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ENCY: Thelin Shows Advantages Relative to Tracleer in STRIDE II

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Encysive Pharmaceuticals# (ENCY, $11.84, NASDAQ, BUY) **February 14, 2005**

#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:

- **Top-line STRIDE II data positive.** This morning, Encysive announced top-line results from the Phase III "STRIDE II" study evaluating Thelin for pulmonary arterial hypertension. Thelin demonstrated a significant improvement in exercise capacity (primary endpoint), WHO functional class, and a trend toward improvement in the rate of clinical worsening, compared to placebo. We expect these data to support an NDA filing in April, with approval to follow within six months.

- **Thelin showed safety, and potentially efficacy, advantages over Tracleer.** We view the relative difference in the incidence of liver function test elevations (3% for Thelin vs. 11% for Tracleer) as rather definitive, and the statistical trend favoring Thelin over Tracleer in the rate of clinical worsening (6.5% for Thelin vs. 16.3% for Tracleer) as intriguing, but not conclusive. Nevertheless, based on conversations with our physician consultants, a greater than 50% reduction in the incidence of liver toxicity is clinically meaningful and will clinically differentiate the two drugs.

- **We model Thelin achieving 6.5% and 28.5% market share in '06 and '08, respectively, accounting for sales of $38M in '06 growing to $238M in '08.** We model Tracleer possessing 93.5% and 57.2% market share in '06, and '08, respectively. Ambrisentan accounts for the remaining market share 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 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.

Rating:	**BUY**	**FY: Dec**	**2003**	**A**	**2004**	**E**	**2005**	**E**	**2006 E**
Price:	**$11.84**	**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):	**$684**	**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**		**NMF**
Risk Level:	**High**	**Revenue (mm)**	**$11.5**		**$11.4**		**$12.4**		**$51.9**

NMF – Not Meaningful.

Important disclosures and analyst's certification in Appendix A.

Top-line STRIDE II Data Positive

This morning, Encysive announced positive Phase III Thelin data in 246 patients with Class II-IV pulmonary arterial hypertension. Patients were randomized to receive 50mg Thelin, 100mg Thelin, placebo, or Tracleer. Only the Thelin and placebo-arms were blinded. The 100mg Thelin-arm demonstrated a significant improvement in exercise capacity (six-minute walk test), the study's primary endpoint, compared to placebo (p=0.03). A significant difference in the percentage of patients improving in WHO functional class (p=0.04) and a trend toward improvement in a decrease in the rate of clinical event worsening (p=0.08) compared to placebo were also observed. The full dataset are expected at the American Thoracic Society meeting (ATS) in May. We expect these data to support an NDA filing in April with approval to follow in six months.

Efficacy & Safety Summary from STRIDE II (% are estimates, assuming equal randomization)

	100mg Thelin	50mg Thelin	Placebo	Tracleer
Improvement in 6MWT (net of placebo)	31.4m	24.2m	--	29.5
p-value	0.03	Not Significant	--	0.05
Improvement in WHO functional class (p-value)	0.04	Not Significant	--	Not Significant
# of events of clinical worsening	5	7	13	15
# of patients with clinical worsening	4 (6.5%)	5 (8.1%)	9 (14.6%)	10 (16.3%)
p-value	0.08	Not Significant	--	Not Significant
# of patients discontinuing the study for efficacy / safety	4 (6.5%)	8 (13.0%)	11 (17.9%)	9 (14.6%)
# of patients discontinuing the study due to adverse events	2 (3.3%)	4 (6.5%)	6 (9.8%)	6 (9.8%)
% of patients with LFT >3x upper limit of normal	3%	5%	6%	11%

Source: Encysive Pharmaceuticals.

Our Analysis of STRIDE II:

- **Overall safety and efficacy:** The results from STRIDE II are consistent with statements expressed by our physician consultants on a conference call we hosted last week – Thelin showed activity similar to Tracleer, but with a lower incidence of liver toxicity. We believe the STRIDE II dataset reaffirms our belief that Thelin is a best-in-class endothelin receptor antagonist, with an improved safety profile, more convenient dosing (once versus twice a day), and the potential for improved efficacy. Hence, we believe the drug is clinically differentiated from Tracleer and therefore possess a relatively competitive profile that could confer significant market share once approved. We model Thelin achieving 6.5% and 28.5% market share in '06 and '08, respectively, accounting for sales of $38M in '06 growing to $238M in '08. (We model Tracleer possessing 93.5% and 57.2% market share in '06, and '08, respectively, with ambrisentan assuming the remaining market share in'08).

- **Comparison to Tracleer:** We caution from over analyzing any difference between Tracleer and Thelin due to: 1) the Tracleer-arm was unblinded, which could have biased the data; 2) it is unclear if there were any imbalances in baseline characteristics between the treatment groups that could have led to differing outcomes; and, 3) the study was not powered to detect differences between the treatment-arms. The most conservative conclusion from STRIDE II is that expressed by our physician consultants – Thelin has similar activity, but an improved safety profile, relative to Tracleer. Nevertheless, we believe there are intriguing differences in safety and efficacy that are worth mentioning, as they may sway physicians to use one drug over the other.

- **Efficacy:** While there was no clinically meaningful difference in exercise capacity observed in this study between both drugs, we believe the difference in the rate of clinical worsening events is intriguing. Indeed, 6.5% of Thelin patients (100mg) experienced one or more clinical worsening events compared to 16.3% of Tracleer patients. Clinical worsening is typically defined as death, lung transplantation, hospitalization or discontinuation of the study treatment due to worsening pulmonary hypertension, a need for prostanoid treatment, or atrial septostomy. The exact definition used in STRIDE II is unknown. Considering the 100mg Thelin dose showed a statistical trend (p=0.08) on this endpoint compared to placebo, and Tracleer did worse than placebo, then we would expect Thelin to show a trend toward a better outcome versus Tracleer with a p-value less than 0.08. Encysive indicated on its conference call that this is the third large study (STRIDE I, II, and IV) in which the p-value for this particular endpoint was 0.08, suggesting a consistency in the data and the potential that the p-value achieves statistical significance ($p<0.05$) when the dataset are pooled together for the integrated summary of efficacy section that is submitted as part of the NDA filing. What is not known is the overall clinical worsening event rate across the three studies and whether there is consistency with this data point – which we believe is a more relevant metric.

  It is unclear how much emphasis to place behind the clinical worsening event rate endpoint. Whereas Thelin demonstrated, as expected, the percentage of patients with clinical worsening with Tracleer is higher than the placebo group (14.6%) and twice the rate observed in the Tracleer Phase III BREATHE-1 study (7%), albeit in a slightly different patient population. We believe the lack of correlation between exercise capacity clinical worsening observed with the Tracleer-group is bothersome, as the six-minute walk test is a validated surrogate endpoint with a correlation with survival. Perhaps the analysis is confounded by the relatively high dropout rate observed with the Tracleer-arm compared to Thelin (14.6% vs. 6.5%). Absent the full data presentation, we view the exploratory analysis on clinical worsening is no more than suggestive of Thelin's activity profile relative to Tracleer.

- **Safety:** Overall, Thelin appears to have better tolerated than Tracleer, as only 3.3% of Thelin patients compared to 9.8% of Tracleer patients discontinued treatment due to adverse events. In BREATE-1, 6.0% of Tracleer patients discontinued due to adverse events. Based on the consistency of liver function test (LFT) elevations with the drugs in numerous studies (Thelin: 3-5%; Tracleer: 11%), we view the STRIDE II data as definitive that Thelin is associated with less than half the incidence in LFT elevation. Based on conversations with our physician consultants, this level of reduction in LFT's is clinically meaningful and enough to drive their treatment decision. Oddly, the 100mg Thelin dose had a lower incidence in LFT elevation than placebo and the 50mg dose. We expect Thelin to receive a similar black box warning as Tracleer in the product label for LFT elevation.

- **Drug interaction with warfarin:** Prior to the release of STRIDE II, one of our physician consultants expressed a concern regarding a couple cases of hospitalizations related elevated INR (a standard measurement for coagulation). Encysive provided clarity on this issue. In over 750 patients involved in the clinical trials, there were two documented cases of patients being hospitalized due to elevated INR: a placebo-treated patient in STRIDE II and a patient in STRIDE I who received a 300mg dose of Thelin. Furthermore, in STRIDE II, while there was a higher incidence of patients, receiving 100mg Thelin, reporting elevated INR levels than placebo, there were no cases of significant bleeding events in the study and only three cases of bleeding episodes in the presence of elevated INR (50mg, 100mg, placebo: 1 each). While the warfarin-Thelin interaction exists, most of our physician consultants who are cardiologists or pulmonologists do not believe it is a material setback for Thelin. It may be a more significant issue with general care physicians or subspecialties (e.g. rheumatologist) that have little experience prescribing warfarin and therefore may choose Tracleer or ambrisentan due to a convenience factor.

Anticipated Milestones

Timing	Event
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										
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)	$0.2
Margin Analysis (w/o 1x Items)										
Product Gross Margin	nmf	nmf	nmf	nmf	nmf	nmf	nmf	nmf	nmf	nmf
Operating Margin	nmf	nmf	nmf	nmf	nmf	nmf	nmf	nmf	nmf	nmf
R&D Expense as a % of Revenue	nmf	nmf	nmf	nmf	nmf	nmf	nmf	nmf	nmf	nmf
SG&A Expense as a % of Revenue	88.8%	80.6%	nmf	nmf	99.4%	nmf	nmf	nmf	nmf	nmf
Thelin Sales ($M)										
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)	$0.4
Margin Analysis (w/o 1x Items)							
Product Gross Margin	nmf	nmf	nmf	nmf	80.0%	85.0%	90.0%
Operating Margin	nmf	nmf	nmf	nmf	nmf	3.7%	33.8%
R&D Expense as a % of Revenue	nmf	nmf	nmf	nmf	nmf	49.0%	33.8%
SG&A Expense as a % of Revenue	86.0%	79.1%	99.4%	nmf	75.3%	34.5%	23.8%
Thelin Sales ($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

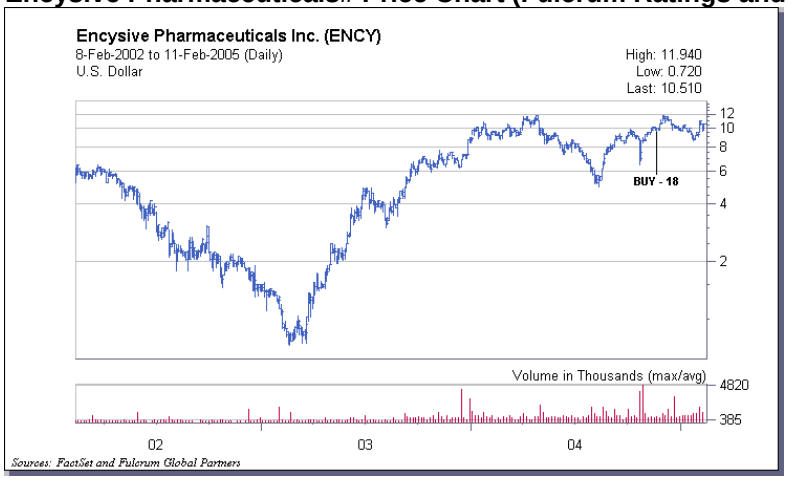
Fulcrum Global Partners LLC ratings are defined as follows:

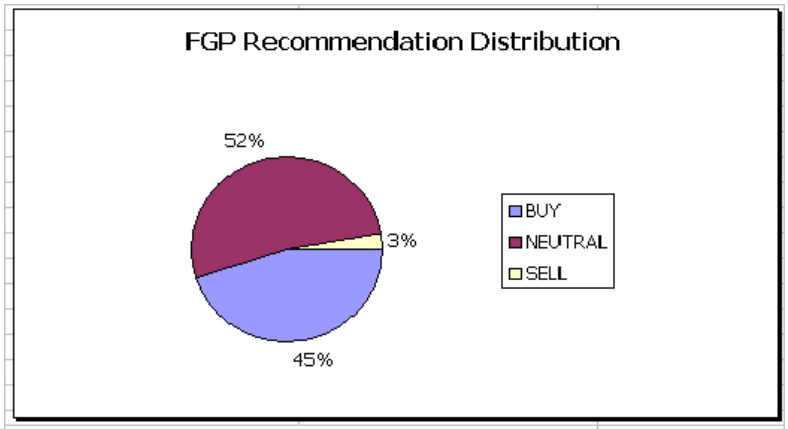
BUY – A stock that is expected at initiation to produce a positive return of 15% or greater over the 12 months following the initial recommendation. The BUY rating may be maintained following initiation as long as it is deemed appropriate, notwithstanding price fluctuations that would cause the target 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, $11.84, 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.

Risks:

- **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.

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

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 intraday, February 14, 2005.

For additional information, please contact your Fulcrum sales representative at (212) 803-9000.