



RATINGS REVISION | COMMENT

JUNE 13, 2011

United Therapeutics Corp. (NASDAQ: UTHR)

Downgrading to SP: It's Not Adding Up; Clinical + Regulatory + Commercial = Risk?

Sector Perform (prev: Outperform)

Above Average Risk

Price:	57.96	Price Target:	60.00 ↓ 75.00
Shares O/S (MM):	62.6	Implied All-In Return:	4%
Dividend:	0.00	Market Cap (MM):	3,628
		Yield:	0.0%

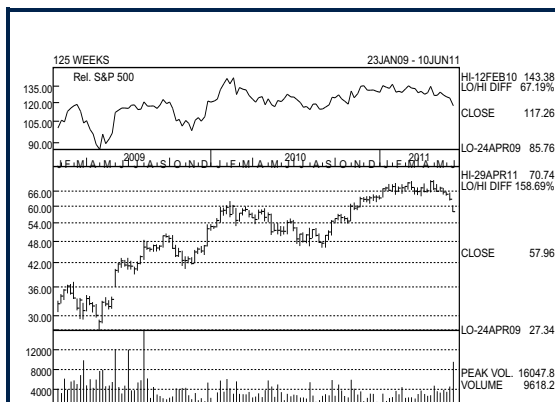
Event

We see unfavorable risk/reward over long term, leading to downgrade.
Conference call at 11 a.m. ET today: 800-602-4090.

Investment Opinion

We see clinical, regulatory, and – most of all – commercial/reimbursement risk. We believe Street is assuming too much optimism for C-2 to be positive, FDA approval will be fine (stock down only 5-6% since release of data), and a big \$1B blockbuster drug. We lower our price target to \$60 from \$75. We can't recommend owning for the regulatory or, longer-term commercial risks and believe risk/reward is not favorable. We don't think UTHR is likely to be acquired anytime soon until there is better visibility on FDA approval and commercial concerns can be resolved.

- **We think C-2 has reasonable clinical risk to not be statistically significant, and in our view, importantly it needs to be clinically meaningful** of at least 15-20m or more (not a low hurdle and Street assumes should be achievable already). If C-2 is negative, there is meaningful regulatory risk for approval on just Freedom-M as one study alone (new NDA with one study and p-value not below $p < 0.01$). Importantly, even if C-2 is positive with a strong result, there is still commercial risk – it is unclear how much use a drug with low-end efficacy (see exhibits on pp. 3-4), titration/tolerability issues (can stay on but still GI tolerability) vs. other orals, and an expected high price can achieve against the headwinds of standard of care going generic in a few years and increasing payor pressures.
- **Issues to consider that don't add up:** 1) Freedom-M average dose of 3.3mg was just not as high as expected (slower than expected titration) and drop-out of 12% (17% including deaths) was higher than expected, in our view (prior suggestions to Street was single digit). Taken together, this means patients just can't dose high enough or fast enough. We also think a 15-20m 6MWD isn't very compelling when compared to ETRAs and PDE5s (23-49m benefits), and if used will be later on top of ETRAs and PDE5s; so, duration on oral won't be that long or it could cannibalize into Tyvaso.
- Our new price target of \$60 is based on \$45 for the base business on a DCF and \$15 for oral remodulin.



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FY Dec	2010A	2011E	2012E	2013E
Revenue (MM)	603.8	722.5	830.4	958.8
EPS (Op) - FD	1.78	1.69	3.21	4.21
P/E	32.6x	34.3x	18.1x	13.8x
Revenue (MM)	Q1	Q2	Q3	Q4
2010	128.9A	137.5A	171.0A	166.5A
2011	165.6A	181.3E	185.3E	190.3E
EPS (Op) - FD				
2010	0.32A	0.62A	0.66A	0.15A
2011	0.26A	0.47E	0.46E	0.46E

All values in USD unless otherwise noted.

Priced as of prior trading day's market close, EST (unless otherwise noted).

For Required Conflicts Disclosures, see Page 10.

Comparative Profiles of Approved and Investigational PAH Therapies

Compound	Indicated	6MWD (median pbo adjusted *)	Market Share	Annual Cost (\$)
Prostacyclins				
Tyvaso	Class III	20m (p =0.0004), w/ Tracleer or Revatio	7%	\$160,000
IV/SubQ Remodulin	Class II/III/IV	16m (p = 0.00064), monotherapy	13%	\$100,000
Oral Remodulin	Class II/III			
PDE5				
Letairis	Class II/III	27 - 39m (p = 0.008), monotherapy	12%	\$65,160
Tracleer	Class II/III/IV	35m mean (p=0.01), monotherapy, stat sig time to clinical worsening	50%	\$53,000
ERAs				
Adcirca	Class II/III	44m mean, monotherapy, 23m mean w/ Tracleer	2%	\$12,000
Revatio	Class II/III	26m mean. w/ IV epoprostenol	16%	\$20,000

Source: Company Reports, Bloomberg and RBC Capital Markets estimates

* Outcomes are placebo adjusted median differences unless otherwise stated

Common Adverse Events of Approved and Investigational PAH Therapies

Drug	Headache	Flushing	Nausea	Vomiting	Pain*
Oral Remodulin	86% vs 38%	49% vs 15%	63% vs 35%	43% vs 9%	42% vs 13%
Letairis	15% vs 14%	4% vs 1%	N/A	N/A	3% vs 1%
Tracleer	15% vs 14%	4% vs 3%	N/A	N/A	5% vs 5%
Revatio	46% vs 39%	10% vs 4%	N/A	N/A	N/A
Adcirca	42% vs 15%	13% vs 2%	10 vs 6%	N/A	12% vs 6%
Ventavis	30% vs 20%	27% vs 9%	13% vs 8%	7% vs 2%	11% vs 3%
Tyvaso	41% vs 23%	15% vs 1%	19% vs 11%	N/A	N/A

Source: Company reports. Adverse events for oral Remodulin are those reported in the FREEDOM C-1 trial, and as described in prescribing information for all other therapies. *Pain is cumulative across jaw, tongue, back, chest and other categories.

- **Reimbursement concerns in face of pending generics and a higher priority for generics are likely.** Because of multiple generics likely in 2015-2016+ (and oral Remodulin's approval likely only in 2013), the low-cost drugs may get pushed ahead of oral Remodulin on the formulary. This may put much more pressure on doctors and providers to use generics before branded prostacyclin, pushing oral Remodulin farther down the treatment sequence before patients start to get the drug (i.e., later in Class III). In fact, we note that BCBS of North Carolina is already trying to block combo use without data, which suggests that it is at least aware of the high price and lack of data, and a new expensive oral without strong clinical benefit is unlikely to better or reverse this trend.
- **Europe is a whole separate risky story.** UTHR has had less success in EU to date even with good regulatory packages in the past, and the potential oral remodulin package may cause issues for EMA approval. Europe may find the efficacy on the lower end of expectations particularly against other therapies, which may lead to lower pricing than expected. Also, based on color from Actelion, EMA may ask for survival endpoints and not view 6MWD alone as a sufficiently compelling endpoint, which may make the oral Remodulin package risky in Europe.