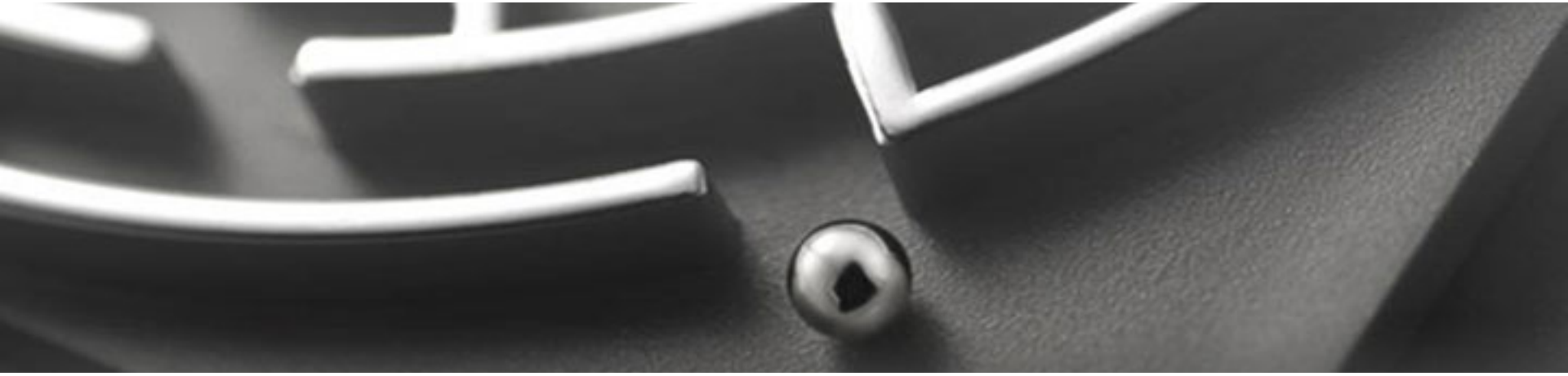

PRESCRIPTION DRUG TRENDS – THE NATIONAL PICTURE

Yohan Cho
Seattle, Washington

Tuesday, June 14th, 2016

Washington Rx Drug Price and Purchasing Summit Series – Part I

Market Access

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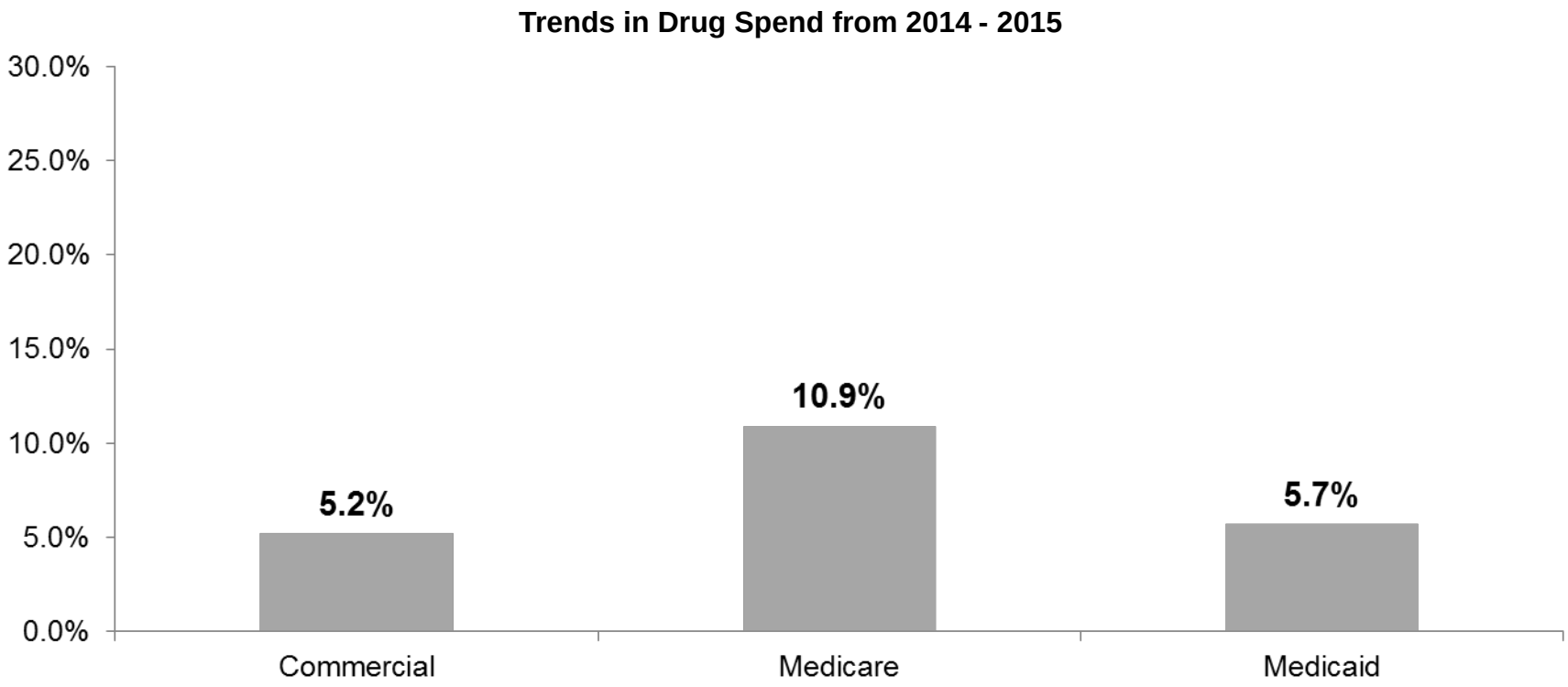
What we saw in 2015…

Overall, drug spend increased in 2015 across all books of business

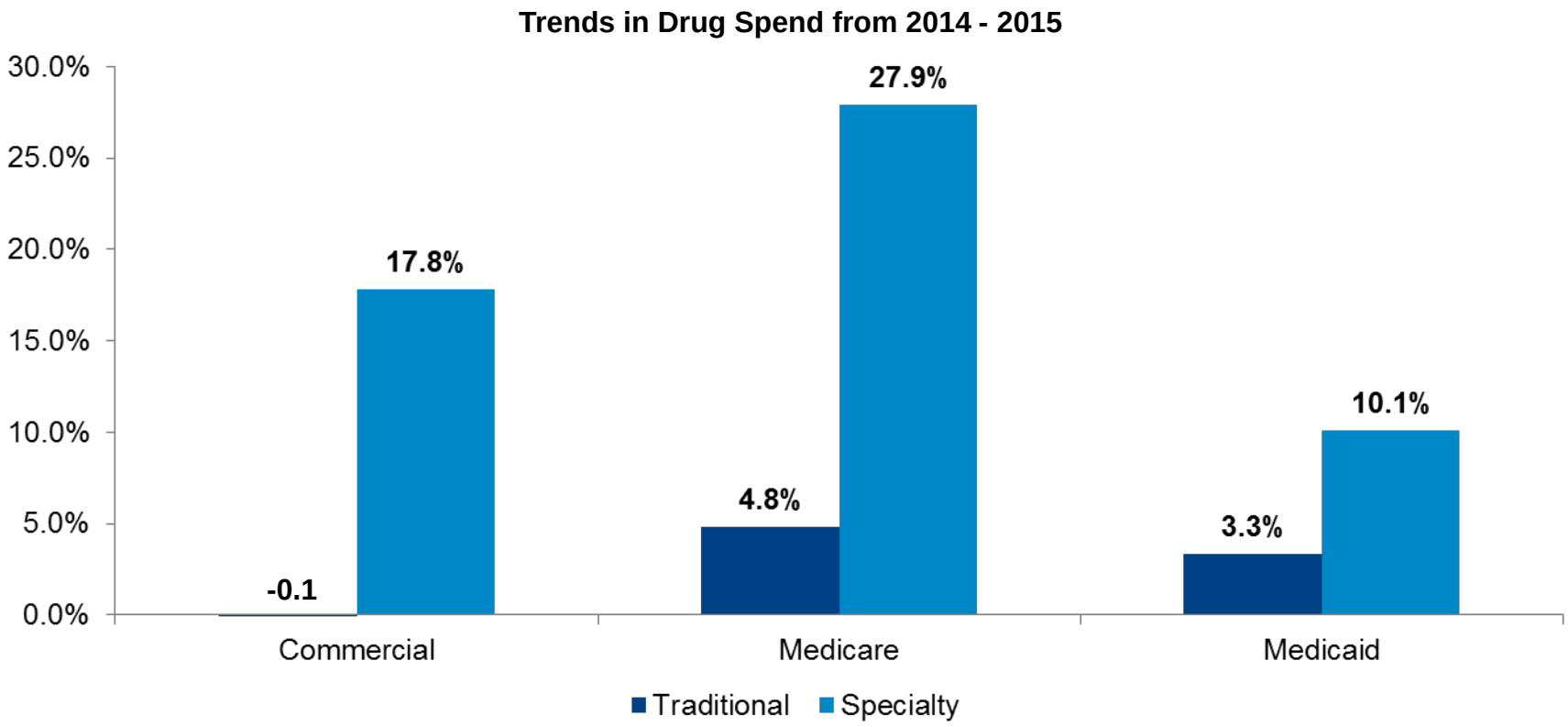
2015 Drug Spend



Source: Express Scripts 2015 Drug Trend Report

However, increases in drug spend was far more significant in specialty drugs

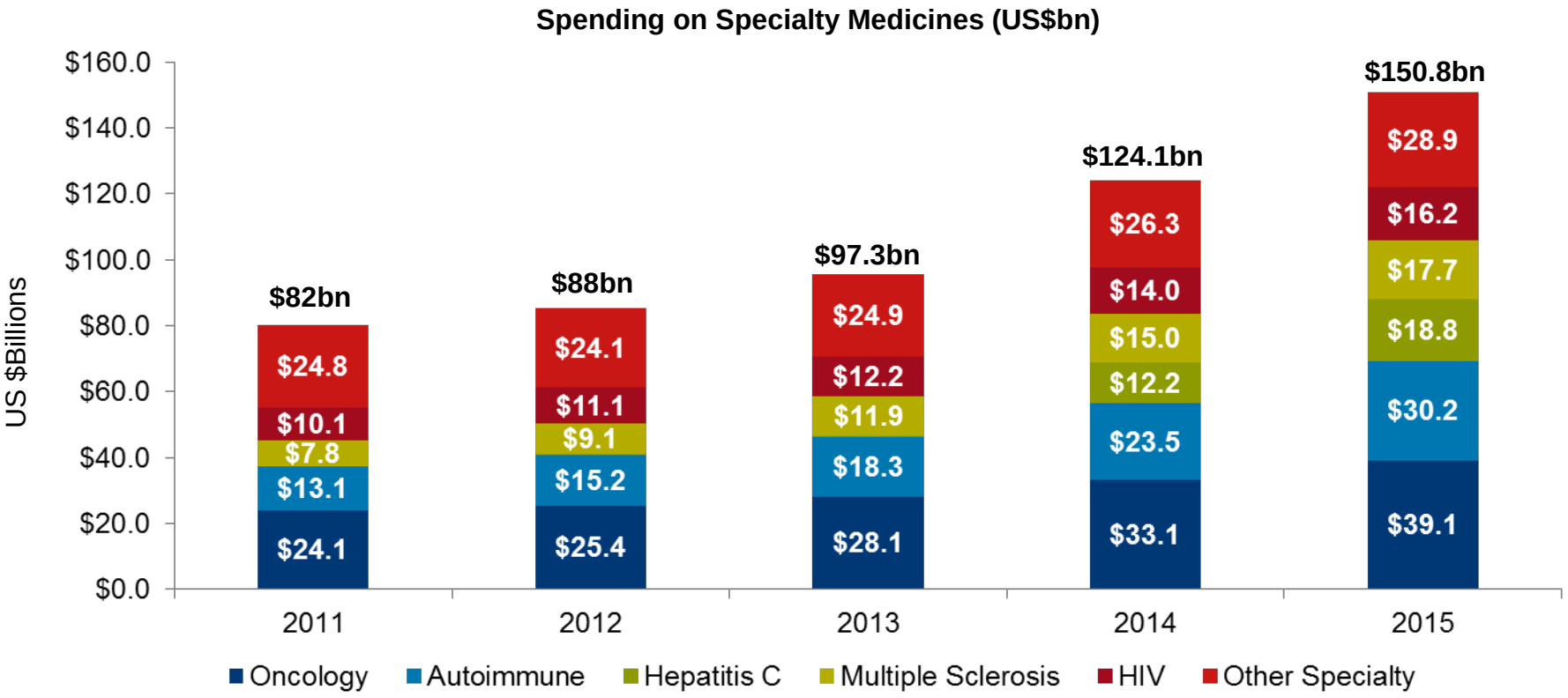
2015 Drug Spend



Source: Express Scripts 2015 Drug Trend Report

Which continues the trend that has been happening for years

Specialty Drug Spend



Source: IMS US Medicines Use and Spending in 2015

Specialty drug spend will continue to grow ~17% from 2016-2018

Trend Forecast for Key Specialty Therapy Classes

Therapy class	2016	2017	2018
Inflammatory conditions	25.5%	25.5%	26.7%
Multiple sclerosis	11.2%	10.2%	7.2%
Oncology	21.1%	20.0%	20.0%
Hepatitis C	10.2%	8.1%	8.0%
HIV	17.7%	17.8%	18.9%
Growth deficiency	9.1%	9.1%	9.0%
Cystic fibrosis	58.2%	36.2%	28.8%
Pulmonary hypertension	16.6%	5.8%	5.9%
Hemophilia	17.3%	18.3%	22.4%
Sleep disorders	22.6%	21.5%	20.5%
Other specialty classes	6.7%	6.4%	6.4%
Total	**17.4%**	**16.8%**	**17.2%**

Source: Express Scripts 2015 Drug Trend Report

2015 Medicaid Drug Spend

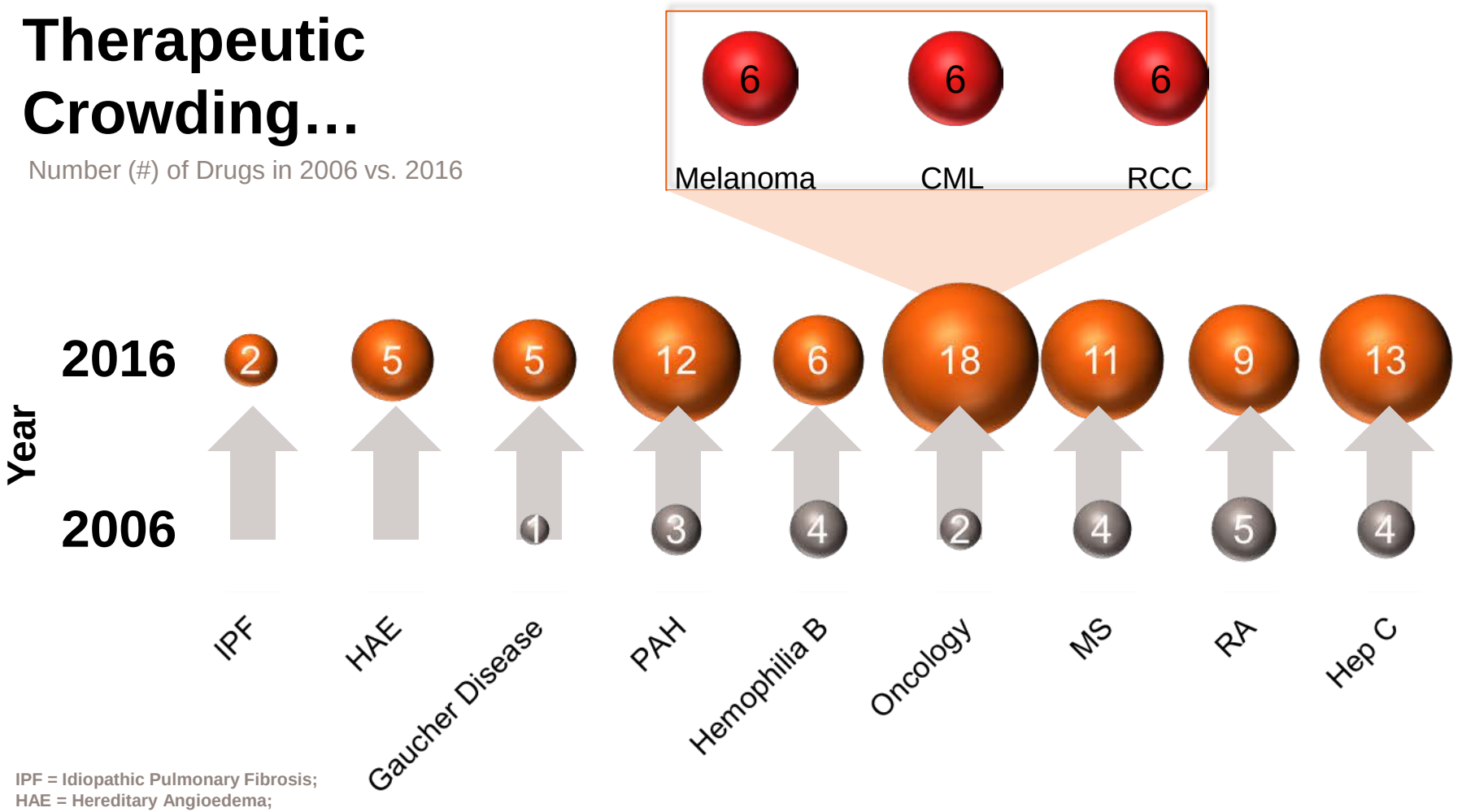
Therapy Class	PMPY	Utilization	Unit Cost	Total
HIV	$131.80	-5.9%	10.8%	4.9%
Hepatitis C	$62.96	-39.9%	30.2%	-9.7%
Inflammatory conditions	$41.30	24.5%	21.1%	45.6%
Oncology	$27.50	12.1%	17.3%	29.4%
Multiple sclerosis	$24.36	6.4%	9.7%	16.0%

Source: Express Scripts 2015 Drug Trend Report

What to expect in 2016…

Therapeutic Crowding…

Number (#) of Drugs in 2006 vs. 2016



IPF = Idiopathic Pulmonary Fibrosis;
HAE = Hereditary Angioedema;
PAH = Pulmonary Arterial Hypertension;
CML = Chronic Myeloid Leukemia;
RCC = Renal Cell Carcinoma;
MS = Multiple Sclerosis,
RA = Rheumatoid Arthritis

2016 Novel Drug Approvals

Drug	Use	Peak Sales (Billions, USD)	Route	Approval
Zepatier (elbasvir+grazoprevir) • Merck	Chronic hepatitis C genotypes 1 & 4	$2.0	Oral	**Jan 28**
Briviact (brivaracetam) • UCB	Seizures in patients 16 years or older with epilepsy	$1.38	Oral	**Feb 18**
Taltz (ixekizumab) • Lilly	Moderate-to-severe plaque psoriasis	$5.0	SC	**Mar 22**
Cinqair (reslizumab) • TEVA	Severe asthma	$0.9	IV	**Mar 23**
Venclexta (venetoclax) • AbbVie / Genentech	Chronic lymphocytic leukemia with specific chromosomal abnormality	$1.7	Oral	**Apr 11**
Nuplazid (pimavanserin) • Acadia	Treat hallucinations and delusions associated w/ psychosis with Parkinson's disease patients	$2.0	Oral	**Apr 29**
Tecentriq (atezolizumab) • Genentech	Urothelial carcinoma (bladder cancer)	$3.0	IV	**May 18**
Zinbryta (daclizumab) • Biogen	Multiple sclerosis	$0.5	SC	**May 27**
Ocaliva (obeticholic acid) • Intercept	Certain patients with primary biliary cirrhosis (PBC)	$2.2	Oral	**May 27**

$14.3 Billion Generic Opportunity: 5 blockbuster drugs coming off patent

Generics

Drug	Use	Annual Sales (Billions, USD)	Anticipated Generic Launch
Gleevec (imatinib) • Novartis	Multiple hematological indications including Ph+ CML and Ph+ AML	$2.5	**Feb 01**
Crestor (rosuvastatin) • AstraZeneca	Multiple indications associated with lowering LDL cholesterol levels	$6.4	**May 02**
Benicar (olmesartan) and Benicar HCT (olmesartan/HCTZ) • Daiichi Sankyo	Hypertension	$1.8	**Oct 25**
Seroquel XR (quetiapine, e.r.) • AstraZeneca	Schizophrenia, bipolar disorder, and major depressive disorder	$1.3	**Nov 01**
Zetia (ezetimibe) • Merck	Multiple indications associated with lowering LDL cholesterol levels	$2.3	**Dec 12**

Source: 2016 Drug Pipeline Full of Blockbuster Potential, Aimee Theraldson, Express Script Website, Accessed May 31, 2016 (http://lab.express-scripts.com/lab/insights/drug-options/2016-drug-pipeline-full-of-blockbuster-potential)

Inflectra, the biosimilar to Remicade, was approved in April 2016

Biosimilars

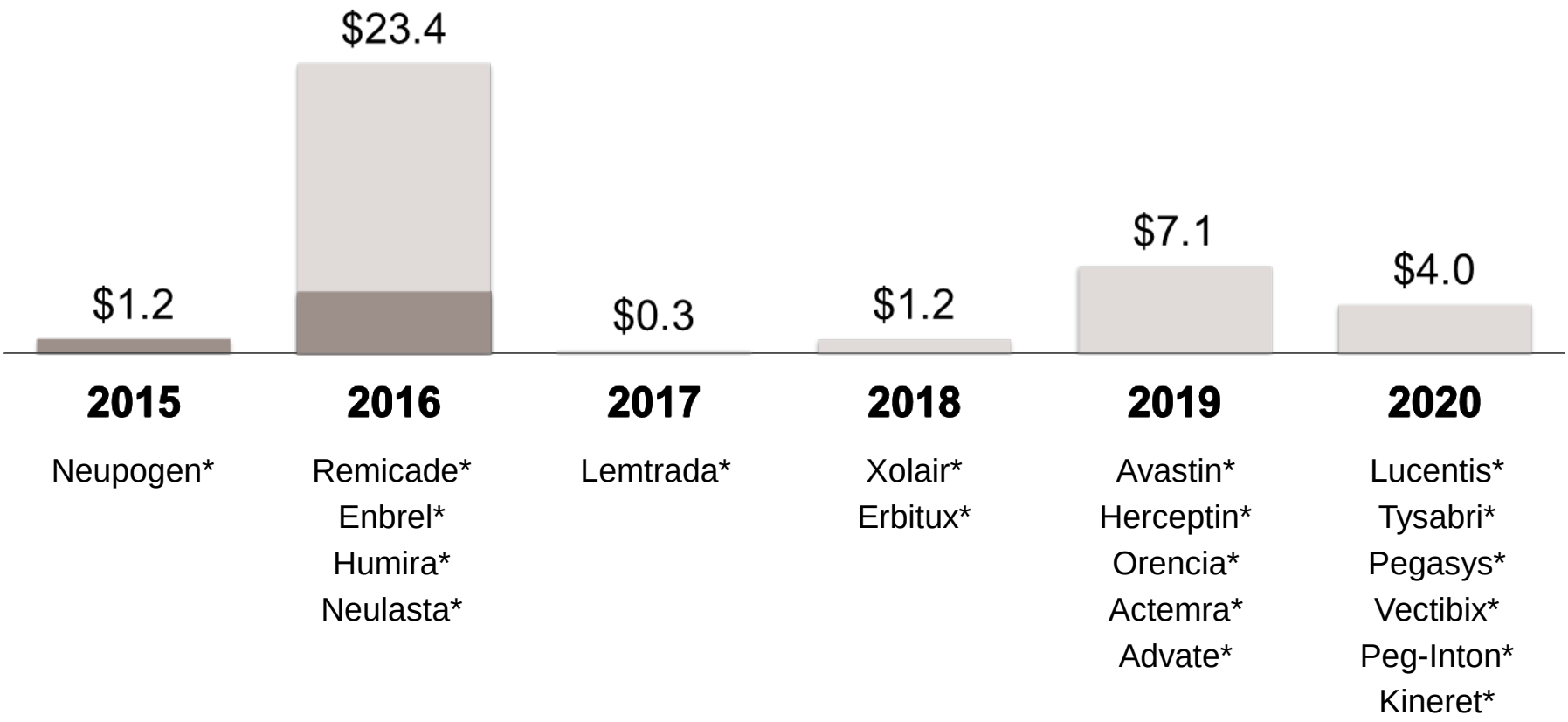
Overall U.S. Market Opportunity (in $ Billions)

Source: U.S. Drug spend estimates are based on IMS Health data for 2015.
The availability of biosimilars is highly variable due to litigation, patent challenges, FDA's establishment of 351(k) pathway, or other factors

With more biosimilars are on the way…

Biosimilars

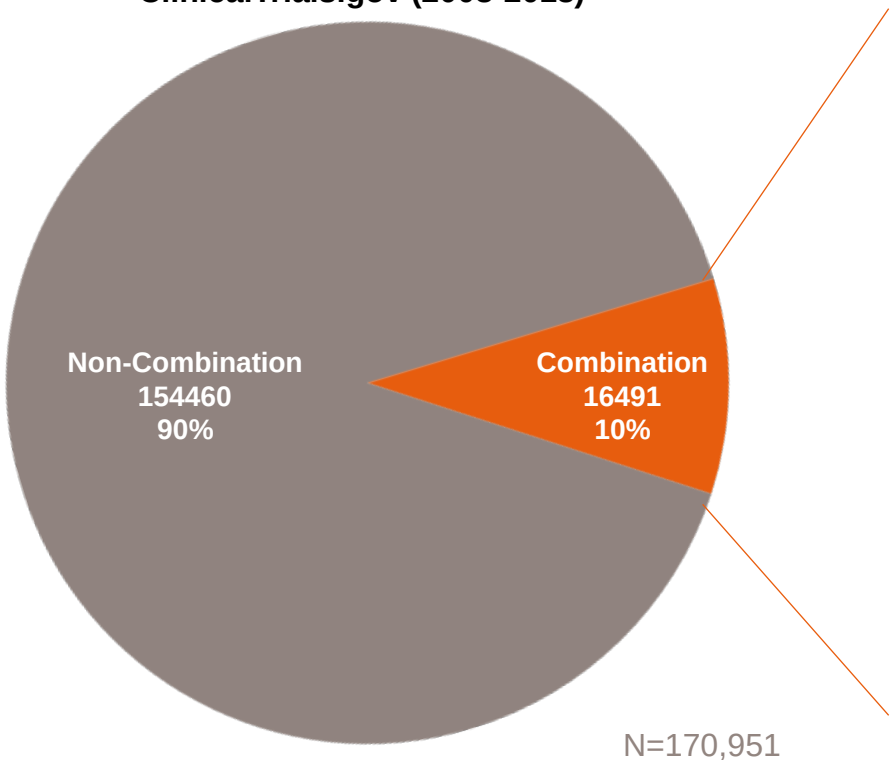
Overall U.S. Market Opportunity (in $ Billions)



Source: U.S. Drug spend estimates are based on IMS Health data for 2015.
The availability of biosimilars is highly variable due to litigation, patent challenges, FDA's establishment of 351(k) pathway, or other factors

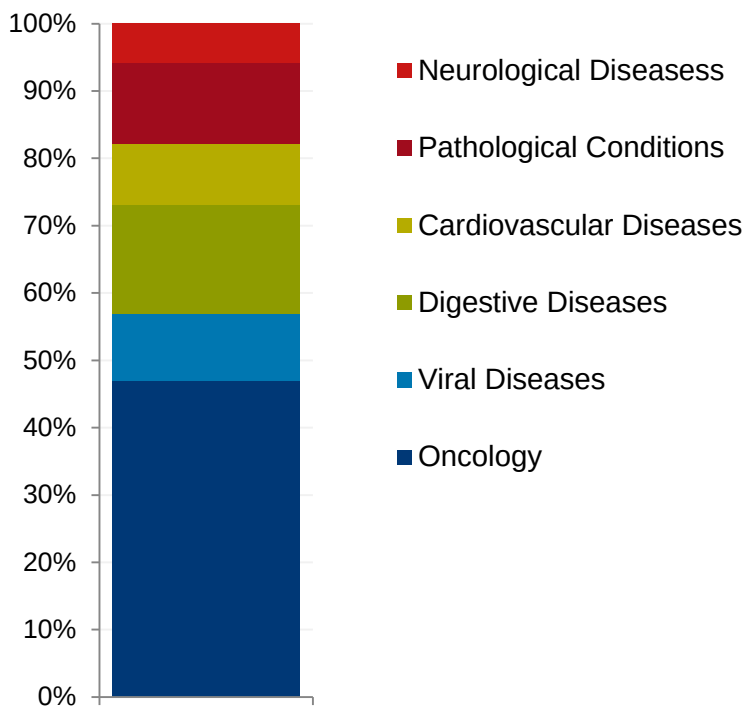
Brand-Brand Combinations

Number of Trials and Combination Trials on ClinicalTrials.gov (2008-2013)



N=170,951

Combination Trials Across Different Disease Types



Nearly half of all combination trials are conducted in oncology and a quarter of oncology trials use combinations therapies

Characteristics of Drug Combination Therapy in Oncology by Analyzing Clinical Trial Data on ClinicalTrials.Gov, Menhua Wu, Stanford

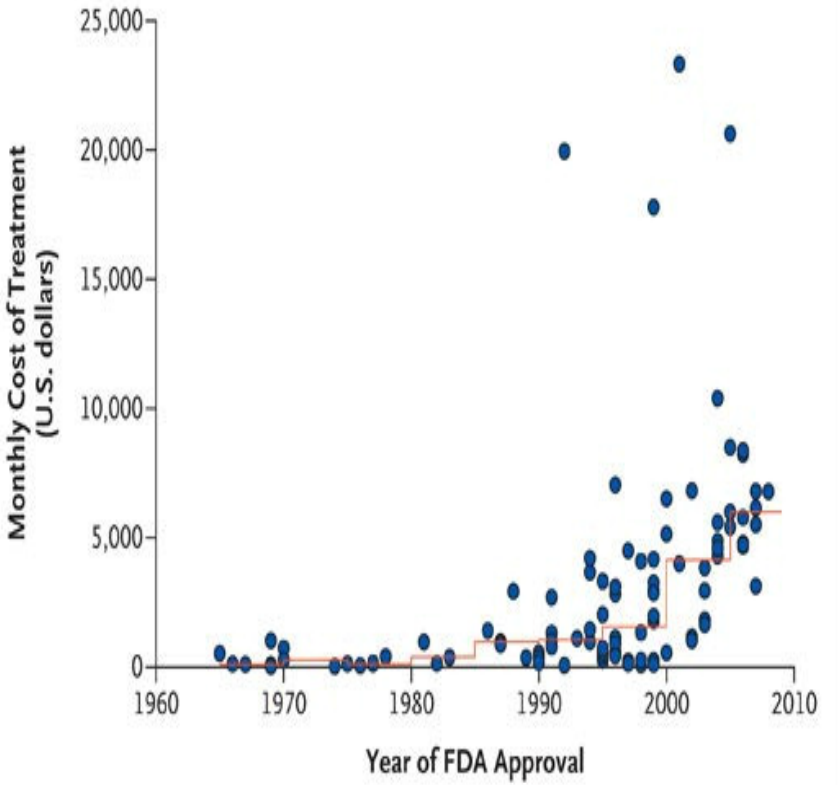
Brand-brand combinations are becoming increasingly prevalent in oncology…

Brand-Brand Combinations

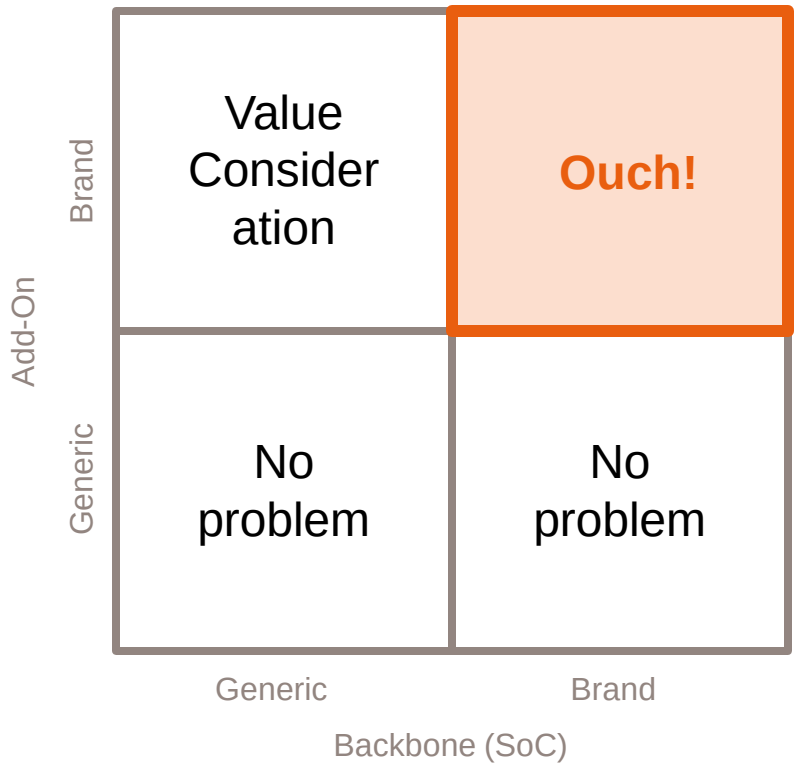
Due to high priced drugs, the combination of multiple expensive branded drugs will test society's willingness to pay

Brand-Brand Combinations

Monthly and Median Costs of Cancer Drugs at the Time of Approval by the FDA



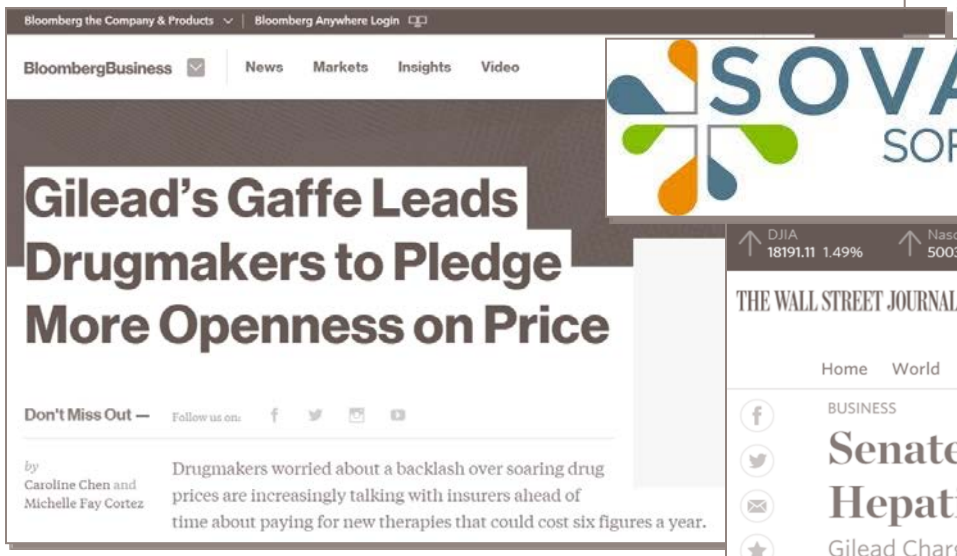
Stack Matrix: Brand and Generic as Backbone or Add-On Positioning

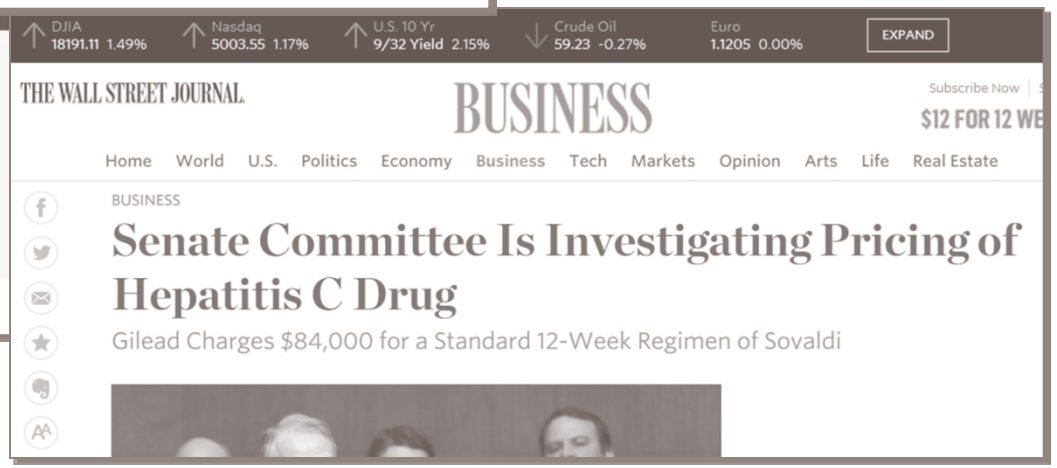


Limits on Medicare's Ability to Control Rising Spending on Cancer Drugs, Peter B. Bach, M.D., N Engl J Med 2009; 360:626-633, February 5, 2009

US Payers React

Drug pricing's "Big Bang" moment…





Source: Various as shown above

Health Economic ROI

- **F**ast-pays: Expensive with short-term healthcare cost
- **S**low-pays: Expensive but decrease costs over long term

- **N**o-pays: Do not save anybody money but they improve people’s lives
- **N**arrow-pays: Expensive but provide cost savings to a narrow population, not providing diffuse , aggregate benefits
- **P**ay-me-laters: Expensive and lower short-term costs but increase long-term costs
- **D**iffuse-pays: Expensive and decrease nonmedical costs

Source: The Price of Progress, J.D. Kleinke, Health Affairs, 20, no.5 (2001): 43-60

Triggers for Contracting

Factor	Impact on Contracting Sensitivity
Competition	• High competition creates opportunity for payers to consider contracting in a TA • Most payers consider a competitive space to have 3 or more comparable products
Utilization	• High utilization triggers attention as well as equips payers with an incentive • Magnitude of utilization control directly impacts the attractiveness of the incentive
Cost	• High costs triggers attention and creates the need for cost savings
Number of Patients	• Higher patient numbers (coupled with high cost products and high utilization) increases the likelihood of payers to feel pressure to contract
Pharmacy Benefit	• Payers have greater ability to manage products that are on the pharmacy benefit
Lack of Clinical Differentiation	• Payers are more comfortable leaving products off formulary in competitive therapy areas that have products are clinically undifferentiated
Physician Acquiescence	• Clinical guidelines or physician consensus for a product being the standard gives the payers confidence to shift patients to a product, increasing utilization and incentive
Political Pressure	• Potentially provides support to payers to explore contracting

What triggers might draw attention for contracting?

"At Risk" Therapy Areas

Factor	HCV	ONC	MS	PAH	Hemo-philia	Asth-ma	Gau-cher's	CV	Migr-aine
Competition	✓	✓	✓	✓	✓	✓	✓	✓	?
Utilization	✓	✓	✓	✗	✗	✓	✗	✗	?
Cost	✓	✓	✓	✓	✓	✓	✓	✓	?
Number of Patients	✓	✓	✓	✗	✗	✓	✗	✓	?
Pharmacy Benefit	✓	✓	✓	✓	✗	✓	✓	✓	?
Lack of Clinical Differentiation	✓	✗	✓	✓	✓	✗	✗	✓	?
Physician Acquiescence	✗	✓	✗	✗	✗	✗	✗	✗	?
Political Pressure	✓	✗	✗	✗	✗	✗	✗	✓	?

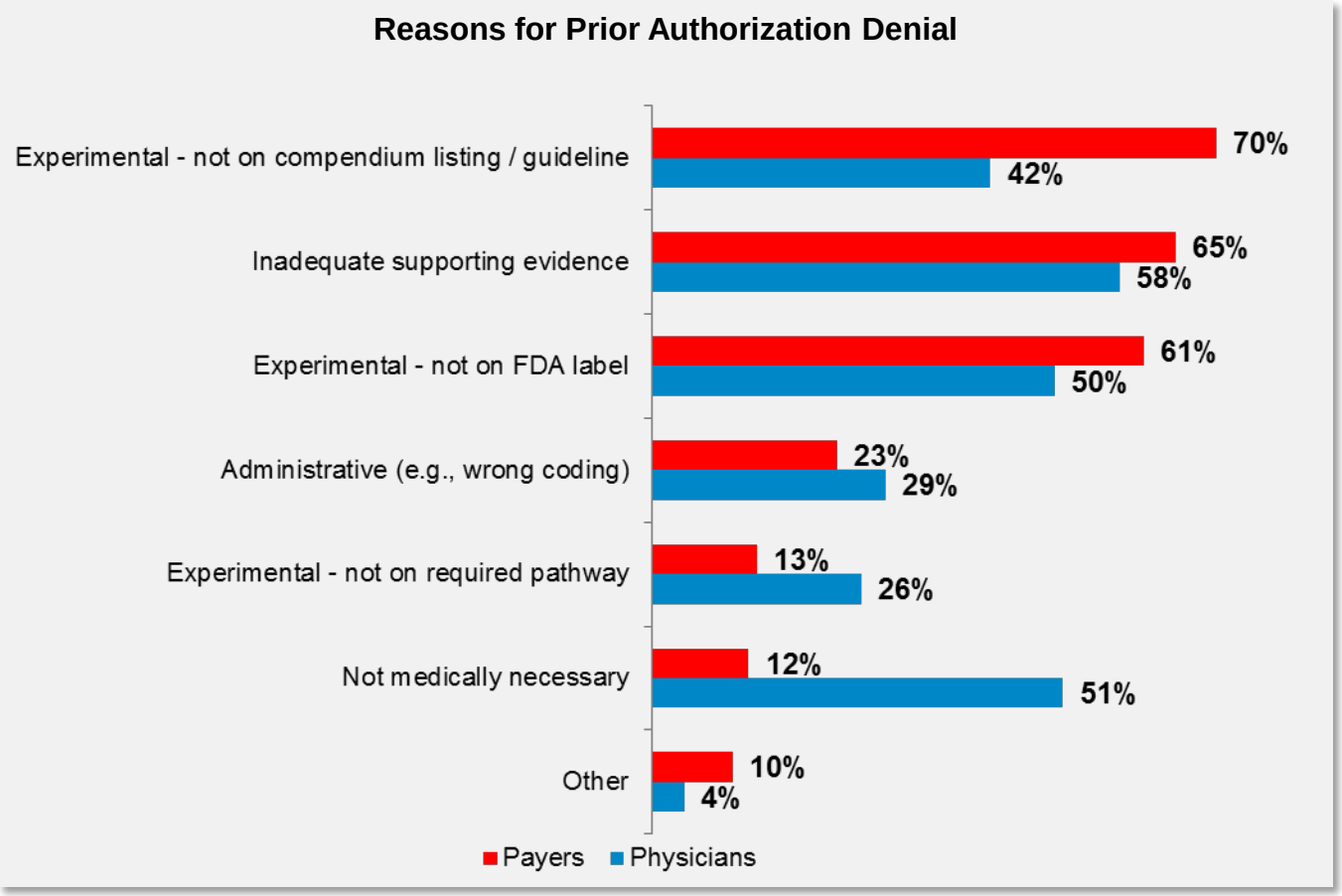
Contracting – But How?

Tools / Mechanisms	Commercial MCOs	PBMs	Medicare	Medicaid
Stricter Prior Authorization Criteria	✓	✓	✓	✓
Closed and Value-based Formularies	✓	✓	Somewhat	?
Outcomes-based Contracts	✓	✗	Somewhat	?
Shifting From Medical to Pharmacy Benefit	✓	N/A	✗	?

Contracting – But How?

Tools / Mechanisms

- **Stricter Prior Authorization Criteria**
- Closed and Value-based Formularies
- Outcomes-based Contracts
- Shifting From Medical to Pharmacy Benefit



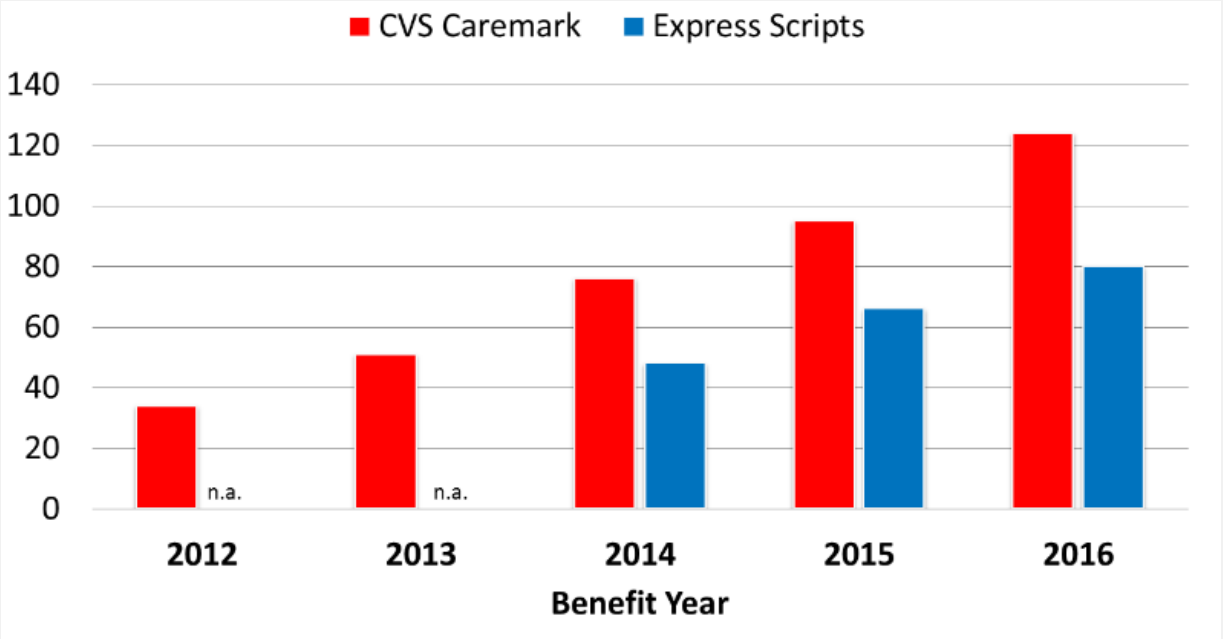
Source: Zitter Group Survey, 2011

Contracting – But How?

Tools / Mechanisms

- Stricter Prior Authorization Criteria
- **Closed and Value-based Formularies**
- Outcomes-based Contracts
- Shifting From Medical to Pharmacy Benefit

Number of Products on PBM Formulary Exclusion Lists, 2012-2016



Note: Express Scripts did not publish exclusion lists for 2012 and 2013

Source: Pembroke Consulting research, Published on Drug Channels on August 4, 2015

Contracting – But How?

Tools / Mechanisms

- Stricter Prior Authorization Criteria
- **Closed and Value-based Formularies**
- Outcomes-based Contracts
- Shifting From Medical to Pharmacy Benefit

PREMERA BLUE CROSS

More from Kai Yeung!

Contracting – But How?

Tools / Mechanisms

- Stricter Prior Authorization Criteria
- Closed and Value-based Formularies
- **Outcomes-based Contracts**
- Shifting From Medical to Pharmacy Benefit

Situation

- Novartis publically proposed a pay-for-performance agreement for Entresto
- Cigna and Aetna announced agreeing to deals with Novartis for Entresto

Agreement Details

- Rebates for the drug will be tied to improvement in relative health of patients; the primary metric is reduction in the proportion of patients with heart failure hospitalizations
- Entresto has preferred brand status on Cigna and Aetna formularies, subject to prior authorization review

Outcome

- Highly publicized pay-for-performance agreement for a potentially blockbuster drug, possibly opening the doors for future outcomes-based agreements in the US

Cigna

Aetna

"Outcomes-based contracts require that prescription medicines perform in the real world at least as well as they did during clinical trials and are a valuable tool for improving health and managing costs."

-Christopher Bradley, Senior Vice President Cigna Pharmacy Management

"We think that's going to become something that becomes more and more popular in the US and around the world."

-David Epstein, Division Head and CEO, Novartis Pharmaceuticals

Contracting – But How?

Tools / Mechanisms

- Stricter Prior Authorization Criteria
- Closed and Value-based Formularies
- **Outcomes-based Contracts**
- Shifting From Medical to Pharmacy Benefit

Situation

- Both PCSK9 inhibitors launched in the US within a few months of each other with similar efficacy and safety profiles
- Being a highly scrutinized drug class, payers were publically acknowledging looking for ways to restrict access to these drugs well before their launch

Agreement details

- Rebates will be tied to the ability of the drug to lower LDL cholesterol levels consistent with results observed in clinical trials
- Repatha has exclusive coverage on Harvard Pilgrim Health Care's formulary

Outcome

- Demonstration of manufacturers willingness to engage in outcomes-based agreements in the US in order to secure access

Cigna

Harvard Pilgrim HealthCare

"This drug is highly effective but by any rational benchmark, it's overpriced. [The deal is a way for Amgen] to put their money where their mouth is."

-Michael Sherman, CMO Harvard Pilgrim Health Care

"Repatha gave us a great opportunity to offer value-based contracts that address payers' concerns about both the impact of the potential patient population on their budget as well as putting a guarantee around the expected efficacy of the drug."

-Amgen Press Release

Contracting – But How?

Tools / Mechanisms

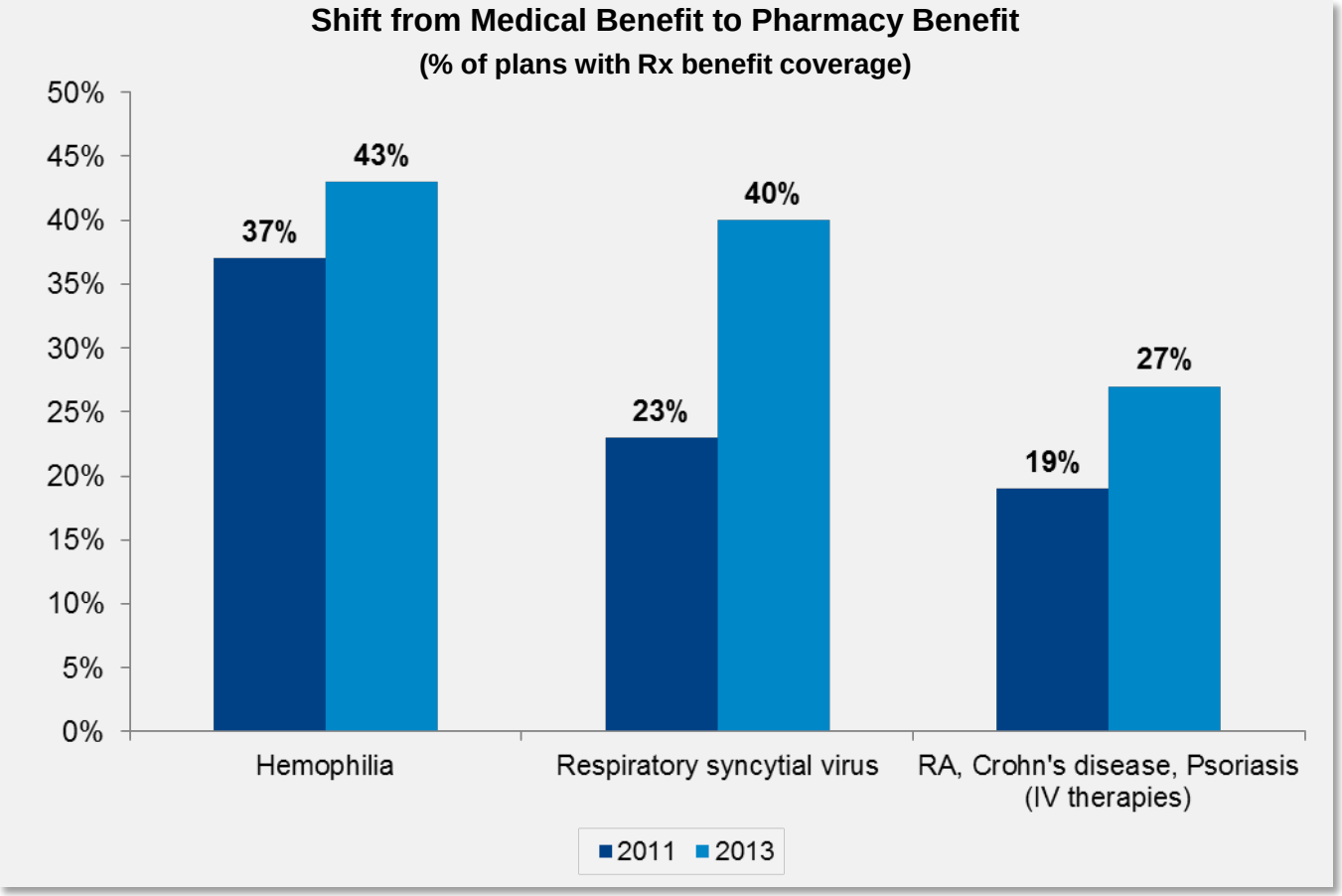
- Stricter Prior Authorization Criteria
- Closed and Value-based Formularies
- **Outcomes-based Contracts**
- Shifting From Medical to Pharmacy Benefit

More from John Carlson!

Contracting – But How?

Tools / Mechanisms

- Stricter Prior Authorization Criteria
- Closed and Value-based Formularies
- Outcomes-based Contracts
- **Shifting From Medical to Pharmacy Benefit**



Source: Should Specialty Drug be Shifted From Medical to Pharmacy Benefit?, Managed Care, January 2015

What does the future hold?

Innovative Management

Tools / Mechanisms	Commercial MCOs	PBMs	Medicare	Medicaid
Stricter Prior Authorization Criteria	✓	✓	✓	✓
Closed and Value-based Formularies	✓	✓	Somewhat	?
Outcomes-based Contracts	✓	✗	Somewhat	?
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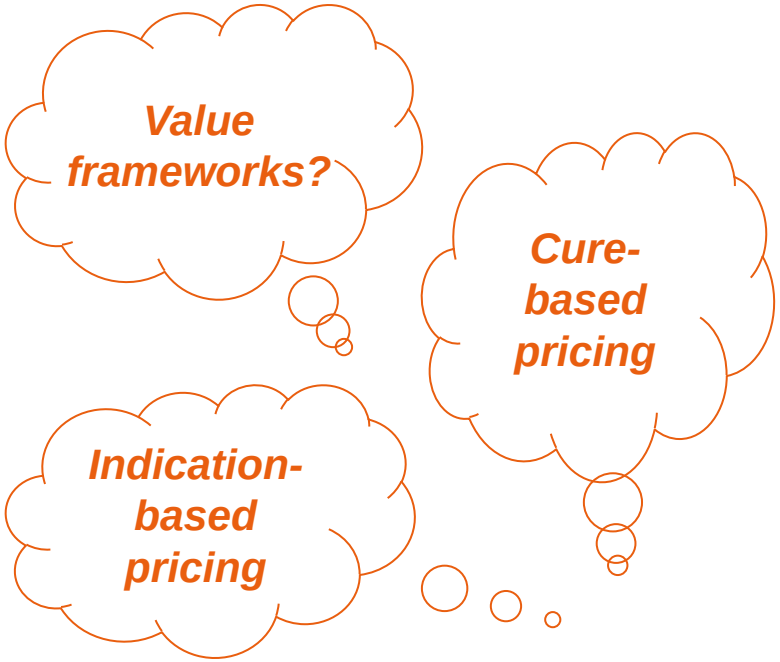
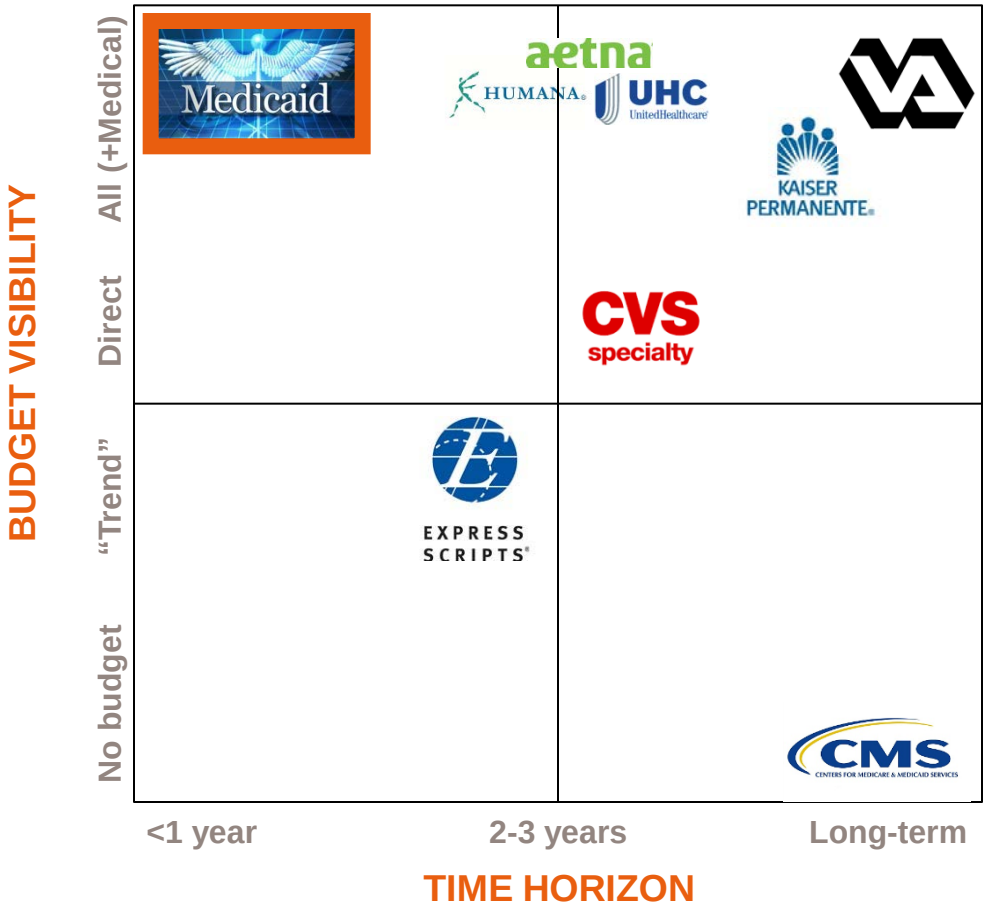


APPENDIX

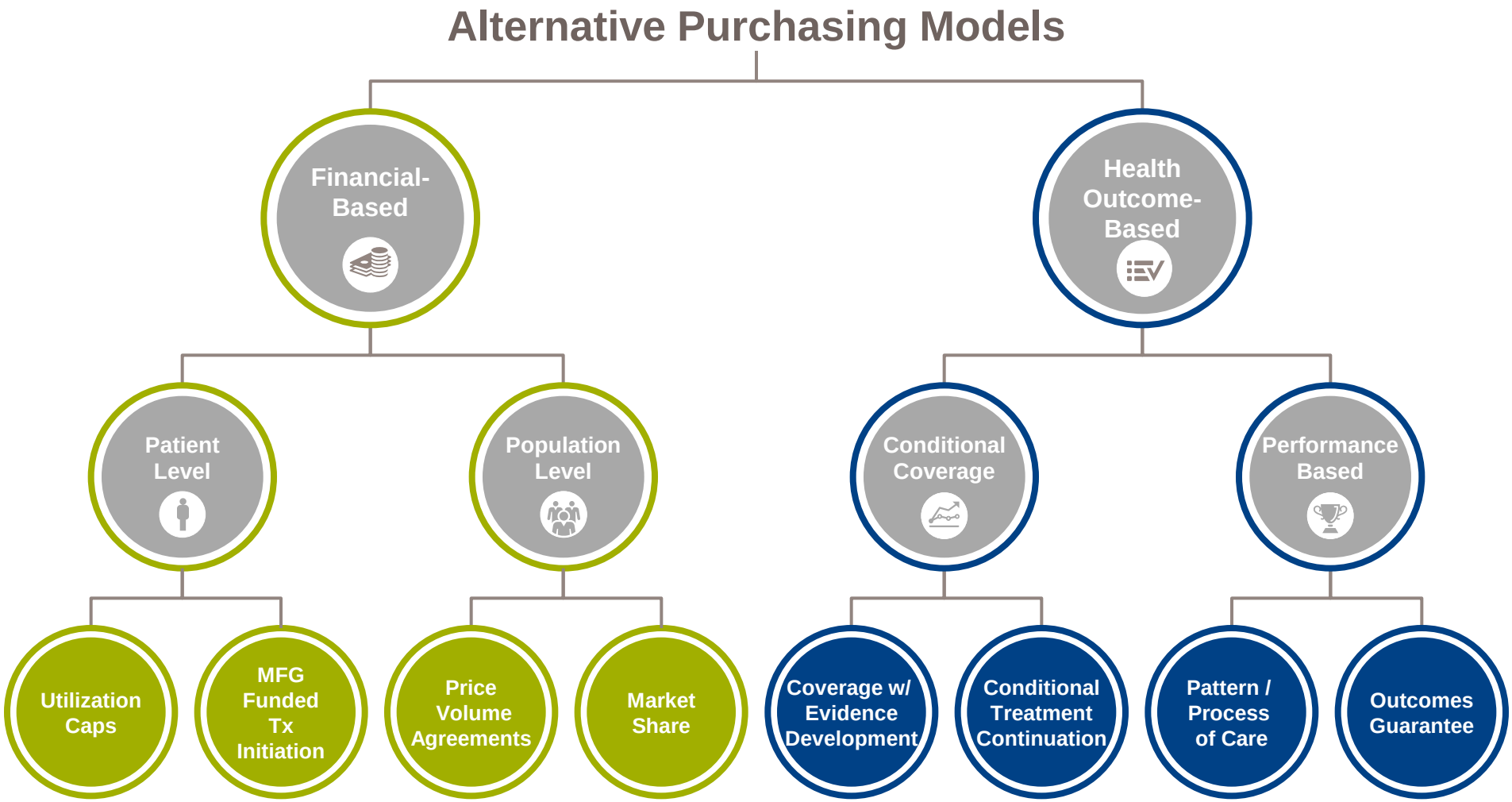
Payer Archetypes

Budget Visibility and Time Horizon



Source; GfK Internal Framework

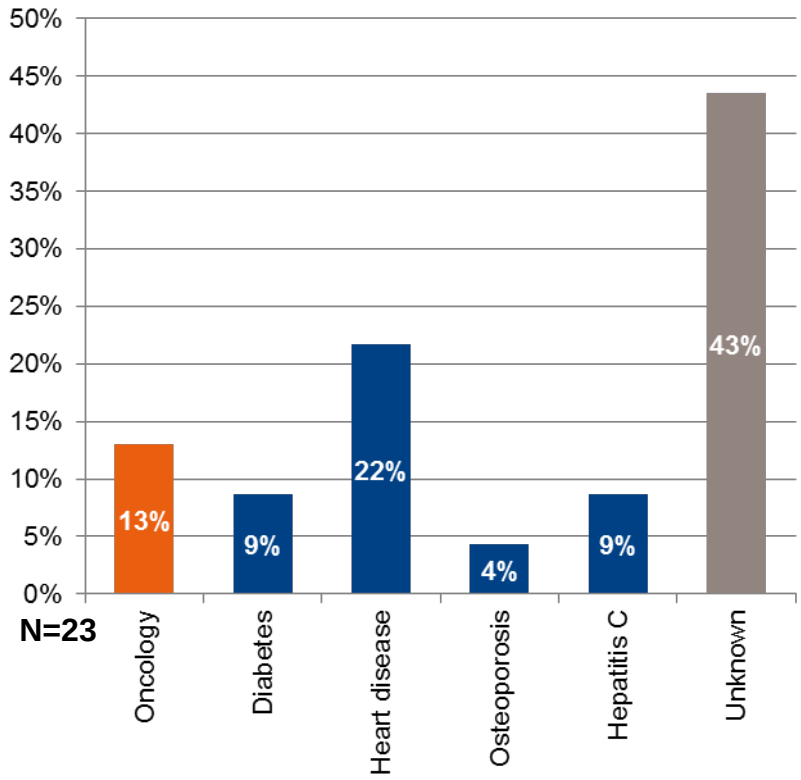
General taxonomy for alternative purchasing models (APMs)



23 APMs with private US payer have been publically acknowledged; however, limited details are available for nearly half of the agreements

Alternative Purchasing Models

Distribution of APMs by disease-type in US



Products with APMs in the US

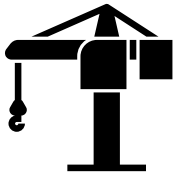
1. **Oncology**
   - Avastin
   - Oncotype Dx
   - Vectibix
2. **Diabetes**
   - Januvia
   - Janumet
3. **Heart disease**
   - Entresto
   - Repatha
   - Praluent
4. **Osteoporosis**
   - Actonel
5. **Hepatitis C**
   - Sovaldi
   - Harvoni

Source: GfK desk research

4 key considerations when planning an APM

Goals

How can this align with addressing our goals and needs?

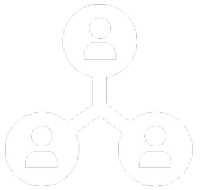


Levers

What already available resources can be leveraged?

Outcomes

Which endpoints and / or outcomes are most appropriate?



Alignment

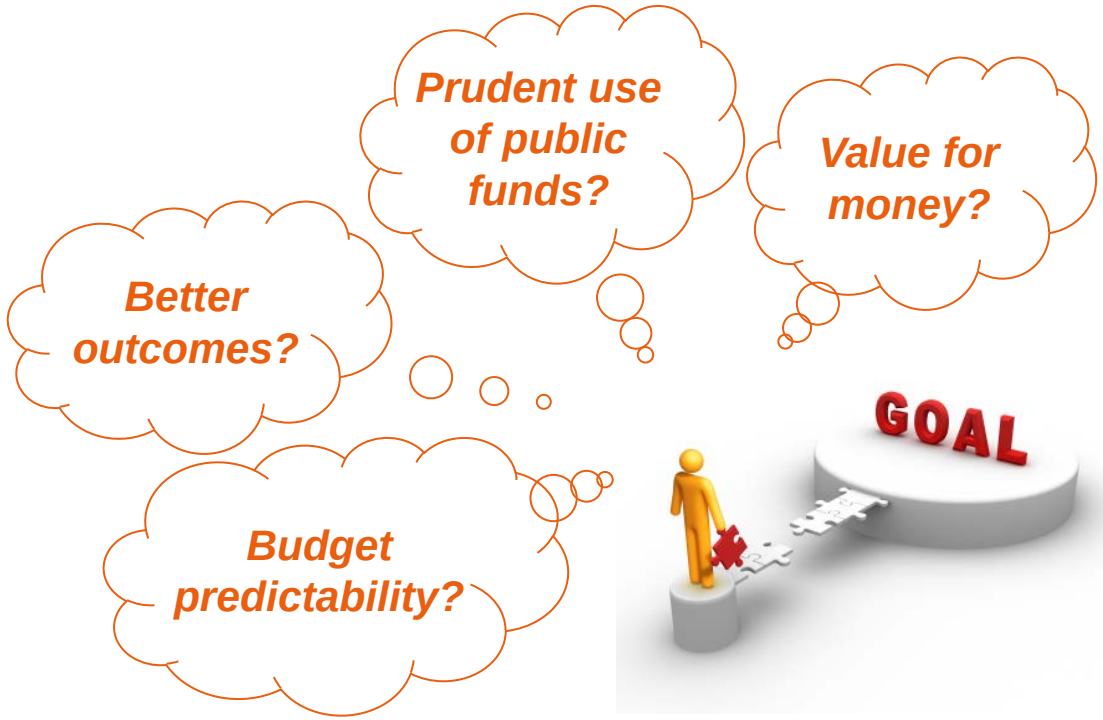
Which stakeholders need to be informed and involved?

APMs should ideally address priority goals and needs

Considerations

Goals & Needs

- APMs have the potential to address both financial and non-financial goals and needs
- Goal #2



Utilizing available levers and resources can lessen initial hurdles during implementation

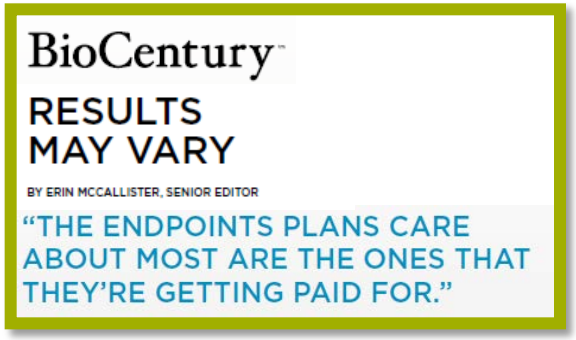
	Considerations
Levers & Resources	• Existing activities and studies can provide a structured base for data tracking and collecting as well as expedite reporting (e.g., Texas) • Agreements need to accommodate for existing capabilities and resources to avoid potential delays or incomplete data reporting • Specific drugs or drug classes may be better targets for an APM – considerations should include PDL exclusion status, competition, patient subtypes, etc.

Endpoints need to be clearly defined with the ability to be collected and reported

Defining Outcomes

Considerations

- It may be prudent to target endpoints and outcomes already included in provider risk agreements
- Potential legal barriers must be considered, particularly if endpoints or outcomes being considered were not evaluated in clinical trials or are not currently in the FDA label
- Outcomes tracking can be patient-level or population-level – choice of data tracking will be dictated by prevalence of the indication and the endpoints tracked



Multiple stakeholders will need to be informed and engaged

Aligning Stakeholders

Considerations

- Any agreement with manufacturers is contingent on CMS approval
- Support from legislators and policy-makers can provide the necessary levers to push an agreement through
- Involvement may be required from other state Medicaid administrators – incentives should be aligned to ensure collaborative efforts
- Alignment with MCOs and multi-state purchasing pools will ensure utilization management efforts do not clash

Taxonomy Definitions

Performance-based health outcomes schemes: price, level, or nature of reimbursement are tied to future performance measures of clinical or intermediate endpoints that are ultimately related to patient quality or quantity of life

Conditional coverage: coverage is granted conditional on the initiation of a program of data collection

- Coverage with evidence development: coverage is conditioned on collection of additional population level evidence, from pre specified study, to support continued, expanded, or withdrawal of coverage
  - Only in research: coverage conditional on individual participation in research (i.e. only patients participating in the scientific study are covered)
  - Only with research: coverage conditional on agreement to conduct a study that informs the use of the medical product in the payer patient population

Performance-linked reimbursement: reimbursement level for covered products is tied, by formula, to the measure of clinical outcomes in the "real world";

- Outcomes guarantees: manufacturer provides rebates, refunds, or price adjustments if their product fails to meet the agreed upon outcome targets
  - Example: J&J agreed to reimburse the NHS in either cash or product for patients who do not respond (Response measure: 50% decrease in serum M protein) after 4 cycles of treatment with Velcade. Responding patients receive additional 4 cycles.
- Pattern or process of care: reimbursement level is tied to the impact on clinical decision making or practice patterns
  - Example: UnitedHealthcare agreed to reimburse OncotypeDx test for 18 months while it and Genomic Health monitor the results.
  - If the number of women receiving chemotherapy exceeds an agreed upon threshold, even if the test suggests they do not need it, the insurer will negotiate a lower price