



Outperform

Encysive Pharmaceuticals (ENCY-NASDAQ)

Company Note

ENCY: STRIDE-2 Physician Follow Up Supports Positive Outcome

January 27, 2005

Price: \$9.11
 52-Wk. Rng.: \$12-5
 Shares Out.: (MM) 56.9
 Market Cap.: (MM) 518.4

EPS FY (Dec.)	2003 A		2004 E		2005 E		REV. 2004		2005
	Current	Prior	Current	Prior	Current	Prior			
Q1 (Mar.)	(\$0.11)	NC	(\$0.21)	A NC	NE	NC	\$2.8	MM	NE
Q2 (June)	(0.32)	NC	(0.23)	A NC	NE	NC	3.4		NE
Q3 (Sep.)	(0.17)	NC	(0.31)	A NC	NE	NC	2.6		NE
Q4 (Dec.)	(0.19)	NC	(0.27)	NC	NE	NC	2.6		NE
Full FY	(\$0.80)	NC	(\$1.03)	NC	(\$0.67)	NC	\$11.7	MM	\$24.3 MM
FYPE	NM		NM		NM				
Full CY	(\$0.80)	NC	(\$1.03)	NC	(\$0.67)	NC			
CYPE	NM		NM		NM				

Source: Company data and Wachovia Capital Markets, LLC estimates NA = Not Available, NC = No Change, NE = No Estimate, NM = Not Meaningful

Float: (MM) 51.7
 Avg. Daily Vol.: 823,809
 S&P 500: 1,174.55
 Div./Yield: \$0.00/0.0%
 Last Reporting Date:

LT Debt: (MM) \$2.0
 LT Debt/Total Cap.: 0.0%
 ROE: NM
 3-5 Yr. Est. Grth. Rate: NE
 CY 2005 Est. P/E-to-Grth.: NE

Company Description

Encysive is a biopharmaceutical company focused on developing small molecule compounds for the treatment of a variety of cardiovascular, vascular and related inflammatory diseases. The company's lead pipeline compound, sitaxsentan for the treatment of pulmonary arterial hypertension is currently in Phase III trials. The company receives revenue from a royalty agreement with Glaxo on sales of Argatroban for the treatment of thrombosis in patients with heparin-induced thrombocytopenia. Encysive's majority-owned affiliate, Revotar Biopharmaceuticals, is developing selectin antagonist bimosiamose, currently in Phase II development for the treatment of asthma and psoriasis.

Investment Thesis

We believe ENCY's lead compound Thelin for treatment of pulmonary hypertension will offer a superior therapy to current standard of care Tracleer, in an expanding PH treatment market.

Key Points

- PHYSICIANS CARRY HIGH EXPECTATIONS FOR THELIN 100MG ARM.** Based on recent dialogue with clinicians involved in STRIDE-2 (representing nearly 25% of the 246 patients enrolled), we expect the Thelin 100mg arm to successfully achieve the trial's primary endpoint and key secondary endpoints.
- INVESTIGATORS UNCONCERNED ABOUT THE RISK OF PLACEBO OUTPERFORMANCE.** Physicians have suggested that STRIDE-2 patients' baseline characteristics will be in the ballpark of Pfizer's recent SUPER-1 trial for sildenafil (60%:40% NYHA Class III:II ratio and a baseline 6-minute walk of about 340m), thus removing the potential for a "ceiling effect". Clinician expectation is for the placebo patients to experience a modest decline in 6-minute walk, consistent with historical evidence.
- LIVER TOXICITY EXPECTED TO BE SUPERIOR TO TRACLEER.** We detect there has been a greater incidence of liver toxicity among the open-label Tracleer patients in STRIDE-2 compared to the patients in the blinded arms (Thelin and placebo) throughout the trial's 18 week study period.
- BELIEVE THERE IS SUBSTANTIAL UPSIDE ON PH. III SUCCESS.** We believe our forecast for \$285 million in 2009 Thelin revenue is readily achievable if Thelin demonstrates efficacy in line with Tracleer with reduced liver toxicity. \$285 million in revenue would support fully-taxed EPS of around \$1.00 or more and potentially provide near-term upside to the mid-teens or better in ENCY shares.

Valuation Range: \$12 to \$14

Our \$12-14 valuation range is based on applying a 32.5x multiple to our 2009 EPS estimate of \$0.94 (fully taxed) on total Thelin sales of \$285 million and discounting back at 32.5% to 2006. Risks to our range include Thelin developmental delays and an increasingly competitive PH treatment market.

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Martin D. Auster, M.D. (212) 451-2691
 martin.auster@wachovia.com
 Zev Cohen (212) 451-2605
 zev.cohen@wachovia.com
 Elizabeth Bernstein (212) 451-9971
 elizabeth.bernstein@wachovia.com

Please see page 6 for rating definitions, disclosure information, and required analyst certifications.



STRIDE-2 Physician Follow Up

With ENCY shares off approximately 25% from their early December highs, we attribute recent weakness to three possible factors:

- Concern that the STRIDE-4 placebo experience has increased the clinical risk in STRIDE-2.
- Possible Tracleer outperformance relative to Thelin in STRIDE-2.
- Risk that ENCY shares may have discounted much of the potential upside from success in the Phase III trial.

As a follow up to our January 20th note “We’re Thelin’ Confident-Recommend Buying Ahead Of STRIDE-2”, we conducted extensive dialogue with physicians representing approximately 25% of the 246 patients enrolled in STRIDE-2. **We have received a consistently positive message from those physicians with whom we have spoken** and reiterate our confidence in Thelin’s ability to demonstrate a statistically significant improvement in the six-minute walk endpoint versus placebo and a relatively low incidence (< 5%) of hepatotoxicity in the 100mg Thelin arm. We regard fears that upside in ENCY may be limited, even with a positive outcome, to be overblown. To this end, **we remind investors of our conservative revenue forecast for Thelin** (we forecast Thelin to conservatively achieve just \$285 million, or about 2/3rds of Tracleer’s current sales rate, despite our expectation that Thelin possesses key differentiating features relative to Tracleer) **and the powerful leverage that exists in the company’s P&L** (due to expected modest selling expenses required to address the PAH physician community).

Consensus Physician Thoughts For Clinical Outcomes of STRIDE-2

Strong expectations for Thelin 100mg arm. The magnitude of the walk improvement is anticipated to at least approximate the 35m-40m improvement demonstrated by Tracleer in its pivotal trial.

No sign of clinical improvement in the placebo arm. Following STRIDE-4 results in December in which placebo patients’ six-minute walk distance actually *improved* rather than deteriorated, we believe investors have had concerns over a repeat placebo outperformance in STRIDE-2. Beyond historical evidence which points to a clinical deterioration in PAH patients receiving placebo, investigators have relayed the existence of patients who clearly underperformed, even to the extent that they had to be pulled out of the trial.

We also believe based on physician dialogue that the baseline characteristics of patients enrolled in STRIDE-2 are similar to those patients enrolled in the Phase III sildenafil monotherapy trial, SUPER-1. As detailed below, patients in the SUPER-1 trial had a baseline six-minute walk of 344m, similar to the baseline walk seen in Tracleer’s pivotal BREATHE-1 trial. This compares favorably to the entry characteristics in STRIDE-1 (398m baseline walk) and could allow Thelin to demonstrate a more pronounced efficacy benefit in this sicker patient population.

Figure 1: Baseline entry characteristics for relevant PAH trials

	STRIDE-1 (sitaxsentan)	SUPER-1 (sildenafil)	BREATHE-1 (bosentan)
N	178	278	213
Baseline walk distance	398m	344m	334m
% NYHA Class II	33%	39%	N/A
% NYHA Class III	66%	58%	N/A
Placebo change in six-minute walk distance from baseline	-13m	-10m	-8m

Note: BREATHE-1 categorized patients by WHO class
Source: New England Journal of Medicine and CHEST 2004

Liver toxicity expected to be superior to Tracleer. Physicians we have consulted with have also noted the scarcity of patients who have been pulled out of one of the blinded arms (meaning Thelin or placebo), but pointed out that there were a few patients who were pulled out of the open-label Tracleer arm due to



elevated liver enzymes. We believe this bodes well for comparison of the rates of hepatotoxicity between Thelin and Tracleer arms.

Efficacy thought to be comparable between Tracleer and Thelin. While investors have voiced concern regarding the relative performance of the Thelin group versus the Tracleer comparator arm in STRIDE-2, we remind investors that clinicians do not regard a 10m, 15m, or even (in most cases) a 20m walk difference as highly clinically meaningful. This is particularly true in STRIDE-2 given that the Tracleer group is open label. That said, **the consensus read from physicians is that results for the two drugs are likely to be in a similar range; if anything, investigators' current best-guess calls for Thelin to perhaps modestly outperform Tracleer in this trial** based on anecdotal assessment of STRIDE-2 performance. Based on Tracleer's BREATHE-1 study, this suggests placebo-adjusted walk improvements of around 40m or better in the Thelin 100mg arm.

Phase III Success Should Support Upside From Current Levels

Our current \$12-\$14 valuation range is based on application of a 33x multiple to our fully-taxed, diluted 2009 EPS estimate of \$0.94, discounted back at 33% annually. Our forecast for global Thelin revenue of \$285 million in 2009 assumes that Thelin will demonstrate efficacy roughly in line with Tracleer while demonstrating a lower incidence of liver toxicity as our physician discussions have suggested. Beyond share gains from Tracleer, we also model a roughly 15% CAGR in the oral segment of the PAH market through 2009. We note that Tracleer is currently expected to have exited 2004 on an annualized run-rate in the range of \$400-\$450 million, with yr/yr growth exceeding 60% through the first nine months of 2004.

Should Thelin perform in line with these expectations in STRIDE-2, we believe a reduction in our discount rate would be appropriate as a great deal of clinical risk associated with investment in Encysive would be removed, supporting a new 6-12 month valuation range in the mid-to-high teens. Based on conversations with physicians we believe there is a possibility that Thelin's STRIDE-2 performance may moderately surpass Tracleer's efficacy. This outcome could lead to higher revenue projections in addition to use of a lower discount rate going forward and could result in a new valuation range closer to \$20/share.

Finally, it is important that investors realize that although we believe the clinical risk of STRIDE-2 is quite low and our field checks consistently support our conclusions stated here, all clinical trials carry risk. We estimate that nearly all of Encysive's current market cap reflects the market's perceived potential for Thelin. As such, failure to produce significantly positive data in STRIDE-2 that supports approval and commercialization of the drug could lead to dramatic downside for Encysive shares—likely in the low-single digits.



Figure 2: Encysive Annual Income Statement

(Dollars in thousands except per-share data)

	2003A	% chg	2004E	% chg	2005E	% chg	2006E	% chg	2007E	% chg	2008E	% chg	2009E	% chg
Thelin - US Sales							35,669		68,968	93%	116,399	69%	171,853	48%
Thelin - EU Sales							21,152		47,992	127%	78,167	63%	112,687	44%
Total WW Sales							\$56,820		\$116,960	106%	\$194,566	66%	\$284,541	46%
Revenues:														
Argatroban Royalties	5,411	241%	8,600	59%	9,288	8%	9,752	5%	9,752	0%	9,752	0%	9,752	0%
Thelin Royalties	-		-		-		5,288		11,998	127%	19,542	63%	28,172	44%
Research Agreements	3,024	(15%)	2,033	(33%)										
Collaborative R&D, Encysive	664	(39%)												
License, milestone and other	2,458	9%	1,025	(58%)	15,000	NM	30,000	100%	5,000	(83%)	5,000	0%	5,000	0%
Total Revenues	\$11,557	11%	\$11,658	1%	\$24,288	108%	\$80,709	232%	\$95,718	19%	\$150,693	57%	\$214,778	43%
Operating Expenses:														
COGS							3,567		6,897	93%	11,640	69%	17,185	48%
% of Sales							10%		10%		10%		10%	
R&D	29,421	47%	57,946	97%	43,459	(25%)	41,286	(5%)	43,144	5%	47,459	10%	51,730	9%
% of Revenues	255%		497%		179%		51%		45%		31%		24%	
SG&A	9,133	2%	11,131	22%	22,262	100%	34,507	55%	43,133	25%	49,603	15%	54,564	10%
% of Revenues	79%		95%		92%		43%		45%		33%		25%	
Equity in loss of Encysive	2,386		-		-		-		-		-		-	
In-process R&D	8,363		-		-		-		-		-		-	
Total Operating Expenses	\$49,303	31%	\$69,077	40%	\$65,722	(5%)	\$79,360	21%	\$93,174	17%	\$108,702	17%	\$123,479	14%
Operating Income (Loss)	(37,746)	NM	(57,419)	NM	(41,434)	NM	1,349	NM	2,544		41,991	NM	91,299	117%
<i>Operating Margin</i>	<i>NM</i>		<i>NM</i>		<i>NM</i>		<i>NM</i>		<i>NM</i>		<i>28%</i>		<i>43%</i>	
Interest and other income	1,228		981		1,350	38%	1,400	4%	1,500	7%	3,500	133%	6,000	71%
Minority interest	1,225		687		-		-		-		-		-	
Pretax Income (Loss)	(\$35,293)		(\$55,751)		(\$40,084)		\$2,749		\$4,044		\$45,491	NM	\$97,299	114%
Provision For Income Taxes	-		-		-		-		-		2,388	NM	5,108	NM
<i>Effective Tax Rate</i>											<i>5.3%</i>		<i>5.3%</i>	
Net Income (Loss)	(\$35,293)		(\$55,751)		(\$40,084)		\$2,749		\$4,044		\$43,103	NM	\$92,191	114%
EPS - Basic	(\$0.80)		(\$1.03)		(\$0.67)		\$0.04		\$0.06		\$0.67		\$1.42	112%
EPS - Diluted	(\$0.80)		(\$1.03)		(\$0.67)		\$0.04		\$0.06		\$0.65		\$1.37	111%
EPS - Diluted, Fully-Taxed	(\$0.80)		(\$1.03)		(\$0.67)		\$0.03		\$0.04		\$0.45		\$0.94	111%
Basic Shares Outstanding ('000s)	44,072		53,971		60,269		63,218		63,689		64,184		64,704	
Diluted Shares Outstanding ('000)	44,072		53,971		60,269		63,218		63,689		66,161		67,111	

Source: Company Reports and Wachovia Capital Markets, LLC estimates



Figure 3: Encysive Quarterly Income Statement

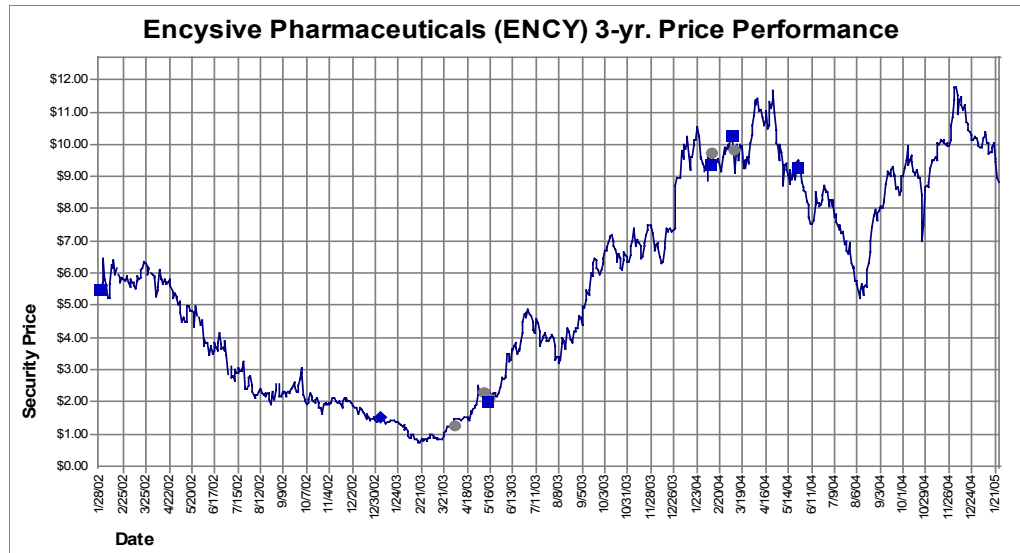
(Dollars in thousands except per-share data)

	Q1 2004A	% chg	Q2 2004A	% chg	Q3 2004A	% chg	Q4 2004E	% chg	2004E	% chg
Revenues:										
Argatroban Royalties	1800	57%	2000	80%	2300	66%	2500	41%	8,600	59%
Research Agreements	700	(6%)	700	(6%)	283	(63%)	350	(55%)	2,033	(33%)
Collaborative R&D, Encysive LP	-		-		-		-		-	
License, milestone and other	335		690		-		-		1,025	
Total Revenues	\$2,835	(12%)	\$3,390	52%	\$2,583	(24%)	\$2,850	6%	\$11,658	1%
Operating Expenses:										
COGS										
R&D	12,015	185%	13,193	109%	16,754	95%	15,984	55%	57,946	97%
SG&A	2,485	15%	2,742	21%	2,893	2%	3,011	60%	11,131	22%
Equity in loss of Encysive	-		-		-		-		-	
In-process R&D	-		-		-		-		-	
Total Operating Expenses	\$14,500	66%	\$15,935	(6%)	\$19,647	72%	\$18,995	56%	\$69,077	40%
Operating Income (Loss)	(11,665)		(12,545)		(17,064)		(16,145)		(57,419)	<i>NM</i>
Interest and other income	350		135		296		200		981	(20%)
Minority interest	194		104		189		200		687	
Pretax Income (Loss)	(\$11,121)		(\$12,306)		(\$16,579)		(\$15,745)		(\$55,751)	
Provision For Income Taxes	-		-		-		-		-	<i>NM</i>
Tax Rate	0.0%		0.0%		0.0%		0.0%		0.0%	<i>NM</i>
Net Income (Loss)	(\$11,121)		(\$12,306)		(\$16,579)		(\$15,745)		(\$55,751)	
EPS, Basic	(\$0.21)		(\$0.23)		(\$0.31)		(\$0.27)		(\$1.03)	<i>NM</i>
EPS, Diluted	(\$0.21)		(\$0.23)		(\$0.31)		(\$0.27)		(\$1.03)	<i>NM</i>
Basic Shares Outstanding ('000s)	52,178		52,550		53,607		57,550		53,971	
Diluted Shares Outstanding ('000s)	52,178		52,550		53,607		57,550		53,971	

Source: Company Reports and Wachovia Capital Markets, LLC estimates



Required Disclosures



Date	Close Price (\$)	Rating Code	Target Price (\$)	Val. Rng. Low	Val. Rng. High
1/28/02	Cann				
1/28/02	5.50	3	NE	NE	NE
1/4/03	1.52	2	NE	NE	NE
4/2/03	1.26	2	NE	1.50	4.25
5/8/03	2.30	2	NE	1.70	5.00
5/13/03	Hausner				
5/14/03	2.10	SR	NE	1.70	5.00
2/9/04	Auster, M.D.				
2/10/04	9.75	1	NE	12.00	14.00
3/8/04	Hausner				
3/9/04	9.82	SR	NE	12.00	14.00
5/25/04	Auster, M.D.				
5/25/04	9.31	1	NE	12.00	14.00

Source: Wachovia Capital Markets, LLC estimates and Bridge data

Beginning 01/04/2004 stock valuation range replaces target price

Symbol Key

- ◆ Rating Scale Conversion
- Rating, Target Price and/or Val. Rnge. Chnge.
- ▼ Rating Downgrade

- ▲ Rating Upgrade
- Analyst Change
- Split Adjustment

Rating Code Key

- 1 Outperform
- 2 Market Perform
- 3 Underperform
- SR Suspended
- NR Not Rated
- NE Not Estimate

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2 = Market Perform: The stock appears appropriately valued, and we believe the stock's total return will be in line with the market over the next 12 months. HOLD

3 = Underperform: The stock appears overvalued, and we believe the stock's total return will be below the market over the next 12 months. SELL

**As of: January 27, 2005**

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Wachovia has provided investment banking services for 35% of its Market Perform-rated companies.
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