



Long Term Forecasting Accuracy

Analysing groupH's long term forecasting track record since 2003

September 2017



groupH Forecasting Experience and Accuracy

Background & Approach

Approach

The question many people ask: How accurate are long term forecasts?

Limitations to analysing one's own track record:

Product not to fall victim to attrition

Product launched

Product close to or past peak sales

Requires to go back to projects conducted at late stage over 10 – 15 years ago

A basket of ~50 drug forecasting projects from the groupH core team

Anonymization of Projects/Case Studies

Checking for available market data for these products

Detailed case-studies analysing the 'Best' and the 'Worst' examples



groupH Core Team Forecasting Experience

Forecasts not evaluable for accuracy (1 of 4)

Year	Therapy Area	Product Forecasted		Overall Project Objective	Geographic Scope	Primary Research		Sales Data	
		MOA / class	Stage			KOL Qual / Semi-Quant	Payer	Available	Reason
2004	Oncology (RCC)	novel	Ph 2	inform internal go/no go decisions	US + EU5	✓	✗	(✓)	Launched, but no indication breakdown
2006	GI	novel	Ph 3	inform internal go/no go decisions	US + EU5	✓	✗	✗	Discontinued
2006	Breast cancer Leukemia	novel	Ph 2	inform internal go/no go decisions	US, EU5	✓	✗	✗	Discontinued
2006	Bipolar disorder	novel	Ph 3	In-licensing opportunity evaluation	EU5	✓	✗	✗	Discontinued
2007	Oncology	novel	Ph 2	inform internal go/no go decisions	US + EU3	✓	✗	✗	Discontinued
2007	CV	novel	Ph 3	inform internal go/no go decisions	US + EU5	✓	✗	✗	Discontinued
2008	Arrhythmia	novel	Ph 2	inform internal go/no go decisions	US, EU5	✓	✗	✗	Discontinued
2009	Menstrual Bleeding	novel	Ph 2	In-licensing opportunity evaluation	US, EU5	✓	✗	✗	Product unspecified (TPP only)
2009	Oncology (total 6 indications)	novel	Ph 2	internal prorization of development options	US, EU5	✓	✗	✗	Still in development
2009	Anemia of cancer & CKD	novel	Preclinical	inform internal go/no go decisions	US, EU5	✓	✗	✗	Still in development
2009	Stem cell mob. for HSCT	novel	Ph 1	inform internal go/no go decisions	US, EU5	✓	✗	✗	Still in development



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Forecasts not evaluable for accuracy (2 of 4)

Year	Therapy Area	Product Forecasted		Overall Project Objective	Geographic Scope	Primary Research		Sales Data	
		MOA / class	Stage			KOL Qual / Semi-Quant	Payer	Available	Reason
2009	Depression	novel	Ph 1	Support partnering decisions	US, EU5	✓	✗	✗	Named-patient
2010	CNS	novel	Ph 2	Inform internal go/no go decisions	US + EU5	✓	✗	✗	Discontinued
2010	Gastric reflux disease	novel	Ph 2	Inform Ph 3 go/no go decision	US, CA, UK, DE, FR, IT, BR	✗	✗	✗	Discontinued
2010	Osteoarthritis	novel	Ph 1/2a Ph 1/2a	Inform internal go/no go decisions	EU5	✓	✓	✗	Still in development
2010	Glaucoma	novel	Ph 2	In-licensing opportunity evaluation	US, EU3	✓	✓	✗	Discontinued
2010	Diabetes (T2D)	novel	Ph 2	Inform internal go/no go decisions	US, EU4, JP, CA, CN, BR	✗	✗	✗	Discontinued
2010	AF - Stroke prevention	novel	Ph 2	Inform internal go/no go decisions	US, EU5, JP	✓	✗	✗	Discontinued
2011	Neuropathic Pain	novel	Ph 2	Inform internal go/no go decisions	G7, CA, MX, RU, CN, BR	✗	✗	✗	Discontinued
2011	Iron overload	novel	Ph 2	inform internal go/no go decisions	US, EU5, JP	✓	✗	✗	Discontinued
2011	Topical anaesthetic	novel	Launched	Inform internal LCM option decisions	US, FR, UK, ES, JP, CN	✓*	✓	✗	LCM opportunities not pursued
2011	Local anaesthetic	novel	Launched	Inform internal LCM option decisions	USA, FR, UK, IT, JP	✓	✗	✗	LCM opportunities not pursued



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Forecasts not evaluable for accuracy (3 of 4)

Year	Therapy Area	Product Forecasted		Overall Project Objective	Geographic Scope	Primary Research		Sales Data	
		MOA / class	Stage			KOL Qual / Semi-Quant	Payer	Available	Reason
2011	Lupus	novel	Ph 2	Inform Ph 3 go/no go decision	US, EU5, RoW roll-up	✗	✗	✗	Discontinued
2011	Pulmonary	novel	Ph 2	Inform internal go/no go decisions	US + EU5	✓	✓	(✓)	Very recently launched
2011	CV	novel	Ph 2	Inform internal go/no go decisions	US + EU5	✓	✓	(✓)	Launched, but no indication breakdown
2011	Pain	novel	Re-launched	Inform internal go/no go decisions	EU5	✓	✓	✗	Discontinued
2011	CV	novel	Ph 1	Inform internal go/no go decisions	US + EU3	✓	✗	✗	Discontinued
2012	IPF	novel	Ph 1	Inform Ph 2 go/no go decision	US, EU5, RoW roll-up	✓	✓	✗	Discontinued
2012	Wound care	novel	Ph 2	Inform internal go/no go decisions	US + EU5	✓	✓	✗	Still in development
2012	Oncology (CRC, NSCLC)	novel	Ph 2	Inform internal go/no go decisions	US, EU5	✓	✗	✗	Still in development
2013	Atopic Dermatitis	novel	Ph 1	In-licensing opportunity evaluation	US, EU5	✓	✗	✗	Still in development
2013	Chronic rhinosinusitis Food allergy	novel	Ph 1	Support internal go/no go decisions	US, EU5 & emerging	✓	✗	✗	Still in development
2013	Wilson's Disease	novel	Ph 2	Inform internal go/no go decisions	US, EU3	✓	✓	✗	Still in development



groupH Core Team Forecasting Experience

Forecasts not evaluable for accuracy (4 of 4)

Year	Therapy Area	Product Forecasted		Overall Project Objective	Geographic Scope	Primary Research		Sales Data	
		MOA / class	Stage			KOL Qual / Semi-Quant	Payer	Available	Reason
2014	Post operative pain	Novel delivery	Concept	Internal prioritisation of development options	US, EU3	✓	✗	✗	Concept stage
2014	Haemonc (NHL)	novel	Ph 1/2	Inform internal go/no go decisions	US, EU3	✓	✓	✗	Still in development
2014	Hyperoxaluria	novel	Ph 2	Inform internal go/no go decisions	US, EU	✓	✓	✗	Still in development
2014	Ophthalmology	novel	Ph 2	Inform Ph 3 go/no go decision	US, EU5	✓	✓	✗	Still in development
2015	COPD	novel	Ph 1	Inform internal go/no go decisions	US, EU5	✓	✓	✗	Still in development
2015	Oncology (breast cancer)	Novel delivery	Concept	Internal prioritisation of development options	US, EU3	✓	✗	✗	Concept stage
2015	Haemonc (MF)	Novel delivery	Concept	Internal prioritisation of development options	US, EU3	✓	✗	✗	Concept stage
2015	Oncology (prostate)	Novel delivery	Concept	Internal prioritisation of development options	US, EU3	✓	✗	✗	Concept stage
2015	Oncology (RCC)	Novel delivery	Concept	Internal prioritisation of development options	US, EU3	✓	✗	✗	Concept stage
2015	Oncology (HCC)	novel	Ph 2	Inform Ph 3 go/no go decision	US, EU, JP, Korea, China	✓	✓	✗	Still in development

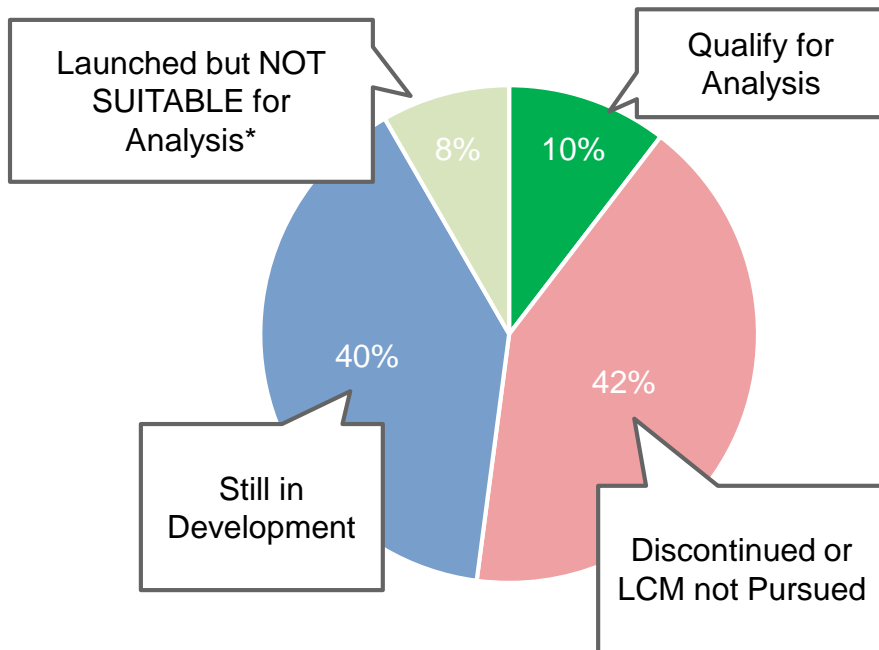


groupH Forecasting Experience and Accuracy

groupH encountered some limitations but five case studies qualified for further analysis

groupH Historic Project Basket

2003 onwards



*includes:

- Launched but no sales data indication breakdown
- Product only launched at named patient basis
- Launch too recent

Limitations



Only around 10% of projects qualify for analysis



Historic lower level forecast assumptions unlikely to find a current data set to compare with



High level sales drivers and major events can be documented and included in the analysis



Required anonymization limits disclosure of a number of details





groupH Core Team Forecasting Accuracy

Anonymised Evaluable Forecasts

Year	Therapy Area	Product Forecasted		Project scope	Geographic Scope	KOL Qual / semi-Quant Research	Forecast		Reported Sales	Forecasting Accuracy*	
		MOA	Stage				Method	Sales in target geography			
2003	Epilepsy	novel	Launch/ Ph3	Informing decision on LCM options	US, EU5, JP	✓	Monte Carlo analysis + patient-based by-year forecast model ('most realistic scenario')	US, EU5, JP Peak (2009): \$1.26bn 2015: \$866mn	WW Peak (2008): \$1.86bn 2015: \$1.01bn	≈ 85%	Case Study 1
2005	MS-related symptoms	novel	Ph 3	In-licensing opportunity evaluation	EU4 (DE, FR, IT, ES)	✓	Patient-based flowchart peak sales calculation	EU4 Peak: €16.8mn (no by-year sales forecast)	Europe 2016: €17.8mn (launched 2011, still growing)	≈ 95%	Case Study 2
2006	PD + 2 follow-on indications	novel	Launch/ Ph 3	In-licensing opportunity evaluation	WW excl. US	✓	Patient-based by-year forecast model ('base case')	Ex-US 2010: \$120mn 2015: \$237mn	Ex-US 2010: \$109mn 2015: \$268mn	≈ 90%	Case Study 3
2006	Epilepsy	novel	Ph 3	In-licensing opportunity evaluation	EU5	✓	Patient-based by-year forecast ('intermediate' scenario)	EU5 2015: €133mn Peak (2017): €148 mn	Europe 2015: €134mn (still growing)	≈ 70%	
2007	Oncology (RCC)	novel	Ph3	Informing commercialisation framework	EU5	✓	Monte Carlo analysis + patient-based by-year forecast model (base case)	EU5 Peak (2010): \$77mn	WW Peak (2010): \$237mn**	≈ 85%	

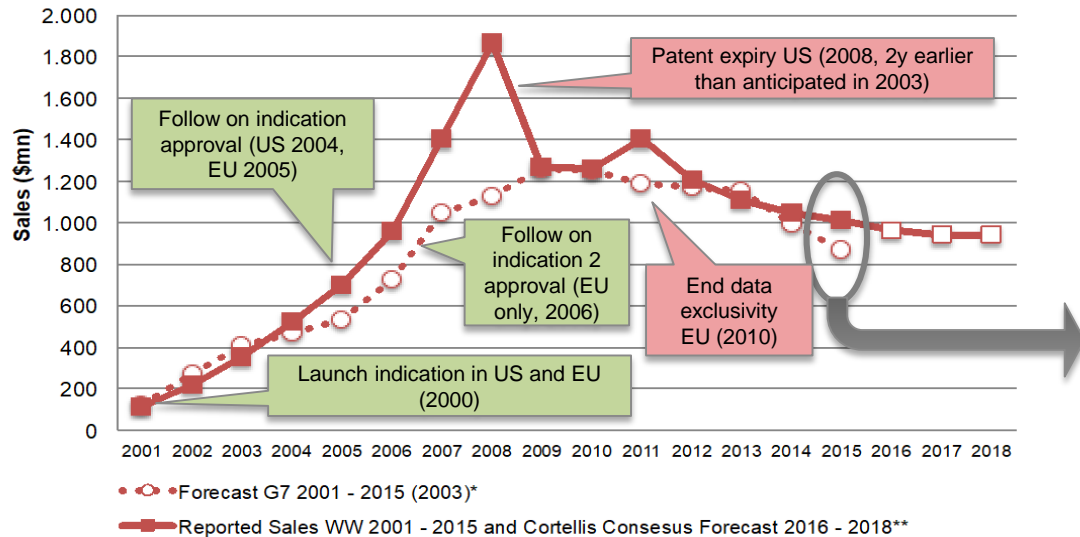
Notes: (*) Forecasting accuracy = 100% - difference between reported and forecasted sales / reported sales; Adjustments in case of mismatch between forecasted geography and reported sales geography: EU4 = 65% of Europe, EU5 = 80% of Europe, G7 = 75% of WW, EU5 = 27% of WW; (**) Also includes minor proportion of sales for R/R MCL (EU only) , Forecast EU4 (G, F, It, Sp) sales = 95% of real EU sales by population



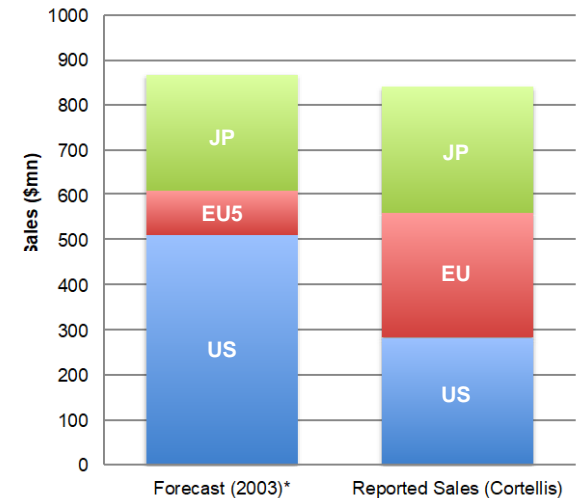
Case study 1 – Product forecast for epilepsy

Sales potential for launch indication and two follow-on indications in epilepsy

Forecasted Product Sales G7 vs. Reported Sales WW - Years 2001 – 2018



Product Sales G7 by Geography - Year 2015



Forecast (2003)

- *Background:* Launched in EU and US in 2000 - *Project scope:* Sales forecast for G7 (US, EU5, JP) until 2015 for approved use and 2 follow-on indications in clinical development
- *General Assumptions:* Approval follow on indications in about 2005 (US and EU); patent expiry 2010 (US & EU) with only moderate impact expected due to reluctance to switch epilepsy patients (max – 20%); Cost pressures in EU to lower market shares vs US
- *Forecasting methodology:* MR findings (incl. extensive physician research) were used in Monte Carlo simulation to calculate most probable scenario for a patient-based forecast model – dotted curve in graph represents total sales from 3 indications

What happened in reality (2003 – 2015)

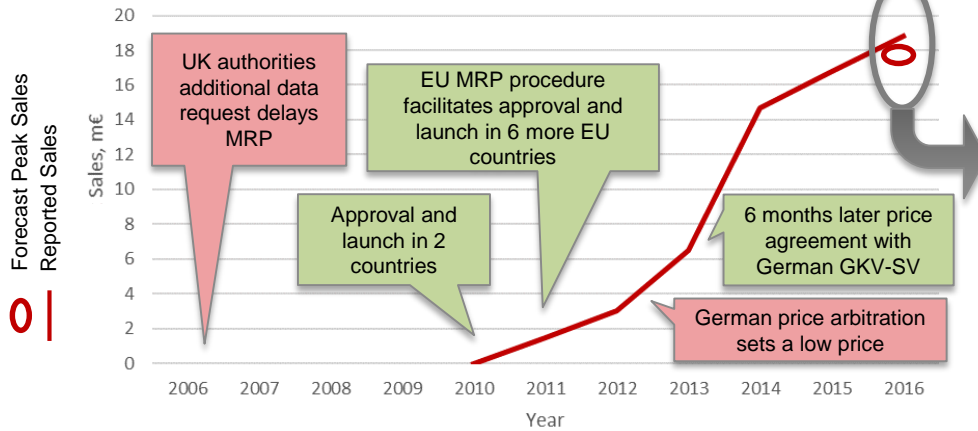
- Reported WW sales were higher than our G7 forecast until 2008 (sales data for G7 not reported) - principally reflected higher pricing achieved than expected in the EU
- Then, patent expiry occurred 2 years earlier than expected and led to dramatic fall in US sales in 2009 vs. 2008 (steadier drop in sales was expected due to physician reluctance to switch epilepsy treatments)



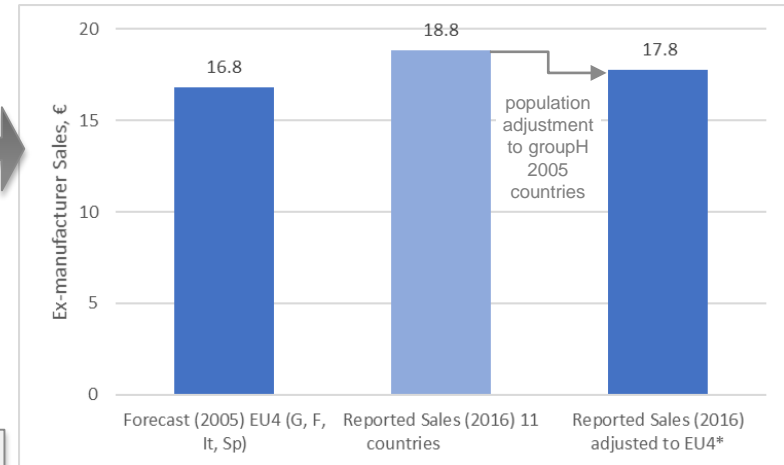
Case study 2 – Product in MS

EU4 in-licencing opportunity in Phase 3 Evaluation

Product EU Sales - Years 2006 – 2016**



Product EU Sales excl. UK - Year 2016 (adjusted to EU4)



Forecast (2005)

- **Background:** In 2005 product was in Phase 3
- **Forecasting methodology:** MR findings (incl. qual. KOL research) were used to generate assumptions supporting a high-level patient-based peak sales framework in chronic progressive and relapsing remittent patients
- **KOL view:** mixed views, novel MOA, but high unmet need due to low efficacy and AEs of existing drugs
- **Base case:** penetration ~25% in chronic progressive and 7.5% in RRMS peak, cost per day €5, 270 treatment days per year (a second scenario assumed cost per day €10, 180 treatment days and a more conservative penetration)

"Analysts at Piper Jaffray say peak sales could hit 121 million pounds in Europe and Canada combined. KBC Peel Hunt's Paul Cuddon and Nomura Code's Samir Devani see only 50 million pounds of European sales" – Reuters, 21st June 2010

What happened in reality (2005 – 2016)

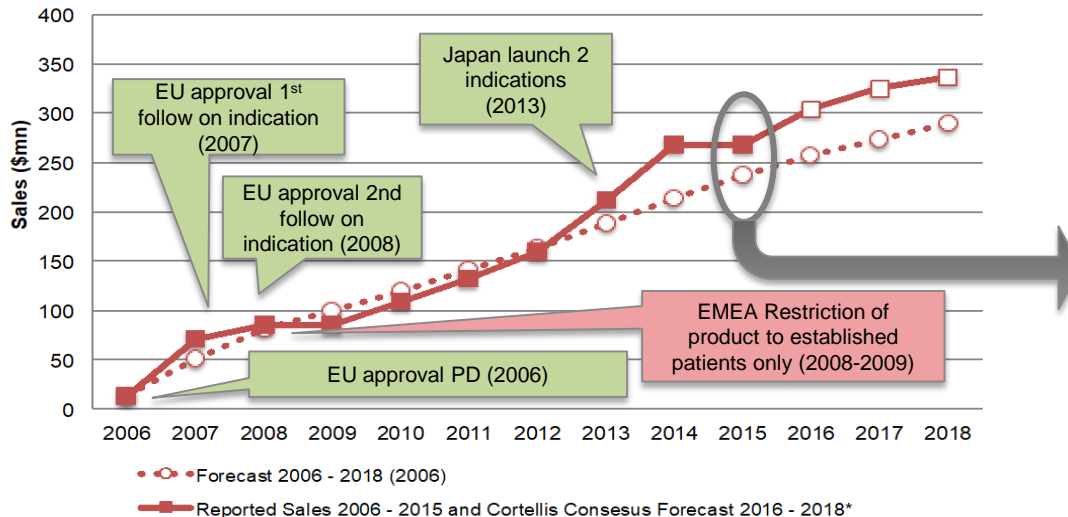
- EU launch delayed as British regulators asked for more trial data. This prevented an EU wide MRP procedure
- Launch in first country in 2010 and two other countries in 2010/2011 plus subsequently more countries
- EU average price of €5-7/day except for Germany G-BA arbitration failed to achieve a similar price, renegotiation brought the price to €10/day in Germany, 52% reimbursed + patient co-payment
- Product standard pack was assumed to last on average 30 days but instead of 8-9 doses per day as in clinical trials, average routine use was lower at 4 doses per day per patient
- 2016 EU Sales (ex-UK) = €18.8m, growing slowly



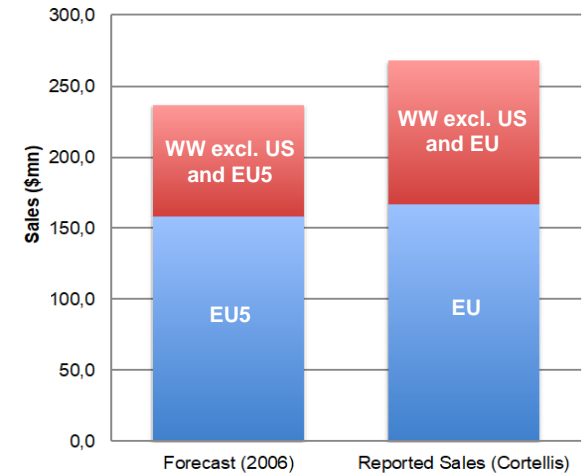
Case study 3 – Product in Parkinson’s Disease

EU in-licencing opportunity for a newly approved product and in Ph 3 for two follow-on indications

Product Sales WW excl. US - Years 2006 – 2018



Product Sales WW excl. US by Geography - Year 2015



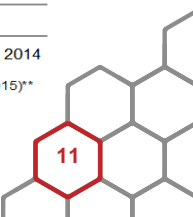
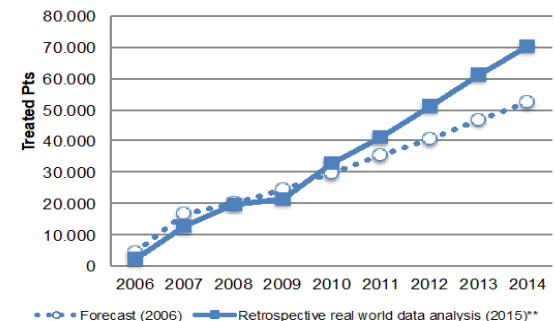
Forecast (2006)

- *Background:* Product was just launched in EU for launch indication based on Feb-2006 approval, follow-on indications were in Ph 3
- *Forecasting methodology:* MR findings (incl. KOL research) was used to generate share assumptions used in a patient-based forecast model – dotted curve in graph represents total sales from launch and follow-on indications

What happened in reality (2006 – 2015)

- EU approval for two follow on indications in 2007 and 2008 as planned
- 2013 Launch in Japan for 2 indications
- From subsequent analogue analysis undertaken by gH (up to 2014 data, see chart on right), we can see our forecast total treated patients matched closely with what happened in reality

Treated Pts EU - Years 2006 - 2014





groupH Forecasting Experience and Accuracy - Summary

Key Insights from case studies

4 out of 5 forecasts over 85% accurate, the 'Worst' at 70%

Too good to be true? – Yes and No

Case Study 1

~85% accuracy in global sales

EU price and hence sales higher than expected

US patent expiry had a bigger hit on sales as expected

Case Study 3

~90% accuracy

ex-US and RoW sales very close to reported sales

EU treated patients closely matched forecast

Case Study 2

~95% accuracy in EU sales

“Late line add-on for non-responders to established treatments”

Simple forecast based on robust KOL qualitative research

Launch suffered a 4 year delay

Real life dosing half of clinical trial setting set off by higher pricing

No launch in France but offset by launch in 9 smaller EU countries

Patient based forecast more accurate than analyst predictions



groupH Forecasting Experience and Accuracy

9 Key Learnings

For forecasting no *'one size fits all'* – If approach is right and no shortcuts in research, a *'right ball park'* forecast for a Ph 3 product is *hard to avoid*

At global or regional level assumption bias and geographical differences often cancel each other out

Better assumptions make better forecasts – academically superior but also more complex modelling such as e.g. Monte Carlo is only better if resources are made available to support the higher # of assumptions required

Product sales are very predictable - unless a trial fails or truly unexpected events happen

The more legs key assumptions stand on the better – use analogues, audit data for calibration and multiple approaches for the all important patient share

Teams and stakeholders involved in assumption setting will benefit from transparent and clear documentation for future reference

groupH to revisit a few years down the road with a higher *n* of anonymized case studies – no really inaccurate example found yet to learn from. Exploring analyst forecast accuracy may also prove to be of value

From all key assumptions and compared to 15 years ago, market access / pricing requires a higher share of resources as it is truly the key to ultimate product value

Bias minimizing and process polishing are likely to remain *'evergreens'* but may add comparably less value compared to using the team's market understanding for actions helping to realize the full potential for a product

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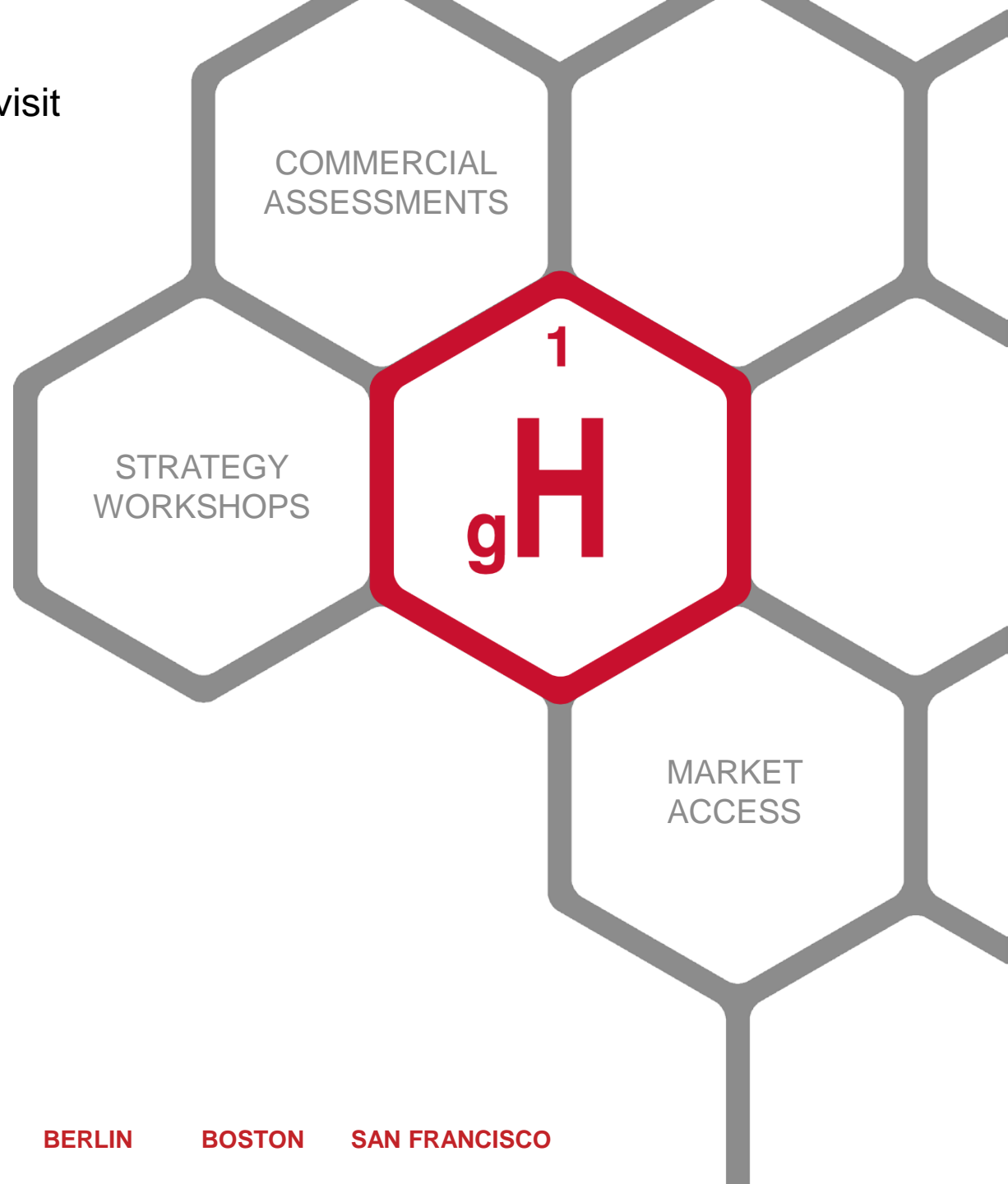
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