

Forecasting and Data Analytics Round Table Discussion

Parallel Session 4 – Handout
26th June

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Round table topics

1. **US Long Term Outlook on Rx Spending** – Share some thoughts on the country mostly responsible for EU future Pharma prosperity
2. **US Pricing Gross to Net** – How much of your US Gross Revenue really arrives as net value in your organisation?
3. **Rx Patient Share - EphMrA Meta-Analysis Project Draft** – Introduction and Discussion
4. **Forecasting Clinic – Ask your peers at the Roundtable!**

The 3 questions *'you always wanted to ask your peers'*

Question 1:

Question 2:

Question 3:

1. US Long Term Outlook on Rx Spending



US Long Term Outlook on Rx Spending - *Share*

*some thoughts on the country
mostly responsible for EU future
Pharma prosperity*

Long Term Drivers and Breaks of US Rx Spending

Drivers

- 1 New high-cost speciality, cell and gene therapies for rare and ultra-rare diseases
- 2 Overall US Healthcare spending increasing faster than Rx spending
- 3 Increasing FDA NME approvals (2016: 22, 2017: 46, 2018: 59)
- 4 Anticipated + 13% CAGR 2016-22 for oncology therapies
- 5 Growth in # of older patients / living longer and demand for HC resources

Shifting value drivers for uptake from clinical data to net price and discount strategy - including in competitive speciality markets

Breaks

- 6 Patent cliffs / generics / biosimilars of high-value drugs e.g. Sitagliptin, Humira up to 2025
- 7 Cheaper Drugs from China e.g. PD-1s / Continued shift to lower cost generic drugs
- 8 Growth of High Deductibles / Lower Premiums Plans increasing consumer anger with high-cost Rx
- 9 Increased payer restrictions, exclusions and utilisation controls of novel Rx's e.g. CGRPs, IL-17s, IL-23s anticipated
- 10 Federal and state price controls on drugs (non-commercial patients) and potential formal or informal international price referencing
- 11 Share of new drugs approved with blockbuster potential (>\$1b) decreasing, 2018: 13 vs. 2017: 23
- 12 Increasing role of ICER in contracting
- 13 Media / patient advocacy backlash against rising cost of Rx / Healthcare and social disparity

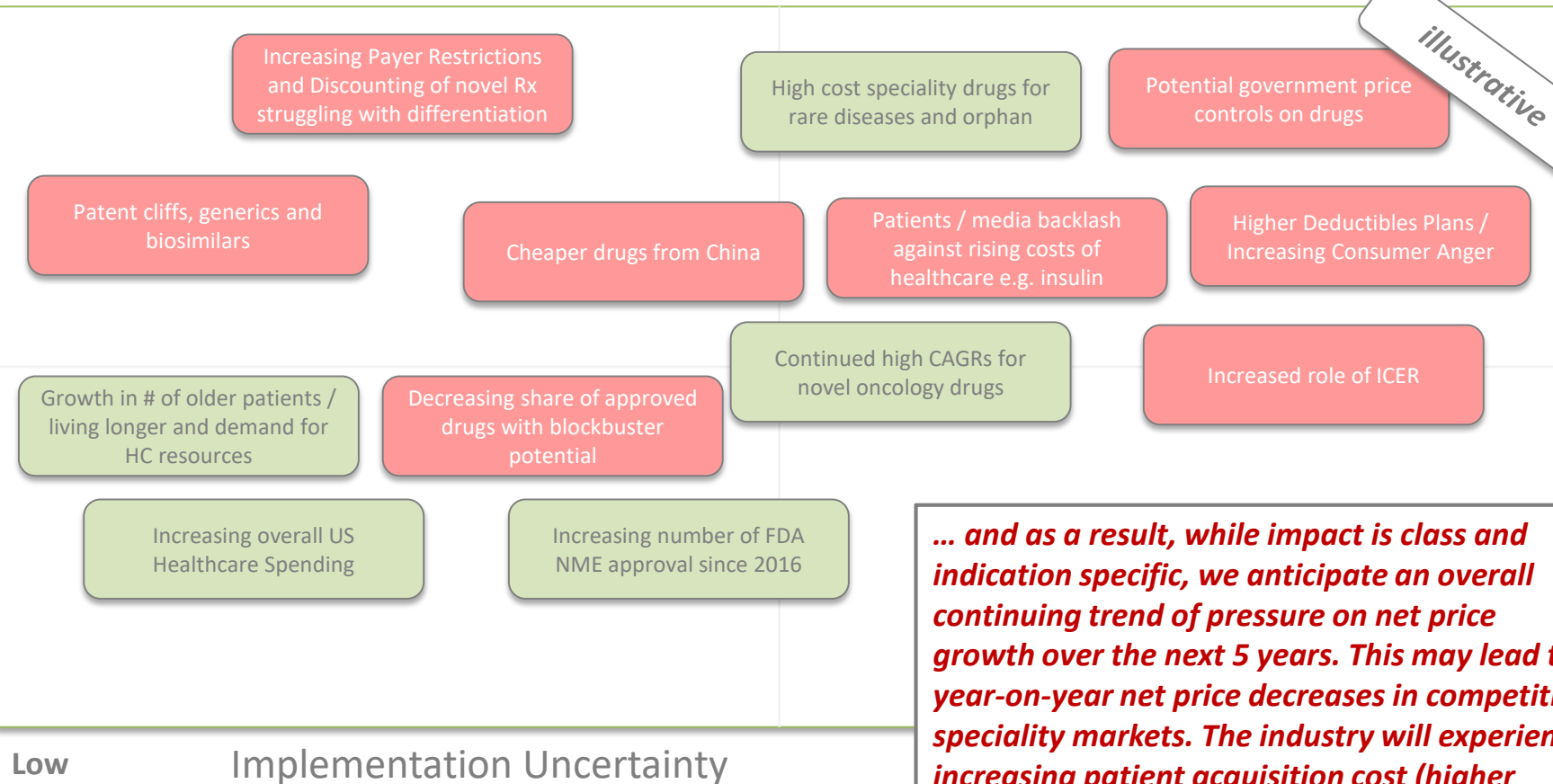
High

illustrative

High

Impact

Low



... and as a result, while impact is class and indication specific, we anticipate an overall continuing trend of pressure on net price growth over the next 5 years. This may lead to year-on-year net price decreases in competitive speciality markets. The industry will experience increasing patient acquisition cost (higher rebates / discounts / performance based agreements) and also more patient access programs (industry covering co-pays)

Appendix - Sources

Pharma spending vs. context of overall healthcare spending increase -

<https://www.insurancejournal.com/news/national/2018/06/22/493065.htm>

<https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/downloads/highlights.pdf>

Patent cliff vs. newer high-cost speciality drugs - <https://healthcare.mckinsey.com/sites/default/files/Pharma-Spending-Growth-Making-The-Most-Of-Our-Dollars.pdf>

Malaysia price controls – will it spread? <https://www.lek.com/insights/ei/malaysia-drug-price-control-impact>

High-cost gene therapies - <https://endpts.com/ned-sharpless-weighs-in-on-gene-therapy-pricing-debate-suggesting-the-messaging-got-lost/>

Future therapy class spending - <https://my.express-scripts.com/rs/809-VGG-836/images/Express%20Scripts%202018%20Drug%20Trend%20Report.pdf>

High deductible plans / lower premiums, <https://www.ajmc.com/newsroom/enrollment-in-highdeductible-health-plans-continues-to-grow>

PD1 – much cheaper in China - <https://www.bloomberg.com/news/articles/2019-06-04/china-s-revolutionary-cancer-drugs-undercut-american-competitors>

<https://info.evaluategroup.com/rs/607-YGS-364/images/WP17.pdf>

Growth in # of older patients - <https://www.cnbc.com/2017/10/03/health-care-dilemma-10000-boomers-retiring-each-day.html>,
<https://www.fqhc.org/blog/2017/8/30/baby-boomers-all-grown-up-the-impact-of-the-aging-population-on-healthcare>

Patient advocacy / media backlash against rise in Rx costs (example insulin NYT 16th June 2019 - <https://www.nytimes.com/2019/06/13/opinion/insulin-price-costs.html>)

Appendix

TREND FORECAST FOR KEY THERAPY CLASSES

2019-2021, in order of 2018 PMPY spend

Show table



Unit cost increases for brand drugs to treat inflammatory conditions will continue, as biosimilar savings are not expected until at least 2020.

Diabetes trend will increase as no new widely used generics are coming to market until Januvia® (sitagliptin) generics become available in 2023. Greater utilization of diabetes medications is expected due to population aging and the obesity epidemic.

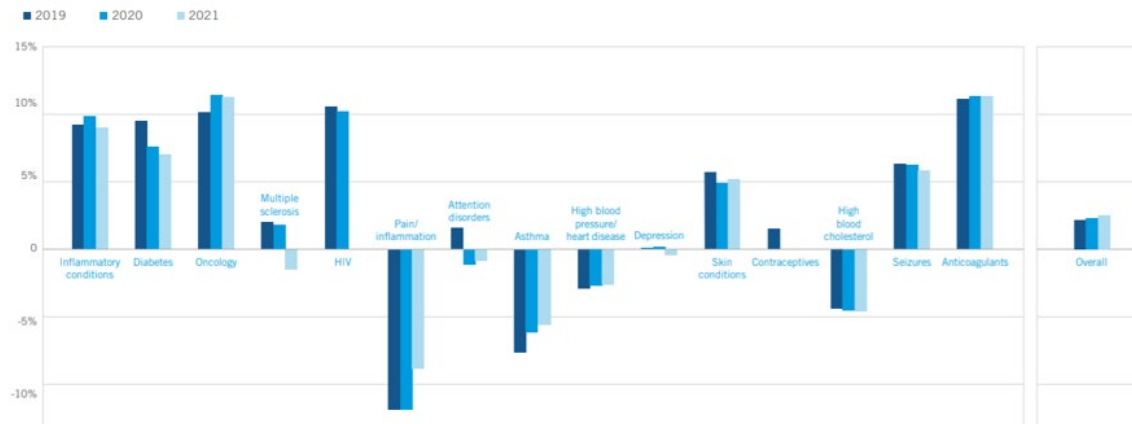
Pain and inflammation trend is expected to be negative through 2021, due to savings from the utilization of the generic for Lyrica® (pregabalin) and to lower opioid utilization, along with the impact of our Advanced Opioid Management solution.

Spending on multiple sclerosis drugs declined in 2018, due in part to negative utilization trend as patients taking Tecfidera® (dimethyl fumarate) moved to Ocrevus® (ocrelizumab), which is typically adjudicated through the medical benefit. The impact of this market share shift may be diminished, leading to positive trend for the next two years.

Attention disorder medications had an unprecedented drop in unit cost in 2018, which is not expected to continue.

Declining prices of PCSK9 inhibitors greatly impacted high blood cholesterol trend in 2018, but are not expected to continue in future years. There are no patent expirations nor generic launches that would likely impact trend.

Newer oral anticoagulants will continue to take market share from older, less expensive drugs, like warfarin, which will continue to drive spending increases through 2021.

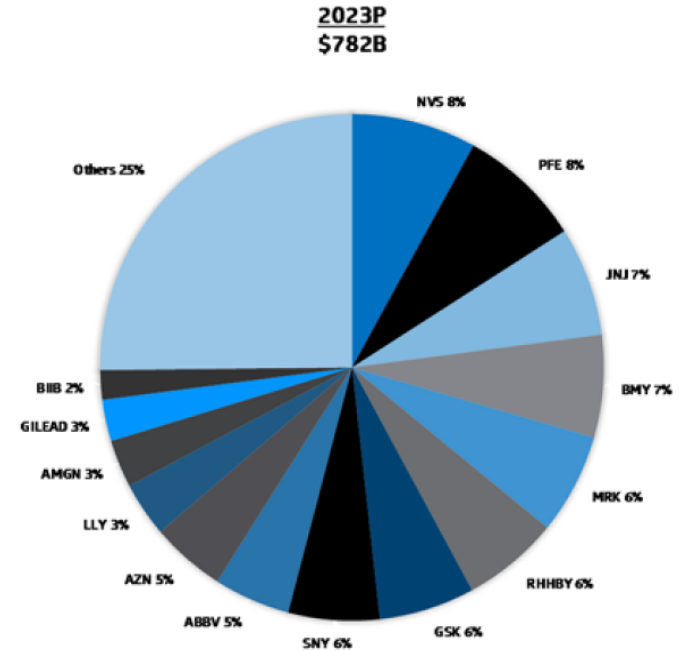
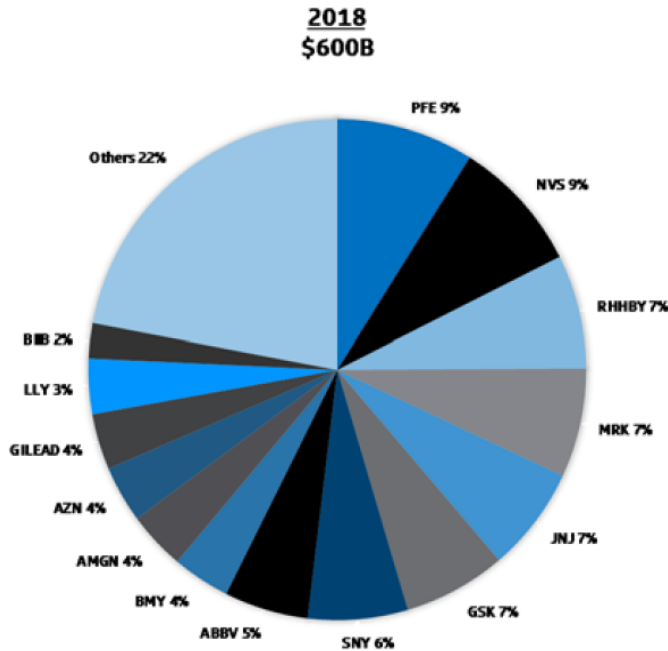


Source: Express Scripts <https://my.express-scripts.com/rs/809-VGG-836/images/Express%20Scripts%202018%20Drug%20Trend%20Report.pdf>

Appendix - US Drug Sales 2018 – 2023 projected, CAGR ~5%

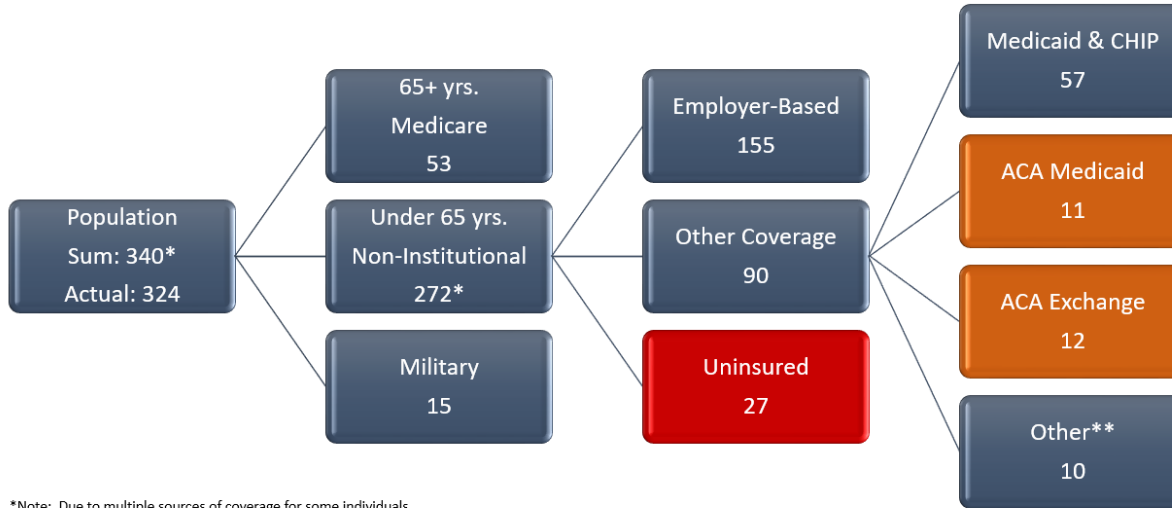
Pharmaceutical Companies: Drug Sales As A Percentage Of The Total Market

Analysis of more than 950 products from the product lines and pipelines of over 85 big- and mid-cap companies in the pharmaceutical and biotechnology industries suggests that drug sales from this group totaled \$600B in 2018. We project that this universe will generate drug sales of \$782B in 2023, implying 5% compounded growth. Pfizer, Novartis, Roche, Merck, and Johnson & Johnson dominated the worldwide market in 2018. Novartis, Pfizer, Johnson & Johnson, Bristol-Myers Squibb, and Merck should be the leaders in 2023. Our analysis of therapeutic categories concludes that oncology / hematology, infectious disease, cardiology, and diabetes/obesity should dominate the worldwide market in 2023.



Appendix – Sources of Health Insurance Coverage 2016 in the US

Sources of Health Insurance Coverage in 2016 (Millions of Persons)



*Note: Due to multiple sources of coverage for some individuals, there is some double-counting in the components. The actual U.S. population in December 2016 was approximately 324m.

**Other: The 10m was reduced to tie to the total for "Other Coverage" of 90m. "Other" includes 23m persons (9m non-ACA marketplaces, 9m disabled in Medicare, 5m other).

Source data:
CBO "Federal Subsidies for Health Insurance Coverage for People Under Age 65: 2016 to 2026" (March 2016)
Census Bureau "Health Insurance Coverage in the United States: 2015 (September 2016)"

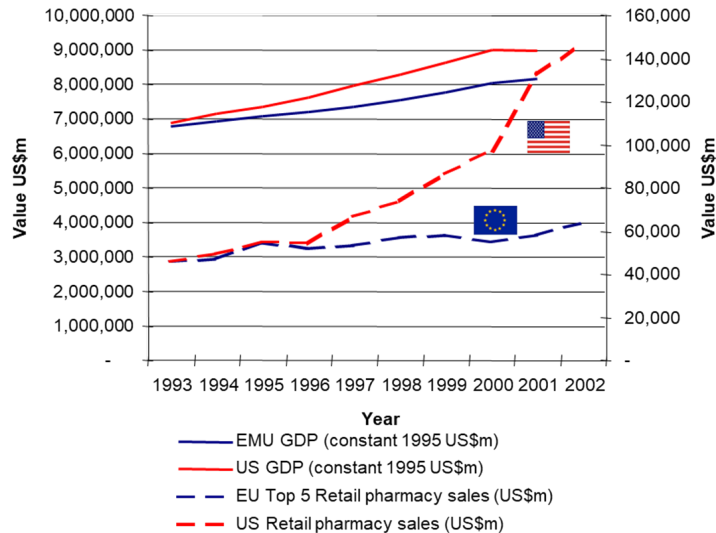
U.S. health insurance coverage by source in 2016. CBO estimated ACA/Obamacare was responsible for 23 million persons covered via exchanges and Medicaid expansion.

Obama-Care halved the number of Americans without insurance coverage, yet ~10% of the population remain uninsured

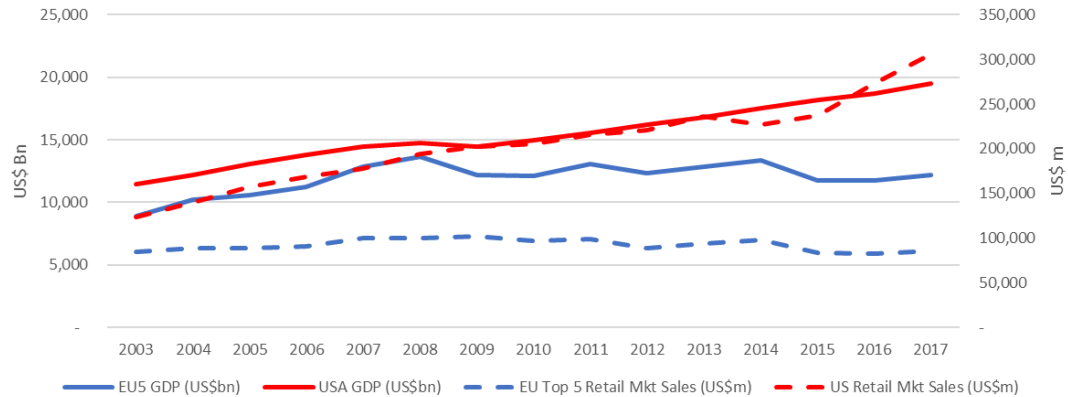
Appendix: historic data on GDP and retail pharmaceutical markets in US and EU Top-5 1993 - 2002 and 2003 – 2017

Note: scales of the two charts are different and GDP and retail sales graphs plotted on secondary vertical axis

GDP versus Retail Pharmaceutical Market Growth
1993 - 2002, US\$m



GDP versus Pharmaceutical Market Growth 2003 - 2017



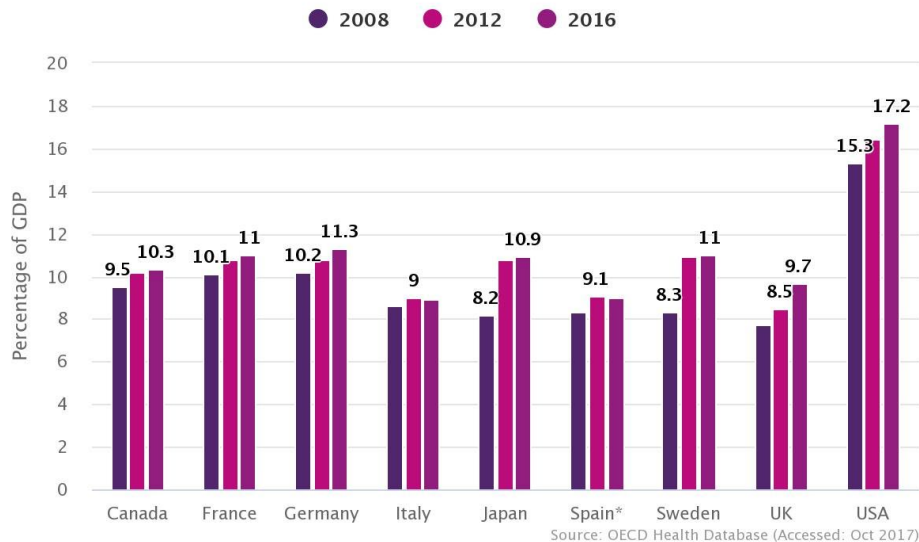
The US and EU5 retail pharma markets used to be of similar size back in the mid nineties. Until recently, the US retail market has picked up in growth and is more than 3 x EU5 while GDP has grown to less than 2 x EU5

Sourced: IMS, IQVIA published data, EPFIA, groupH research & analysis

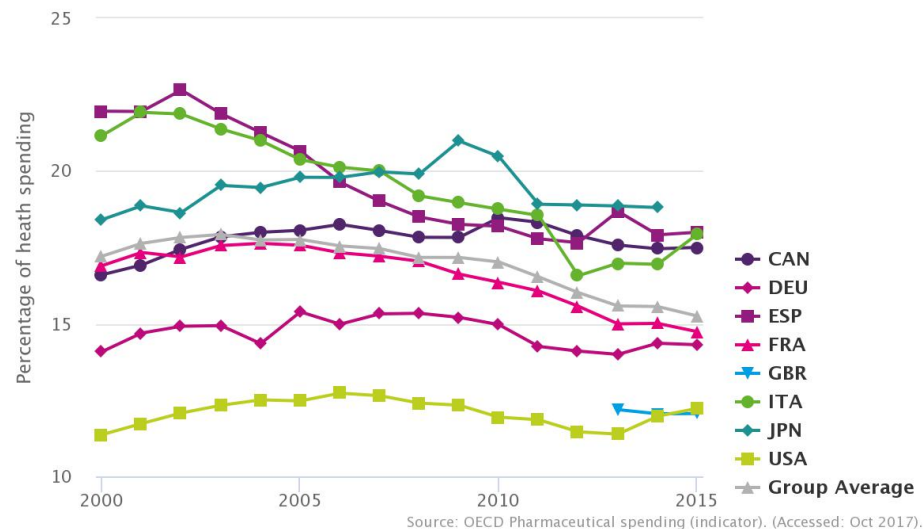
Appendix: historic health expenditure as percent of GDP and Pharma spending as percent of health spending

Note: latest figures from OECD

Health Expenditure as per cent of GDP



Pharmaceutical spending as a percentage of health spending 2000–2015



2. US Pricing Gross to Net



“Would that be ‘net’ or ‘gross’?”

1. US Pricing Gross to

Net – *How much of your US
Gross Revenue really arrives as net
value in your organisation?*

Gross to Net

Manufacturers at present only publish aggregate gross to net discounts across the entire portfolio. New legislation creating transparency at a product level could increase future competitive dynamics

- Payor Discounts, Rebates and Charge Backs (includes government e.g. Medicaid***/US Dept. of Veteran Affairs, employers and insurers)

- Hospital and Clinic Discounts for inclusion and 340B Drug Discount Programs

- Patient Access Programs / Coupons + Discount Cards*****

- Patient Access Services*****

- Wholesaler Fees (as applicable)

- Product Returns / Accruals

- Prompt Pay Discounts

TOP SECRET

TOP SECRET

Gross / List Price

At ex-manufacturing / WAC level*

Net Price 1

Net Price Definition may vary between manufacturers depending on cost centres

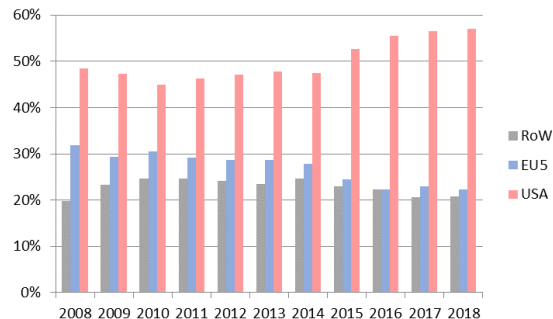
Net Price 2

- Gross prices displayed initially by manufacturers or reported by market audit data are not the same as the **negotiated net prices** paid in the end by insurers, employers or PBMs on behalf of patients
- A **presidential directive currently under discussion [May 2019]** would ask federal agencies to force price disclosures at product level across the industry and increase future competitive dynamics** leading to lower future net prices

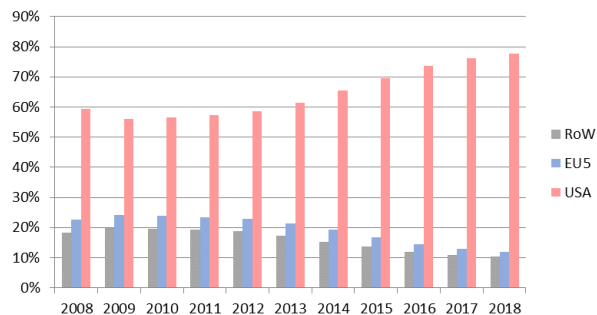
Source: groupH research & analysis, Michael Hy, *after wholesaler and pharmacy margins and distribution costs, **<https://www.fiercepharma.com/pharma/trump-to-unveil-executive-order-to-force-drug-cost-disclosure-wsj>, ***supplemental and statutory rebates, ****for healthcare practices e.g. <https://www.genentech-access.com/hcp/my-patient-solutions.html>, *****to get patients from unpaid to paid scripts and to mitigate list price increases for patients on co-insurance or deductibles

US oncology and speciality Rx sales share from global Rx sales based on list prices have been increasing since 2010

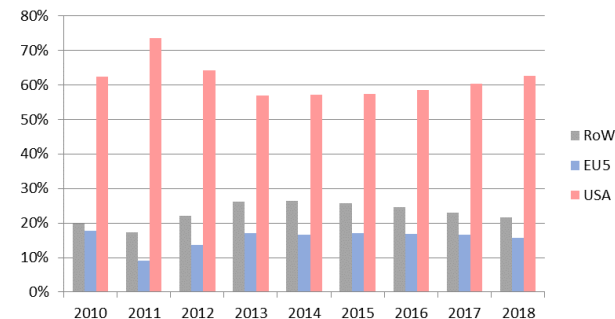
Oncology Product Basket
2012 – 2018, % of Global Revenue



Specialty Care Product Basket
2012 – 2018, % of Global Revenue



Primary Care Product Basket
2012 – 2018, % of Global Revenue



Includes: Afinitor (everolimus), Alimta (pemetrexed), Erbitux (cetuximab), Herceptin (trastuzumab), Ibrance (palbociclib), Keytruda (pembrolizumab), Nexavar (sorafenib), Opdivo (nivolumab), Sutent (sunitinib), Tarceva (erlotinib), Xeloda (capecitabine)



Includes: Cubicin (daptomycin), Enbrel (etanercept), Gardasil (HPV), Humira (adalimumab), Kuvan (sapropterin), Repatha (evolocumab), Zytiga (abiraterone)

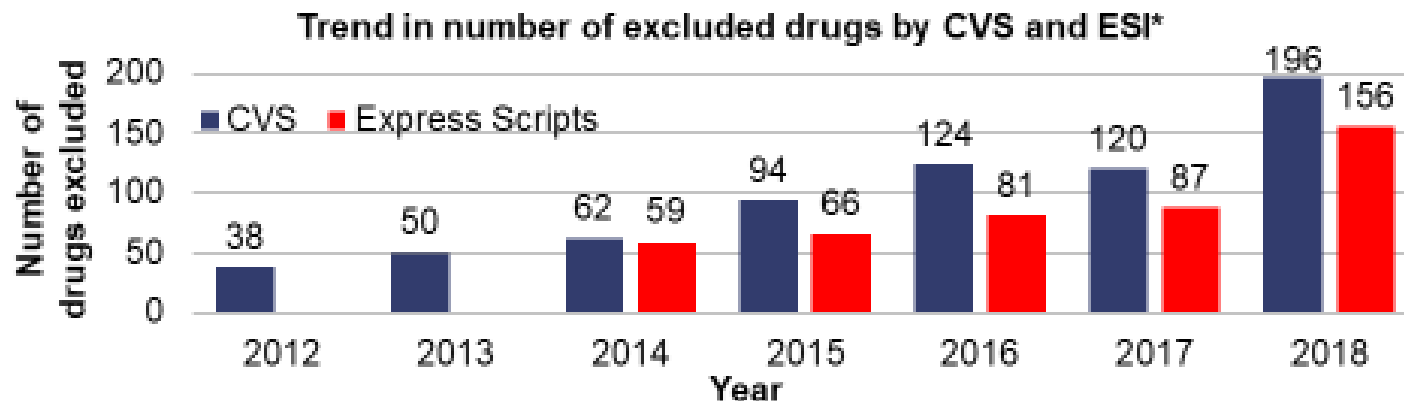


Note: 2007 – 2009 excluded as products not yet available in most countries

Includes: Eliquis (apixaban), Jardiance (empagliflozin), Onglyza (saxagliptin), Pradaxa (dabigatran), Praluent (alirocumab), Pristiq (desvenlafaxine), Tradjenta (linagliptin), Trintellix (vortioxetine), Xarelto (rivaroxaban)

Source: IQVIA, analysis based on Global Revenue LC€, Note: IQVIA gross revenue not gross/net adjusted, groupH research & analysis, BI

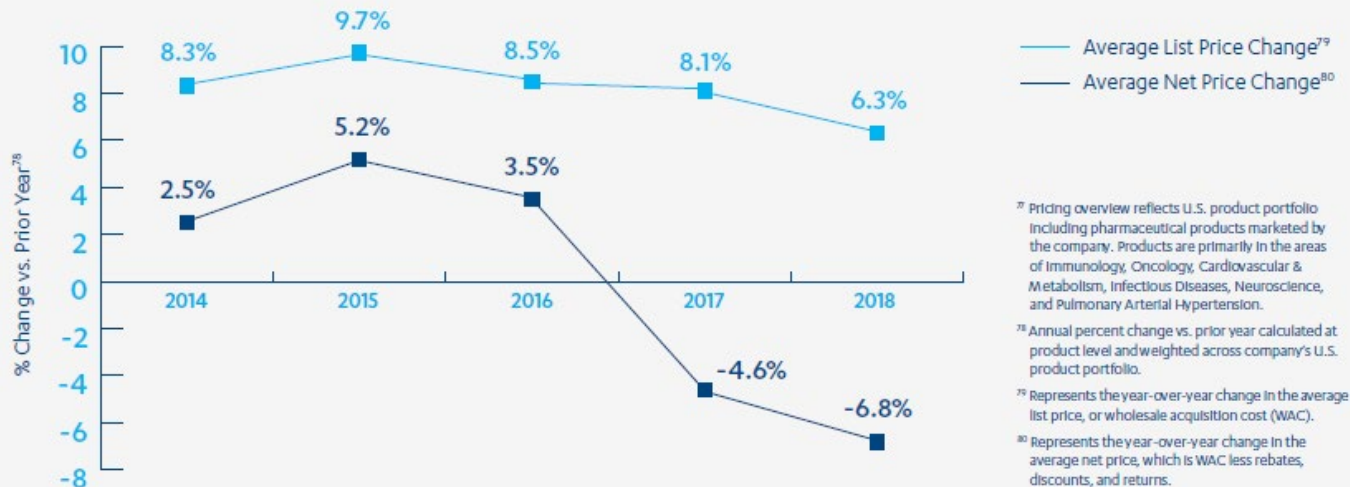
However, leading US PBMs continue to increase the number of drugs excluded each year – some solely due to the amount of price increases



Source: Compass Strategic Consulting Inc. research & analysis, CVS: https://www.caremark.com/portal/asset/Formulary_Exclusion_Drug_List.pdf
ESI: https://www.express-scripts.com/art/pdf/Preferred_Drug_List_Exclusions2018.pdf

And individual companies such as J&J calculate a difference between gross to net of 13.1% with a net price decrease of -6.8% in 2018

JANSSEN U.S. PRICING OVERVIEW⁷⁷



Source: <https://jnj-janssen.brightspotcdn.com/30/0e/a365aea641e28a57573355358e01/2018-janssen-us-transparency-report.pdf>

*IQVIA 2019, <https://www.iqvia.com/institute/reports/the-global-use-of-medicine-in-2019-and-outlook-to-2023>, **U.S. Department of Labor. Bureau of Labor Statistics. "CONSUMER PRICE INDEX – DECEMBER 2018," ***<https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/Downloads/highlights.pdf>, ****Ibid

- Average discount rate of 47% in 2018
- The average net prices for branded medicines in the U.S. grew an estimated 1.5% in 2018*
- Total rate of medical inflation in the U.S. rose approximately 2%**
- Total prescription drug spending grew 0.4%*** in 2017 while overall healthcare expenditures increased 3.9%****

Sanofi shows similar gross to net discounts for 2018 suffering a price decrease of 8% net compared to the previous year at 55% overall discount

CONTINUED TRANSPARENCY IN THE U.S.

U.S. Portfolio Annual Aggregate Price Changes*

Year	Average Aggregate List Price	Average Aggregate Net Price
2016	4.0% INCREASE	2.1% DECREASE
2017	1.6% INCREASE	8.4% DECREASE
2018	4.6% INCREASE	8.0% DECREASE

**Aggregate across Sanofi's prescription portfolio*

In 2018, 55 percent of our gross sales were given back to payors as rebates, including \$4.5 billion in mandatory rebates to government payors and \$7.3 billion in discretionary rebates.

Source: : https://www.sanofi.us/-/media/Project/One-Sanofi-Web/Websites/North-America/Sanofi-US/Home/corporateresponsibility/Prescription_Medicine_Pricing_2019.pdf

MSD could increase its net prices by 3% in 2018 but the average discount taken off from gross revenue is at 44%

	2010	2011	2012	2013	2014	2015	2016	2017	2018
US Product Portfolio ¹ % Change vs. Prior Year ²									
List Price Change (WAC) ³	7.4	9.5	9.2	9.6	10.5	9.8	9.6	6.6	5.5
Net Price ⁴	3.4	5.1	6.2	5.5	3.7	5.5	5.5	(1.9) ⁵	2.99
	2010	2011	2012	2013	2014	2015	2016	2017	2018
US Product Portfolio									
Avg. Discount ⁶ (%)	27.3	28.9	29.9	32.1	37.0	38.2	40.9	45.1	44.3

¹ US Product Portfolio includes human health pharmaceutical and vaccine products marketed by the company, excluding partnered products. The product sales utilized in the analysis represent ~97% of the total US Product Portfolio in 2010, increasing each year to approach 99.8% of coverage in 2017.

² Annual percent change vs. prior year was calculated at a product level and weighted across the company's US Product Portfolio.

³ Represents the year-over-year change in the average list price or wholesale acquisition cost (WAC).

⁴ Represents the year-over-year change in average net price, which is WAC less rebates, discounts and returns.

⁵ In 2017, the average annual net price across our portfolio declined by 1.9 percent, reflecting specific in-year dynamics, including the impact of loss of patent protection for three major medicines.

⁶ Weighted average annual discount is calculated by dividing annual rebates, discounts and returns by annual gross sales.

Source: : https://s3.amazonaws.com/msd18-assets/wp-content/uploads/2019/02/28155345/2018-US-PRICING-TRANSPARENCY-REPORT_02.2019.pdf

Novo Nordisk's average discount rate in 2018 was at 51.5%

2.1 Net sales and rebates (continued)

Gross-to-net sales reconciliation

DKK million	2018	2017	2016
Gross sales	230,701	216,174	198,924
US Managed Care and Medicare	(65,207)	(53,077)	(40,874)
US wholesaler charge-backs	(29,469)	(28,324)	(25,416)
US Medicaid rebates	(11,950)	(12,491)	(10,862)
Other US discounts and sales returns	(6,606)	(5,771)	(5,147)
Non-US rebates, discounts and sales returns	(5,638)	(4,815)	(4,845)
Total gross-to-net sales adjustments	(118,870)	(104,478)	(87,144)
Net sales	111,831	111,696	111,780

Sales discounts and sales rebates are predominantly issued in the US. As such, rebates amount to 68% of gross sales in the US (64% in 2017 and 59% in 2016). Novo Nordisk sales are impacted by exchange rate changes. For development in key currencies refer to note 4.2 on p 83.

Source:

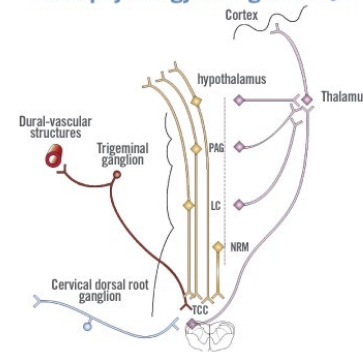
https://www.novonordisk.com/content/dam/Denmark/HQ/investors/irmaterial/annual_report/2019/NN-AR18_UK_Online.pdf

- Average discount rate was 51.5% in 2018 (after conversion into DKK)
- Net sales stayed more or less constant since 2016 while gross sales increased year-on-year (after conversion into DKK)

Case Study CGRPs in Migraine



Pathophysiology of migraine Fig. 1



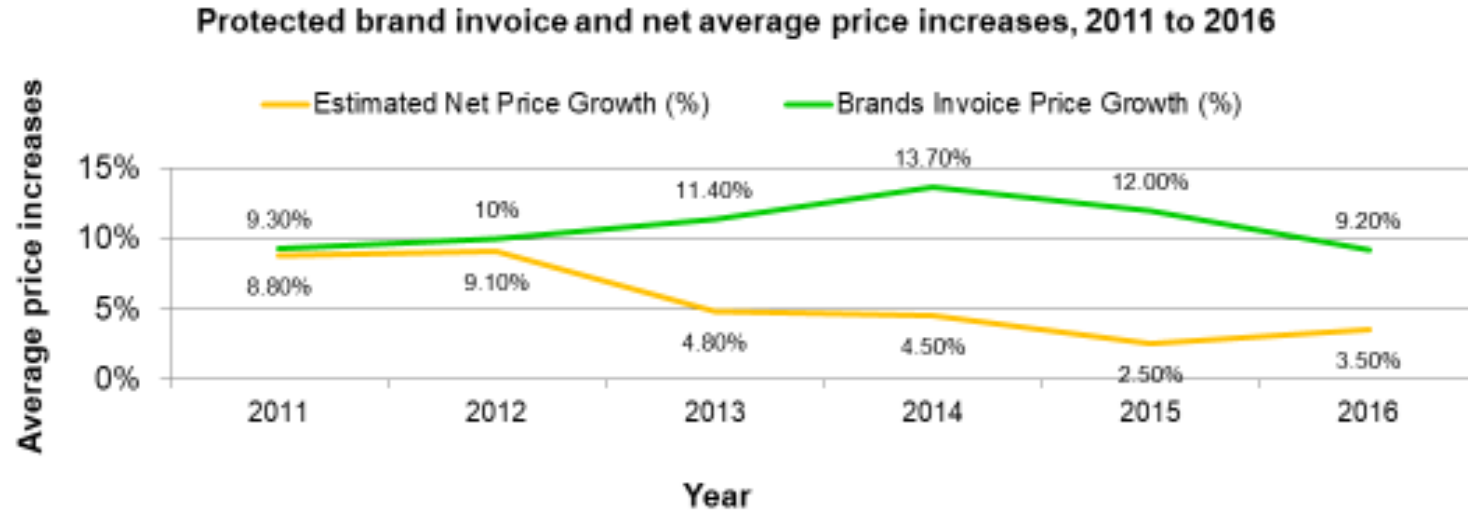
Lilly

- New anti-CGRP migraine **prevention** drug class launched last year
- In launch order: 1. erenumab (Aimovig) / Amgen + Novartis, 2. fremanezumab (Ajovy) / Teva and 3. galcanezumab (Emgality) / Lilly
- Despite minor differences in MOA, the clinical profiles of all three drugs is seen as interchangeable in terms of efficacy, tolerability, safety and administration**
 - Once monthly sc injection after loading dose, Ajovy offers also a once quarterly sc injection alternative
- All three FDA-approved treatments rely on monoclonal antibodies designed to target CGRP or its receptor in trigeminal pain pathways
- Interestingly, the new market leader in new Rx as of end of April 2019 is the third to market
- Lilly's therapy Emgality claimed the largest share of first-time patients at 37.7%, outstripping Amgen's Aimovig, whose share dropped to 37.2%; Teva came in at a 25.1%
- Leadership position led by having best formulary position across 3 major PBMs (Cigna Inc's Express Scripts, UnitedHealth Group's OptumRx and CVS Health)

- **Fierce battle for patient share decided by market access / contracting**
- **Lilly aiming for favourable insurance coverage by heavy discounting with PBMs + First-Month-Free patient access programs**
- **Too early to call a winner in this battle after <12 months after launch of Aimovig**
- **Lilly may have used its T2D primary care experience competing in markets lacking differentiation over Amgen who has mostly a speciality care background to its advantage**

*calcitonin-gene-related peptide, <https://www.reuters.com/article/us-lilly-migraine-share/lillys-new-migraine-drug-pulls-ahead-of-amgen-in-fierce-battle-for-new-prescriptions-idUSKCN1SG28C>, groupH analysis and research, **no data on head to head trials, migrain.com, groupH research & analysis and Michael Hy

While US brand prices may continue to increase, all important net prices show a significant slowing over recent years



Source: Compass Strategic Consulting Inc. research & analysis, https://structurecms-staging-psyclone.netdna-ssl.com/client_assets/dwonk/media/attachments/590c/6aa0/6970/2d2d/4182/0000/590c6aa069702d2d41820000.pdf?1493985952

3. Rx Patient Share - EphMrA Meta-Analysis Project Draft

for Discussion

Background

- The EphMrA Forecasting Forum was set-up in 2018 and had its first online dial-in meeting on 11th October 2018
- Currently 36 individuals from 11 Pharma companies (AZ, Bayer, BI, Celgene, Eisai, J&J, Roche, Sanofi, Pierre Fabre and others), and 5 agencies (Aurum, groupH, JD, Kantar, SKIM) are forum participants
- The highest scoring topic* of interest to forum participants is *Forecasting Methodologies* and Process, and one of most critical assumptions driving product forecasts is *future Patient Share* for any particular product
- *Patient Share* assumptions can be derived by different means of market research and analysis, most involving qualitative and quantitative primary research with physicians, online or through telephone interviews
- Forecasters in Pharma companies or agencies may then choose to adjust or not adjust the shares for physician bias and other market factors (not least e.g. market access strategy considerations) before their use in a forecasting model, others may choose to derive patient shares through Conjoint / Differential Analysis
- While there is broad agreement in principle that adjustments are needed and inevitable in many cases, there is little consensus and relatively little evidence behind what this adjustment factor should be and how it should be derived. The topic is complex, there is a need for an as high as possible precision, individual studies show discrepancies

* Survey Monkey Feedback, January 2019, n = 15

Background ... (continued)

- There is also no real clarity on which forecasting methodology in general or which factors in particular are likely to lead to long term forecasting outcomes or accuracy – hence the idea to conduct a **systematic review**
- The EphMrA Forecasting Forum offers the unique opportunity to assemble a sufficiently large sample of historic market research from >10 years ago to compare with real world outcomes of products and their respective patient share at peak revenue
- If successful, a large sample of suitable, high-quality, >10 year old market research reports combined with suitable real-world patient shares would represent high grade evidence and the project team is hopeful that it will allow deeper insights into the predictive qualities of some of the methodologies that are being used
 - In the absence of RCTs and cohort trials in forecasting methodologies, a META analysis (provided statistical methods are applicable to the sample of projects being analysed) is an attractive approach/strongest form of evidence as so far evidence is limited to case reports and expert opinion

for Discussion

Objectives



for Discussion

Primary Objectives

- To understand better, qualitatively and quantitatively, the relationship between '*Patient Preference Share*' stated by physicians as part of primary market research ahead of product launch and real-world product shares as reported by market audit data
- If possible, to understand better this relationship considering different possible biases/impact such as indication, treatment positioning, geography and chosen research methodology (including physician, consultant or market research agency bias)

Secondary Objectives

- Based on the available insights, to propose methodological improvements to forecasting and market research methodology
- To understand better the role of payer contracting and market access strategies in the uptake and peak revenue of a product

The geographic scope of this project includes the US and EU markets plus Japan

Geographic Scope

- United States



- Europe



- Japan



Secondary Research scope will be broader and may include additional countries as required

Comments

- The geographic scope, in principle is world-wide and covers all markets frequently included in long-term and strategic market opportunity assessments

step 1

Scoping, Roles & Responsibilities & Alignment

June, July 2019

step 2

Data Gathering, Data Analysis

September – December 2019 (n = 20 – 50 products)

step 3

Insights & So What?

Early 2020

TCs as required



Soft Kick Offs

Stakeholder Briefings

- Forum members (industry, agencies)
- Academic Partner

Preparation & Alignment

- Consensus on modus operandi, CDAs
- Refining the Question
- Align on: Objectives, scope, approach, timing, project outputs
- Project eligibility criteria (data specifications)
- Informal project ID and data gathering
- Roles & responsibilities fine-tuning

Data Gathering – 2nd Round

- Historic project documentation from EphMrA members
- Associated IQVIA data pull (or similar) for real-world patient shares
- Research & analysis for real-world peak patient share as needed



Interim



Interim

- View and validate available data set for eligibility/inclusion
- Is the question still valid?
- Data clarifications, alignment and adjustments as needed
- Revise roles and objectives as needed

Data Analysis by Product

- Historic project documentation from EphMrA members
- Associated IQVIA data pull (or similar) for real-world patient shares

Part A – Academic Partner

- **Statistical analysis**
- Read all projects
- Data abstraction
- Data analysis and quantitative insights
- Other outputs, to be agreed

Part B – Agencies + Industry

- **Non-statistical analysis**
- Secondary research and analysis
- Primary research (e.g. industry, brand manager interviews as needed)

for Discussion

Documentation

- Document in and analysis for each product case study

So What?

- What are the results?
- Are the results valid?
- How can we apply them?

Final Draft

- Share & discuss draft report in forum
- Final edits



Final

4. Forecasting Clinic – Ask your peers at the Roundtable

Thank You!

For your diary - Upcoming EphMrA Forecasting Forum Events

4h Face-to-face meeting

- Friday, 11th October – 4h face-to-face Roundtable in Ingelheim, sponsored by BI and groupH
- Attendance is free and for EphMrA members only
- Topics
 - Guest speaker Prof. Paul Goodwin, University of Bath
 - Author of: ‘Decision Analysis for Management Judgement’ and ‘Forewarned - a sceptics guide to prediction’ among other publications
 - Other topics to be announced post EphMrA 2019

1h TC dial-ins July – December 2019

- Dates and topics to be published post EphMrA 2019

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For joining the EphMrA Forecasting Forum
please contact Bernadette Rogers,
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