November 3, 2017

OUTPERFORM

Reason for report:

PROPRIETARY INSIGHTS

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LEERINK

VERTEX PHARMACEUTICALS INCORPORATED

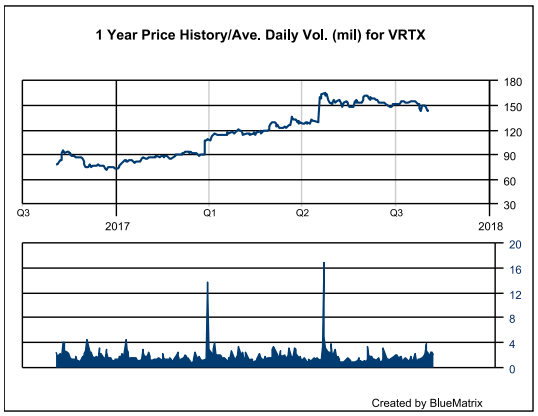
GLPG Has Great Molecules, But Does it Have a Drug (in the US)?

• Bottom Line: We are attending the North American Cystic Fibrosis Conference in Indianapolis this week, primarily to catch up on the latest progress for Vertex's CF combinations, and to understand the prospects and profile of their rival Galapagos. The main conclusion from our participation so far, is that Galapagos has well researched molecules that have intriguing activity in a variety of laboratory systems and molecular models for CF, but so far it is difficult to know if these molecules will actually make viable drugs. The company appears to be compressing, and in some cases attempting to outright skip over, many of the usual stages of traditional drug development (dose ranging and establishing each component, showing proof of concept for their combinations, dose ranging combinations prior to phase III), and there are already some idiosyncrasies to their molecules that are raising questions for investors. Given their lack of progress with their combinations in the US, we don't foresee the sort of rapid development timeline for GLPG's combinations in the US that they are proposing and planning for Europe.

(Continued inside...)

Key Stats:	**(NASDAQ: VRTX)**
Sector:	**Biotechnology**
S&P 500 Health Care Index:	**936.30**
Price :	**$144.90**
Price Target:	$179.00
Methodology:	Avg. of 23.0x '21E EPS, 9.2x '22E revs. disc. to '18, and DCF at 9% WACC and 2% TG
52 Week High:	$167.86
52 Week Low:	$71.46
Shares Outstanding (mil):	256.0
Market Capitalization (mil):	$37,094.4
Book Value/Share:	$3.63
Cash Per Share:	$6.63
Net Debt to Total Capital:	(194)%
Dividend (ann):	$0.00
Dividend Yield:	0.0%
Est LT EPS Growth:	55%
P/E to LT EPS Growth (FY18):	1.13

Completion: November 03, 2017, 5:57AM EDT.
Distribution: November 03, 2017, 5:57AM EDT.
Est LT EPS Growth: '17-'21E



Dec Yr	1Q	2Q	3Q	4Q	FY Rev	1Q	2Q	3Q	4Q	FY EPS	P/E
2016A	$397.2	$431.5	$413.5	$458.5	$1,700.7	$0.09	$0.24	$0.16	$0.35	$0.84	NM
2017E	$482.3A	$516.9A	$551.9A	$590.3	$2,141.3	$0.41A	$0.39A	$0.53A	$0.52	$1.85	78.3x
2018E	--	--	--	--	$2,525.2	--	--	--	--	$2.34	61.9x

Source: Company Information and Leerink Partners LLC Research
Revenues in millions.
EPS diluted, excluding options expense

INVESTMENT THESIS

Our price target for Vertex (VRTX) is $179 and we rate the stock Outperform. Our thesis is based on our expectation of continued capture of cystic fibrosis (CF) patient subpopulations by Vertex with its successive iterations of CF modulating oral combination medicines. We expect that Vertex's CF revenue line will grow steadily from ~$1.7bn in 2016 to ~$2.5bn by 2018E. Our probability of success for the triple combination is now 100% and our valuation accounts for our full expected value of the CF portfolio. While we consider competitors in our forecasts and valuation, we believe their development path and time to market are challenging, and Vertex is well positioned to partner with or acquire any that show promise. After flirting with profitability in the past, Vertex seems determined to maintain its recently recovered profitability and appears capable of growing its operating margin to ~27% by the end of 2017E and 30% by the end of 2018E and beyond. The company still aspires to discover and develop drugs in other categories, and large diversifying investments and associated expenses are a risk to our thesis and valuation. However, with the potential for sizable near-term growth, the stock offers strong valuation upside potential in the next 12-18 months.

Galapagos Advancing Multiple Drugs in Many Combinations. As is by now well known to investors, Galapagos is advancing multiple drugs in three different drug classes – CFTR potentiators and CFTR correctors from two different drug classes. These medicines, respectively 2737 and 3221 (C2 correctors), 2222 and 2851 (C1 correctors) and 2451 and 3067 (potentiators), are designed to be used in combination, and are the only real rival to Vertex's more advanced combinations in the CF category. The company and their investigators have impressed us at this meeting with their thorough pre-clinical research, and the validation of their molecules in multiple pre-clinical assays and model systems. Even more than Vertex, Galapagos is willing to disclose where and how their medicines work, and what they expect their effects to be in humans, based on the pre-clinical characterization. The company has developed compounds with mostly long half-lives, and with so far excellent pre-clinical and clinical tolerability and safety. Their drugs bind different sites on CFTR, thus achieving what they believe is best in class synergy and clinical benefit.

Galapagos' lead program is currently '2222, which is a C1 corrector, ostensibly binding to CFTR at the same site and in the same way as Vx809 and Vx661. Pre clinically, Galapagos suggest that '2222 alone can achieve almost as much CFTR correction as the combination of Vertex's tezacaftor and Kalydeco, and with the addition of a potentiator they believe they can achieve correction several fold higher than tez/iva. '2222 is in a 50 patient, 4 week, placebo-controlled four dose monotherapy study in F508del patients in the US and EU. This study (FLAMINGO) is exploring four doses of '2222, and is fully recruited with results anticipated by year end. If the company's assertions about the drug's activity, compared to tezacaftor/ivacaftor, are correct, the drug's activity should be somewhere between Orkambi and Tez/Iva. Galapagos is also studying '2222 in combination with Kalydeco (ivacaftor) in patients with F508del and class III CFTR mutations (including presumably G551d). This 35 patient, 4 week study (ALBATROSS) is exploring two doses of '2222 – 150mg qd and 300mg qd. This study is also scheduled to read out later this year, or next year, and is being conducted outside the US only. These studies should give Galapagos substantial information for dose selection for '2222, and also some safety data to discuss

further development with the FDA. However, the company has not conducted such exploratory development and dose finding for the other components of their combination, at least not in patients and not in combination. Beyond these two studies with '2222, Galapagos is also studying their first C2 corrector, '2737, at a single dose in combination with Orkambi in the PELICAN trial. In this 18 patient, 4 week study, patients in Germany are being treated with the combination of Orkambi and '2737 or with Orkambi alone, also for four weeks.

The rest of the company's portfolio of CF medicines have been through Single and Multi-Ascending Dose human safety studies in healthy subjects and have, in some cases even been through combination study healthy volunteer trials. The most advanced of their potentiators now appears to be '2451, which the company has already disclosed has an ADME problem in the form of an active metabolite with a half-life of 1 month or more. While there are some theoretical advantages to such a compound, in practice it makes it more difficult to work with than the ideal 8-16 hour half-life for daily dosing. Galapagos is proposing to develop the drug with an initial loading dose, and then very small daily "maintenance" doses, but whether the FDA will endorse a drug with such a profile, and its inherent liabilities, remains to be seen. At the very least this profile will require more extended monitoring for safety during development, and at the worst, might require larger and more complex studies, particularly in the US, in order to secure approval. GLPG indicated that their next steps are to move '2451 ahead into a three drug combination trial, which appears to be the company's intent next year. GLPG also outlined their timing and plans for '2737, which is the company's C2 corrector. This molecule is first being tested in a triple combination phase II study with Vertex's Orkambi – this study should get underway outside the US in 2017. '2737 also has unusual pharmacokinetics, displaying a very high, even escalating, spike in plasma drug levels after dosing followed by a steady state plasma concentration between doses. GLPG is also advancing another potentiator, GLPG3067 which is now in phase I studies in initially healthy volunteers. The trials with '3067 should start enrolling in early 2018.

During their poster and oral presentations at the NACFC, and at their investor event afterwards, the company outlined an ambitious and complex development strategy, that involves introducing different molecules via single drug and add-on studies first, and then advancing into novel triple combination trials very rapidly. The company seems to be attempting to avoid traditional phase II trials, instead aiming to jump directly from phase Ib first-in-patient trials with a combination regimen, all the way to phase III. When we asked the company about the regulatory endorsement of this strategy, the company indicated that the FDA had not endorsed any aspect of their combination development, and had in fact required that the company file individual drug IND's in the US, which had only been completed for '2222 at this stage. This means that all the current and soon-to-start trials of the Galapagos combinations will be conducted only in Europe, other than the '2222 combination trial with Kalydeco which is ongoing in the US. Furthermore, it was not clear that Galapagos had regulatory endorsement from the EMA for their accelerated development program either, and the company suggested that they had not yet decided, even in Europe, whether they would in fact have to conduct a second phase II trial with any of the triple combinations entering the clinic in late 2017 or 2018. It appears that the decision about whether to do further dose ranging in phase III, or insert another trial for that purpose, will depend in part on the results of the next trials, and in part on further discussions

with regulators. Proceeding to phase III is not a foregone conclusion for any of these programs, even if the initial phase II results are positive. It became clear last night that Galapagos has not even discussed these drugs and their development plans with the FDA, and only expect to start those conversations sometime in the middle of 2018, after they file the 5 individual IND's (assuming the company wants to study all the drugs and combinations in the US as well as Europe). Privately Galapagos suggested that they expect to have their pre-IND meetings with the FDA sometime in 2018, and then later in the year to present all the results of the next suite of studies to the agency, to start the discussion about next trials, and what would be required before phase III, and then in phase III.

The key questions about these molecules, and this strategy, are how safe and effective the individual drugs are, and how viable their development strategy is.

Does Galapagos Have a Path Forward in the US? During their investor presentation GLPG outlined a portfolio of combination trials that they are planning with their array of drugs in the coming year. These trials are designed to advance their combination to phase III by their claimed timeline of 2019. During the presentation the company's representatives explained that their upcoming phase II trials may not be their final phase II's and that depending on the results of those trials, the company would either incorporate dose ranging into their phase III plans, or conduct another dose ranging study prior to approaching the FDA about starting phase III.

Galapagos/AbbVie Diverging Interests? Who Carries on In the Event of Divergence…

AbbVie acquired the rights to Galapagos' CF combination development programs many years ago, and now, with successive waves of data emerging from these trials, we are approaching the point when AbbVie (ABBV, OP) would be required to opt in, or not. This decision is probably going to be made in 2018, and could well result in another significant delay in regulatory timelines and approval. AbbVie still seems quite uninterested in this project, and definitely qualify their level of enthusiasm and degree of positive sentiment. For AbbVie, who has to fund and execute phase III trials, they would presumably prefer a more traditional, and complete, package before going ahead and committing to those expensive trials. AbbVie is also reportedly unhappy with the single LFT elevation in an otherwise healthy group of patients. There are signs from different directions that this relationship is being viewed less positively in Chicago than in the past. Should AbbVie discontinue, or delay a decision about going forward, this would be viewed negatively for Galapagos, and positively for Vertex. Such a decision doesn't seem imminent, which is fortunate for GLPG, but will make for challenging times for GLPG if AbbVie opts out, or doesn't advance any of the combinations.

VALUATION

Our price target for Vertex (VRTX) 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 high growth large cap biopharmaceutical companies; price to sales multiples for mid and large cap high growth biopharmaceutical companies, and discounted cash flow (DCF). Using a current average high growth large cap biopharma multiple of 2018 EPS (ALXN, REGN) of 22.2x, applied to our current 2021E EPS estimate for VRTX of $9.57, and discounted back 2 years at the company's 9% cost of equity,

gives a value of $178 in one year. Using an average high growth large cap biotech price-to-revenue multiple of 2018E sales (REGN, ALXN, BMRN) of 8.1x, applied to our 2022E revenue estimate for VRTX (post-triple) of $6.3bn, and discounted back 3 years at the company's 9% cost of equity, gives a value in one year of $174. Lastly, our DCF valuation given a 9% WACC and a terminal cash flow growth rate of 2% gives a present value of $186. The average of these three methods is our current price target of $179.

RISKS TO VALUATION

The risks to our view, outlook, and valuation for Vertex include any major change in the price or reimbursement coverage, labelling, or competitive position for Kalydeco and Orkambi, the company's main products today. The other major risk is any disappointment, delay, or failure in the company's development and regulatory filings of its second first generation CF corrector, tezacaftor, or of the company's much-anticipated dual corrector/potentiator triple combination program. Other risks include accelerated or successful development of alternative modulators of CFTR, or alternative approaches to treating CF, such as gene therapy. Finally, the company has a history of spending much of its potential earnings, and expensive diversifying acquisitions could undermine the future expected value of the company's CF portfolio. Opportunities for better-than expected performance include realization of significant revenue from the company's current CF dual combination in markets outside the US, as well as accelerated clinical development of a viable triple combination regimen.

Leerink Vertex Revenue Forecast ($ in millions)	**2016A**	**1Q17A**	**2Q17A**	**3Q17E**	**4Q17E**	**2017E**	**2018E**	**2019E**	**2020E**	**2021E**	**2022E**
Non-Product Sales Revenue											
Non-Product Sales Revenue	18	2	3	3	4	11	10	9	9	9	9
Product Sales (all POS adjusted)											
Kalydeco monotherapy	704	186	190	213	232	820	909	854	738	643	633
Orkambi (Vx809/Kalydeco)	979	295	324	336	355	1,310	1,406	1,424	1,176	808	613
Combo Vx661/Kalydeco (2017 approval/2018 full year sales)	-	-	-	-	-	-	200	1,160	2,365	2,395	2,070
Triple Combination of Kalydeco, Vx661, second corrector (2020 full year	-	-	-	-	-	-	-	-	200	1,850	3,010
Total Product Sales (booked by VRTX)	1,683	481	514	549	586	2,130	2,515	3,438	4,479	5,696	6,325
Total Revenues (Non-GAAP)	1,701	482	517	551.9	590.3	2,141	2,525	3,448	4,488	5,705	6,334
ANNUAL GROWTH											
Non-Product Sales Revenue											
Non-Product Sales Revenue	-7%	-20%	-18%	-16%	-14%	-38%	-10%	-6%	-4%	-2%	-2%
Product Sales (all POS adjusted)											
Kalydeco monotherapy	11%	9%	5%	21%	31%	17%	11%	-6%	-14%	-13%	-2%
Orkambi	179%	32%	32%	44%	28%	34%	7%	1%	-17%	-31%	-24%
Combo Vx661/Kalydeco	0%	0%	0%	0%	0%	0%	0%	480%	104%	1%	-14%
Triple Combination	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	63%
Total Product Sales (booked by VRTX)	70%	22%	21%	34%	29%	27%	18%	37%	30%	27%	11%
Total Revenues (Non-GAAP)	69%	21%	20%	33%	29%	26%	18%	37%	30%	27%	11%

Source: Leerink Partners Research and Company Filings

Leerink Vertex Income Statement Model											
($ in millions)	**2016A**	**1Q17A**	**2Q17A**	**3Q17E**	**4Q17E**	**2017E**	**2018E**	**2019E**	**2020E**	**2021E**	**2022E**
Revenues:											
Product sales (direct product sales by Vertex)	$1,683	$481	$514	$549	$586	$2,130	$2,515	$3,438	$4,479	$5,696	$6,325
Other revenue (includes royalties, milestones)	$18	$2	$3	$3	$4	$11	$10	$9	$9	$9	$9
Total revenues	**$1,701**	**$482**	**$517**	**$552**	**$590**	**$2,141**	**$2,525**	**$3,448**	**$4,488**	**$5,705**	**$6,334**
Expenses:											
Cost of sales	$210	$47	$71	$73	$77	$268	$309	$421	$548	$660	$692
R&D	$861	$227	$240	$243	$255	$965	$1,123	$1,183	$1,141	$1,177	$1,143
SG&A	$344	$86	$93	$91	$97	$367	$378	$446	$517	$609	$645
Profit share	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Other expenses	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Total expenses	$1,415	$360	$405	$407	$429	$1,600	$1,810	$2,050	$2,206	$2,446	$2,480
Operating income (EBIT)	$285	$122	$112	$145	$161	$541	$715	$1,397	$2,282	$3,259	$3,854
Nonoperating income (interest), net	($77)	($17)	($17)	($15)	($17)	($66)	($66)	($57)	($43)	($24)	($0)
Pre-tax income	$208	$105	$95	$131	$144	$475	$650	$1,340	$2,239	$3,235	$3,854
Tax (incl. NOL adjustment)	($0)	$4	($4)	($6)	$10	$4	$45	$94	$233	$647	$771
Pro Forma Earnings (Excluding Options Expense):											
Net income	**$208**	**$101**	**$99**	**$136**	**$134**	**$471**	**$604**	**$1,246**	**$2,006**	**$2,588**	**$3,083**
Earnings per share (basic):	**$0.85**	**$0.41**	**$0.40**	**$0.54**	**$0.53**	**$0.00**	**$2.38**	**$4.82**	**$7.65**	**$9.73**	**$11.44**
Earnings per share (diluted, *excluding option expense*)	**$0.84**	**$0.41**	**$0.39**	**$0.53**	**$0.52**	**$1.85**	**$2.34**	**$4.74**	**$7.52**	**$9.57**	**$11.26**
Weighted ave. shares (basic):	245	246	248	250	251	249	254	258	262	266	269
Weighted ave. shares (diluted):	247	249	252	256	257	254	258	263	267	270	274
MARGIN ANALYSIS:											
Gross margin (1-COGS/total revenue)	88%	90%	86%	87%	87%	87%	88%	88%	88%	88%	89%
R&D to total revenue	51%	47%	47%	44%	48%	45%	44%	34%	25%	21%	18%
SG&A to total revenue	20%	18%	18%	16%	16%	17%	15%	13%	12%	11%	10%
Operating margin (EBIT/total revenue)	17%	25%	22%	26%	27%	25%	28%	41%	51%	57%	61%
Effective tax rate	0%	3%	-4%	-4%	7%	1%	7%	7%	10%	20%	20%
Net margin (net income/total revenue)	12%	21%	19%	25%	23%	22%	24%	36%	45%	45%	49%
ANNUAL GROWTH											
Total revenues	69%	21%	20%	33%	29%	26%	18%	37%	30%	27%	11%
EPS (diluted)	-176%	343%	67%	229%	48%	120%	26%	103%	59%	27%	18%

Source: Leerink Partners Research and Company Filings

Analysis of Stock Price and Leerink Target for Vertex Pharmaceuticals

Method 1 - Large-Cap Healthcare 2018 EPS Multiple on 2021 LP VRTX Normalized Earnings	
Current Average High Growth **Large Cap** High Growth Biopharma Multiple of 2018 EPS (ALXN, REGN)	22.2x
Leerink EPS for VRTX (2021)	$9.57
Implied Price for 2020 on 2021 EPS (using current consensus high growth large cap multiple of 2017	**$212**
Cost of Equity	**9.0%**
Number of Periods (2020-2018)	2
Implied One Year Target Price by approach	**$178**
Method 2 - Discounted Future Value of Normalized Revenue Using Mid and Large Cap Biotech Comparables	
Average Growth Large Cap and Mid Cap Biotech Price-to-Revenue Multiple of 2018 Sales (REGN, ALXN, BMRN)	8.1x
Vertex 2022 Recurring Revenue (+triple) ($mm)	$6,334
Implied Vertex Enterprise Value in 2021 on 2022 Sales Est ($mm)	$51,571
Est. Net Cash in 2021	$6,945
Implied Vertex Equity Value in 2021 ($mm)	$58,516
Cost of Equity	9.0%
Number of Periods (2021-2018)	3
Implied Vertex Value in 2018 ($mm)	$45,304
Anticipated Share Count End 2018 (mm)	260
Implied One Year Target Price by approach	**$174**
Method 3 - DCF Based on Current Products and POS Adjusted Outlook for CF Franchise Only Using 9% WACC and 2% terminal cash flow growth rate	
Present Value of Late Stage and Marketed Product Cash Flows	$46,689
Cash Net of Debt end 2017	$1,583
Total Value	$48,271
Shares O/S End 2018	260
Implied One Year Target Price	**$186**
Average of Methods	**$179**
Leerink Target Price	**$179**

Source: Leerink Partners Research and Company Filings, Factset

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

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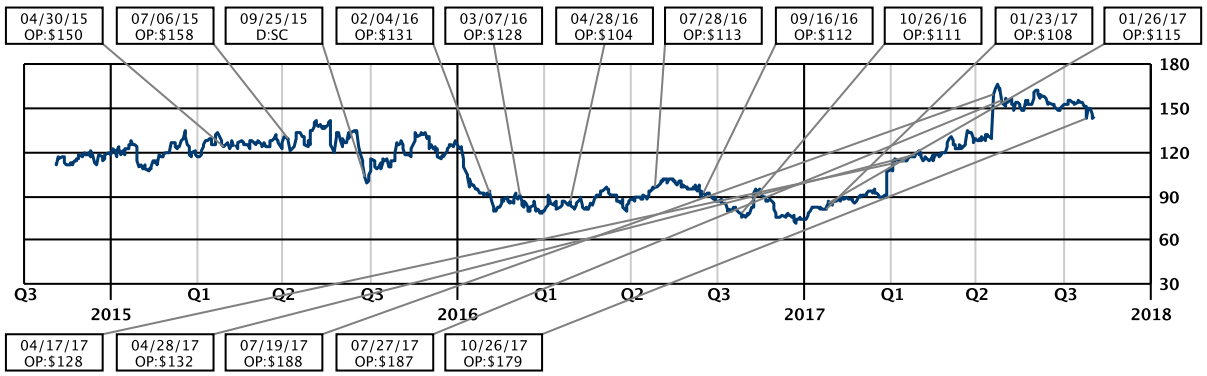

Leerink placed an Outperform rating on VRTX on April 1, 2008.

OP=Outperform MP=Market Perform UP=Underperform D=Drop Coverage I=Initiate SC=Suspend Coverage

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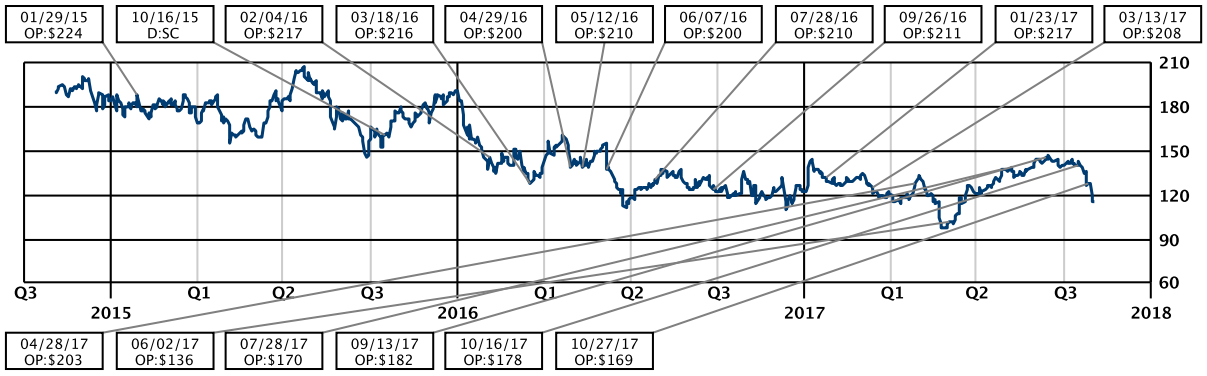

Leerink initiated coverage of ALXN with an Outperform rating on Feb. 9, 2009.

OP=Outperform MP=Market Perform UP=Underperform D=Drop Coverage I=Initiate SC=Suspend Coverage

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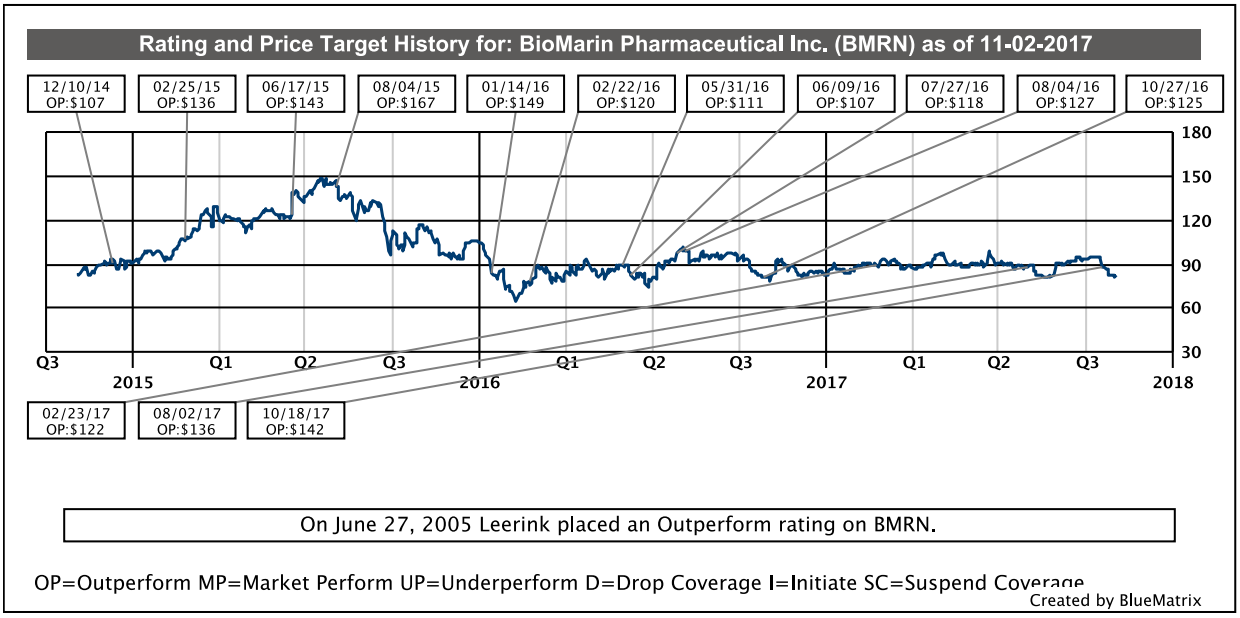
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02/25/15 OP:$136
06/17/15 OP:$143
08/04/15 OP:$167
01/14/16 OP:$149
02/22/16 OP:$120
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07/27/16 OP:$118
08/04/16 OP:$127
10/27/16 OP:$125
02/23/17 OP:$122
08/02/17 OP:$136
10/18/17 OP:$142
180
150
120
90
60
30
Q3 Q1 Q2 Q3 Q1 Q2 Q3 Q1 Q2 Q3
2015 2016 2017 2018
On June 27, 2005 Leerink placed an Outperform rating on BMRN.
OP=Outperform MP=Market Perform UP=Underperform D=Drop Coverage I=Initiate SC=Suspend Coverage
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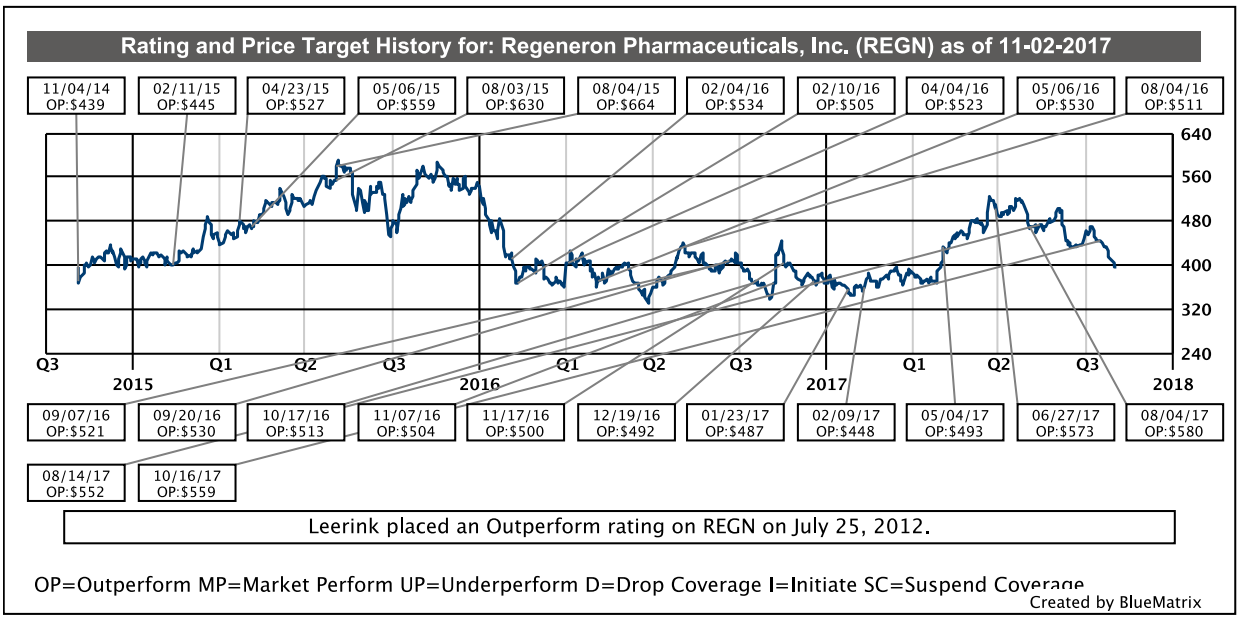
Rating and Price Target History for: Regeneron Pharmaceuticals, Inc. (REGN) as of 11-02-2017
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02/11/15 OP:$445
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11/17/16 OP:$500
12/19/16 OP:$492
01/23/17 OP:$487
02/09/17 OP:$448
05/04/17 OP:$493
06/27/17 OP:$573
08/04/17 OP:$580
08/14/17 OP:$552
10/16/17 OP:$559
640
560
480
400
320
240
Q3 Q1 Q2 Q3 Q1 Q2 Q3 Q1 Q2 Q3
2015 2016 2017 2018
Leerink placed an Outperform rating on REGN on July 25, 2012.
OP=Outperform MP=Market Perform UP=Underperform D=Drop Coverage I=Initiate SC=Suspend Coverage
Created by BlueMatrix

Distribution of Ratings/Investment Banking Services (IB) as of 09/30/17				
			IB Serv./Past 12 Mos.	
Rating	Count	Percent	Count	Percent
BUY [OP]	122	67.4	40	32.8
HOLD [MP]	59	32.6	4	6.8
SELL [UP]	0	0.00	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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Important Disclosures

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Leerink Partners LLC makes a market in Vertex Pharmaceuticals Incorporated, Alexion Pharmaceuticals, Inc., BioMarin Pharmaceutical Inc. and Regeneron Pharmaceuticals, Inc.

Leerink initiated coverage of ALXN with an Outperform rating on Feb. 9, 2009.

On June 27, 2005 Leerink placed an Outperform rating on BMRN.

Leerink placed an Outperform rating on REGN on July 25, 2012.

Leerink placed an Outperform rating on VRTX on April 1, 2008.

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