Cara Therapeutics Inc. (CARA) — Overweight

Pipeline in a Product Could Become More Visible Soon

CONCLUSION

Cara announced this AM that it has initiated the human abuse liability (HAL) study for its kappa-opioid agonist I.V. CR845 and guided to data in 4Q. While the initiation of the study itself is not a major event, we now have refined timelines for data for this important study. Also of importance is the comparator for the study: Schedule IV drug pentazocine. We think the choice of a Schedule IV drug favorably indicates the FDA expectations regarding '845's abuse risk (i.e., it's low, despite previous concerns regarding the target). As a result of this incremental positive and growing visibility that we anticipate for '845's potential to become a pipeline-in-a-product over the next ~12 months, we reiterate our Overweight rating and $23 price target on Cara.

- **"Active comparator" sets bar low for positive HAL results.** Pentazocine makes sense to us as it is a mixed mu-opioid/kappa-opioid agonist. Recall that CR845 is a pure kappa agonist. Since the majority of euphoria and likeability comes from mu-opioid activation, we expect CR845 to perform well vs. pentazocine. Part of the definition of DEA Schedule IV drugs is: "defined as drugs with a low potential for abuse and low risk of dependence." We expect that CR845 will be, at worst, Schedule IV, putting it in the class with Talwin (pentazocine combined with naloxone), Xanax, and Valium. At best CR845 is unscheduled, and we'd estimate there's a 50% probability of this scenario.

- **Study timelines bode well for an active YE14.** The HAL results should arrive about the same time as the single-ascending-dose and multiple-ascending-dose data for oral CR845, leading to a catalyst rich 4Q14 for Cara. We could also see data in uremic pruritus by year end, but more likely 1H15. This is a 2 part study in patients with kidney disease. Part 1 will look at PK and peak dosing, part 2 is a 2-week treatment phase in about 60 patients. We don't currently model pruritus projections, however note its incidence in hemodialysis patients is estimated at ~40% (Nephrol Dial Transplant. 2006;21(12):3495) and there are over 350k hemodialysis patients in the U.S. (NIDDK Kidney Disease Statistics, 2009 data), so success in this indication could represent meaningful upside to our valuation.

COMPANY DESCRIPTION

Cara develops novel peripherally-resctricted candidates for pain indications.

PRICE: US$12.57
TARGET: US$23.00
DCF of I.V. CR845 revenues for post-op pain in the U.S.

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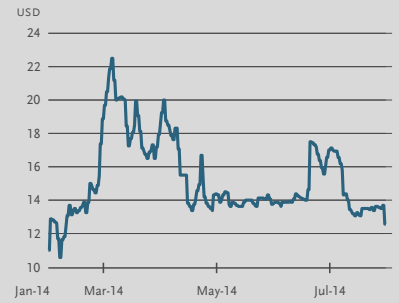
RISKS TO ACHIEVEMENT OF PRICE TARGET

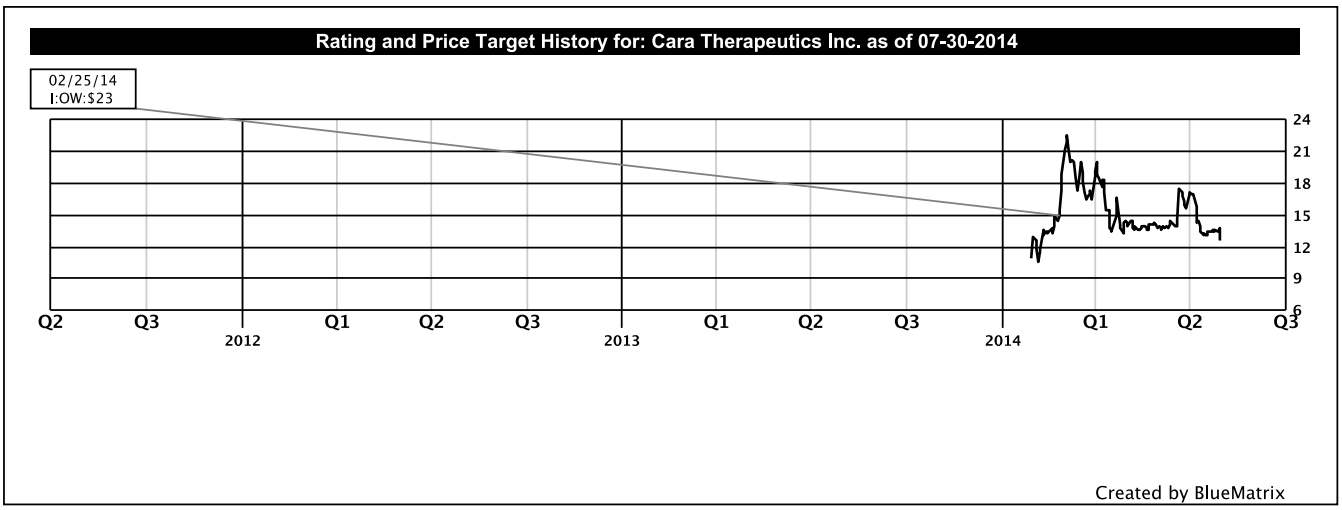
Failure of lead candidate I.V. '845 in pivotal studies, DEA scheduling, or safety signals.

Price Performance - 1 Year



Source: Bloomberg

IMPORTANT RESEARCH DISCLOSURES



Notes: The boxes on the Rating and Price Target History chart above indicate the date of the Research Note, the rating, and the price target. Each box represents a date on which an analyst made a change to a rating or price target, except for the first box, which may only represent the first Note written during the past three years.

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I: Initiating Coverage
R: Resuming Coverage
T: Transferring Coverage
D: Discontinuing Coverage
S: Suspending Coverage
OW: Overweight
N: Neutral
UW: Underweight
NA: Not Available
UR: Under Review

Distribution of Ratings/IB Services
Piper Jaffray

			IB Serv./Past 12 Mos.	
Rating	Count	Percent	Count	Percent
BUY [OW]	361	62.35	94	26.04
HOLD [N]	206	35.58	21	10.19
SELL [UW]	12	2.07	0	0.00

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