and Mylan – have acquired smaller generic firms, and Teva is acquiring giant generic division of Allergan). New owners have transformed low-margin commodity products into very high margin products, particularly in cases where markets are small and there are few competitors (e.g., Valeant, Turing). But with high prices, why hasn't there been extensive and rapid generic entry?
- Entry into these and other generic markets has been constrained by FDA ANDA backlog – in spite of GDUFA. At the time of GDUFA passage in October 2012, the backlog of submitted but not approved ANDAs was 3000 with median review time of 27 months, but according to GPhIA by June 2015 the backlog had grown to more than 4000 ANDAs and a median review time of more than 40 months. According to ASPE report, FDA has made progress in reducing backlog and median review times, and GDUFA renewal is up in 2017, so it appears plausible to expect that recent increasing generic price trends will be moderated in the next few years. But some provisions of the GDUFA fee structure may be increasing barriers to entry and exacerbating incentives to exit old, low margin products.

What to Expect from the New Product Innovation Pipeline?

- While the share and number of new expensive orphan drugs has increased in recent years, 2013-2014 saw the launch of several truly innovative treatments for diseases affecting large populations such as hepatitis C, diabetes and multiple sclerosis, impacting overall drug spending.
- A dramatic example is the market for hepatitis C medicines.

Nearly 250,000 new patients received treatment for hepatitis C in 2015

Patients Treated with Hepatitis Medicines



Source: IMS Health, National Prescription Audit, NPA New to Brand, PayerTrak, IMS Institute for Healthcare Informatics, Mar 2016

Innovation in the Market for Hepatitis C Treatments: I

- Prior to May 2011, standard therapy of interferon and ribavirin, taken up to 48 weeks with severe side effects, and cure rate of about 50%.
- May 2011 – Merck launches Victrelis™, reduces treatment duration to 24 weeks, increases cure rate to 60+%. Several days later, Vertex's Incivek™ approved, reducing treatment to 12 weeks in some cases, number of daily tablets from 12 to 6, but keeping cure rate at 60+%.
- In late 2013 and into 2014, J&J launches Olysio™, Gilead launches Sovaldi™ and then Harvoni™, followed by AbbVie's Viekira Pak™. These successive innovations reduced or eliminated interferon and ribavirin, reduced daily number of tablets to one, and achieved cure rates of 90-95% for an 8-12 week treatment regimen. Treat all genotypes of the hepatitis C virus.

Innovation in the Market for Hepatitis C Treatments: II

- Gilead list priced Sovaldi™ and Harvoni™ at \$84K and \$93.5K -- at parity per expected cure for previous generation hepatitis C treatments, with average rebates of 22% off list price in 2013 and 46% in 2014. 17,000 hepatitis C patients were treated in US in 2013, but 141,000 in 2014, and net real spending for the new generation hepatitis C treatments increased by \$7 billion, accounting for almost 40% of the net increase in overall US drug spending in 2014. Conclusion: Dramatic innovation from new drug pipeline had very substantial impact on overall US drug spending in 2014
- Incidentally, having been made obsolete due to successive innovations, Vertex withdrew Incivek from US market in 2015 and entirely abandoned research in the hepatitis C space, and later in 2015 Merck announced it was withdrawing Victrelis from the US market.
- These are dramatic examples of Schumpeter's "creative destruction". Should we expect more of the same over the next few years?

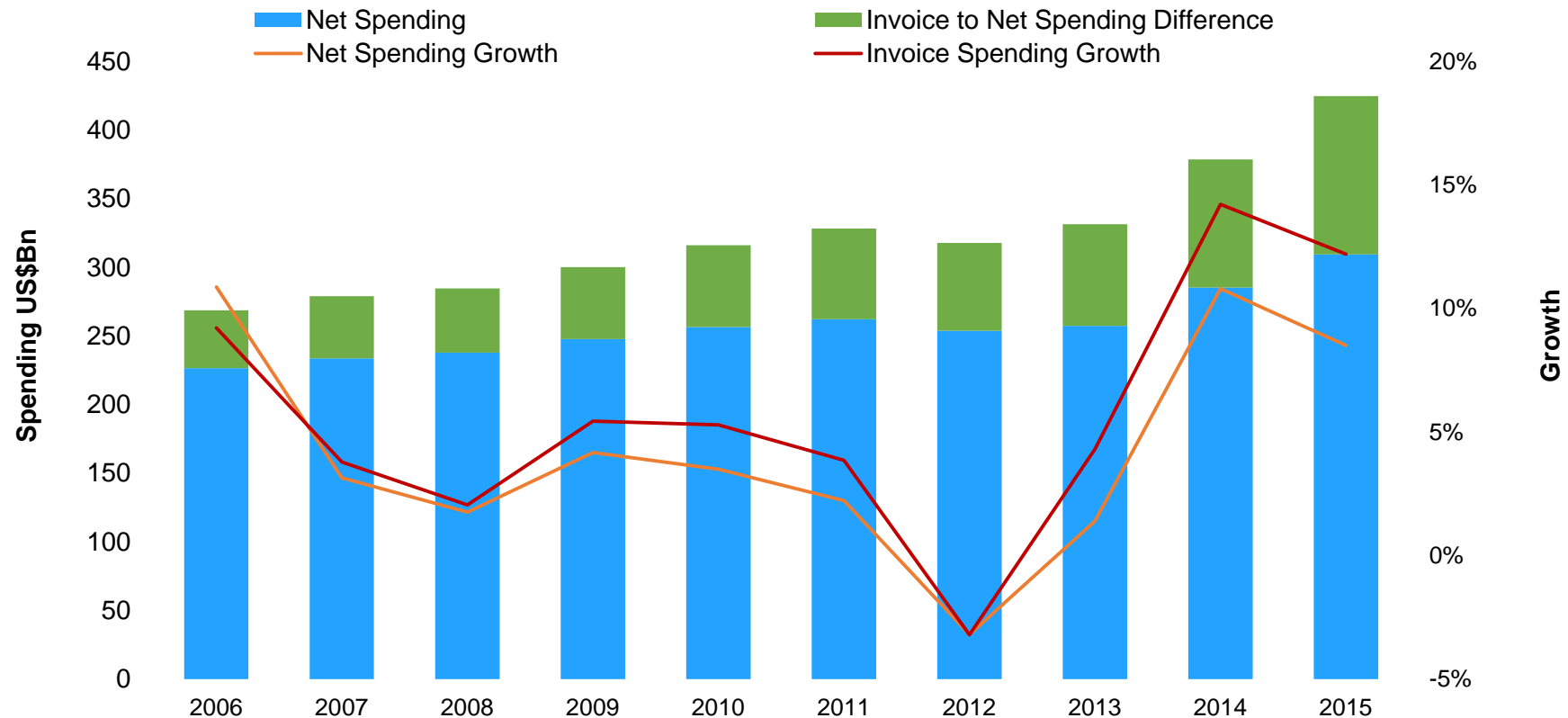
Some Final Thoughts on Future US Drug Spending Trends

- Recent CMS Office of Actuary forecast for 2015-2024 of 6.3% annually
- Many recent innovations on the supply side: Realizing benefits finally from Human Genome project, plus increasingly patient-friendly and efficacious formulations? Incentives provided by FDA's breakthrough designation? But also developments on the demand side: Consolidation among insurers, PBMs, wholesalers, pharmacy chains and providers. Insurers' shifts to greater patient cost-sharing. Highly visible brand (and generally isolated generic) price increases in presidential election year make government intervention more likely?
- Only certain outcome: ***There will be no détente in the pharms race.***

Additional Optional Appendix Slides from IMS

Spending on medicines in 2015 increased 8.5% on a net price basis to \$309.5Bn and 12.2% to \$424.8Bn on an invoice basis

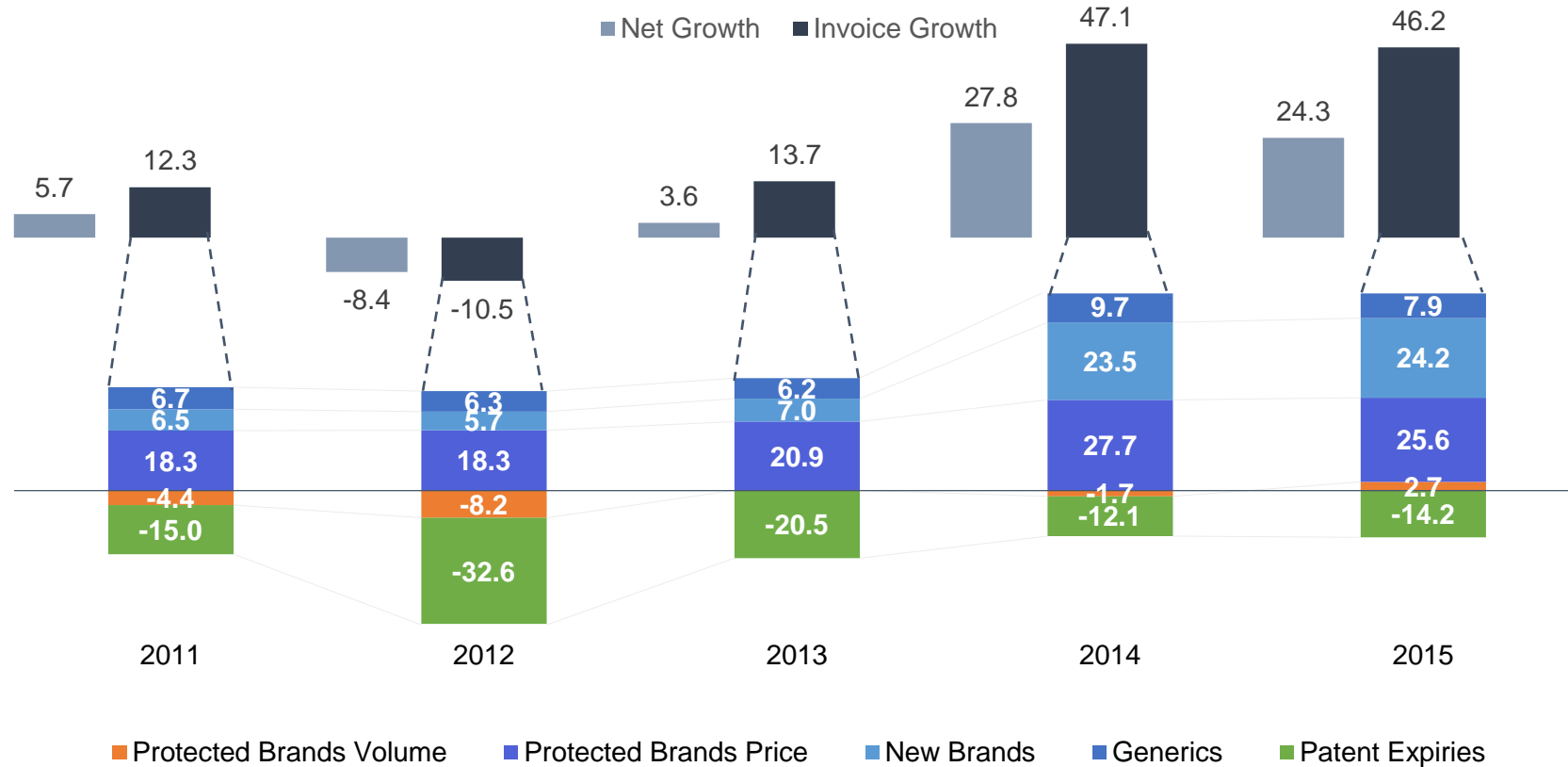
Total Spending on Medicines US\$Bn



Source: U.S. Census Bureau; U.S. Bureau of Economic Analysis; IMS Health, National Sales Perspectives, Jan 2016

The 2015 increase of \$24.3Bn in spending on a net basis and \$46.2Bn on an invoice basis has five major drivers

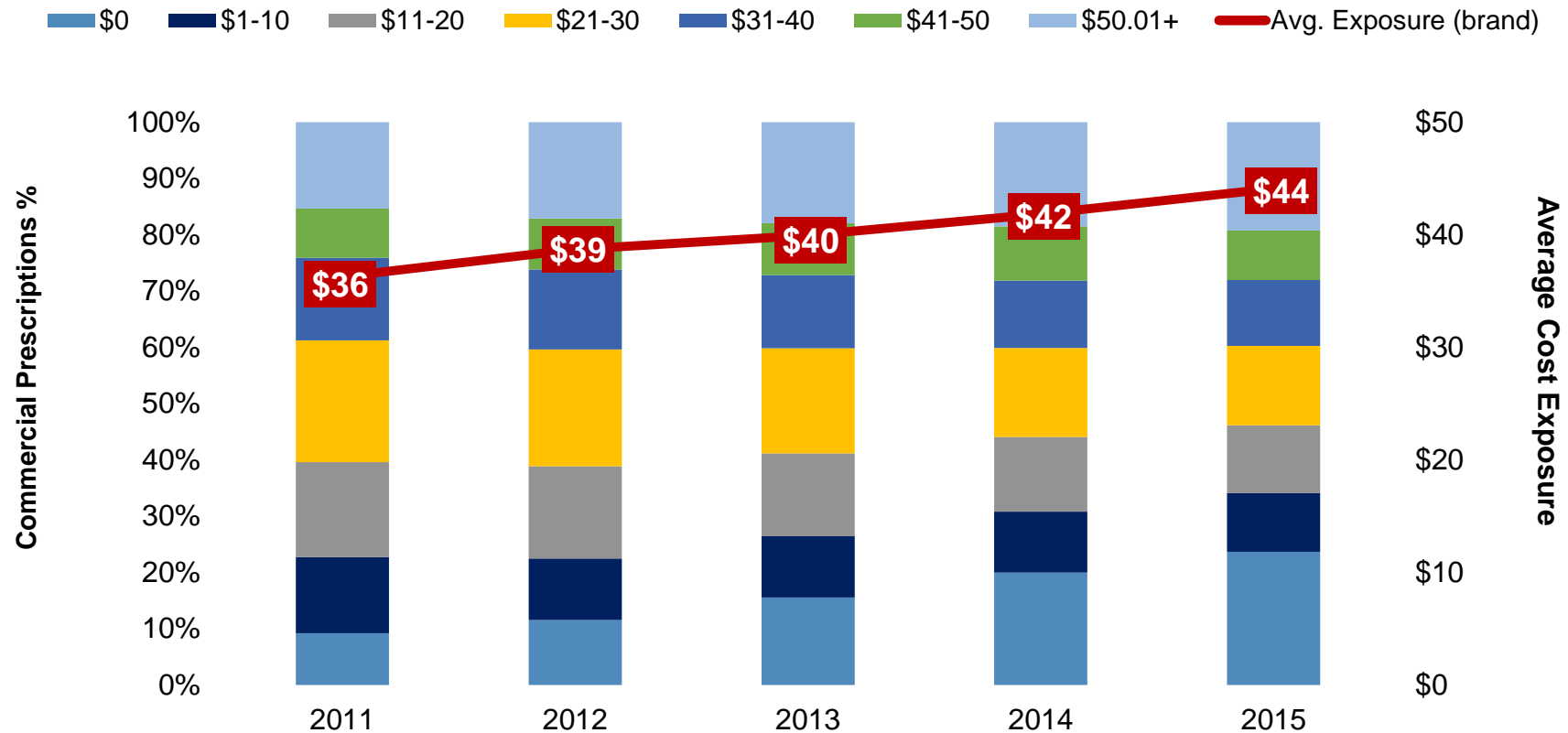
Spending Growth Drivers US\$Bn



Source: IMS Health, National Sales Perspectives, Jan 2016

Patients faced higher average cost exposure for branded medicines as coinsurance and pharmacy deductible plans evolve

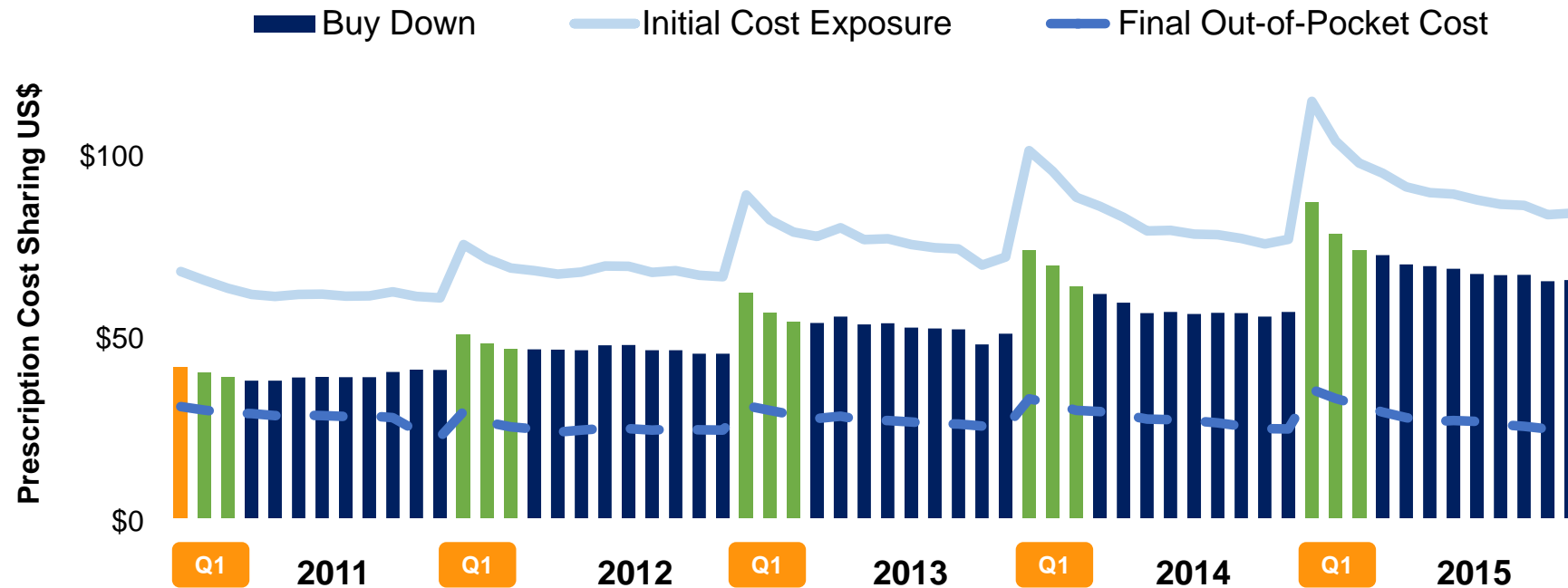
Patient Cost Exposure Distribution for Brands in Commercial Plans



Source: IMS Health, Formulary Impact Analyzer; IMS Institute for Healthcare Informatics, Dec 2015

Brand manufacturer “buy-downs” have increased steadily to offset increasing patient cost exposure

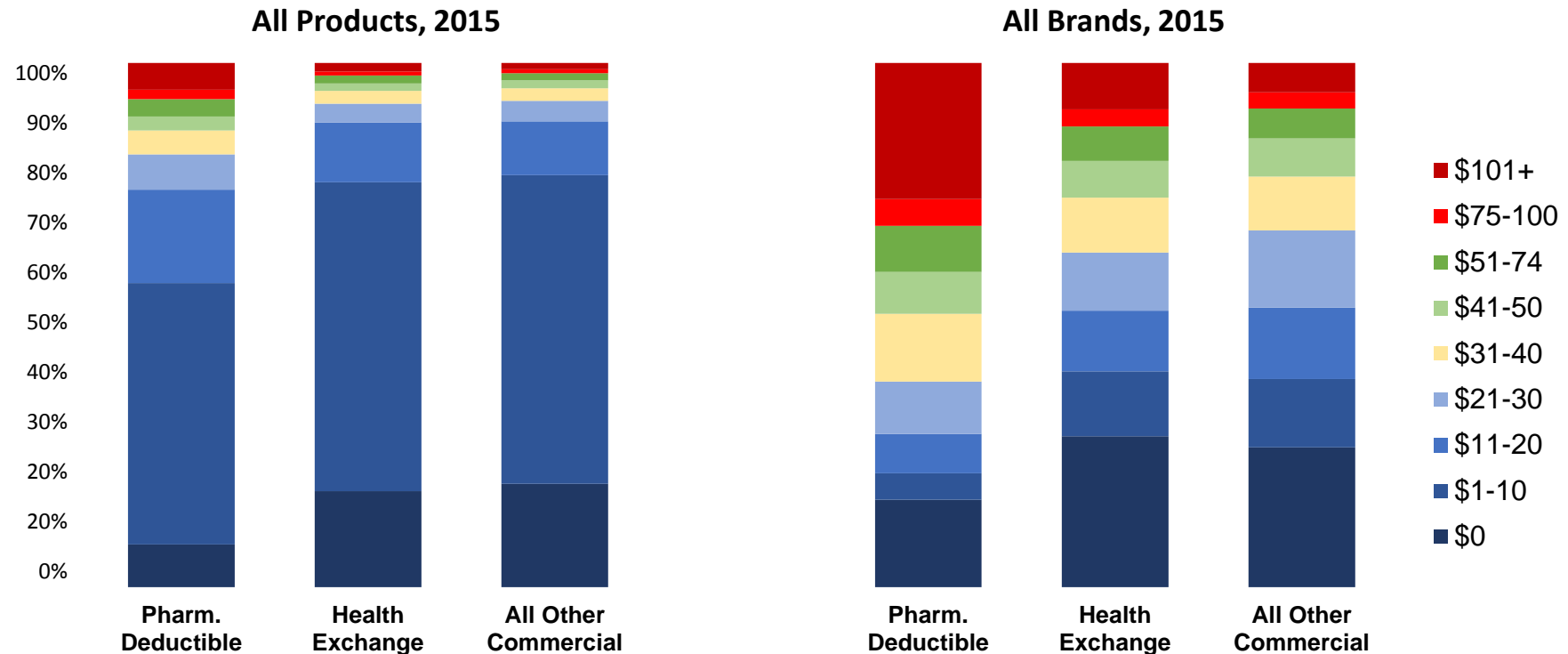
Patient Cost-Sharing and Manufacturer Buy-Down (Commercial, Brands)



Source: IMS Health, Formulary Impact Analyzer, IMS Institute for Healthcare Informatics, Dec 2015

Even after patient savings programs are applied, patients with pharmacy deductibles have high cost exposure

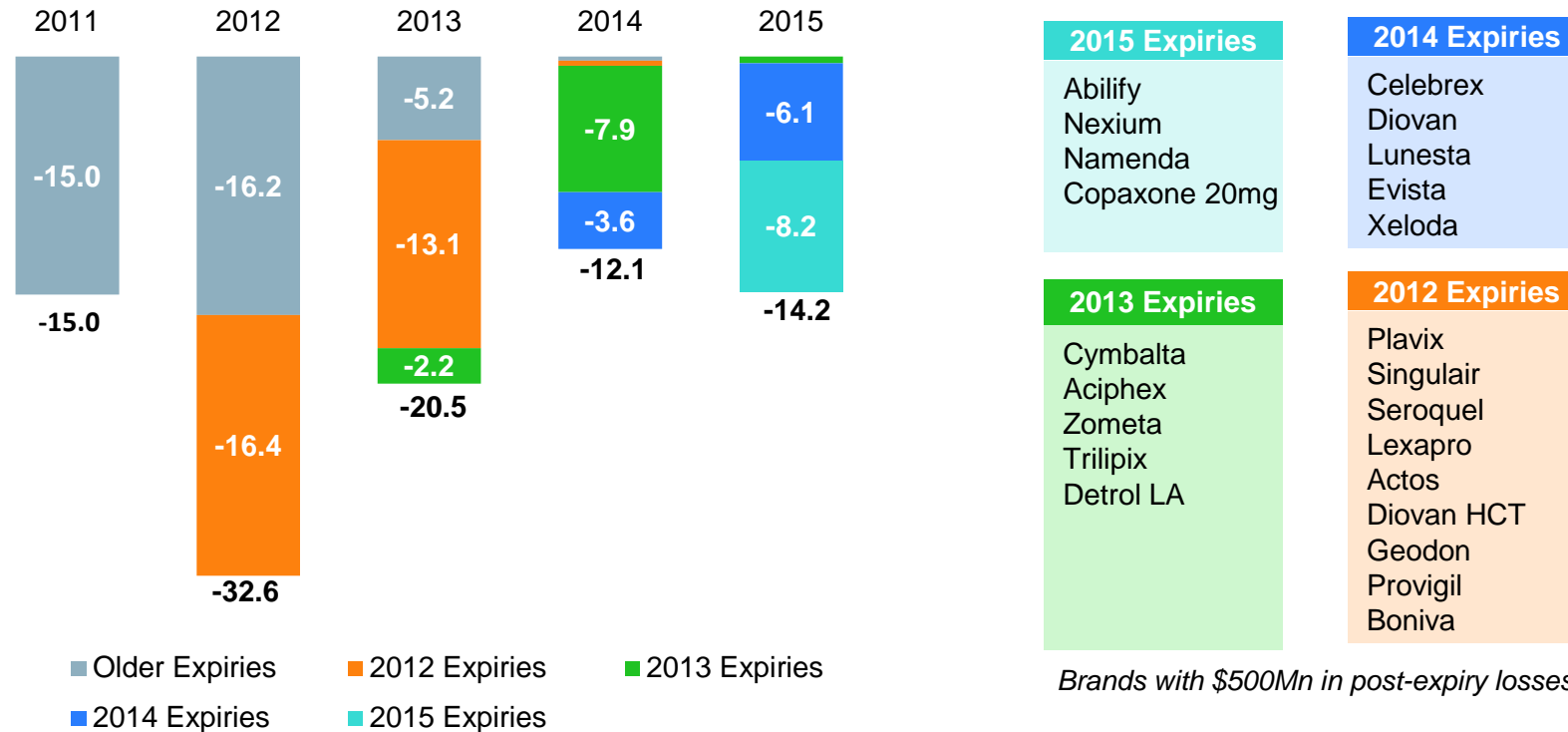
Distribution of Commercial Prescriptions by Payer Type and Final Cost Sharing After Patient Savings Programs are Applied



Source: IMS Health, Formulary Impact Analyzer; IMS Institute for Healthcare Informatics, Dec 2015

Spending on brands without exclusivity reduced growth by \$14.2Bn in 2015, slightly higher than the impact in the prior year

Decline in Brand Spending from Loss of Exclusivity US\$Bn

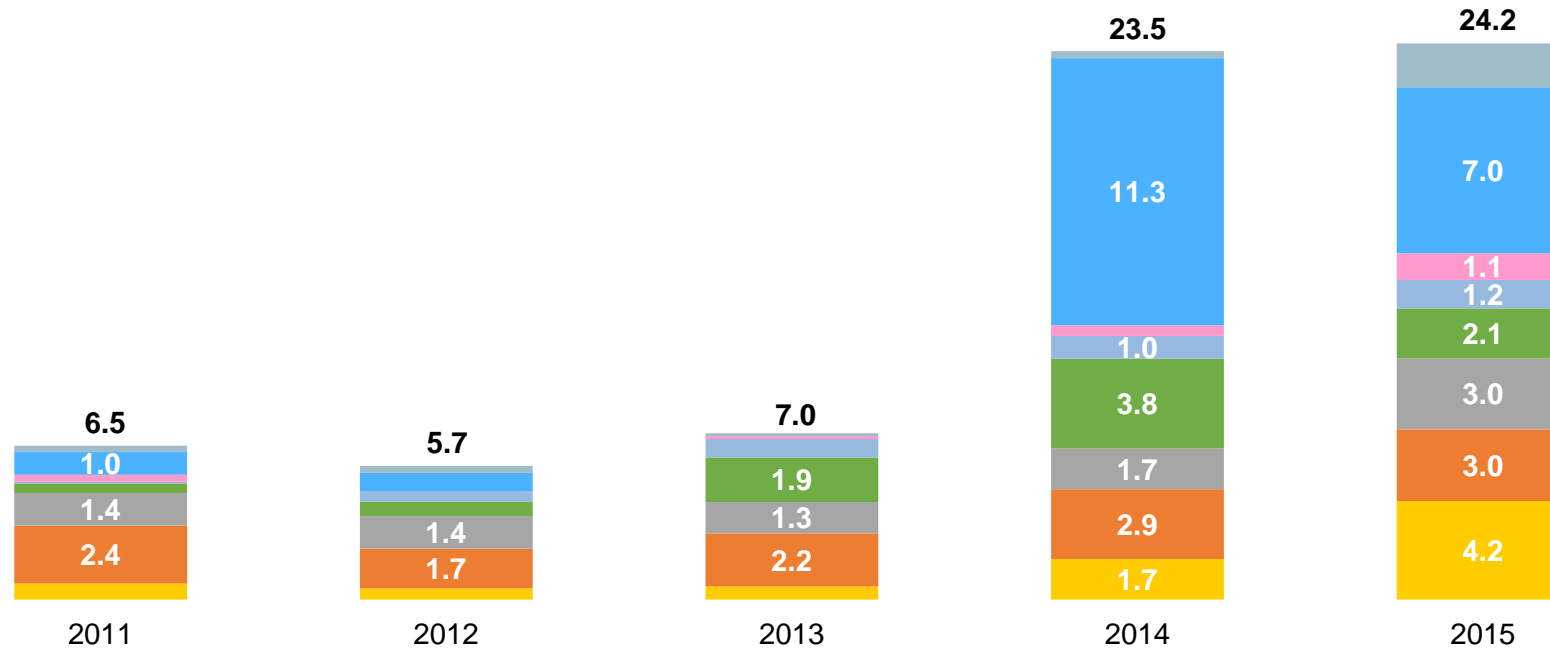


Source: IMS Health, National Sales Perspectives, Jan 2016

Patient use of new treatments drove a historically high level of \$24.2Bn of growth in 2015

New Brand Spending Growth US\$Bn

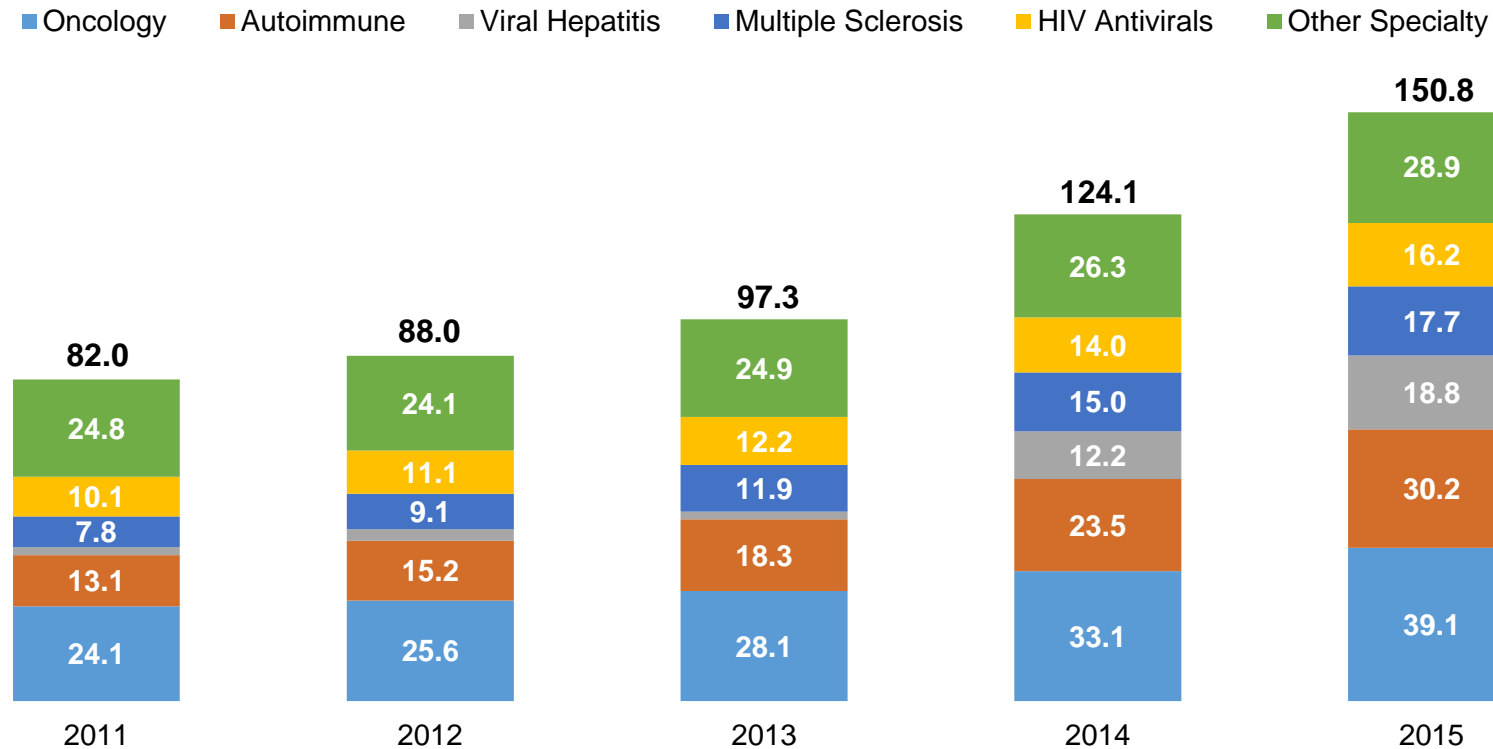
■ Diabetes ■ Other Traditional ■ Oncology ■ Multiple Sclerosis ■ HIV Antivirals ■ Autoimmune ■ Viral Hepatitis ■ Other Specialty



Source: IMS Health, National Sales Perspectives, Jan 2016

Spending on specialty medicines in 2015 increased 21.5% to \$150.8Bn on an invoice price basis

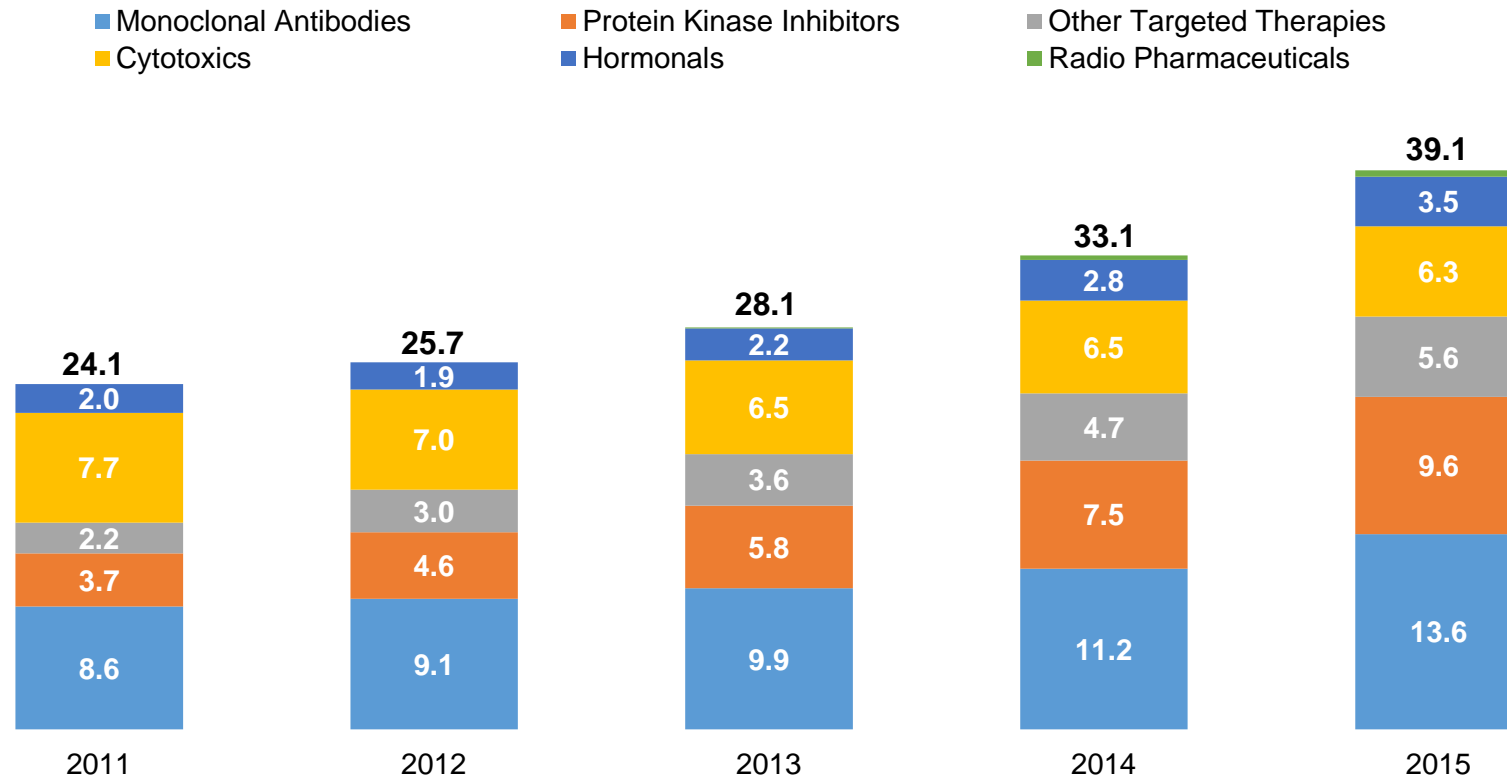
Spending on Specialty Medicines US\$Bn



Source: IMS Health, National Sales Perspectives, Jan 2016

Oncology spending increased 18.0% to \$39.1Bn in 2015, driven by new breakthrough treatments for cancer patients

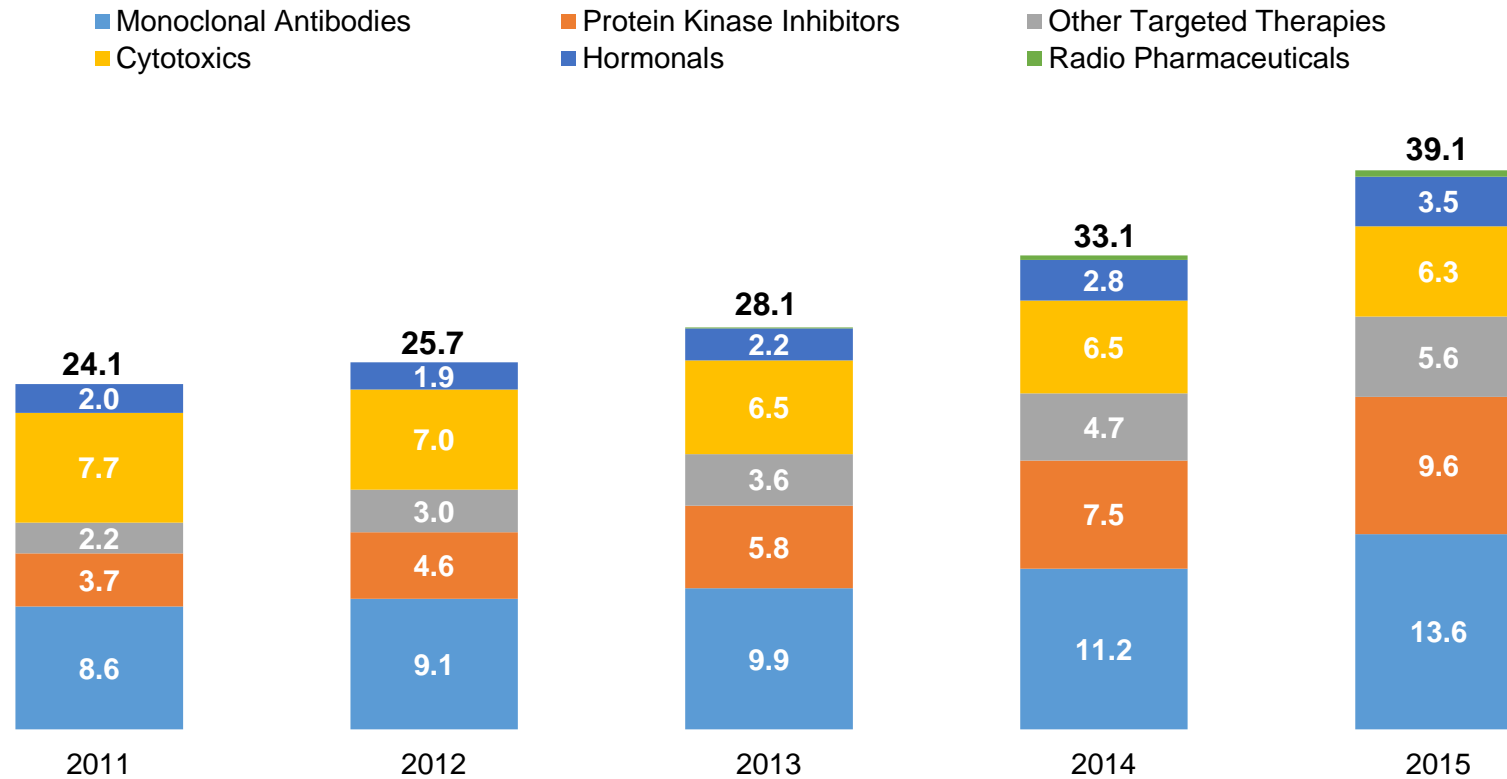
Spending on Oncology Medicines US\$Bn



Source: IMS Health, National Sales Perspectives, Jan 2016

Oncology spending increased 18.0% to \$39.1Bn in 2015, driven by new breakthrough treatments for cancer patients

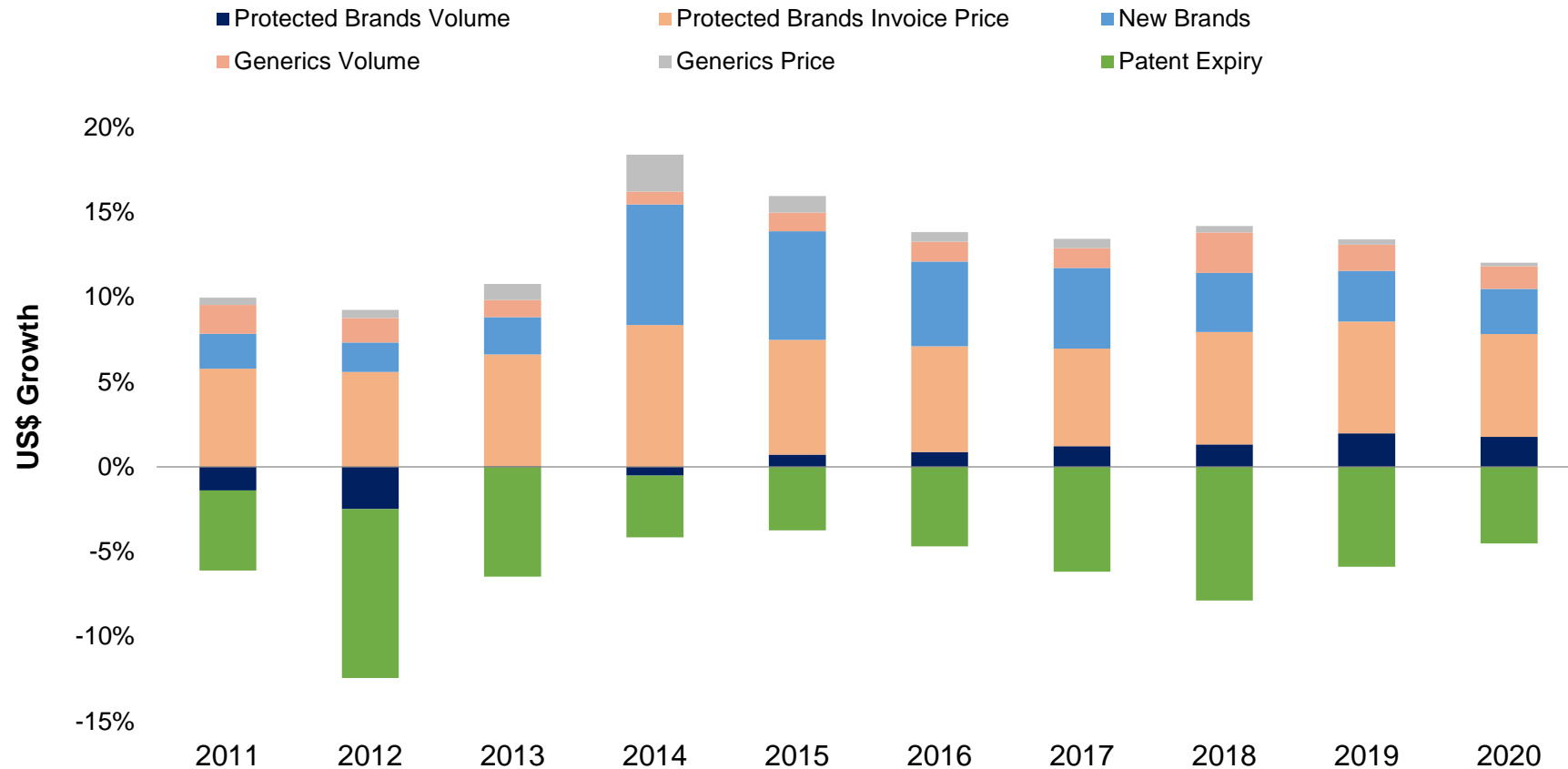
Spending on Oncology Medicines US\$Bn



Source: IMS Health, National Sales Perspectives, Jan 2016

U.S. spending on medicines will reach \$610-640Bn in 2020 on an invoice price basis, with steady mid-single digit growth

U.S. Spending Growth 2010-2020 US\$Bn



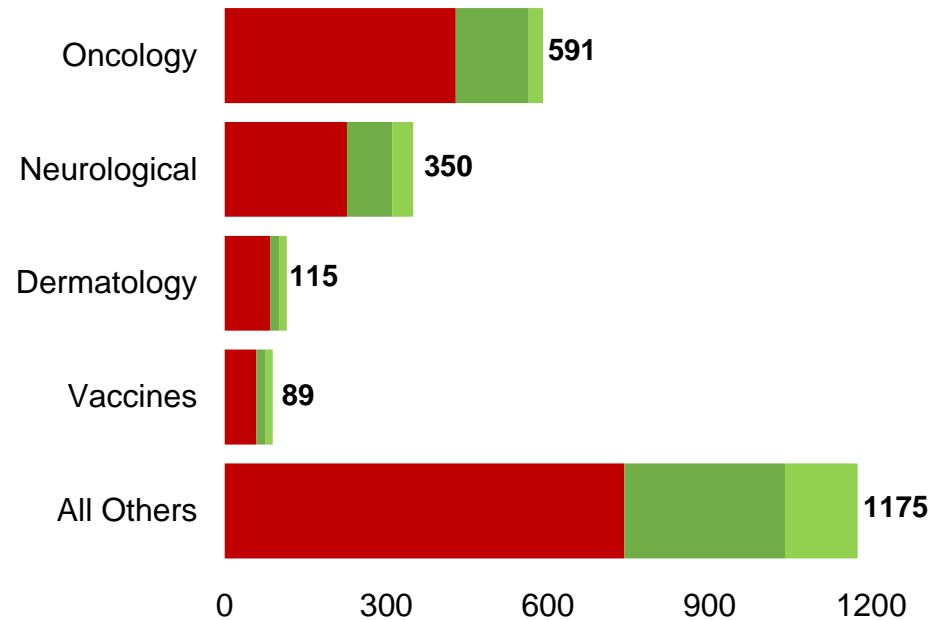
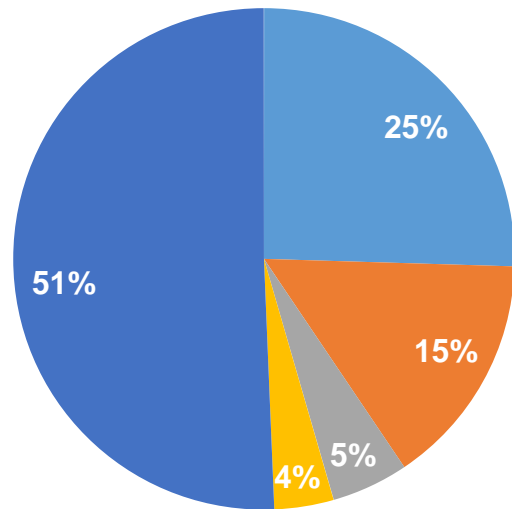
Source: IMS Health, Market Prognosis, National Prescription Audit, IMS Institute for Healthcare Informatics, Jan 2016

The late phase R&D pipeline remains robust and will ensure an ongoing high number of new brand launches by 2020, especially cancer treatments

Late Phase R&D Pipeline by Top Therapy Area

■ Oncology ■ Neurological ■ Dermatology ■ Phase 2 ■ Phase 3 ■ Pre-Reg/Registered
■ Vaccines ■ All Others

43-49 NAS/Year Expected by 2020



Source: IMS Health, LifeCycle R&D Focus, Dec 2015; IMS Institute for Healthcare Informatics, Mar 2016