Cara Therapeutics Inc. (CARA) — Overweight

Possible New Paradigm in Post-Op & Chronic Pain; Initiating w/ OW

CONCLUSION

We are initiating coverage on Cara with an Overweight rating and $23 price target. We believe Cara's lead candidate CR845 ('845) will prove to be an effective solution to targeting kappa opioid receptors for treating pain, by restriction of its activity to the peripheral nervous system. With positive Phase II data in the post-op setting, both for efficacy vs. placebo and in reduction of mu-opiate consumption and side effects, we believe this early data has higher than usual predictive value for success in remaining clinical development work. Soon to begin pivotal trials and other near-term clinical catalysts should keep investors engaged in 2014 and beyond, and an approval in 2016 could usher-in a new paradigm for the treatment of post-operative pain, and perhaps beyond. Upside scenarios to our current valuation include oral formulations of '845, currently in Phase I, and/or use in pre-surgical settings or other indications and non-U.S. markets.

- **I.V. '845 expectations.** We model peak sales of ~$1.6bn for both in-patient and out-patient post-surgical use of '845. Major competitors currently include Exparel and Ofirmev, both of which we have used to project our market expectations for '845. The multi-modal pain space continues to evolve, driven by prospective new entrants and the interest in patients, physicians, and regulators to reduce overall opioid exposure.

- **Abuse liability study important near-term catalyst.** Cara is conducting an abuse-liability study for I.V. '845 with data expected in 2Q (Exhibit 1). The study is required by the FDA but should also support marketing as a less addiction-prone opioid alternative and presumably a lack of DEA scheduling, which should give it a market advantage over standard opioids, in our view. We see it also as a test of the selectivity of peripheral kappa activation.

- **Pipeline-derived upside.** An oral '845 would be an important addition to the pain management armamentarium in our view. Cara needs to show activity in the Phase II proof-of-concept study that we anticipate will start in 2H14. We maintain oral '845 in the "show me" category pending the single- and multiple-ascending dose studies which should readout in 2H14. Cara also has a cannabinoid receptor agonist for neuropathic and inflammatory pain, CR701, in preclinical studies on which we await greater visibility on (Exhibit 2).

RISKS TO ACHIEVEMENT OF PRICE TARGET

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

COMPANY DESCRIPTION

Cara develops novel peripherially-resctricted candidates for pain indications.

PRICE: US$14.48
TARGET: US$23.00
DCF of I.V. CR845 revenues for post-op pain in the U.S.

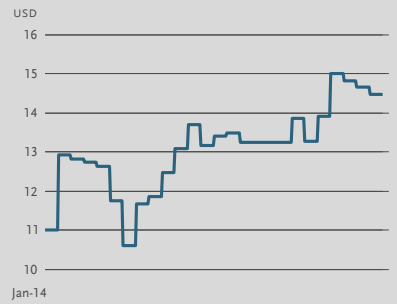
Charles C. Duncan, PhD
Sr. Research Analyst, Piper Jaffray & Co.
212 284-5025, charles.c.duncan@pjc.com

Roy Buchanan, Ph.D.
Research Analyst, Piper Jaffray & Co.
212 284-9458, roy.d.buchanan@pjc.com

Changes	Previous	Current
Rating		Overweight
Price Tgt		US$23.00
FY14E Rev (mil)	—	0.0
FY15E Rev (mil)	—	0.0
FY14E EPS	—	(0.56)
FY15E EPS	—	(1.00)

52-Week High / Low	US$15.69 / US$10.40
Shares Out (mil)	21.8
Market Cap. (mil)	US$315.7
Book Value/Share	US$3.00
Net Cash Per Share	US$3.20
Debt to Total Capital	0%
Div (ann)	NA
Fiscal Year End	Dec

Price Performance - 1 Year



Source: Bloomberg

YEAR	REVENUE (m)						EARNINGS PER SHARE ( )					
	Mar	Jun	Sep	Dec	FY	FY RM	Mar	Jun	Sep	Dec	FY	FY P/E
2013E	—	—	—	0.0	11.0	28.7x	—	—	—	(0.11)	(0.21)	NM
2014E	0.0	0.0	0.0	0.0	0.0	NA	(0.10)	(0.13)	(0.16)	(0.20)	(0.56)	NM
2015E	—	—	—	—	0.0	NA	—	—	—	—	(1.00)	NM

Exhibit 1

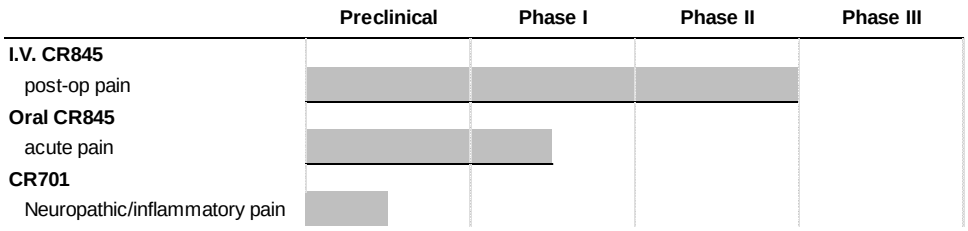
CARA EXPECTED CATALYSTS

Expected date	Event
I.V. CR845	
2Q14	End-of-Phase II meeting with FDA
2Q14	* Data from human abuse liability study
4Q14	Start 3 Phase IIIs for post-surgical pain
2Q15	* Data from Phase IIIs
1Q16	File NDA
2017	U.S. launch
oral CR845	
early 2014	* Start Phase I SAD/MAD studies with tablet formulation (data YE14)
4Q14	Phase IIa POC study start

Source: Company reports, Piper Jaffray. * indicates high likelihood for share price impact

Exhibit 2

CARA PIPELINE



Source: Company reports, Piper Jaffray

VALUATION AND MARKETS

Our valuation of Cara considers only potential sales of CR845 ('845) for post operative pain (for both in- and out-patient procedures) in the U.S. We assume that Cara completes Phase III testing of '845 in 2015 (management has guided to data in 2Q15), and we conservatively project a launch in the U.S. in 2Q17 following NDA submission in 2H15 and a 2H16 approval.

Company valuation

We value Cara using an NPV methodology applied to projected revenues from I.V. '845 (Exhibit 3) derived from our post-op pain market model (Exhibit 4). Our costs assume eventual 75% gross margins, reductions in R&D spending growth following the conclusion of the I.V. '845 Phase III studies, and that Cara builds a specialty sales force for I.V. '845 in the U.S. of approximately 80 hospital-focused representatives.

Exhibit 3

CARA NPV AND VALUATION

Cara sum of the parts (000s $)	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
U.S. I.V. CR845 net sales	0	0	0	13,324	102,320	242,815	384,811	555,373	813,499	1,088,198	1,334,243	1,470,094	1,559,034	1,621,863
Operating Costs	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
COGS	0	0	0	4,250	26,311	60,704	96,203	138,843	203,375	272,049	333,561	367,523	389,759	405,466
R&D	16,500	36,373	40,059	30,939	30,103	30,103	30,103	30,103	30,103	30,103	30,103	30,103	30,103	30,103
SG&A	4,700	7,658	11,504	20,650	24,162	25,143	26,164	27,226	28,332	29,482	30,679	31,925	33,221	34,570
Fixed Operating Costs	21,200	44,030	51,563	55,839	80,576	115,950	152,470	196,173	261,810	331,635	394,343	429,552	453,083	470,139

	NPV (MM$)		NPV Per Share ($)
I.V. CR845 (U.S. only)	1,094,024	$	45.67
Oral CR845 (U.S. only)	0	$	-
Operating costs	(614,758)	$	(25.67)
Terminal value	0	$	-
Pipeline value	0	$	-
Cash (YE14 est)	68,850	$	2.87
Long-term debt (YE14 est)	0	$	-
Total NPV	**548,116**	**$**	**22.88**

Source: Piper Jaffray

We discount estimated I.V. '845 revenues by 25% annually (a typical discount rate for specialty-pharma type candidates we view as partially validated in terms of clinical data and market potential) to YE14 and apply no terminal value beyond the expiry of the first to expire '845 patent (expires November 2027). We apply a 20% discount rate to projected expenses as we view these as being more likely to be realized, even in the event I.V. '845 doesn't make it to market. This results in a NPV for Cara of $1.1bn. We divide this by approximately 24mn estimated post-IPO fully diluted shares (21.8mn common shares plus 2.1mn options and 0.02mn warrants) to derive our $23 price target for Cara.

Exhibit 4

I.V. '845 MARKET MODEL

	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
I.V. CR845															
U.S. in- & out-patient surgeries (000s)	**86,100**	**86,961**	**87,831**	**88,709**	**89,596**	**90,492**	**91,397**	**92,311**	**93,234**	**94,166**	**95,108**	**96,059**	**97,020**	**97,990**	**98,970**
% growth (year-over-year)	*1.0%*	*1.0%*	*1.0%*	*1.0%*	*1.0%*	*1.0%*	*1.0%*	*1.0%*	*1.0%*	*1.0%*	*1.0%*	*1.0%*	*1.0%*	*1.0%*	*1.0%*
CR845 penetration rate	*0.0%*	*Phase III*	*Phase III*	*NDA*	*0.1%*	*1.1%*	*2.3%*	*3.5%*	*4.8%*	*6.6%*	*8.3%*	*9.6%*	*10.0%*	*10.0%*	*10.0%*
U.S. CR845 units (000s)	-	-	-	-	*130*	*950*	*2,147*	*3,241*	*4,455*	*6,215*	*7,918*	*9,246*	*9,702*	*9,799*	*9,897*
% growth (year-over-year)	*na*	*na*	*na*	*na*	*na*	*631%*	*126%*	*51%*	*37%*	*40%*	*27%*	*17%*	*5%*	*1%*	*1%*
CR845 price per procedure	*$ 112.5*	*$ 118.1*	*$ 124.0*	*$ 130.2*	*$ 136.7*	*$ 143.6*	*$ 150.8*	*$ 158.3*	*$ 166.2*	*$ 174.5*	*$ 183.3*	*$ 192.4*	*$ 202.0*	*$ 212.1*	*$ 218.5*
% growth (year-over-year)		*5.0%*	*5.0%*	*5.0%*	*5.0%*	*5.0%*	*5.0%*	*5.0%*	*5.0%*	*5.0%*	*5.0%*	*5.0%*	*5.0%*	*5.0%*	*3.0%*
U.S. CR845 wholesale sales (000s $)		-	-	-	17,765	136,426	323,753	513,081	740,497	1,084,665	1,450,931	1,778,991	1,960,125	2,078,712	2,162,485
% growth (year-over-year)		*na*	*na*	*na*	*na*	*na*	*na*	*na*	*na*	*na*	*na*	*na*	*na*	*na*	*na*
gross-to-net, other adjustments	*0.75*	*0.75*	*0.75*	*0.75*	*0.75*	*0.75*	*0.75*	*0.75*	*0.75*	*0.75*	*0.75*	*0.75*	*0.75*	*0.75*	*0.75*
Net I.V. CR845 sales (000s $)	**0**	**0**	**0**	**0**	**13,324**	**102,320**	**242,815**	**384,811**	**555,373**	**813,499**	**1,088,198**	**1,334,243**	**1,470,094**	**1,559,034**	**1,621,863**

Source: Piper Jaffray

Relative valuation

A comparison of enterprise values of companies we feel are similar in many ways to Cara is shown in Exhibit 5. These include a list of development or early commercial stage companies, as well as established companies, whose pipeline is focused on pain and particularly post-op multi-modal offerings (Pacira, Cadence). This valuation suggests that Cara may be trading at a discount relative to a basket of its peers, though we note the inclusion of a number of high-value commercial stage companies.

Exhibit 5

RELATIVE VALUE COMPARISON

Company Name	Ticker	Price / share	Shares	Market cap	Cash	Debt	EV
Pacira	PCRX	$73.33	33.5	2459	84	0	2376
Cadence	CADX	$13.97	86.1	1203	55	21	1169
Horizon Pharma	HZNP	$12.15	65.9	800	59	30	770
Zogenix	ZGNX	$4.91	138.4	680	17	29	691
Depomed	DPMD	$12.89	57.0	735	81	10	664
AcelRx	ACRX	$11.77	43.0	507	76	2	433
Pozen	POZN	$8.20	30.5	250	90	0	160
Cumberland	CPIX	$4.71	18.1	85	65	5	25
	Median			**707**			**677**
	Mean			**840**			**786**
Cara Therapeutics	CARA	$14.48	21.8	316	24.4	1	293
		Derived price/share					
Cara Therapeutics - at group median	**CARA**	**$31.01**	**21.8**	**677**		**0**	**677**
Cara Therapeutics - at group mean	**CARA**	**$35.99**	**21.8**	**786**		**0**	**786**

Source: Thomson Reuters, Piper Jaffray, 2/24/2014 close pricing

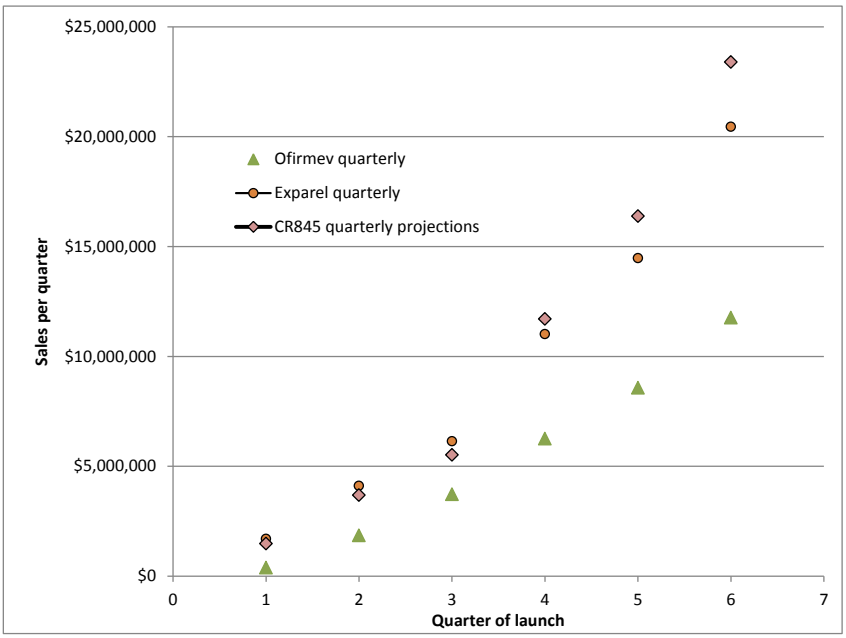
Post-op pain market model

We assume ~86mn eligible surgeries in the U.S. in 2013, ~51mn in-patient (CDC National Hospital Discharge Survey 2010) and ~35mn out-patient (National Health Statistics Reports 2006), and we increase that number by 1% annually. These estimates may be conservative given the slightly dated nature of the cited references. Into these patient populations we project I.V. '845 achieves penetration of 0.1% in its launch year, 2017, and peak penetration of 10% in 2025 and subsequent years (compare to Exparel and Ofirmev launch sales in Exhibit 6). The post-op pain space is relatively fragmented, beyond the level we include in our model. For example, Exparel on launch was targeted primarily at

colorectal surgery and cosmetic surgery based on the existing data. We do not have sufficient visibility on market granularity at this point to include it in our model. Conservatively, we project no sales beyond 2027 in the U.S. based on the first to expire composition patent for '845 which expires in November 2027 (U.S. Patent No. 7,402,564). Our pricing estimate for I.V. '845 is derived from our estimate of the per-surgical-procedure cost for Exparel of $90 in 2013, in turn derived from assumed use of Exparel according to its label. We assume I.V. '845 is priced at $113/procedure (25% higher than Exparel) in 2013 and increase that cost by 5% annually through the end of our model. We arrive at a higher per-procedure cost for '845 due to its novel mechanism, differentiated safety profile, and its demonstrated ability to significantly reduce opioid-derived side effects.

Exhibit 6

I.V. '845 PROJECTIONS VS. COMPARABLE-DRUG LAUNCHES



Source: Piper Jaffray, IMS Health

Ex-U.S. markets

Cara retains ownership of CR845 globally except for Korea and Japan, where it has partnered with Maruishi (Japan, in April 2013) and Chong Kun Dang (Korea, April 2012). The partnerships cover both I.V. and oral '845 but are limited to acute pain and uremic pruritus in the case of Maruishi. Upfronts and milestones to date have provided approximately $24mn in capital to Cara. The partnerships may provide tiered royalties from low double digits to low twenties (Maruishi) and high single digits to high teens (Chong Kun Dang) on net sales plus milestones, ~$14.3mn total in development and regulatory milestones. While we believe there is significant market potential for analgesics for surgical use outside the U.S., we lack a view on how '845 might fit in the treatment paradigm, and Cara has not communicated plans to develop '845 beyond the existing partnerships plus plans for a global (ex-U.S., Japan, and Korea) partnership for the oral formulation in acute pain.

Oral '845

Cara has completed an initial Phase I study utilizing a capsule formulation of '845 to examine oral bioavailability, which the company estimated to be ~16%. Cara observed activation of peripheral kappa receptors at doses as low as 0.5mg. The results warrant moving forward with additional clinical testing and the company is doing so with a tablet formulation of the drug that should provide more predictable pharmacokinetics and greater stability. Cara plans to complete Phase I single ascending dose (SAD, CLIN1002-PO, up to ~100 patients) and multiple ascending dose (MAD, CLIN1003-PO, ~45 patients in 3 cohorts) studies in 1H14 followed by a Phase IIa proof of concept study in bunionectomy with a SPID-48 primary endpoint to begin in 2H14 (assuming positive SAD/MAD results).

Cara expects oral '845 to compete in the moderate-to-severe chronic pain and step-down therapy markets. Current offerings include the standard oral mu-opioid agonists, non-steroidal anti-inflammatory drugs (NSAIDs such as oral ibuprofen and Celebrex), and anticonvulsants (Topamax, Lyrica, and Neurontin, among others). '845 would have definite advantages over mu-opioid agents if it ends up without DEA scheduling, in our view, for the same reasons the I.V. agent has potential advantages: less abuse potential and lower rates of mu-typical AEs. As '845 would be highly differentiated in this market, we believe the potential for the drug could be much larger than the surgical market. However, we would like to see additional efficacy and safety data in this setting before including oral '845 in our valuation.

Other multi-modal pain agents

Multi-modal post-surgical pain control typically involves the mainstay opioid medication plus infusion of local anesthetic, or more recently injection of liposomal bupivacaine (Exparel), and possibly oral or I.V. NSAIDs (Ofirmev, Caldolor, Toradol). However, these agents are not without drawbacks, the most severe likely being cardiotoxicity risk for bupivacaine and risk of liver damage for acetaminophen and CV and bleeding risk for other NSAIDs. '845 hopes to provide another effective option for pain management and presents a differentiated profile vs. existing agents (Exhibit 7).

Exhibit 7

TYPICAL POSTSURGICAL ANALGESICS COMPARISON

	CR845	Exparel (bupivicaine)	Ofirmev (acetaminophen)
Use/formulation	I.V.	Local injection	I.V.
Target	Peripheral kappa-opioid receptors	Local anesthetic (Na+ channels)	Unknown
Safety	Urinary frequency/volume	CNS and CV (particularly w/ accidental I.V. delivery)	Liver toxicity
Reduction in opioid adverse events	Decrease in opioid consumption. Reduced nausea/vomiting, pruritis	Reduction in opioid consumption. Effect on AEs unclear	No
Last-12-month sales (mn$)	na	$52	$97
Current year-over-year sales growth	na	~400%	~100%

Source: Piper Jaffray, Company reports

The multi-modal postsurgical pain market is evolving, with continuing pressures to reduce opioid use, and ever-present reimbursement issues from multiple parties. We believe an overlying theme that is likely to persist for the foreseeable future in the U.S. is for reduced opioid consumption as physicians, patients, and other interested parties recognize the burden of mu-opioid caused adverse events. Exparel, for one, has data demonstrating significant reductions in both opioid consumption and the proportion of patients completely avoiding opioid use, in certain settings. Ofirmev also has demonstrated reductions in opioid use, but to our knowledge, no observed improvement in opioid-derived adverse events. Regardless, we expect the use of local anesthetics like Exparel and NSAIDs like Ofirmev to continue to grow as part of the multi-modal approach. Cara management believes that a scenario of an opioid-free post op (mu opioid at least) is feasible through the use of '845 along with other agents.

Other agents on the horizon that may fit into a multi-modal approach include Nektar's NKTR-119 (Naloxegol and opioid co-formulation) and NKTR-192 (an oral, peripherally restricted mu-opioid agonist designed for acute activity), NKTR-192 is in Phase I; or Trevena's TRV130, an I.V.-formulated "biased ligand" for mu-opioid receptors that demonstrated reduced opioid side effects vs. morphine in Phase Ib and will start Phase II in 2Q14.

DEVELOPMENT AND OUTLOOK FOR I.V. '845

Kappa-opioid receptor background

As mentioned above, the adverse events that arise from opioid consumption -- respiratory depression, somnolence, constipation, pruritis, etc., as well as the tendency to cause euphoria and thereby addiction -- are generally due to activation of the mu receptor subtype. For this reason, attempts have been made to develop activators of the kappa opioid receptor subtype to treat pain to avoid those adverse effects. To date, these attempts have failed due to adverse events observed including dysphoria (feelings of unhappiness) and hallucinations, diuresis, and constipation. Additionally, the analgesic efficacy of the kappa agents appeared lower than the mu-receptor agonists. The mixed kappa-agonist/mu-antagonist pentazocine (and its combinations) are approved for treating moderate-to-severe pain as an oral with similar analgesic effect to codeine and is DEA Schedule IV. As with other kappa agonists, pentazocine can cause visual hallucinations, likely limiting its wider use. A kappa-agonist, Remich (nalfurafine), is approved in Japan for the treatment of pruritis (itching). It received a negative CHMP opinion for lack of clinical benefit.

'845 background

'845 is a tetrapeptide made from all "un-natural" D-amino acids that was discovered and patented by Cara. The drug's structure prevents it from entering the brain and it is also secreted by the kidneys intact and not metabolized, therefore is unlikely to create problems with drug-drug interactions. Preclinical studies have both demonstrated the broad spectrum activity of '845 (i.e., multiple pain models, including those of chronic and acute inflammatory and neuropathic pain) and verified the peripheral site of action through examinations of the brains of treated animals.

'845 has been studied in over 300 human subjects across 7 clinical trials. The adverse events/signals that have been seen so far in clinical testing of '845 include most prominently: facial tingling, somnolence/fatigue, dizziness (these three being the most frequent), and hypernatremia (possibly as a result of aquaresis). The hypernatremia was observed in earlier studies and effectively addressed by using water or low-saline solution for the patient's I.V. Cara has not observed the dysphoria or hallucinations that plagued prior kappa opioid agonist development programs. Also importantly, the studies have demonstrated a lack of respiratory depression or clinically meaningful EKG changes. The studies have also shown reductions in common mu-opioid side effects like pruritus, nausea and vomiting for subjects taking '845. The Phase II studies discussed below also proved I.V. '845 to be statistically significantly superior to placebo in the primary efficacy endpoints that are typical of pain studies of this type and will be used in the planned Phase III studies. Cara intends to conduct 3 Phase III studies:

'845 Phase II studies

Cara has successfully completed 3 Phase II studies, 2 in soft tissue surgery (laparascopic hysterectomy) and 1 in a hard tissue model (bunionectomy). The characteristics of the 3 studies are summarized in Exhibit 8. All the studies were placebo-controlled, double-blind, and randomized.

Exhibit 8

'845 PHASE II SUMMARY TABLE

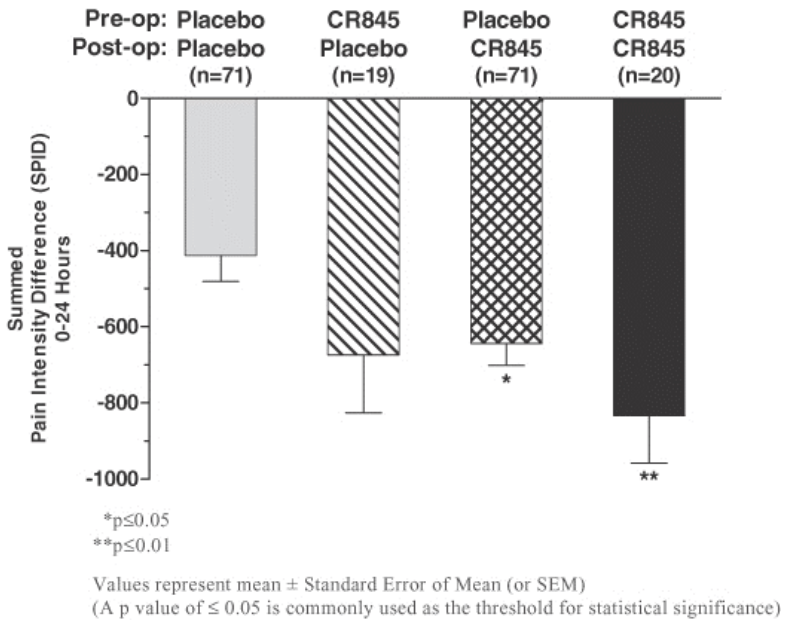
Phase	IIb	II	IIa
ID	CLIN2002	CLIN2003	CLIN2001
Indication	laparoscopic hysterectomy	bunionectomy	laparoscopic hysterectomy
# patients	203	51	114
# sites	22	1	12
Site locations	U.S.	U.S.	U.S.
Sex	F	M/F	F
Age	21-65	18+	21-60
Enrollment criteria		moderate-to-severe pain (≥40 on 100 pt scale)	
Dosing	0.04 mg/kg I.V. '845 pre-op and/or post-op	0.005 mg/kg I.V., + as-needed 30-60 min later, then every 8 hours max through 48-hours	0.008 or 0.024 mg/kg I.V., 24 hrs. post surgery, or 0.024 mg/kg, 3 hrs post surgery
Primary endpoint	Morphine consumption in 1st 24-hours	SPID-24	Patient reported measures of pain
Secondary endpoints	Pain intensity scores, % requiring morphine rescue	Other pain intensity scores, amount rescue opioid	Multiple efficacy and safety
Rescue medication	Morphine	Fentanyl allowed	Morphine

Source: Company reports

The following exhibits illustrate the efficacy results from the Phase II studies. Data images are taken from the IPO prospectus. The main efficacy endpoint likely for approval in the Phase III studies, the summed pain intensity differences (SPID), for the laparoscopic hysterectomy is shown in Exhibit 9. Note that I.V. '845 was statistically significantly superior to placebo for both the pre-surgery-placebo/post-surgery-'845 and pre- and post-'845 patient groups.

Exhibit 9

SPID 0-24: '845 VS. PLACEBO – CLIN2002

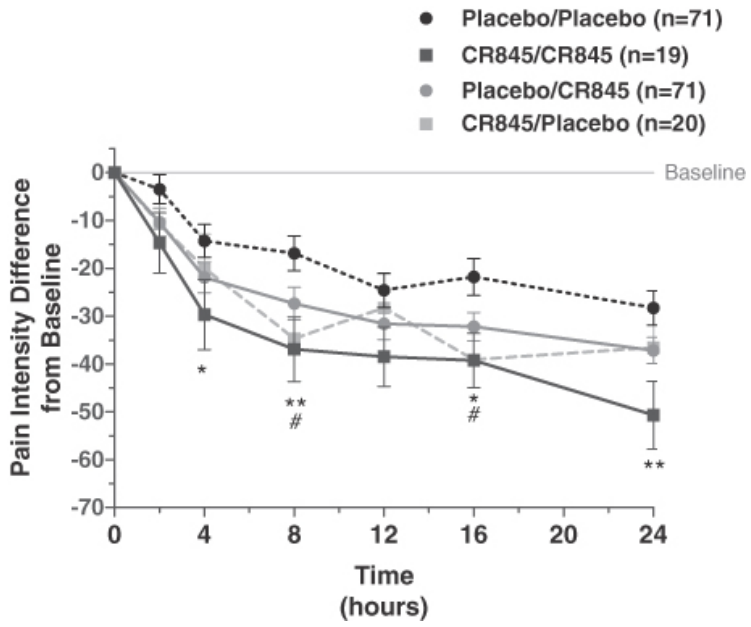


Source: Company reports

In more granularity, the pain intensity differences from baseline at different time points is shown in Exhibit 10. A single asterisk (*) indicates p≤0.05, ** indicates p≤0.01 for the pre-'845/post-'CR845 patients, and # indicates p≤0.05 for both pre-placebo/post-'845 and pre-'845/post-placebo.

Exhibit 10

PID TIMECOURSE – CLIN2002

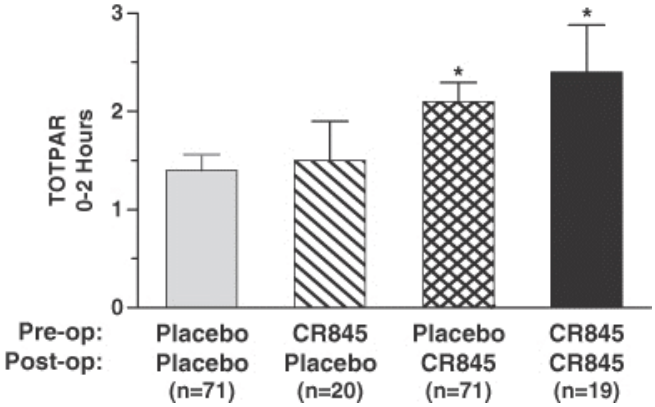


Source: Company reports

An indication of the speed of '845's activity is seen in the total pain relief at 2 hours (Exhibit 11).

Exhibit 11

TOTAL PAIN RELIEF 2 HOURS POST-OP – CLIN2002



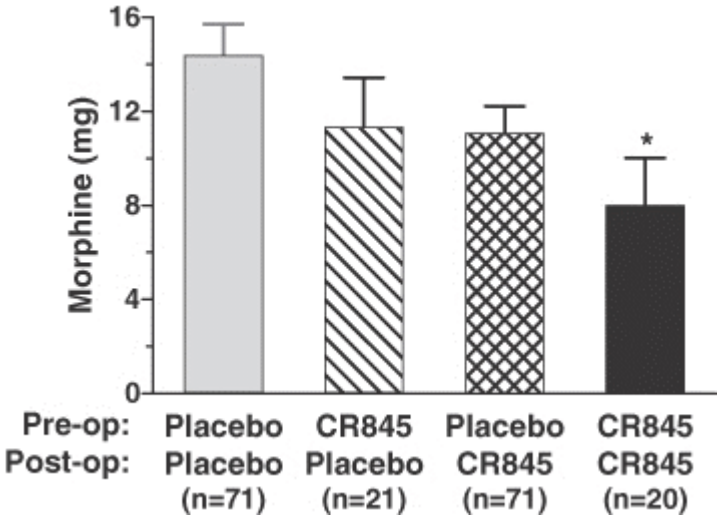
Source: Company reports

Morphine consumption data for 2-24 hours post surgery (i.e.. recovery) (Exhibit 12) are not necessarily important for approval, but likely to be for marketing and clinical acceptance of '845. * indicates $p \leq 0.05$. Concomitantly with the reduction in morphine consumption,

investigators observed a reduction in common opioid side effects -- nausea, vomiting, and pruritus -- for the '845 patients (Exhibit 13). * indicates a p=0.035 and ** p≤0.01.

Exhibit 12

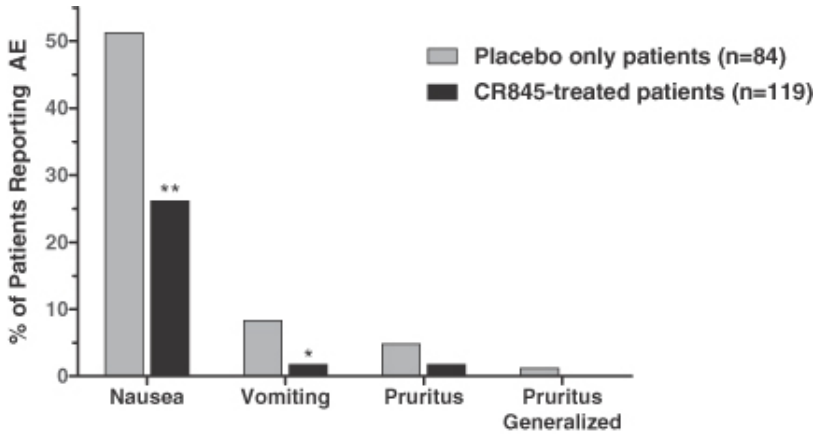
MORPHINE CONSUMPTION 2-24 HOURS – CLIN2002



Source: Company reports

Exhibit 13

TYPICAL OPIOID SIDE EFFECTS – CLIN2002

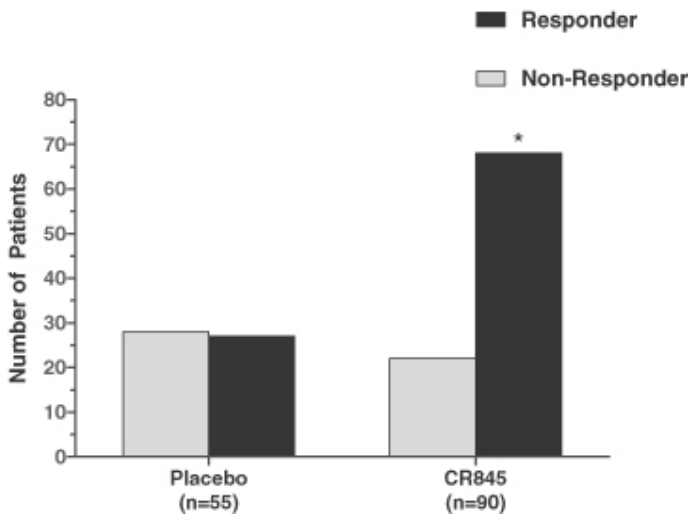


Source: Company reports

Another measure is the proportion of patients considered responders. In this study, a responder was defined as a patient describing their pain treatment as "very good" while non-responders characterized it as "fair" or "poor." The CLIN2002 study produced a highly significant (p=0.001) proportion of responders among the '845 treated patients vs. those that only received placebo (Exhibit 14).

Exhibit 14

RESPONDER ANALYSIS – CLIN2002

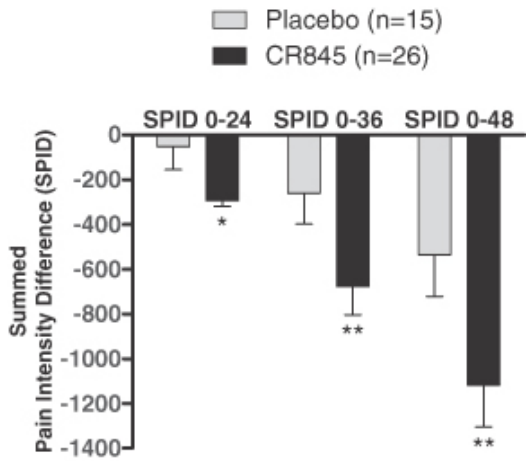


Source: Company reports

CLIN2003 was the Phase II of I.V. '845 for bunionectomies. Cara conducted analyses looking at the population of "completers," those patients that completed the study and the modified intent to treat (mITT) population which included completers and drop-outs. The differences in SPID vs. placebo at various time points was highly significant for the completer population but not for the mITT, though there were evident differences in SPID for the treatment arm (Exhibits 15 and 16, * $p \leq 0.05$, ** $p \leq 0.03$, one-sided ANOVA). Considering the small number of patients vs. what will be included in Phase III, we expect the results to be significant for both patient populations in Phase III. In particular, Cara is using the mITT results to power the Phase III studies.

Exhibit 15

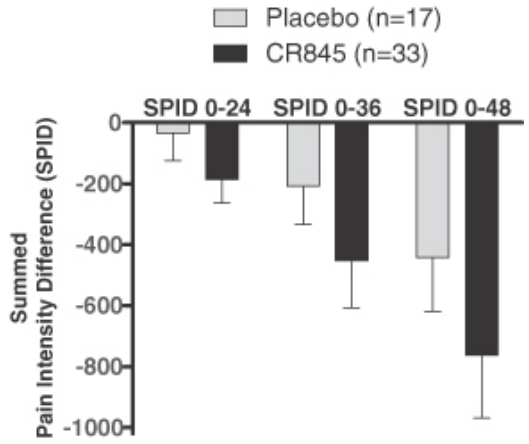
SPID – CLIN2003 COMPLETERS



Source: Company reports

Exhibit 16

SPID – CLIN2003 MODIFIED ITT

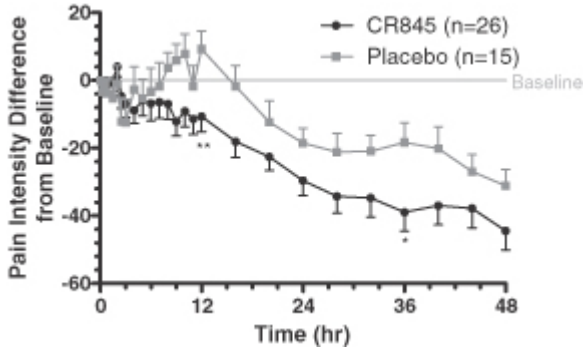


Source: Company reports

Pain intensity time courses for each patient population provide insights into the activity of '845 at up to 48 hours (Exhibits 17 and 18, * $p \leq 0.05$, ** $p \leq 0.01$).

Exhibit 17

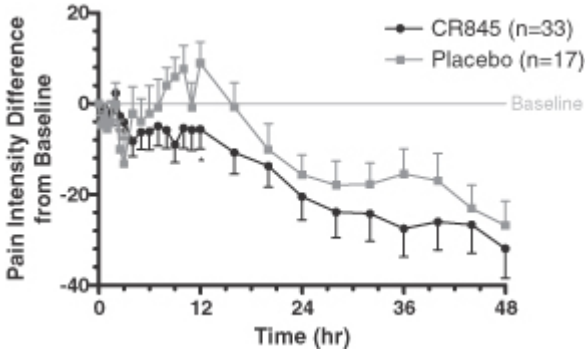
PID TIMECOURSE – CLIN2003 COMPLETERS



Source: Company reports

Exhibit 18

PID TIMECOURSE – CLIN2003 MODIFIED INTENT TO TREAT

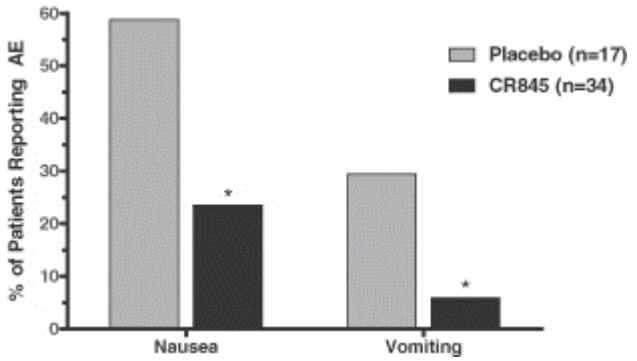


Source: Company reports

Unlike the case in CLIN2002, there was not an observed reduction in rescue opioid use, though there was a reduction in observed nausea and vomiting (Exhibit 19).

Exhibit 19

OPIOID ADVERSE EVENTS – CLIN2003 MODIFIED INTENT TO TREAT



Source: Company reports

Cara believes that the lack of observed reduction in mu-opioid use may have been due to the use of fentanyl, a particularly powerful opioid, or the severe pain of the hard-tissue surgery. In the Phase III studies, the company will limit the rescue medication to morphine.

Interestingly, the reduction in nausea and vomiting may be due to the action of kappa agonism on a set of neurons in the chemoreceptor trigger zone and thus representative of an effect of '845 over the simple reduction in the use of standard mu-opioids. This effect has been previously noted with kappa-opioid agonists (Chavkin C, *Neuropsychopharmacology* (2011) 36, 369–370).

The 3rd Phase II, CLIN2001, also in laparascopic hysterectomy, provided the interesting observation that, likely due to lack of severe pain in this setting, 30% of patients do not require narcotic medications for 24-hours following the surgery. This prevented an observation of efficacy in the two 24-hours-post-surgery dose arms. The third cohort looked at 0.04 mg/kg dosed at 3-hours post-surgery and demonstrated both a meaningful reduction in morphine consumption as well as significant ($p \leq 0.05$) reductions in pain intensity vs. placebo.

Phase III plans

Cara intends to conduct 2 Phase III studies, one in soft tissue surgery (CLIN3001) and one in hard tissue (CLIN3002), based on feedback from the FDA. These studies will use either the SPID vs. placebo at 24 hours (SPID-24) or at 48 hours (SPID-48). The soft tissue study is expected to be a laparoscopic hysterectomy study in ~600 women and the hard tissue a bunionectomy study also in ~600 patients. Cara also plans to run a 3rd "optional" study (CLIN3003) of ~450 patients undergoing laparoscopic hysterectomy or bunionectomy that will compare pre- and post-surgical use of I.V. '845, and we believe might support a broad label for '845 on approval. All the studies will look at total pain scores at 24 and 48 hours as well as measure reductions in nausea and vomiting.

Abuse liability study

Prior to starting the Phase III studies, but important for indicating DEA scheduling of '845, Cara is completing a human abuse liability study. The study looks at the "likability" of the drug. Cara expects '845 to not require DEA scheduling due to the lack of CNS access.

CR701

Similarly to the rationale with '845, Cara has targeted peripheral cannabinoid receptors to avoid unwanted CNS effects. The lead compound in this program is CR701 ('701) which is currently in preclinical testing. Cara is targeting peripheral CB2 cannabinoid receptors present on cells like mast cells and leukocytes and that the company believes may be involved in inflammation and pain. According to Cara, the company has data indicating '701 is orally bioavailable, is active in preclinical models of inflammatory and neuropathic pain, and hasn't produced signals of CNS effects such as sedation and/or hypothermia. The earliest to expire patent covering '701 and related compounds expires in June 2028.

FINANCIALS

We project eventual cost of goods of 25% for I.V. 845, and therefore our gross margin for Cara as a whole is 75% based on our current model. We model increasing R&D expenses through the expected Phase III studies for I.V. '845, then a flattening of R&D. We expect SG&A to ramp approaching the NDA preparation and filing, then we project a flattening here as well. Greater visibility on the development plans for pipeline candidates such as oral '845 or CR701, or partnering for any of the candidates, would likely change our projections. Based on our model, we project that Cara has sufficient cash through 2016.

RISKS

Lack of compelling efficacy for CR845 in Phase III

- While '845 has shown compelling early data so far, these results could fail to translate to sufficient activity in pivotal testing.
- The oral candidate could fail to achieve adequate efficacy in POC studies.

Emergence of a concerning safety signal for '845 or other drug candidates

- Kappa-opioid agonists have a history of poor safety (CNS effects, GI effects)
- '845 safety appears good (no CNS, limited GI, manageable hypernatremia), however this needs to continue to be true in the pivotal studies.

Regulatory risk from the FDA and other agencies

- Despite the company's possible views on the efficacy and safety of its drug candidates, the agencies may deny or delay their approval for a number of reasons.

Inability to raise additional capital

- Our model assumes a secondary offering in 4Q16. Inability to complete this transaction might constrain Cara's cash position, limiting its ability to successfully develop '845 and the other candidates.

MANAGEMENT

Derek Chalmers, Ph.D., D.Sc. - President, CEO

Dr. Chalmers co-founded Cara, and has been President and CEO since September 2004. Prior, he co-founded Arena Pharmaceuticals (NASDAQ: ARNA). He earned his B.Sc. and Ph.D. (Pharmacology) from the University of Glasgow.

Josef Schoell - CFO

Mr. Schoell has been CFO since May 2006, having joined Cara in May 2005. From 2003 until joining Cara, he was a consultant with Robert Half Management Resources. From 1995 to 2002, he was CFO of American Biogenetic Sciences. Mr. Schoell earned his B.S. in Accounting from the New York University Stern School of Business. He is a CPA and a member of the American Institute of Certified Public Accountants and Financial Executives International.

Frédérique Menzaghi, Ph.D. - VP R&D

Dr. Menzaghi co-founded Cara, and has been VP of R&D since September 2004. From 1999 to 2003, she was Research Director of In Vivo Pharmacology at Arena. From 2003 to 2004, she was VP of Pharmacology and Business Development at Psychogenics. Dr. Menzaghi earned her Ph.D. in Neurosciences from the Louis Pasteur University and M.Sc. in Clinical Psychology from the University of Nancy.

Michael E. Lewis, Ph.D. - CSA

Dr. Lewis co-founded Cara and has been Chief Scientific Advisor since September 2004. He was a member of Cara's board of directors from September 2004 to July 2010. Prior, he co-founded Arena Pharmaceuticals and was Chief Scientific Advisor from 1997 to 2004, and director from 1997 to 2000. He also co-founded Adolor and was Chief Scientific Advisor from 1994 to 1997. Prior, he co-founded Cephalon, and was Director of Pharmacology from 1988 to 1992 and Senior Director of Scientific Affairs from 1992 to 1993. Dr. Lewis earned his Ph.D. in Psychology from Clark University and subsequently focused his research on opioid receptors.

Cara ($ in thousands, except per share amounts)	2011	2012	1st 9 months 2013	4Q13E	2013E	1Q14E	2Q14E	3Q14E	4Q14E	2014E	2015E	2016E	2017E	2018E
Income Statement														
Revenue														
License and milestone fees	-	1,190	9,637	-	9,637	-	-	-	-	-	-	7,400	6,900	-
% total revenue	*100%*	*88%*			*88%*	*na*	*na*	*na*	*na*	*na*	*na*	*100%*	*34%*	*0%*
Revenues under collaborative agreements	-	-	1,354	-	1,354	-	-	-	-	-	-	-	-	-
% total revenue	*0%*	*12%*			*12%*	*na*	*na*	*na*	*na*	*na*	*na*	*0%*	*0%*	*0%*
Product sales and royalties	-	-	0	-	-	-	-	-	-	-	-	-	13,324	102,320
% total revenue	*0%*	*0%*			*0%*	*na*	*na*	*na*	*na*	*na*	*na*	*0%*	*66%*	*100%*
Total Revenues	**-**	**1,190**	**10,991**	**-**	**10,991**	**-**	**-**	**-**	**-**	**-**	**-**	**7,400**	**20,224**	**102,320**
Costs & Expenses:														
Cost of product revenue	-	-	0	-	-	-	-	-	-	-	-	-	4,250	26,311
R&D	7,159	4,597	6,707	2,500	9,207	2,500	3,500	4,500	6,000	16,500	36,373	40,059	30,939	30,103
SG&A	2,407	2,829	2,457	1,000	3,457	1,000	1,000	1,200	1,500	4,700	7,658	11,504	20,650	24,162
Total Operating Expenses	**9,566**	**7,426**	**9,164**	**3,500**	**12,664**	**3,500**	**4,500**	**5,700**	**7,500**	**21,200**	**44,030**	**51,563**	**55,839**	**80,576**
Operating Income (loss)	**(9,566)**	**(6,236)**	**1,827**	**(3,500)**	**(1,673)**	**(3,500)**	**(4,500)**	**(5,700)**	**(7,500)**	**(21,200)**	**(44,030)**	**(44,163)**	**(35,616)**	**21,744**
Investment income	-	-	0	-	-	-	-	-	-	-	-	-	-	-
Income (loss) before income taxes	**(9,841)**	**(6,302)**	(1,897)	**(3,500)**	**(5,397)**	**(3,500)**	**(4,500)**	**(5,700)**	**(7,500)**	**(21,200)**	**(44,030)**	**(44,163)**	**(35,616)**	**21,744**
Income tax (benefit) provision	(35)	(31)	(27)	(1,225)	(1,252)	(1,225)	(1,575)	(1,995)	(2,625)	(7,420)	(15,411)	(15,457)	(12,465)	7,610
Tax rate	*0*	*0*	0	*35.0%*		*35.0%*	*35.0%*	*35.0%*	*35.0%*	*35.0%*	*35.0%*	*35.0%*	*35.0%*	*35.0%*
Net operating loss offset			0	1,225	1,225	1,225	1,575	1,995	2,625	7,420	15,411	15,457	12,465	(7,610)
Net income (loss) available to common stockholders	**(9,806)**	**(6,271)**	**(1,870)**	**(2,275)**	**(4,145)**	**(2,275)**	**(2,925)**	**(3,705)**	**(4,875)**	**(13,780)**	**(28,620)**	**(28,706)**	**(23,150)**	**14,134**
Net income (loss) to common shareholders - basic	**(9,806)**	**(6,271)**	**(979)**	**(2,275)**	**(3,254)**	**(2,275)**	**(2,925)**	**(3,705)**	**(4,875)**	**(13,780)**	**(28,620)**	**(28,706)**	**(23,150)**	**14,134**
Net income (loss) to common shareholders - diluted	**(9,806)**	**(6,271)**	**(1,870)**	**(2,275)**	**(4,145)**	**(2,275)**	**(2,925)**	**(3,705)**	**(4,875)**	**(13,780)**	**(28,620)**	**(28,706)**	**(23,150)**	**14,134**
Basic Earnings Per Share	(1.21)	(0.75)	(0.10)	($0.11)	($0.16)	($0.10)	($0.13)	($0.16)	($0.20)	($0.56)	($1.00)	($0.87)	($0.60)	$0.33
Diluted Earnings Per Share	**(1.21)**	**(0.75)**	**(0.18)**	**($0.11)**	**($0.21)**	**($0.10)**	**($0.13)**	**($0.16)**	**($0.20)**	**($0.56)**	**($1.00)**	**($0.87)**	**($0.60)**	**$0.28**
Basic Shares Outstanding	8,089	8,322	10,202	20,000	20,000	21,842	22,498	23,173	23,868	24,584	28,499	33,039	38,301	42,287
Diluted Shares Outstanding	**8,089**	**8,322**	**10,202**	**20,000**	**20,000**	**21,842**	**22,498**	**23,173**	**23,868**	**24,584**	**28,499**	**33,039**	**38,301**	**50,745**

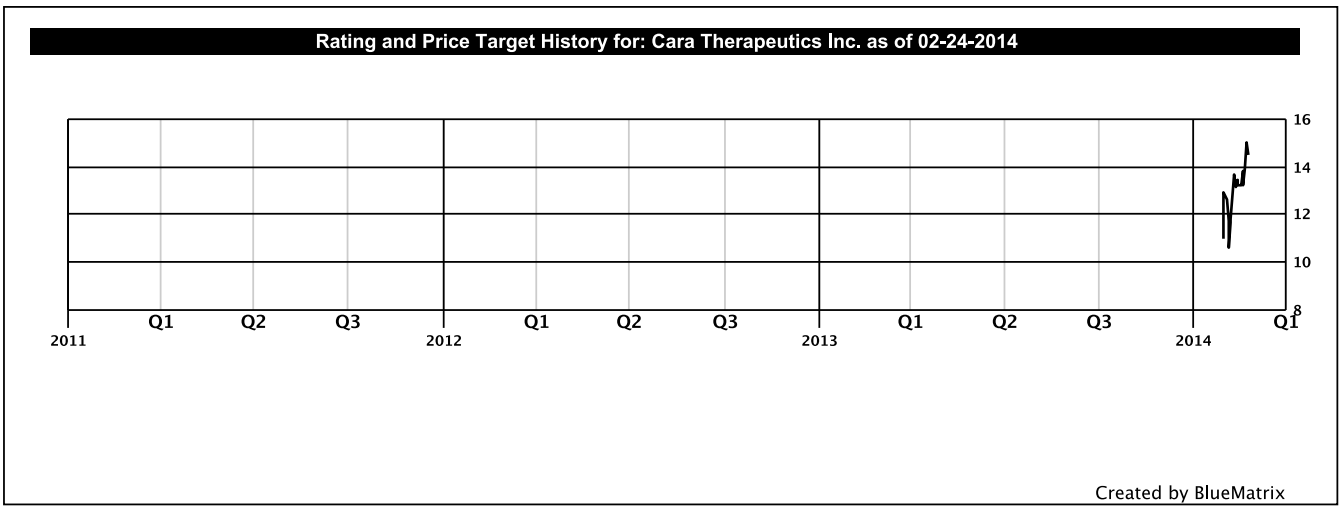
Balance Sheet	2011	2012	1st 9 months 2013	4Q13E	2013E	1Q14E	2Q14E	3Q14E	4Q14E	2014E	2015E	2016E	2017E	2018E
Current assets														
Cash and cash equivalents	4,097	1,117	17,733	16,084	16,084	10,745	10,357	9,589	8,850	8,850	(8,385)	50,016	23,621	18,405
Marketable securities, AFS	0	0	0	0	0	60,000	60,000	60,000	60,000	60,000	60,000	60,000	60,000	60,000
Accounts receivable	18	0	58	0	0	0	0	0	0	0	0	0	3,446	15,202
Inventories, net	0	0	0	0	0	0	0	0	0	0	0	0	3,446	15,202
Prepaid expenses and other current assets	443	111	556	0	0	0	0	0	0	0	0	0	3,446	15,202
Total current assets	**4,558**	**1,228**	**18,347**	**16,084**	**16,084**	**70,745**	**70,357**	**69,589**	**68,850**	**68,850**	**51,615**	**110,016**	**93,958**	**124,011**
Total property, plant and equipment, net	5,427	3,609	3,021	2,771	2,771	2,271	1,771	1,271	771	771	(1,229)	(2,229)	(3,229)	(4,229)
Other assets	700	700	700	700	700	700	700	700	700	700	700	700	700	700
Total assets	**10,685**	**5,537**	**22,068**	**19,555**	**19,555**	**73,716**	**72,828**	**71,560**	**70,321**	**70,321**	**51,086**	**108,487**	**91,429**	**120,482**
Current liabilities														
Accounts payable & accrued expenses	2,176	906	2,530	350	350	350	450	570	750	750	1,212	1,280	1,577	2,316
Convertible promissory notes, including accrued interest payable of $2 and $147 a	0	473	311	0	0	0	0	0	0	0	0	0	0	0
Deferred revenue, current portion	0	0	4,434	1,400	1,400	1,400	1,800	2,280	3,000	3,000	4,847	5,119	6,309	9,263
Current portion long term debt	753	307	0	0	0	0	0	0	0	0	0	0	0	0
Total current liabilities	**2,929**	**1,686**	**7,275**	**1,750**	**1,750**	**1,750**	**2,250**	**2,850**	**3,750**	**3,750**	**6,059**	**6,399**	**7,886**	**11,579**
Deferred revenue, net of current portion	0	0	0	5,250	5,250	5,250	6,750	8,550	11,250	11,250	18,178	19,198	23,658	34,737
Long-term debt, net	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Deferred obligation	1,592	1,377	1,202	1,202	1,202	1,202	1,202	1,202	1,202	1,202	1,202	1,202	1,202	1,202
Other long-term liabilities	60	35	0	0	0	0	0	0	0	0	0	0	0	0
Total liabilities	**4,581**	**3,098**	**8,477**	**8,202**	**8,202**	**8,202**	**10,202**	**12,602**	**16,202**	**16,202**	**25,439**	**26,799**	**32,746**	**47,518**
Commitments														
Stockholders' equity:														
Convertible preferred stock	58,168	58,522	65,586	65,586	65,586	0	0	0	0	0	0	0	0	0
Beneficial conversion feature on convertible promissory notes	0	2,050	0	0	0	0	0	0	0	0	0	0	0	0
Common stock	8	8	4	4	4	4	4	4	4	4	4	4	4	4
Additional paid-in capital	1,041	1,243	8,364	8,401	8,401	130,423	130,460	130,497	130,533	130,533	130,680	215,427	215,573	215,720
Accumulated deficit	(53,113)	(59,384)	(60,363)	(62,638)	(62,638)	(64,913)	(67,838)	(71,543)	(76,418)	(76,418)	(105,038)	(133,743)	(156,893)	(142,760)
Total stockholders' equity	**6,104**	**2,439**	**13,591**	**11,353**	**11,353**	**65,514**	**62,626**	**58,958**	**54,119**	**54,119**	**25,646**	**81,687**	**58,684**	**72,964**
Total liabilities and stockholders' equity	**10,685**	**5,537**	**22,068**	**19,555**	**19,555**	**73,716**	**72,828**	**71,560**	**70,321**	**70,321**	**51,086**	**108,487**	**91,429**	**120,482**

Proprietary to Piper Jaffray & Co. February 25, 2014
CARA: Charles Duncan; 212.284.2505
Current disclosure information for this company can be found at:
http://www.piperjaffray.com/researchdisclosures

Cara ($ in thousands, except per share amounts)

Cash Flow Statement	2011	2012	1st 9 months 2013	4Q13E	2013E	1Q14E	2Q14E	3Q14E	4Q14E	2014E	2015E	2016E	2017E	2018E
CASH FLOWS FROM OPERATING ACTIVITIES														
Net Income (Loss)	(9,806)	(6,271)	(1,870)	(2,275)	(4,145)	(2,275)	(2,925)	(3,705)	(4,875)	(13,780)	(28,620)	(28,706)	(23,150)	14,134
Adjustments to reconcile to cash used in operating activities:														
Stock-based compensation expense	95	61	110	37	147	37	37	37	37	147	147	147	147	147
Change in fair value of liability under license agreement	(20)	(25)	(35)	-	(35)	-	-	-	-	-	-	-	-	-
Change in fair value of investor rights / obligations	179	-	-	-	-	-	-	-	-	-	-	-	-	-
Accrued interest and amortization of beneficial conversion feature on promissory notes	-	25	3,605	-	3,605	-	-	-	-	-	-	-	-	-
Depreciation and amortization	1,186	1,025	709	250	959	250	250	250	250	1,000	1,000	1,000	1,000	1,000
Deferred rent costs	(191)	(214)	(175)	-	(175)	-	-	-	-	-	-	-	-	-
Long-term debt, non-cash interest expense	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Loss (gain) on disposal of equipment	(9)	286	-	-	-	-	-	-	-	-	-	-	-	-
Change in operating assets and liabilities:														
Other receivable	6	26	(27)	58	31	-	-	-	-	-	-	-	(3,446)	(11,756)
Inventories	-	-	-	-	-	-	-	-	-	-	-	-	(3,446)	(11,756)
Prepaid expenses and other assets	228	367	(78)	556	478	-	-	-	-	-	-	-	(3,446)	(11,756)
Accounts payable and accrued expenses	1,487	(1,311)	1,220	(2,180)	(960)	-	100	120	180	400	462	68	297	739
Deferred revenue	-	-	4,434	2,216	6,650	-	1,900	2,280	3,420	7,600	8,775	1,292	5,649	14,033
Net cash used in operating activities	**(6,845)**	**(6,031)**	**7,893**	**(1,338)**	**6,555**	**(1,988)**	**(638)**	**(1,018)**	**(988)**	**(4,633)**	**(18,236)**	**(26,199)**	**(26,395)**	**(5,216)**
CASH FLOWS FROM INVESTING ACTIVITIES														
Purchases of marketable securities, net	-	-	-	-	-	(60,000)	-	-	-	(60,000)	-	-	-	-
Purchase of property, plant and equipment, net	45	511	(4)	-	(4)	250	250	250	250	1,000	1,000	-	-	-
Net cash provided by (used in) investing activities	**45**	**511**	**(4)**	**-**	**(4)**	**(59,750)**	**250**	**250**	**250**	**(59,000)**	**1,000**	**-**	**-**	**-**
CASH FLOWS FROM FINANCING ACTIVITIES														
Proceeds from convertible promissory notes		2,538	1,462	(311)	1,151	0	0	0	0	-	-	-	-	-
Financing costs on convertible promissory notes		(47)	(70)	0	(70)	0	0	0	0	-	-	-	-	-
Proceeds from issuance of common stock, net		86	-	0	-	56,400	0	0	0	56,400	-	84,600	-	-
Stock option exercise	2	55	-	0	-	0	0	0	0	-	-	-	-	-
Repayment of LTD	(848)	(446)	(307)	0	(307)	0	0	0	0	-	-	-	-	-
Proceeds from issuance of convertible preferred stock	9,982	354	7,642	0	7,642	0	0	0	0	-	-	-	-	-
Proceeds from issuance of common stock under equity incentive plans, net		-	-	0	-	0	0	0	0	-	-	-	-	-
Net cash provided by (used in) financing activities	**9,136**	**2,540**	**8,727**	**(311)**	**8,416**	**56,400**	**0**	**0**	**0**	**56,400**	**0**	**84,600**	**0**	**0**
Net increase in cash and cash equivalents	2,336	(2,980)	16,616	(1,649)	14,967	(5,338)	(388)	(768)	(738)	(7,233)	(17,236)	58,401	(26,395)	(5,216)
Cash and cash equivalents at beginning of period	1,761	4,097	1,117	17,733	1,117	16,084	10,745	10,357	9,589	16,084	8,850	(8,385)	50,016	23,621
Cash and cash equivalents at end of period	4,097	1,117	17,733	16,084	16,084	10,745	10,357	9,589	8,850	8,850	(8,385)	50,016	23,621	18,405

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.

Legend:
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]	350	59.52	77	22.00
HOLD [N]	218	37.07	22	10.09
SELL [UW]	20	3.40	0	0.00

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Analyst Certification — Charles C. Duncan, PhD, Sr. Research Analyst
— Roy Buchanan, Ph.D., Research Analyst

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