Vertex Pharmaceuticals, Inc. (Nasdaq: VRTX)

Rating: Buy

Price Target: $500.00 (was $550.00)
Share Price: $397.27

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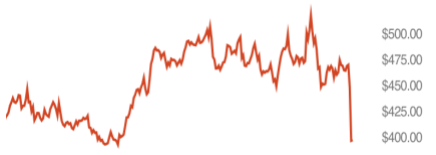
December 23, 2024

Company Data	
Average Daily Volume (M)	1.37
52-Week Range	377.85-519.88
Shares Outstanding (M)	257.53
Market Cap (B)	102.31
Enterprise Value (B)	97.49
Total Cash (B), mrq	6.52
Total Debt (B), mrq	1.77
Total Debt to Cap	10.19%

GAAP Estimates				
FYE: Dec		2023A	2024E	2025E
EPS	Q1	2.69	4.21	3.86
	Q2	3.52	(13.92)	3.90
	Q3	3.97	4.01	3.96
	Q4	3.71	4.00	4.06
	FY	13.89	(1.57)	15.79
P/E		28.6x	NM	25.2x
Rev	Q1	2,374.8	2,690.6	2,750.0
	Q2	2,493.2	2,645.6	2,790.0
	Q3	2,483.5	2,771.9	2,845.0
	Q4	2,517.7	2,775.0	2,920.0
	FY	9,869.2	10,883.1	11,305.0
EV/Sales		9.9x	9.0x	8.6x

One-Year Performance Chart



As of December 20, 2024. Source: E*Trade.

Vertex Pharmaceuticals Announces Two FDA Approvals in Cystic Fibrosis and Potentially Troubling Phase 2 Results in Chronic Pain

Markets reacted to suzetrigine failing to outperform placebo in a Phase 2 sciatica study, despite showing a statistically significant reduction from baseline pain scores

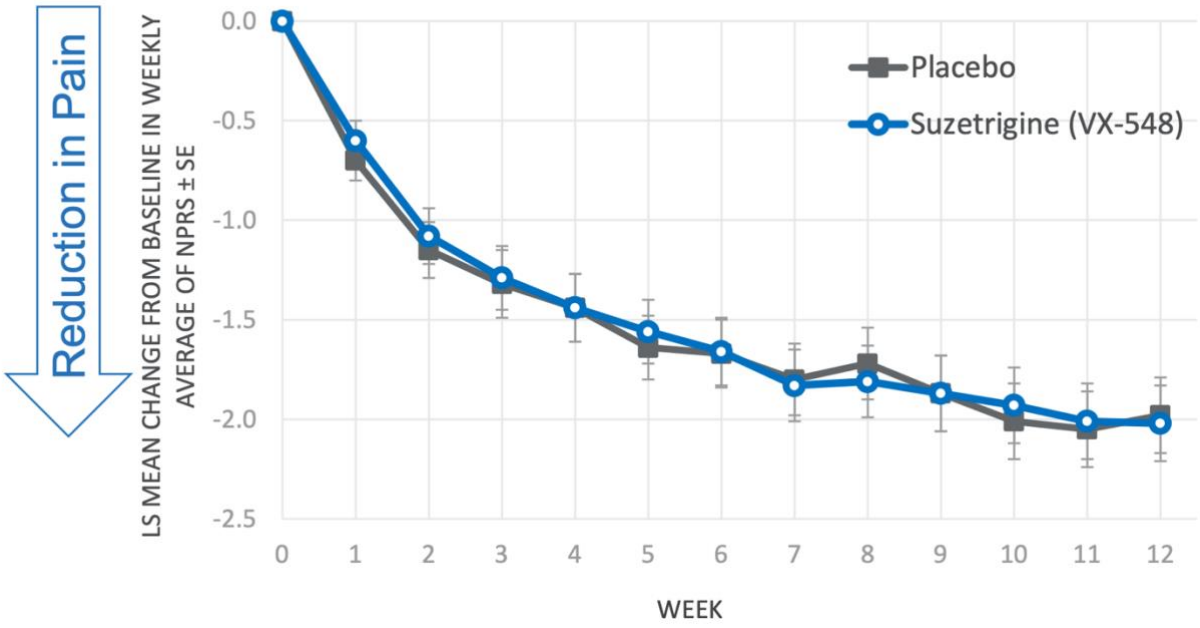
Summary

Shares of Vertex Pharmaceuticals dropped 15% last week on news that its closely watched pain drug, suzetrigine, met its primary endpoint of reducing pain from baseline in a statistically significant and clinically meaningful manner, but failed to outperform a placebo in the company's Phase 2 proof of concept sciatica study.

In the trial, suzetrigine was administered to 102 of 202 patients with lumbosacral radiculopathy (LSR), a condition in which compressed nerves in the spine lead to back and leg pain. The study employed the 11-point Numeric Pain Rating Scale (NPRS), which asks patients to rank pain from 0 (no pain) to 10 (worst pain imaginable).

Valuation. Based on our analysis of available clinical data, we expect the regulatory approval of suzetrigine for acute pain in 2025, followed by accelerating revenue and EPS growth in 2026. We recommend investors begin accumulating shares of Vertex during the next 12-18 months. Our 12-month price target of $500.00 (down from $550.00) is based on 2025 projected earnings of $15.79 and a P/E multiple of 31.7x.

Figure 1: Reduction in Pain on NPRS Scale, Suzetrigine versus Placebo



Source: Vertex Pharmaceuticals, Inc.

The study's primary endpoint was a within-group change from baseline in the weekly average of daily leg pain intensity on the NPRS at week 12. The suzetrigine arm (blue) showed a within-group pain reduction from baseline of 2.02 points, from a mean of 6.33 points at baseline to 4.31 points at Week 12. However, the placebo reference arm (gray) essentially matched these results, showing a within-group pain reduction from baseline of 1.98 points, from a mean of 6.05 points at baseline to 4.07 points at Week 12. The p-value for both arms was a highly statistically significant <0.0001.

Secondary and other endpoints were consistent with the study's primary endpoint.

Suzetrigine was well tolerated, with incidence of mostly mild to moderate adverse events at 22.9%, compared to 32.4% in the placebo group. There was one serious adverse event observed in the suzetrigine arm, which was not related or possibly related to suzetrigine, compared with two serious adverse events in the placebo arm.

Management commented that there was variability in the placebo response across study sites, with about 40% of sites scoring lower placebo responses and thus generating a correspondingly greater separation of the suzetrigine arm from the placebo arm. Management intends to advance suzetrigine into Phase 3 trials for treatment of painful LSR following discussions with regulators on study design and regulatory package. Trial design innovation will be needed to better control the placebo response in pivotal trials.

Efforts to minimize the placebo response could involve a placebo run-in phase for the Phase 3 trial (starting both study arms on placebo and excluding patients with a pronounced placebo effect), enrichment (run patients in on the study drug and only include patients showing a response to the study drug), or a combination of both.

Withdrawal of study drug or placebo constitutes another technique whereby trial participants temporarily stop taking the active medication or placebo they were previously receiving before starting a new treatment phase. This is often done in a randomized withdrawal design where participants who show a positive response to the study drug during the initial treatment phase are then randomly assigned to either continue receiving the active drug or switch to placebo, allowing researchers to compare the outcomes between the two groups and assess the true efficacy of the treatment.

Vertex's suzetrigine pivotal trial in painful diabetic peripheral neuropathy (DPN) remains ongoing, and suzetrigine is under FDA review for treatment of moderate-to-severe acute pain, with a Prescription Drug User Fee Act target action date of January 30, 2025.

While we expect an approval on the strength of the acute pain data, the perplexing Phase 2 results raise doubts about the drug's ability to succeed in the lucrative chronic pain market.

On December 20, Vertex announced FDA approvals for its blockbuster drug TRIKAFTA to include additional non-*F508del* TRIKAFTA-responsive genetic variants in patients aged 2 years and older with cystic fibrosis (CF), as well as for ALYFTREK™, a once-daily next-in-class cystic fibrosis transmembrane conductance regulator (CFTR) modulator for the treatment of CF in patients aged 6 years and older.

The TRIKAFTA (elexacaftor/tezacaftor/ivacaftor and ivacaftor) approval covers patients who have at least one *F508del* (phenylalanine deletion at position 508) mutation in the CFTR gene or a mutation that is responsive to TRIKAFTA based on clinical and/or *in vitro* data, resulting in the addition of 94 non-*F508del* CFTR mutations to the TRIKAFTA label. This will benefit approximately 300 patients in the U.S. who will now be able to treat the underlying cause of their disease for the first time.

The ALYFTREK (vanzacaftor/tezacaftor/deutivacaftor, aka "vanzacaftor triple") approval covers patients who have at least one *F508del* mutation of another mutation in the CFTR gene that is responsive to ALYFTREK, including 31 mutations not responsive to other CFTR modulator therapies. This will benefit approximately 150 CF patients in the U.S. with one of the 31 mutations who are now eligible for a CFTR modulator for the first time.

ALYFTREK Phase 3 studies in patients aged 12 years and older met their primary endpoint of non-inferiority on absolute change from baseline in percent predicted forced expiratory volume in one second (ppFEV1) compared to TRIKAFTA. ppFEV1 is a measurement of how much air a person can exhale in the first second and is used to monitor the progression of CF lung disease.

The studies also met all key secondary endpoints, including demonstrating statistically significant lowering of sweat chloride levels compared to TRIKAFTA, an advancement for the treatment of CF. The ALYFTREK Phase 3 study in children aged 6-11 years demonstrated safety, the primary endpoint.

ALYFTREK was generally well tolerated across all studies. The therapy is the first once-daily CFTR modulator, providing more convenient dosing for CF patients, and is under regulatory review in the EU, UK, Canada, Switzerland, Australia, and New Zealand.

We reiterate our BUY rating on Vertex Pharmaceuticals based on the fundamental strengths of Vertex's business and pipeline but lower our target price from $550 to $500 given the uncertainty introduced by the Phase 2 suzetrigine results in LSR.

Company Description

Founded in 1989, and headquartered in Boston, MA, and London, U.K., Vertex Pharmaceuticals, Inc., is a global biotechnology company focused on discovering, developing, manufacturing, and commercializing small molecule treatments for chronic and genetic diseases, for which there is acute medical need.

The firm's initial focus, and subject of ongoing research and development, is cystic fibrosis (CF), a genetic disease affecting the lungs and other organs. The Vertex portfolio of marketed CF medicines includes KALYDECO, ORKAMBI, SYMDEKO, and TRIKAFTA, which improve lung function and reduce hospitalizations in CF patients.

The company has also received regulatory approval for CASGEVY™, the first CRISPR/Cas9 gene editing therapy that treats the underlying causes of two chronic, life-shortening diseases: sickle cell disease and transfusion-dependent beta thalassemia.

Vertex has a robust clinical pipeline of investigational therapies for other debilitating diseases and conditions, including non-opioid treatment of acute and chronic pain, Type 1 diabetes, alpha-1 antitrypsin deficiency, kidney disease, Duchenne muscular dystrophy, and myotonic dystrophy type 1.

The company has research and development sites and commercial offices in the United States, Canada, Latin America, the Middle East, Japan, Australia, and several European countries.

Valuation

As an established company in the cystic fibrosis space, Vertex leads its competitors across a spectrum of solvency, valuation, and profitability metrics, including having a 2023 P/E of 34.2x versus the competitor group median of 17.0x. The firm's 2023 enterprise value (EV)/Revenue was 11.1x versus its competitor group median of 6.6x. Vertex's 2023 EV/EBIT was 25.4x, versus its competitor group median of 15.6x. The company's 2023 gross margin was 87.2%, contrasted with its competitor group median of 74.2%, and its 2023 net margin was 36.7% against the competitor group median of 19.0%.

Combined with the above metrics, Vertex's rich valuation is, in our opinion, justified by its formidable cash resources, deep and broadening pipeline, historical successes in clinical trials, and the marketing of its drugs in key strategic regions.

We believe that additional shareholder value will be unlocked as Vertex's portfolio of approved products broadens. One example is the company's global launch of and reimbursement coverage for CASGEVY™, its gene therapy for SCD and beta thalassemia. Another near-term product launch opportunity is the vanzacaftor/tezacaftor/deutivacaftor triple oral small molecule combination for cystic fibrosis, which employs a similar mechanism of action as Vertex's blockbuster drug TRIKAFTA.

Vertex's non-opioid treatment for moderate to severe acute pain, Suzetrigine (VX-548), completed Phase 3 clinical trials in December 2023. It is now in regulatory review by the U.S. FDA. Non-opioid pain management is a significant, unmet medical need worldwide. It is possible that Suzetrigine could be approved within one calendar year, and capture a significant first mover share of the $80-90 billion global pain management market.

Based on our analysis of available clinical data, we expect the regulatory approval of suzetrigine for acute pain in 2025, followed by accelerating revenue and EPS growth in 2026. We recommend investors begin accumulating shares of Vertex during the next 12-18 months. Our 12-month price target of $500.00 (down from $550.00) is based on 2025 projected earnings of $15.79 and a P/E multiple of 31.7x.

Vertex Pharmaceuticals Financial Forecast											
	FY 23 A	MAR 24 A	JUN 24 A	SEP 24 A	DEC 24 E	FY 24 E	MAR 25 E	JUN 25 E	SEP 25 E	DEC 25 E	FY 25 E
Revenue	9,869.2	2,690.6	2,645.6	2,771.9	2,775.0	10,883.1	2,750.0	2,790.0	2,845.0	2,920.0	11,305.0
Cost of Sales	1,262.2	342.6	371.9	392.6	395.5	1,502.6	337.5	345.6	355.6	365.0	1,403.7
Gross Profit	**8,607.0**	**2,348.0**	**2,273.7**	**2,379.3**	**2,379.5**	**9,380.5**	**2,412.5**	**2,444.4**	**2,489.4**	**2,555.0**	**9,901.3**
Operating Expenses:											
R&D	3,162.9	789.1	966.6	875.9	888.0	3,519.6	935.0	948.6	967.3	992.8	3,843.7
Acquired in-process R&D	527.1	76.8	4,449.1	15.0	30.0	4,570.9	30.0	30.0	30.0	30.0	120.0
SG&A	1,136.6	342.7	372.2	371.8	374.6	1,461.3	357.5	362.7	369.9	379.6	1,469.7
Change in Fair Value of Contingent Consideration	-51.6	-0.1	0.5	0.3	0.5	1.2	-15.0	-15.0	-15.0	-15.0	-60.0
Total Operating Expenses	**4,775.0**	**1,208.5**	**5,788.4**	**1,263.0**	**1,293.1**	**9,553.0**	**1,307.5**	**1,326.3**	**1,352.2**	**1,387.4**	**5,373.4**
Operating Income	**3,832.0**	**1,139.5**	**-3,514.7**	**1,116.3**	**1,086.4**	**-172.5**	**1,105.0**	**1,118.1**	**1,137.3**	**1,167.6**	**4,528.0**
Interest Expense/Income, net	570.6	170.8	146.6	124.7	135.0	577.1	88.0	89.0	90.0	91.0	358.0
Other Income/Expense, net	-22.8	-31.2	-23.1	-16.9	-	-71.2	-	-	-	-	-
Earnings Before Tax	**4,379.8**	**1,279.1**	**-3,391.2**	**1,224.1**	**1,221.4**	**333.4**	**1,193.0**	**1,207.1**	**1,227.3**	**1,258.6**	**4,886.0**
Income Tax Expense	760.2	179.5	202.4	178.7	178.3	738.9	179.0	181.1	184.1	188.8	732.9
Net Income	**3,619.6**	**1,099.6**	**-3,593.6**	**1,045.4**	**1,043.1**	**-405.5**	**1,014.1**	**1,026.0**	**1,043.2**	**1,069.8**	**4,153.1**
Weighted Average Basic Shares Outstanding	257.7	258.2	258.1	258.0	257.9	258.0	259.8	260.0	260.4	260.7	260.2
Weighted Average Diluted Shares Outstanding	260.5	261.1	258.1	261.0	260.9	259.0	262.9	263.0	263.2	263.6	263.1
Net Income per Share, GAAP, Basic	$14.05	$4.26	-$13.92	$4.05	$4.04	-$1.57	$3.90	$3.95	$4.01	$4.10	$15.96
Net Income per Share, GAAP, Diluted	$13.89	$4.21	-$13.92	$4.01	$4.00	-$1.57	$3.86	$3.90	$3.96	$4.06	$15.79
All figures in millions of U.S. Dollar except per share items.											

Sources: Capital IQ, Kingswood Capital Partners Estimates.

Risks to Our Price Target

Clinical trial setbacks: The success of Vertex's drug development pipeline depends on the outcomes of clinical trials, which are subject to risks and uncertainties, including unexpected safety issues, serious side effects, or lack of efficacy.

Regulatory: Vertex may face delays caused by, or rejections from regulatory agencies of its applications for regulatory clearance and marketing authorizations, which in turn would delay or prevent commercialization.

Pricing and reimbursement: Payers such as medical insurers or government-underwritten health systems may limit patient access, or decline to reimburse Vertex's therapies if Vertex's prices are deemed too high, or the efficacy of its therapies are deemed insufficient.

Dependence on a few key products: Vertex's revenue is heavily dependent on its cystic fibrosis products, and any setbacks or competition in this area could have a significant impact on the company's financial performance.

Intellectual property challenges: Vertex's patents may be challenged by competitors, declared invalid by the Patent Trial and Appeal Board, or in court, which could lead to loss of intellectual property or formulary exclusivity, and increased competition.

Competition: Vertex operates in a highly competitive industry, and its competitors may develop equivalent or superior therapies, thereby eroding its market share and revenue.

Supply chain disruptions: Vertex relies on a complex global supply chain to manufacture its therapies, and disruptions or quality issues could impact production, sales, as well as clinical trial timelines.

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			Investment Banking Services/Past 12 Months	
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BUY	4	80.00	1	25.00
HOLD	0	0.00	0	0.00
SELL	0	0.00	0	0.00
NOT RATED	1	20.00	1	100.00

As of December 2024.

Vertex Pharmaceuticals Rating History as of December 23, 2024

Source: E-Trade.

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