April 24, 2018

Reason for report:

PROPRIETARY INSIGHTS

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BIOPHARMA

Cool AdComm Reception Likely to Leave Market for ABBV/GILD JAKs; Key Data H2

S&P 500 Health Care Index: 953.60

Companies Highlighted:
ABBV, GILD

• **Bottom Line: Yesterday after the market close the FDA's Arthritis Advisory Committee for baricitinib (JAK1/2 inhibitor) for rheumatoid arthritis (RA) voted 10-5 in favor of the newly-proposed 2mg dose's benefit-risk, but with clear reservations and recommended restrictions, and voted 5-10 against the original 4mg dose (see our mid-meeting note discussing the FDA and Lilly's presentations here: "Bari AdComm Mid-Meeting Report: FDA Not Such a Pushover After All"). The major issues that limited the approval were the venous thromboembolic event (VTE) risk associated with both doses of baricitinib, but particularly the higher dose, and the limited efficacy data in support of the lower dose.** This vote follows the FDA's original rejection of Lilly's 4mg application in April 2017, which now appears unlikely to be approved at all. Based on the AdComm's cautious commentary and divided vote in favor of the 2mg approval, and the negative interpretation of Lilly's data by the FDA entering the committee, we also believe the 2mg dose is at risk of another CRL, or outright rejection, and seems likely to only be approved with substantial limitations (PDUFA mid-2018) on its use (post anti-TNF's rather than pre). We believe the 2mg dose is likely to be indicated only for multi-DMARD and/or biologic failures, and that the label will include a laundry list of warnings and precautions, including the characterization of VTE risk, without reliable surrogate markers for monitoring for the risk of these events. Any panel discussion that includes comparisons to Vioxx is never going to end well for the sponsor, and given the liabilities and reservations disclosed in the discussion, unfortunately baricitinib is likely going to come out of the gate mostly exciting future plaintiff's attorneys. With only the lower dose and a compromised label in the US, baricitinib is likely to struggle to meet prior revenue expectations, if approved. However, both the FDA and the AdComm appeared to clearly delineate and separate the profiles of baricitinib and Pfizer's JAK1/3 inhibitor Xeljanz (tofacitinib), and we reiterate our view that each of the forthcoming JAK inhibitors will be judged on the merits of their respective phase III data sets. This may be advantageous for Gilead's (GILD, MP) filgotinib if the drug avoids a phase III VTE imbalance due to its beneficial reduction of platelets, but could be detrimental to AbbVie's (ABBV, MP) upadacitinib given the program's VTE imbalance to date. We believe both these JAKs still have an opportunity to thread the needle on dose, efficacy, safety, and tolerability with larger data sets and long-term follow-up, and then potentially be awarded with approval in broader all-comers populations. Results for both drugs from ongoing pivotal trials that read out in H2 will clarify the opportunities of these drugs with data from AbbVie's 1,000-patient SELECT-EARLY trial and Gilead's first 449-patient phase III RA trial.

• **(Continued Inside...)**

Panel Reached Near-Unanimous Vote for Efficacy of Both Doses. The panel was asked to vote if the data provide substantial evidence of the efficacy of baricitinib for the treatment of RA patients with an inadequate response to or who are intolerant to methotrexate (MTX). The vote was 14 yes to 1 no in favor of the 2mg dose and 15 yes to 0 no in favor of the 4mg dose. The panel believed the superior results of the 2mg and 4mg against placebo were demonstrated in the phase III program and that consistent superiority was seen across multiple subgroup analyses. However, the panel found it difficult to definitively assess the 2mg compared to the 4mg, and believed a different conclusion could be drawn based on different cuts of the data. The one no vote for 2mg was due to the lack of radiographic evidence of benefit, as the voter wanted to be able to tell a patient about to be initiated on baricitinib that his/her x-ray results would improve. However, this panel member admitted that baricitinib 2mg demonstrated clear clinical benefit on ACR (American College of Rheumatology) scores and SDAI (Simplified Disease Activity Index) scores which established at least the clinical effect for the drug and dose.

AdComm Voted in Favor of 2mg Safety with Unenthusiastic Support. The panel was asked to vote if the data provide substantial evidence of the safety of baricitinib for the treatment of RA. The panel was asked to address the adequacy of the 2mg safety database and the specific safety issues of both doses, including VTEs and infections, and discuss if one dose was more favorable versus the other. The vote was 9 yes to 6 no in favor of the 2mg dose, but 4 yes and 11 no against the 4mg dose. On overall safety, the panel suggested that the difference between 4mg and 2mg was not remarkable, and any increased risk of adverse events for 4mg would be expected given the potency of the mechanism. The AdComm was also reassured by the drug's approval in Europe and a lack of postmarketing safety findings so far in that geography. However, the panel was more cautious about the rare event rates, particularly the VTEs, which they believed did not have enough data to make a reasonable comparison between the doses. The VTEs were also concerning because the AdComm found them unpredictable. While Rheumatologists routinely screen for abnormal laboratory findings in patients on potent anti-inflammatory medicines, and are competent for monitoring infection risks, they do not typically monitor for VTEs. Since platelet count elevations do not correlate to VTEs and cannot be used as a surrogate marker for VTE risk, there is nothing available to guide rheumatologists on their monitoring practices. For the 2mg, the minority "no" voters were principally concerned with the lack of long-term data and randomized data, which in turn led to a reduced exposure and inadequate characterization of the drug's actual safety. Even the "yes" votes found the question to be difficult and most hedged their answers with the statement that more data would be preferable (one panelist described the vote as an "uncomfortable yes"). Further, some panelists who voted in favor of the 2mg suggested that only heavily-pre-treated and treatment refractory patients justify the risks of the medicine even at this reduced dose. The 4mg dose met much more resistance from the AdComm for its safety profile, with many members referencing the clear signal for risk of VTEs that needed further investigation. Ironically, it was the better characterization of 4mg (more patients and exposure) that soured the panel on the dose, as the relatively larger amount of data convinced more panel members that the observed safety signals were real. In general, the panelists believed the overall safety looked a little worse for the 4mg.

Mixed Panel Supported Benefit-Risk Profile of 2mg, but Voted Against 4mg. The panel was ultimately asked to vote if benefit-risk profile was adequate to support the approval of the 2mg and 4mg baricitinib doses separately for the treatment of RA patients who have had an inadequate response or are intolerant to MTX. The vote was 10 yes to 5 no in favor of the 2mg dose, but 5

yes and 10 no against the 4mg dose. The vote was generally in line with the results of the safety assessment of the individual doses. Again, several panelists remarked that the 2mg risk-benefit was most suitable for later-line patients, such as those failing a prior biologic (one panelist voted yes but commented the risk is too high for MTX-IR patients). The AdComm also suggested extensive labeling to inform physicians and patients about safety risks and also suggested that large postmarketing observational studies be completed by the sponsor. The "no" votes for the 2mg dose largely centered on a lack of confidence in the safety database and a need to have more than 400 randomized patients in the data set to better inform a decision.

Exhibit 1: FDA AdComm Baricitinib Votes

Vote 1:
Do the data provide substantial evidence of the efficacy of baricitinib **2 mg** for the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response or are intolerant to methotrexate (MTX)?

Yes	14
No	1

Vote 2:
Do the data provide substantial evidence of the efficacy of baricitinib **4 mg** for the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response or are intolerant to methotrexate (MTX)?

Yes	15
No	0

Vote 3:
Are the safety data adequate to support approval of baricitinib **2 mg** for the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response or are intolerant to methotrexate (MTX)?

Yes	9
No	6

Vote 4:
Are the safety data adequate to support approval of baricitinib **4 mg** for the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response or are intolerant to methotrexate (MTX)?

Yes	4 (1 panelist originally voted yes in error)
No	11

Vote 5:
Is the benefit-risk profile adequate to support approval of baricitinib **2 mg** for the proposed indication of the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response or are intolerant to methotrexate (MTX)?

Yes	10
No	5

Vote 6:
Is the benefit-risk profile adequate to support approval of baricitinib **4 mg** for the proposed indication of the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response or are intolerant to methotrexate (MTX)?

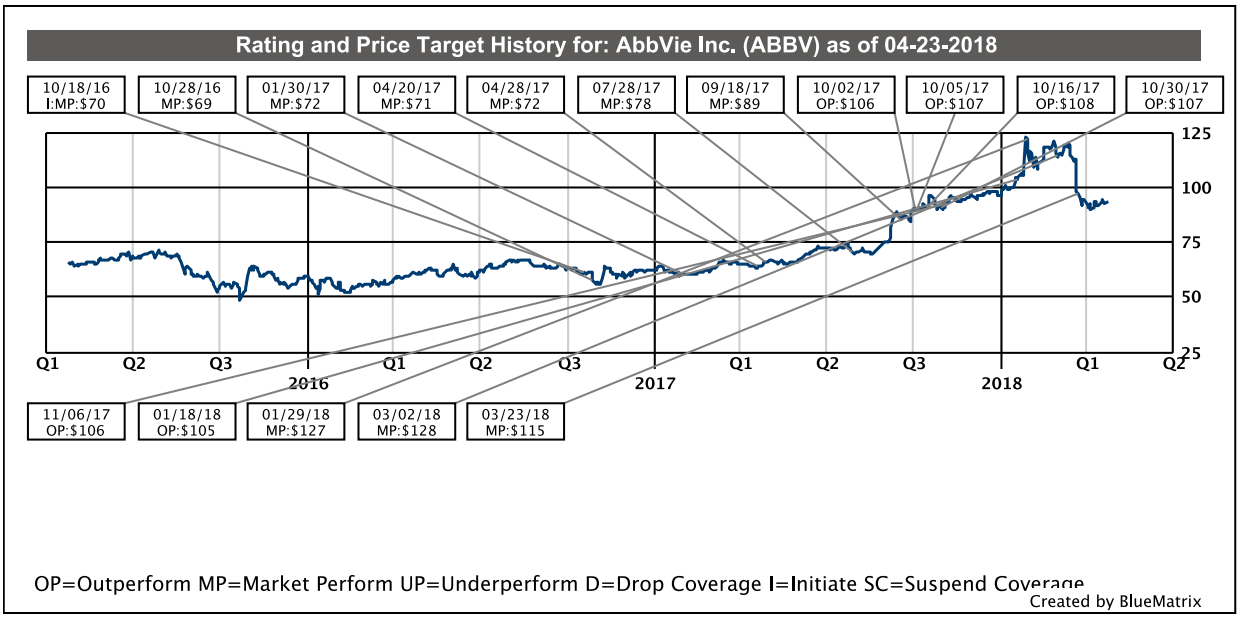
Yes	5
No	10

Source: FDA Arthritis Advisory Committee (April 23 2018)

Disclosures Appendix

Analyst Certification

I, Geoffrey C. Porges, MBBS, certify that the views expressed in this report accurately reflect my views and that no part of my compensation was, is, or will be directly related to the specific recommendation or views contained in this report.



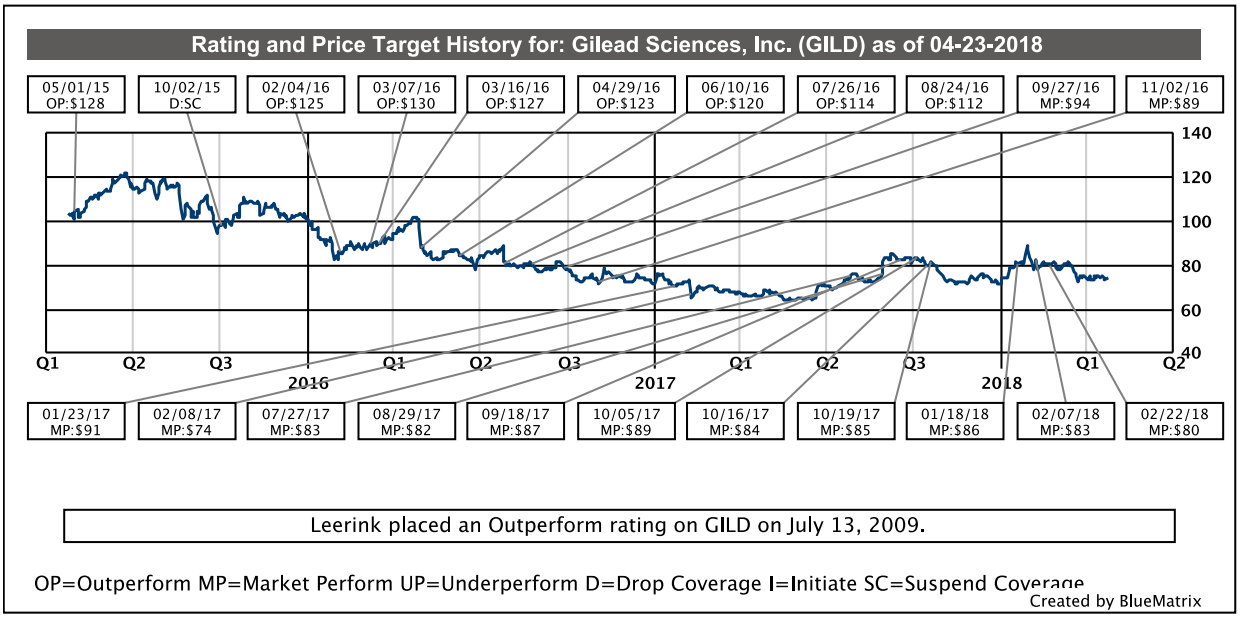
Valuation

Our price target for AbbVie (ABBV) is based on a simple average of three approaches that we believe are a reasonable basis for valuing the stock today. These approaches are simple price to earnings multiples for comparable large biopharmaceutical companies; price to sales multiples for large cap peer companies' stocks; and discounted cash flow (DCF). We apply peer EPS and revenue multiples using an average for large cap, large molecule therapeutic companies with mid-term growth and tail risk (RHHBY, SNY, MRK, PFE, NVS, LLY, AMGN, BIIB, CELG). Their average 2018 consensus EPS multiple of 13.0x applied to our current 2019 EPS estimate for ABBV of $9.08, gives a value of $118 in 2018. Using a 2018E revenue multiple for similar companies of 5.1x 2018E consensus sales, and applied to our 2019 revenue estimate for ABBV of $35.1bn, gives a 2018 value of $112. Lastly, our DCF valuation given a 6.9% WACC and a terminal cash flow growth rate of +1.5% beginning 2029E (after Humira biosimilar entry) gives present value of $121. The average of these three methods is our current price target of $115. Upon completion of our analysis of quarterly results, we will revisit our price targets and at present they remain unchanged

Risks to Valuation

The risks to our view, outlook, and valuation for AbbVie include any major change in the price outlook, reimbursement coverage, labeling, or competitive position for Humira, the company's main product. Other risks include commercial or development disappointments for the company's follow-on programs in inflammatory diseases, for Imbruvica and Venclexta in expanded hematological malignancies, as well as the competitive positioning of the company's next-generation HCV therapy. We assume operating margins will increase from their current level towards 50% by 2020E; should they fail to reach and sustain that level it would adversely affect our forecast and valuation. Also, the company remains highly levered and committed to a growing dividend, and any reduction to forecasted EBITDA due to negative

business trends would place the company's capital allocation strategy and dividend growth at risk. Opportunities for upside from our expectations include stronger-than-expected pricing, volume and share for Humira and emergence of more tangible demand for underappreciated elements of the company's early-to-mid stage pipeline assets, and potential label expansion opportunities to late stage opportunities.



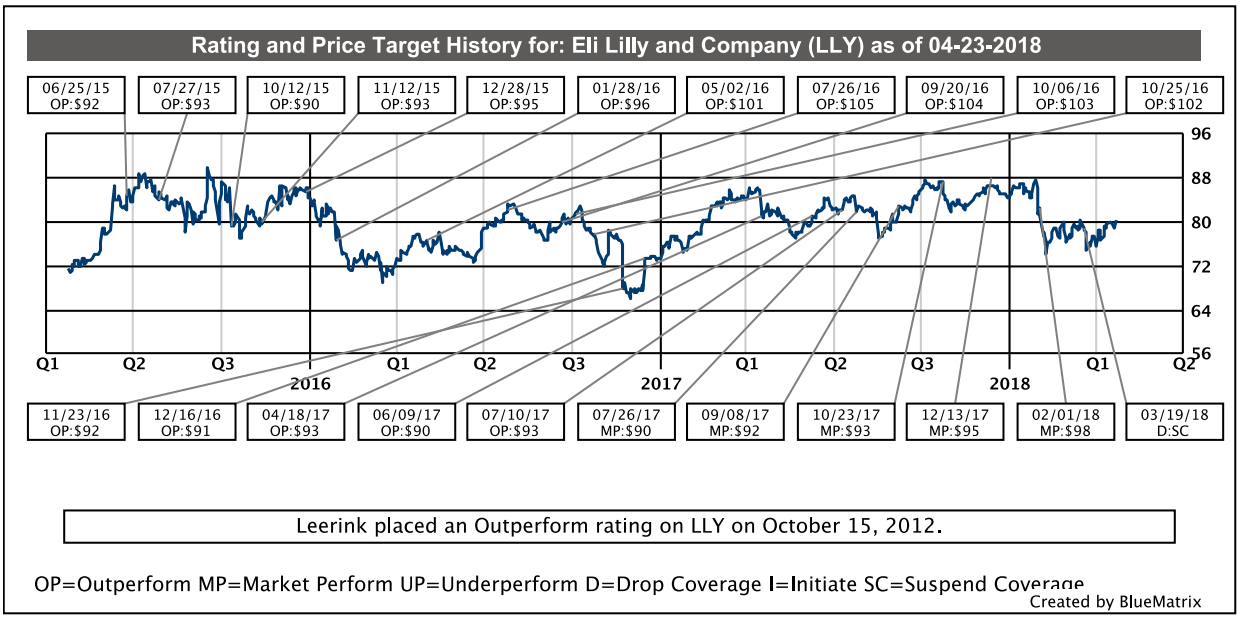
Valuation

Our $80 price target for Gilead Sciences, Inc. (GILD) is based on an average of four approaches that we believe are a reasonable basis for valuing the stock today. These approaches are trough price to earnings multiples for large cap, slow-growth medical products businesses long term; revenue multiples for large cap medical products stocks with slow growth outlooks; sum of the parts valuation for existing franchises; and discounted cash flow (DCF). Using a trough consensus forward earnings (2018E) multiple for slow-growth medical products stocks (CELG, PFE, MRK, SNY) of 12.3x, applied to our 2019 EPS estimate for Gilead, gives a price of $80. Alternatively we apply a slow-growing, large-cap medical products (US Pharma, Spec Pharma, EU Pharma) revenue multiple (4.9x) to 2019 revenue estimates to derive a 2018 implied value of $106bn, implying a one year price target of $80. Using a sum of the parts valuation for existing franchises, we get a price of $82, consisting primarily of a price of $59 for the company's HIV franchise and $6 for its HCV products. Lastly, our DCF uses our forecast of free cash flow through 2028E and then applies a -7% growth rate to our terminal cash flow forecast and discounts the values back to the present at a 7.8% WACC to give a present value of $79. The average of these four approaches is $80, which is our price target. Upon completion of our analysis of quarterly results, we will revisit our price targets and at present they remain unchanged

Risks to Valuation

The risks to our view, outlook, and valuation for Gilead include any major change in the labeling, price, or reimbursement coverage for the company's existing HIV or HCV products, emergence of further aggressive price discounting, rebating, or other value erosion in the HIV and HCV categories, over and above our current forecast, or any failure of the company's principal pipeline assets, bictegravir (HIV) and filgotinib (RA, IBD) to advance through development to commercialization. Opportunities for better performance and value than our expectations include delays or limitations in the development, profile, and adoption of competitive HIV and HCV products, successful development of

underappreciated elements of the company's portfolio, such as momelotinib, selonsertib, or entospletinib and stronger-than-expected conversion of current HIV patients to Gilead's next generation TAF-based HIV treatment regimens.

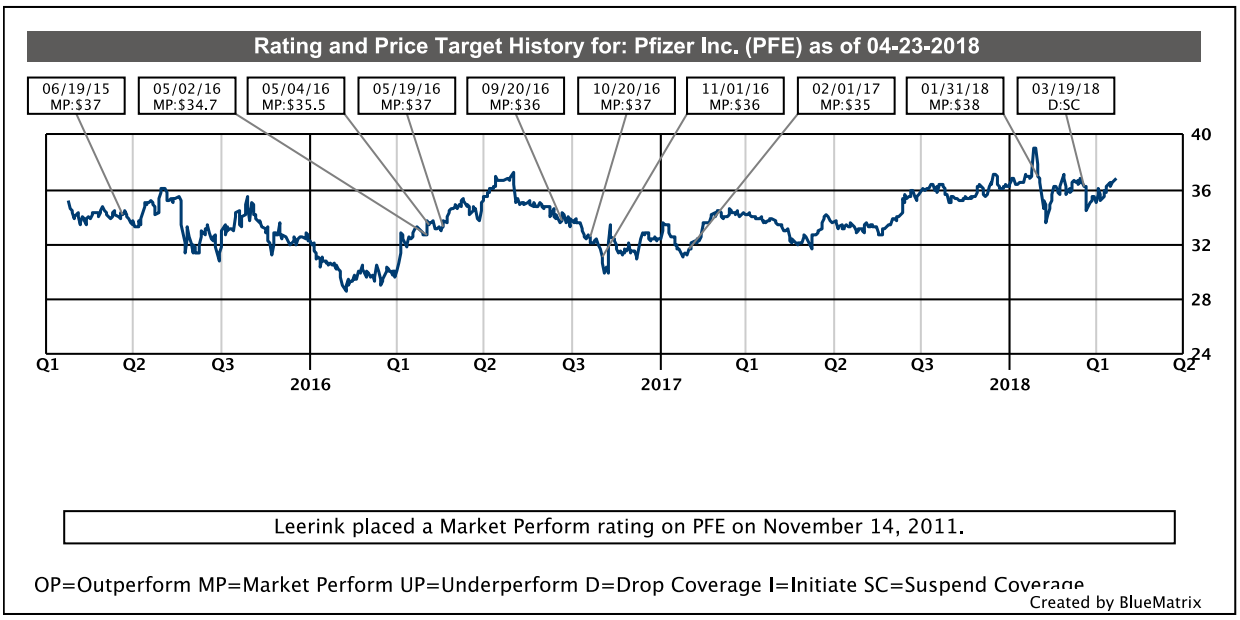


Valuation

Since we have suspended coverage of LLY shares, we no longer put forth a valuation.

Risks to Valuation

Since we suspended coverage of LLY, we no longer put forth risks to valuation.



Valuation

As we have suspended coverage of PFE shares, we no longer put forth a statement of valuation.

Risks to Valuation

Since we suspended coverage of PFE, we no longer put forth risks to valuation.

Distribution of Ratings/Investment Banking Services (IB) as of 03/31/18

Rating	Count	Percent	IB Serv./Past 12 Mos. Count	IB Serv./Past 12 Mos. Percent
BUY [OP]	110	71.0	49	44.5
HOLD [MP]	44	28.4	1	2.3
SELL [UP]	1	0.6	0	0

Explanation of Ratings

Outperform (Buy): **We expect this stock to outperform its benchmark over the next 12 months.**

Market Perform (Hold/Neutral): **We expect this stock to perform in line with its benchmark over the next 12 months.**

Underperform (Sell): **We expect this stock to underperform its benchmark over the next 12 months.**

The degree of outperformance or underperformance required to warrant an Outperform or an Underperform rating should be commensurate with the risk profile of the company.

For the purposes of these definitions the relevant benchmark will be the S&P 600® Health Care Index for issuers with a market capitalization of less than $2 billion and the S&P 500® Health Care Index for issuers with a market capitalization over $2 billion.

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