

ENCY: Physician Conference Call Focuses on Safety & Efficacy of Thelin

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Encysive Pharmaceuticals# (ENCY, \$10.01, NASDAQ, BUY)

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#Fulcrum Global Partners LLC makes a market in this security.

Company description: Encysive is a late-stage biotechnology company focused on developing and commercializing small molecules addressing diseases of the vasculature. The lead product, Thelin, is in Phase III trials for pulmonary arterial hypertension.

Decision points:

- **On Wednesday morning, we sponsored a physician consultant call to discuss the emerging market for pulmonary hypertension.** Dr. Jim Gossage from the Medical College of Georgia and Dr. Harold Palevsky from the University of Pennsylvania participated in the call. Dr. Gossage is or was involved in the Thelin STRIDE studies and Dr. Palevsky is on the Thelin data safety monitoring board.
- **Both physicians expect positive Thelin data.** While our consultants believe Thelin will show similar activity as Tracleer, they noted that a 30% relative difference between the drugs in exercise capacity would be clinically meaningful. Furthermore, they differed in their expectations on liver toxicity, in addition to the relative importance of the warfarin-Thelin interaction. But both agreed that if Thelin shows half the incidence in liver toxicity of Tracleer, it would be considered clinically relevant. Finally, **Dr. Palevsky mentioned concern over certain hospitalizations related to the warfarin-Thelin interaction that we believe is likely associated with the STRIDE I trial and will not be an issue with the STRIDE II dataset.** Importantly, the overall incidence of major bleeding events is rather low in the STRIDE program and not a cause for concern. Overall, we believe their comments support our view that Thelin could be a best-in-class endothelin antagonist, as we expect it to show a reduction in liver toxicity and possibly a clinically relevant improvement in exercise capacity compared to Tracleer.
- **Other drugs discussed include Actelion's Tracleer, Myogen's Ambrisentan, Pfizer's Revatio/Viagra, GlaxoSmithKline's Flolan, United Therapeutic's Remodulin, and CoTherix's Ventavis.** We included their comments on each drug in this report.
- **Phase III Thelin data from STRIDE II are on track for this month.** We expect positive results to support a NDA filing in April and approval in Q4:05. We estimate Thelin sales of \$38M in '06, growing to \$233M in '08. Encysive owns 100% of the rights to the drug and plans to commercialize it in the U.S. Ex-U.S. commercialization is still unclear (out-license, strategic alliance, or build a sales force). Since the PAH market is relatively efficient (concentrated prescribing that requires a modest sales force of 35 to 50 individuals to adequately detail the physicians), we model Encysive achieving profitability on \$100M in sales. We project first-year profitability of \$0.05 per share in '07 growing to \$0.85 in '08.

- **We reiterate our BUY rating and \$18 YE:05 price target.** ENCY is among our favorite small-cap biotech names that should benefit from expected positive Phase III data and approval for its lead product during 2005. Our \$18 price target is based on 30x our FY'08 EPS estimate of \$0.85 and a 20% discount rate. It equates to a \$1 billion market capitalization, which is on par with existing biotechnology companies with late-stage drugs with a high-probability of success. We believe upside exists to the valuation if Thelin demonstrates a statistically significant difference (or trend) to Tracleer in the STRIDE II study.

Rating:	BUY	FY: Dec	2003	A	2004	E	2005	E	2006	E
Price:	\$10.01	Mar	(\$0.11)	A	(\$0.21)	A	(\$0.26)	E	--	
52-Week Range:	\$5.00–\$11.94	Jun	(\$0.13)	A	(\$0.23)	A	(\$0.25)	E	--	
Market Cap (mm):	\$577	Sep	(\$0.17)	A	(\$0.31)	A	(\$0.24)	E	--	
Avg. Daily Volume:	822,681	Dec	(\$0.19)	A	(\$0.30)	E	(\$0.30)	E	--	
3-Yr. Est. Grwt Rate:	--	FY	(\$0.61)	A	(\$1.07)	E	(\$1.05)	E	(\$0.87)	E
Investment Theme:	Growth	Previous								
		Consensus				(\$1.06)	(\$0.86)			
Target Price:	\$18	P/E				NMF	NMF			
Risk Level:	High	Revenue (mm)	\$11.5		\$11.4		\$12.4		\$51.9	

NMF – Not Meaningful.

Both Consultants Expect Positive Thelin Data in STRIDE II

- **A 30% relative difference between Thelin and Tracleer would be viewed as clinically meaningful.** While the consultants expect all three drugs arms (50mg & 100mg Thelin, 125mg Tracleer) to show a significant benefit over the placebo group, they were less certain that Thelin would demonstrate a marked improvement over Tracleer in the six-minute walk test. However, they stated that a 30% relative difference between treatments would be clinically meaningful.

Given the historical performance of Tracleer in the Phase III BREATH trials (~35m-40m net improvement) and the post-hoc STRIDE I and European subset from STRIDE IV data on Thelin (~55m-60m net improvement), we believe Thelin has “wobble room” to show a meaningful improvement in exercise capacity. We are cognizant there are several caveats in analyzing post hoc and subset data for any drug. Yet our conviction in the possibility that Thelin could be a more effective drug lies in the STRIDE VI dataset, in which approximately 33% of patients who failed prior Tracleer treatment responded to Thelin. However, it is unclear if the converse would hold true as well, given the lack of data in that setting.

- **The consultants differed in their opinions regarding the safety profile.**
 - **Liver function test (LFT) elevations:** Dr. Gossage expects a 3% to 5% incidence with Thelin and a 10%+ incidence with Tracleer at 18 weeks. These are typical rates observed in the STRIDE and BREATH trials for Thelin and Tracleer, respectively. On the other hand, Dr. Palevsky does not expect a material difference in the incidence of LFT elevations between either drug, citing numerous reasons for LFT elevation other than Thelin or Tracleer, such as alcohol consumption or other medications (statins, etc). Both physicians agreed it would be a significant advantage should Thelin show half the incidence of LFT elevation as Tracleer. We believe the Thelin data have consistently shown a 5% incidence of LFT elevation in the STRIDE I and III datasets. The wildcard may be the LFT elevation in the Tracleer-arm. Similar to Tracleer, we expect Thelin to receive a black-box warning for LFT elevation that requires monthly monitoring.

- **Drug interaction with warfarin:** Warfarin is a commonly prescribed blood thinner in PAH patients (~65-75% of patients). Since it has a relatively tight therapeutic index (too much can lead to bleeding), physicians must constantly monitor a patient's ability to coagulate. Thelin is the only endothelin antagonist to interact with warfarin, thereby requiring a 90% dose reduction in the blood thinner, which is usually titrated back to an effective dose in the patient. Virtually all the cardiologists and pulmonologists we have spoken with have indicated this drug interaction is not a problem with Thelin, provided an appropriate dose-adjustment scale is included in the package insert that they can use as a guide.

HOWEVER, on our call Dr. Palevsky indicated the warfarin-Thelin interaction might be a material issue among the primary care physicians (PCP) and certain physician subspecialties (e.g., rheumatologist) that are not accustomed to adjusting warfarin doses. Indeed, he cited cases in the STRIDE studies in which patients were hospitalized due to elevated INR (International Normalization Ratio; a measure of blood coagulation), possibly due to the warfarin-Thelin interaction. Dr. Palevsky stressed that none of the hospitalizations were associated with a major bleeding episode and to the best of his knowledge, the overall incidence of major bleeding events is rather low across the STRIDE studies, possibly due to the studies being conducted by cardiologists and pulmonologists accustomed to prescribing warfarin.

After an additional follow-up conversation with Dr. Palevsky (off-line) and a check-in with Encysive management, we believe the cases of hospitalizations are isolated to the STRIDE I trial. Specifically, approximately two-thirds of the patients enrolled in that study prior to the implementation of the dose-adjustment scale that is currently used in the STRIDE II and subsequent trials. It is unclear if all of the hospitalizations were observed in the 100mg or the 300mg-arm in STRIDE I. In addition, in STRIDE IV there was no difference in the incidence or severity of bleeding episodes between Thelin and placebo. Hence, we would not expect either bleeding or hospitalization due to elevated INR to be an issue with the STRIDE II dataset.

HOWEVER, we believe the essence of Dr. Palevsky's comment warrants further attention. Our belief is that in order for the PAH market to continue growing significantly, the prescriber base must expand to include physicians other than pulmonologists and cardiologists. The approval of Pfizer's Revatio/Viagra in mid-05E could accelerate this expansion. If PCP and rheumatologists treating PAH patients are following the current recommended American College of Cardiology (ACC) and American College of CHEST physician treatment guidelines, they most likely are prescribing warfarin. Absent a significant efficacy advantage of Thelin over Tracleer and for the sake of simplicity, a large portion of these PCP and rheumatologists may elect to use either Tracleer or ambrisentan over Thelin.

- **The "placebo effect" observed in STRIDE IV is an anomaly and not expected to be repeated in STRIDE II.** Recall, patients in the placebo-arm improved by 34m in the six-minute walk test over baseline measurements. This improvement resulted in the study failing to show a significant improvement in exercise capacity with the 100mg Thelin dose, despite it demonstrating an impressive 58m improvement over baseline scores. Interestingly, placebo-treated patients experienced a greater improvement than patients receiving the 50mg Thelin dose (22m improvement), in addition to the 100mg-arm achieving a statistically significant benefit over the 50mg-arm. Since the release of these data in mid-December, investors have been concerned over the potential for a similar placebo effect in STRIDE II. While neither consultant could explain why there was a placebo effect, they noted that no other PAH study has demonstrated a marked improvement in the placebo-arm and they would not expect it to occur in STRIDE II.

Other drugs discussed on the call.

- **Tracleer (Actelion):** Neither doctor expressed concerns regarding possible drug interactions with Viagra. Both prescribe Tracleer as a front-line agent in PAH patients. The introduction of Thelin will impact Tracleer use, although absent the STRIDE II data it is difficult to conclude exactly in what manner. For example, should Thelin only show comparable efficacy and safety (similar LFT evaluations) as Tracleer, then Tracleer's use may not be significantly impacted in front-line. However, if Thelin shows a marked improvement in EITHER safety or efficacy over Tracleer, then it could become a treatment of choice. Finally, Dr. Gossage expressed enthusiasm for the STRIDE VI results, in which Thelin showed activity in Tracleer failures. He did not believe these data would limit Thelin to use in this setting, which represents up to 30% of patients after 12 months of Tracleer treatment.
- **Ambrisentan (Myogen):** Dr. Gossage is involved in the ongoing Phase III ambrisentan trial. He noted slow patients accrual that has not accelerated over the last couple of months. The patient accrual is affected by the number of treatment-naïve patient referrals. Myogen recently announced a delay in enrollment completion to Q4:05 from Q2:05. We believe this timeline is still at risk and may be more difficult to achieve should Thelin be approved and launched in Q4:05. Dr. Palevsky indicated that he believed ambrisentan could be associated with a lower incidence of LFT elevation. However, we note he is not involved in the clinical trials, nor is he on the data safety monitoring board for that drug. Furthermore, the reported incidence of LFT elevation in the Phase II ambrisentan study is 6% at 24 weeks, a rate similar to Thelin.
- **Revatio/Viagra (Pfizer):** Both doctors were critical of the Revatio data from SUPER-1 that was released last fall. This is somewhat surprising given the "buzz" surrounding the drug among pulmonologists and cardiologists after the release of the data. Specifically, our consultants emphasized the lack of long-term efficacy data and the potential that the improvements in exercise capacity observed at 12 weeks will not be sustained at 12 months. Dr. Palevsky cited a particular study conducted at the Mayo clinic in which PAH patients treated with Revatio monotherapy experienced a clinical benefit at 12 weeks that waned over time. At this point, it is unknown if the lack of sustained benefit is due to a loss in biologic effect or disease progression. The long-term follow-up data from SUPER-1 are possible at the American Thoracic Society meeting this spring. Currently, neither physician is using Revatio significantly, due to insurance reimbursement issues and the lack of clinical data. They are currently using Revatio primarily in patients who are poor candidates for Tracleer due to LFT elevations. Several of our other consultants are using Revatio in combination with Tracleer. We expect the reimbursement issue to be resolved upon approval in mid-05E, and for Revatio to be used primarily in combination with an endothelin antagonist, as this class is now associated to modify disease progression.
- **Flolan (GlaxoSmithKline):** Flolan remains the treatment of choice among severe Class IV PAH patients due to the physicians' familiarity in titrating up to the effective dose. However, we believe that as physicians become better acquainted with the IV Remodulin formulation a large number of patients will be transitioned over due to the potential quality of life benefit associated with not requiring ice packs (Remodulin is stable at room temperature whereas Flolan requires ice packs) or daily reconstitution of the drug (Remodulin comes premixed).
- **Remodulin (United Therapeutics):** Both physicians disliked the subcutaneous formulation of Remodulin, but believe the IV formulation is a big advance. However, Dr. Gossage expressed that it may not be as effective as Flolan in severe Class IV patients, due to difficulty in titrating the dose. Furthermore, he expressed frustration over United Therapeutic's pricing strategy, as IV Remodulin appears more expensive than Flolan.
- **Ventavis (CoTherix):** Dr. Gossage expressed considerable interest in "trying out" Ventavis in his stable Class III patients when the drug become commercially available. Ventavis is an inhaled formulation of a prostanoid called iloprost that received FDA approval in late December. Due to the necessity for frequent administrations (6 to 9 inhalations a day through a nebulizer) and the inability to easily titrate the dose, neither consultant believed Ventavis would be used in severe patients who need sustained blood concentrations (especially through the nighttime) or require high doses.

Anticipated Milestones

Timing	Event
Feb '05	Phase III STRIDE II data evaluating Thelin for pulmonary arterial hypertension.
Q1:05	Encysive discusses pipeline and clinical programs for other Thelin indications during Q4 conference call.
April '05	File NDA for Thelin in PAH.
Q4:05	FDA approval of Thelin in PAH.
2005	Schering-Plough initiates Phase I trial with TBC4746 in asthma.

Sources: Encysive and Fulcrum Global Partners LLC.

Encysive Pharmaceuticals, Income Statement (\$M)

Fiscal Year Ending in December

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	2004E				FY	2005E				FY
	Mar(A)	Jun(A)	Sep(A)	Dec	2004E	Mar	Jun	Sep	Dec	2005E
U.S. Thelin Sales	-	-	-	-	-	-	-	-	-	-
Thelin Royalty Revenue	-	-	-	-	-	-	-	-	-	-
Argatroban Royalty Revenue	1.8	2.0	2.3	2.4	8.5	2.5	2.6	2.7	2.8	10.6
Contract / R&D / Other Revenue	1.0	1.4	0.3	0.3	2.9	0.5	0.5	0.5	0.5	2.0
Total Revenue	\$2.8	\$3.4	\$2.6	\$2.7	\$11.4	\$2.8	\$3.1	\$3.2	\$3.3	\$12.4
Cost of Goods Sold	-	-	-	-	-	-	-	-	-	-
Gross Profit	\$2.8	\$3.4	\$2.6	\$2.7	\$11.4	\$2.8	\$3.1	\$3.2	\$3.3	\$12.4
R&D Expense	12.0	13.2	16.8	17.5	59.5	15.0	13.5	12.0	12.5	53.0
SG&A Expense	2.5	2.7	2.9	3.3	11.4	3.5	4.0	5.5	8.5	21.5
Equity in Loss of Affiliate	-	-	-	-	-	-	-	-	-	-
In-Process R&D	-	-	-	-	-	-	-	-	-	-
Total Operating Expense	14.5	15.9	19.6	20.8	70.8	18.5	17.5	17.5	21.0	74.5
Operating Income	(\$11.7)	(\$12.5)	(\$17.1)	(\$18.1)	(\$59.4)	(\$15.7)	(\$14.4)	(\$14.3)	(\$17.7)	(\$62.1)
Net Interest Income / Expense	0.4	0.1	0.3	0.3	1.1	0.4	(0.1)	0.0	(0.0)	0.2
Minority Interest in Revotar	0.2	0.1	0.2	-	0.5	-	-	-	-	-
Pretax Income (Loss)	(\$11.2)	(\$12.3)	(\$16.6)	(\$17.8)	(\$57.8)	(\$15.4)	(\$14.5)	(\$14.3)	(\$17.7)	(\$61.9)
Income Tax	-	-	-	-	-	-	-	-	-	-
Tax Rate	-	-	-	-	-	-	-	-	-	-
Net Income (Loss)	(\$11.2)	(\$12.3)	(\$16.6)	(\$17.8)	(\$57.8)	(\$15.4)	(\$14.5)	(\$14.3)	(\$17.7)	(\$61.9)
Reported EPS	(\$0.21)	(\$0.23)	(\$0.31)	(\$0.30)	(\$1.07)	(\$0.26)	(\$0.25)	(\$0.24)	(\$0.30)	(\$1.05)
EPS (ex one-time items)	(\$0.21)	(\$0.23)	(\$0.31)	(\$0.30)	(\$1.07)	(\$0.26)	(\$0.25)	(\$0.24)	(\$0.30)	(\$1.05)
Shares Outstanding	52.2	52.6	53.6	58.5	54.2	58.7	59.0	59.2	59.5	59.1
Fully Diluted Shares	57.2	57.6	58.6	63.5	59.2	63.7	69.0	69.2	69.5	67.8

Cash Model

	2004E	2004E	2004E	2004E	2004E	2005E	2005E	2005E	2005E	2005E
Beginning Cash (incl. LT investments)	\$85.5	\$71.6	\$60.6	\$83.2	\$85.5	\$65.4	\$50.0	\$135.5	\$121.2	\$65.4
Net Income	(11.2)	(12.3)	(16.6)	(17.8)	(57.8)	(15.4)	(14.5)	(14.3)	(17.7)	(61.9)
Funds Raised / Distributed	-	-	36.5	-	36.5	-	100.0	-	-	100.0
Other	(2.7)	1.2	2.7	-	1.2	-	-	-	-	-
Ending Cash (incl. LT investments)	\$71.6	\$60.6	\$83.2	\$65.4	\$65.4	\$50.0	\$135.5	\$121.2	\$103.5	\$103.5
Average Cash (incl. LT investments)	\$78.6	\$66.1	\$71.9	\$74.3	\$75.4	\$57.7	\$92.8	\$128.4	\$112.4	\$84.4
Yield	0.4%	0.2%	0.4%	0.4%	1.4%	0.4%	0.4%	0.4%	0.4%	1.8%
Interest Income	\$0.4	\$0.1	\$0.3	\$0.3	\$1.1	\$0.4	\$0.3	\$0.4	\$0.4	\$1.5
Long-term Debt	-	-	-	-	-	-	\$100.0	\$100.0	\$100.0	\$100.0
Interest Rate	-	-	-	-	-	-	0.4%	0.4%	0.4%	1.8%
Interest Expense	-	-	-	-	-	-	\$0.4	\$0.4	\$0.4	\$1.3
Other Income / Expense	-	-	-	-	-	-	-	-	-	-
Net Interest Income / Expense	\$0.4	\$0.1	\$0.3	\$0.3	\$1.1	\$0.4	(\$0.1)	\$0.0	(\$0.0)	\$0.2

Margin Analysis (w/o 1x Items)

	2004E	2004E	2004E	2004E	2004E	2005E	2005E	2005E	2005E	2005E
Product Gross Margin	nmf	nmf	nmf	nmf	nmf	nmf	nmf	nmf	nmf	nmf
Operating Margin	nmf	nmf	nmf	nmf	nmf	nmf	nmf	nmf	nmf	nmf
R&D Expense as a % of Revenue	nmf	nmf	nmf	nmf	nmf	nmf	nmf	nmf	nmf	nmf
SG&A Expense as a % of Revenue	88.8%	80.6%	nmf	nmf	99.4%	nmf	nmf	nmf	nmf	nmf

Thelin Sales (\$M)

	2004E	2004E	2004E	2004E	2004E	2005E	2005E	2005E	2005E	2005E
U.S. Sales	-	-	-	-	-	-	-	-	-	-
ROW Sales	-	-	-	-	-	-	-	-	-	-
Total Sales	-	-	-	-	-	-	-	-	-	-
annual growth	-	-	-	-	-	-	-	-	-	-

Sources: Company reports and Fulcrum Global Partners LLC.

Encysive Pharmaceuticals, Income Statement (\$M)
Fiscal Year Ending in December

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	FY 2002	FY 2003	FY 2004E	FY 2005E	FY 2006E	FY 2007E	FY 2008E
U.S. Thelin Sales	-	-	-	-	\$38.3	\$111.3	\$179.7
Thelin Royalty Revenue	-	-	-	-	-	4.6	12.9
Argatroban Royalty Revenue	3.5	5.5	8.5	10.6	11.7	12.8	14.1
Contract / R&D / Other Revenue	6.9	6.1	2.9	2.0	2.0	2.0	2.0
Total Revenue	\$10.4	\$11.5	\$11.4	\$12.4	\$51.9	\$130.8	\$208.7
Cost of Goods Sold	-	-	-	-	7.7	16.7	18.0
Gross Profit	\$10.4	\$11.5	\$11.4	\$12.4	\$44.3	\$114.1	\$190.8
R&D Expense	20.1	29.4	59.5	53.0	58.3	64.1	70.5
SG&A Expense	9.0	9.1	11.4	21.5	39.1	45.2	49.7
Equity in Loss of Affiliate	8.6	2.4	-	-	-	-	-
In-Process R&D	-	8.4	-	-	-	-	-
Total Operating Expense	37.6	49.3	70.8	74.5	97.4	109.3	120.2
Operating Income	(\$27.2)	(\$37.8)	(\$59.4)	(\$62.1)	(\$53.1)	\$4.8	\$70.5
Net Interest Income / Expense	2.5	1.2	1.1	0.2	(0.2)	(0.6)	0.4
Minority Interest in Revotar	1.2	1.2	0.5	-	-	-	-
Pretax Income (Loss)	(\$23.5)	(\$35.3)	(\$57.8)	(\$61.9)	(\$53.3)	\$4.2	\$71.0
Income Tax	-	-	-	-	-	0.2	6.7
Tax Rate	-	-	-	-	-	5%	10%
Net Income (Loss)	(\$23.5)	(\$35.3)	(\$57.8)	(\$61.9)	(\$53.3)	\$4.0	\$64.2
Reported EPS	(\$0.54)	(\$0.80)	(\$1.07)	(\$1.05)	(\$0.87)	\$0.05	\$0.85
EPS (ex one-time items)	(\$0.54)	(\$0.61)	(\$1.07)	(\$1.05)	(\$0.87)	\$0.05	\$0.85
Shares Outstanding	43.7	44.1	54.2	59.1	61.5	63.5	65.5
Fully Diluted Shares	48.7	49.1	59.2	67.8	71.5	73.5	75.5

Cash Model

Beginning Cash (incl. LT investments)	\$95.4	\$68.0	\$85.5	\$65.4	\$103.5	\$50.2	\$54.1
Net Income	(23.5)	(35.3)	(57.8)	(61.9)	(53.3)	4.0	64.2
Funds Raised / Distributed	-	48.6	36.5	100.0	-	-	-
Other	(4.0)	4.2	1.2	-	-	-	-
Ending Cash (incl. LT investments)	\$68.0	\$85.5	\$65.4	\$103.5	\$50.2	\$54.1	\$118.4
Average Cash (incl. LT investments)	\$81.7	\$76.7	\$75.4	\$84.4	\$76.8	\$52.1	\$86.2
Yield	3.0%	1.6%	1.4%	1.8%	2.0%	2.3%	2.5%
Interest Income	\$2.5	\$1.2	\$1.1	\$1.5	\$1.5	\$1.2	\$2.2
Long-term Debt	-	2.9	-	\$100.0	\$100.0	\$100.0	\$100.0
Interest Rate	-	-	-	1.8%	1.8%	1.8%	1.8%
Interest Expense	-	-	-	\$1.3	\$1.8	\$1.8	\$1.8
Other Income / Expense	-	-	-	-	-	-	-
Net Interest Income / Expense	\$2.5	\$1.2	\$1.1	\$0.2	(\$0.2)	(\$0.6)	\$0.4

Margin Analysis (w/o 1x Items)

Product Gross Margin	nmf	nmf	nmf	nmf	80.0%	85.0%	90.0%
Operating Margin	nmf	nmf	nmf	nmf	nmf	3.7%	33.8%
R&D Expense as a % of Revenue	nmf	nmf	nmf	nmf	nmf	49.0%	33.8%
SG&A Expense as a % of Revenue	86.0%	79.1%	99.4%	nmf	75.3%	34.5%	23.8%

Theelin Sales (\$M)

U.S. Sales	-	-	-	-	\$38.3	\$111.3	\$179.7
ROW Sales	-	-	-	-	-	\$15.4	\$43.1
Total Sales	-	-	-	-	\$38.3	\$126.8	\$222.8
annual growth	-	-	-	-	-	231.3%	75.7%

Sources: Company reports and Fulcrum Global Partners LLC.

APPENDIX A

IMPORTANT DISCLOSURES AND ANALYST’S CERTIFICATION

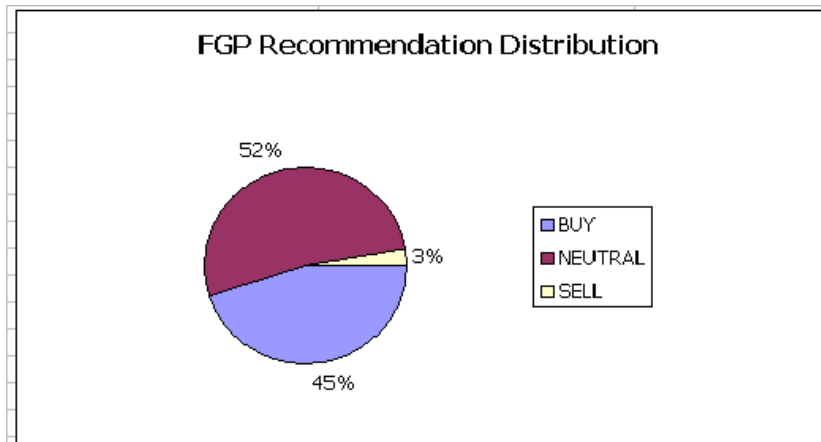
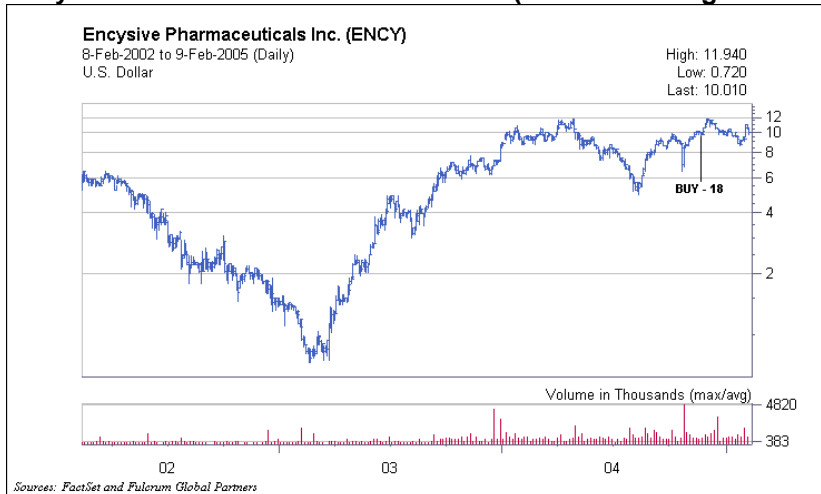
Fulcrum Global Partners LLC ratings are defined as follows:

BUY – A stock that is expected at initiation to produce a positive return of 15% or greater over the 12 months following the initial recommendation. The BUY rating may be maintained following initiation as long as it is deemed appropriate, notwithstanding price fluctuations that would cause the target to fall outside of the 15% return.

SELL – A stock that is expected at initiation to produce a negative return of 15% or greater over the 12 months following the initial recommendation. The SELL rating may be maintained following initiation as long as it is deemed appropriate, notwithstanding price fluctuations that would cause the target to fall outside of the 15% return.

NEUTRAL – A stock that is not expected to appreciate or depreciate meaningfully over the next 12 months.

Encysive Pharmaceuticals# Price Chart (Fulcrum Ratings and Price Targets Designated)



Source: FactSet and Fulcrum Global Partners

Note: The percentage of subject companies in each rating category for which FGP has provided investment banking services within the last 12 months is 0%.

All required disclosures, including price charts, designating ratings and price targets on all Fulcrum Global Partners LLC-rated stocks are available upon request by contacting rmenasian@fulcrumgp.com.

VALUATION, PRICE TARGET METHODOLOGY, RISKS TO ACHIEVING PRICE TARGET

Encysive Pharmaceuticals# (ENCY, \$10.01, NASDAQ, BUY)

#Fulcrum Global Partners LLC makes a market in this security.

Valuation: Our \$18 price target is based on 30x our FY'08 EPS estimate of \$0.85 and a 20% discount rate. It equates into a \$1 billion market capitalization, which is on par with existing biotechnology companies with late-stage drugs with a high probability of success. We believe upside exists to the valuation if Thelin demonstrates a statistically significant difference (or trend) to Tracleer in the STRIDE II study.

Risks:

- **Thelin may not demonstrate a benefit to either placebo or Tracleer in STRIDE II.** The study is designed for Thelin to show superiority to placebo, but not Tracleer. Nevertheless, it is likely the company will run a statistical comparison between Thelin and Tracleer. While we expect a numerical difference in the six-minute walk test between the two drug arms, we are cautiously optimistic that the statistical analysis will show a trend toward significance favoring Thelin. Some investors may expect Thelin to demonstrate superiority to Tracleer.
- **The pulmonary arterial hypertension market may become crowded with endothelin antagonists.** Currently, we expect Thelin to compete with two other endothelin receptor antagonists — Tracleer and ambrisentan. However, other companies may develop endothelin receptor antagonists for PAH, thereby limiting the commercial opportunity for Thelin.
- **Viagra may directly compete with, rather than be complementary to, endothelin antagonists.** Based on our discussions with physicians, we expect Viagra to be primarily used in combination with either an endothelin antagonist or prostacyclin analogue. Should Viagra be more directly competitive to endothelin antagonists, our sales assumptions for the class and Thelin could be aggressive.
- **Additional financing is expected.** For 2004, the company expects a net loss of \$54 million to \$57 million, and a year-end cash balance of \$60 million to \$62 million. At the current pace, we expect Encysive will need to raise capital in 2005. We model the company issuing \$100 million in convertible notes during Q2 — an event expected to occur after the Phase III STRIDE II data and possibly the NDA filing in April.

Other Companies Mentioned:

Actelion (ALIOF.PK, \$95.05, Pink Sheets, not rated)

CoTherix# (CTRX, \$8.98, NASDAQ, not rated)

GlaxoSmithKline (GSK, \$45.72, NYSE, not rated)

Myogen# (MYOG, \$7.95, NASDAQ, not rated)

Pfizer (PFE, \$25.05, NYSE, not rated)

United Therapeutics# (UTHR, \$44.57, NASDAQ, not rated)

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ANALYST'S CERTIFICATION

I, Patrick E. Flanigan III, hereby certify that the views expressed in this research report accurately reflect my personal views about the subject company(ies) and its (their) securities. I also certify that I have not been, and will not be, receiving direct or indirect compensation in exchange for expressing the specific recommendation(s) in this report.

Unless otherwise noted, all prices are as of the close, February 9, 2005.

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