

Box S1 | Data sources and methodology**Data sources**

EvaluatePharma® data. EvaluatePharma® provides coverage on over 7,600 companies and over 50,000 active products both marketed and in R&D.

EvaluatePharma® has company reported sales back to 1986 and consensus forecasts for products and company revenues to 2018. The consensus forecasts are an arithmetic average of up to six equity research analysts from the top 20+ major sell side institutions as available and they are updated monthly as revised by equity analysts.

The Archive Forecast Module is a component of EvaluatePharma®. It contains over 210,000 forecasts starting from January 2003. It also details products' lifecycle from R&D through marketed stage and the corresponding change in consensus forecasts or sales.

Key data elements from EvaluatePharma® and the Archive Forecast Module used in this analysis include:

- Market Status - the current status of a product within its lifecycle.
- Annual Sales Worldwide (Archive) – including both historic (previously published, actual company reported numbers) and forecast sales (based on consensus product sales estimates).
- Forecast Comment (Archive) – an annotation detailing the sell-side institutions used to build the consensus estimate, including the forecast report date and the furthest forecasted year.

Other sources. Information on disease area for each drug is published by the European Pharmaceutical Marketing Research Association (EphMRA).

Clinical trial activity for each drug, including a list of trials and number of patients enrolled, is publicly available at clinicaltrials.gov.

Methods

Consensus estimate versus actual peak sales. For the 260 drugs with consensus

forecasts available in the year pre-launch, the difference δ between consensus estimate of peak sales versus actual peak sales was calculated for each drug i as:

$$\delta_i = \frac{(\text{consensus estimate of peak sales})_i - (\text{actual peak sales})_i}{(\text{actual peak sales})_i}$$

A histogram of δ_i is plotted in Figure 1a. Note that although analyst coverage varies by drug — both in terms of the number of institutions providing estimates as well as the frequency with which they update their estimates — only a single consensus estimate was taken for each drug in the year pre-launch, to prevent ‘over-indexing’ on drugs with more extensive coverage.

Of the 260 drugs used in the analysis above, 54 ‘outliers’ — drugs whose consensus forecasts were >160% higher than actual revenues — were excluded from subsequent analyses.

Variance in consensus versus actual sales over time. Variance is a statistical measure of how far a set of numbers is ‘spread out’. For example, in Figure 1a, if the data points in the histogram were more heavily concentrated in a narrow band, the

variance of the data set would be lower, while if it was more spread out, variance would be higher.

For the drugs remaining after excluding the ‘outliers’ in Figure 1a, the difference δ for each drug i was calculated in each year y , where $y = 0$ for each drug corresponds to its launch year. The variance $Var(y)$ across all drugs for each year was then calculated as:

$$Var(y) = \frac{1}{n} \sum_{i=1}^n (\delta_{i,y} - \mu_y)^2$$

where n is the total number of drugs with forecasts available in that year, and μ_y is the ‘bias’, or arithmetic mean of all $\delta_{i,y}$ in year y . $Var(y)$ for $y = -2$ to $+7$ is plotted in Figure 1b.

Forecast accuracy using different segmentations. Using the same methodology as above, the analysis was repeated after segmenting the database by:

- Company size: drugs originated by top pharmaceutical companies by 2011 revenues (Pfizer, Novartis, Merck, Sanofi, GSK, Roche, AstraZeneca, Johnson & Johnson, Eli Lilly, Abbott, BMS, Bayer) versus drugs originated by all other companies (plotted in Figure 2a)
- Disease area: drugs categorized by EphMRA disease area (plotted in Figure 2b)

Other analyses (data not shown in main article)

Forecast bias for large pharmaceutical companies versus ‘all other’ companies. To better understand how the accuracy of forecasts evolve over time for large pharmaceutical companies versus other companies, we repeated the analysis shown in Figure 2a — which represents a ‘snapshot’ performed in the first year post-launch — for a range of 3 years pre-launch to 7 years post-launch. The results, shown in Figure S1, demonstrate that drugs from large pharmaceutical companies tend to be heavily discounted pre-launch, over-corrected in the immediate years post-launch, then stabilize over time, while forecasts for “all other” companies tend to be systematically overestimated, particularly in the peri-launch years.

Novelty. To test the hypothesis that ‘follow-on’ drugs are easier to forecast than ‘first-in-class’ therapies, we compared the variance and bias of these two segments in the first year post-launch. The results, shown in Figure S2, suggest that there is in fact no meaningful improvement in forecast accuracy for follow-on drugs.

Clinical trial activity versus analyst forecasts. Some pharmaceutical companies might be better at forecasting than analysts. Although we did not have access to a systemic database of internal pharmaceutical company forecasts to compare with the consensus forecasts, we did have access to a rough proxy of a company’s conviction behind a drug, which is the number and size of its Phase II and III clinical trials. Simplistically, a company will not invest hundreds of millions of dollars in a large-

scale cardiovascular or diabetes trial program if it does not have conviction that the drug can become a blockbuster. Conversely, a company will be more circumspect in designing a clinical trial program for a drug with estimated peak sales of \$250 million.

We assessed whether clinical trial activity or analyst forecasts better correlated with actual sales. For each of 72 drugs, originated across 8 companies, we collected data on the total number of patients enrolled in any completed or ongoing Phase II or Phase III clinical trials. For each company, we calculated the Pearson correlation coefficient between actual peak sales for each drug and:

- Consensus estimate peak sales for each drug, across all drugs originated by that company for which data was available (the x-axis in Figure S3)

- Number of patients enrolled in clinical trials for each drug, across all drugs originated by that company for which data was available (the y-axis in Figure S3)

Interestingly, the results shown in Figure S3 were mixed, depending on the company in question. Novartis, Roche, Sanofi and Amgen had the highest strength of correlation between their clinical trial investments and actual peak revenues, while GSK had very low correlation.

Figure S-1: Big pharma drugs are discounted heavily pre-launch, while non-big pharma drugs are consistently overestimated

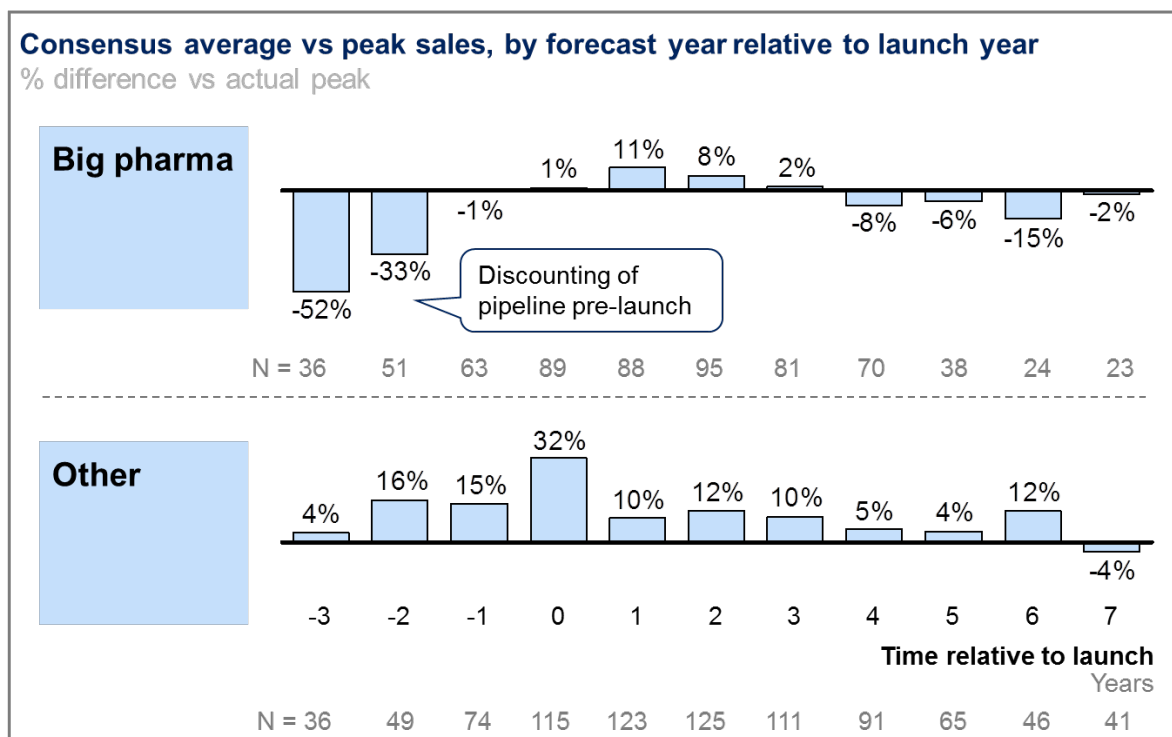


Figure S-2: Novelty. There does not appear to be a discernible difference in forecasting accuracy for “first-in-class” vs “follow-on” drugs, despite greater understanding around the disease pathway, market adoption, usage patterns, etc.

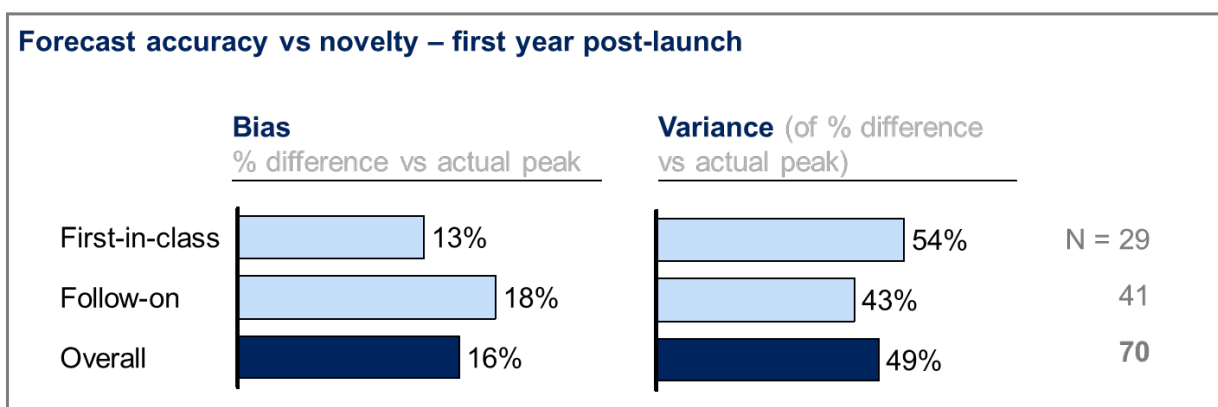


Figure S-3: Accuracy of analyst forecasts vs clinical investment.

Using clinical trial resourcing as a proxy for PharmaCo internal estimates of drug potential, certain PharmaCos (top left) are more accurate at 'placing bets' than if they were to rely on consensus analyst forecasts

Bubble size =
of drugs
(7 shown)

