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Company Report

April 28, 2015

Cara Therapeutics (CARA - $11.61)

Healthcare / Biotechnology

Initiation of Coverage

Ticker:	CARA
Rating:	**Buy**
Price Target:	**$20.00**

We are initiating coverage of Cara Therapeutics (CARA) with a BUY rating and $20 price target. CARA is a clinical-stage biopharmaceutical company focused on developing and commercializing novel and proprietary chemical entities that selectively target kappa-opioid receptors involved with pain. The lead product candidate is intravenous CR845, an injectable version of a first-in-class kappa-opioid receptor-based peripheral analgesic. It is designed to provide pain relief without stimulating mu-opioid receptors, which trigger many unwanted side effects. CARA has completed two phase II trials investigating IV CR845 in both soft- (laparoscopic hysterectomy) and hard-tissue (bunionectomy) surgeries, successfully demonstrating significant pain relief and a consistent ability to decrease opioid-related adverse events. Currently, CARA is expecting to begin phase III pivotal trials for IV CR845 in 1H15. CARA recently reported positive phase 1a/1b data on the oral tablet formulation of CR845.

- **First-in-class kappa in acute pain:** CR845 is a first-in-class novel pain therapeutic. As it is an opioid receptor, CR845 has, much like its mu-opioid receptor cousin, demonstrated effective acute pain relief in both of its phase IIb acute pain trials following soft- and hard-tissue surgeries. Due to its specific formulation, CR845 does not cross the blood/brain barrier and affect the central nervous system (CNS), thus negating the side effects that sidelined kappa-receptor agonists in the 1980s.

- **Opioid pain relief without the side effects**: Though mu-opioids are considered the standard of care in acute pain, they have many unwanted side effects. As CR845 is a selective kappa-opioid receptor agonist, it does not activate the mu-receptors that generate the adverse reactions, such as respiratory depression, euphoria, nausea, and vomiting.

- **Low abuse potential could lead to unscheduled drug status:** One of the significant benefits of CR845 is that is does not produce the euphoria typical in mu-opioids. With this lack of euphoria, there is a decrease in potential abuse and addiction. In the company's human abuse liability study CR845 had a significantly ($p<0.0001$) lower "liking" score compared to IV Talwin (pentazocine). CARA management believes they may be able to get CR845 as a schedule V drug or with no designation, which would make for a significant advantage over current therapies.

- **Our $20 target price is based on a sum-of-the-parts analysis.**

Trading Data:

Last Price (04/27/2015)	$11.61
52–Week High (07/07/2014)	$17.77
52–Week Low (10/13/2014)	$7.53
Market Cap. (MM)	$265.0
Shares Out. (MM)	22.82

Earnings Estimates: (per share)

(Sep)	1Q	2Q	3Q	4Q	FY	P/E
FY16E	NA	NA	NA	NA	(1.30)	NA
FY15E	(0.36)	(0.29)	(0.30)	(0.31)	(1.25)	NA
FY14A	(0.22)	(0.16)	(0.28)	(0.18)	(0.85)	NA
FY13A	NA	NA	NA	NA	(0.74)	NA

Source: Laidlaw & Company estimates

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Summary and Investment Thesis

We are initiating coverage of Cara Therapeutics (CARA) with a BUY rating and $20 price target. CARA is a clinical-stage biopharmaceutical company focused on developing and commercializing novel and proprietary chemical entities that selectively target kappa-opioid receptors involved with pain. The lead product candidate is intravenous CR845, an injectable version of a first-in-class kappa-opioid receptor-based peripheral analgesic. It is designed to provide pain relief without stimulating mu-opioid receptors, which trigger many unwanted side effects. CARA has completed two phase II trials investigating IV CR845 in both soft- (laparoscopic hysterectomy) and hard-tissue (bunionectomy) surgeries, successfully demonstrating significant pain relief and a consistent ability to decrease opioid-related adverse events. Currently, CARA is expecting to begin phase III pivotal trials for IV CR845 in 1H15. CARA reported positive phase 1a/1b data on the oral tablet formulation of CR845 in 4Q14.

- First-in-class kappa in acute pain: CR845 is a first-in-class novel pain therapeutic. As it is an opioid receptor, CR845 has, much like its mu-opioid receptor cousin, demonstrated effective acute pain relief in both of its phase IIb acute pain trials following soft- and hard-tissue surgeries. Due to its specific formulation, CR845 does not cross the blood/brain barrier and affect the central nervous system (CNS), thus negating the side effects that sidelined kappa-receptor agonists in the 1980s.
- Opioid pain relief without the side effects: Though mu-opioids are considered the standard of care in acute pain, they have many unwanted side effects. As CR845 is a selective kappa-opioid receptor agonist, it does not activate the mu-receptors that generate the adverse reactions, such as respiratory depression, euphoria, nausea, and vomiting.
- Low abuse potential could lead to unscheduled drug status: One of the significant benefits of CR845 is that is does not produce the euphoria typical in mu-opioids. With this lack of euphoria, there is a decrease in potential abuse and addiction. In the company's human abuse liability study CR845 had a significantly ($p<0.0001$) lower "liking" score compared to IV Talwin (pentazocine). CARA management believes they may be able to get CR845 as a schedule V drug or with no designation, which would make for a significant advantage over current therapies.
- Large market opportunity with significant unmet need: The post-operative pain market is estimated to be ~$6B in the US, with ~300 million IV units dosed per year. With the multi-modal analgesia as a

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standard of care and 75% of patients reporting adverse events from their pain medications, we believe CR845 has the ability to draw significant market share if approved.

- Pruritus opportunity could ultimately dwarf pain indication: The company is conducting a phase II trial in uremic pruritus, with PK data expected in December 2014 and topline results in 2Q15. Uremic pruritus (itching) is an unmet medical need that presents in 40-50% of adults with chronic kidney disease, while generalized pruritus affects up to 8% of the US adult population. Should CARA demonstrate positive phase II data in December 2014/2Q15 this could be a significant value driver for the shares

Figure 1. Upcoming Potential Catalysts

Event	Expected Timing
Start IV formulation phase 3 trials	1H15
Start phase 2 proof of concept trial in oral version	1H15
Phase 2 data CR845 for uremic pruritis	2Q15
Start phase 3 trial CR845 for uremic pruritis	4Q15

Source: Company reports: Laidlaw & Company estimates

Valuation

We value CARA at $20/share based on a sum-of-the-parts analysis, with IV CR845 valued at $11/share based on a 3.5x multiple of 2019 sales of $303MM discounted five years at 25%, oral CR845 valued at $3/share based on a 3.5x multiple of 2020 sales of $175MM discounted five years at 50%, CR845 for Uremic Pruritus valued at $3.5/share based on a 3.5x multiple of 2020 sales of $350MM discounted five years at 60%, and our remaining value based on cash (end 2015) and technology of $3/share. We estimate an ~$70MM raise in 2015.

Figure 2. Sum-of-the-Parts Analysis

Sum-of-the-parts value: CARA		
Segment	Valuation (000's)	Per share value
CR845: IV post-op pain	$346,092	$11.0
CR845 - Uremic Pruritus	$116,825	$3.5
CR845 - oral formulation	$80,658	$2.5
Cash (end '15) & tech value	$100,532	$3.0
SUM	**$644,107**	**$20**
Shares out '15E (000)		30,666

Source: Company reports; Laidlaw and Company estimates

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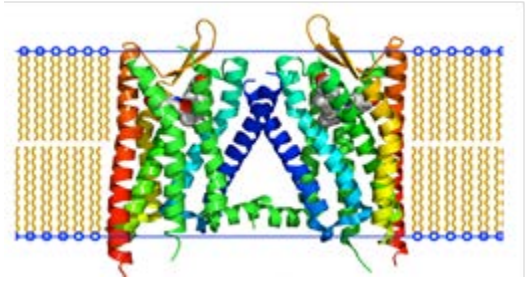
Company Description

CARA is an emerging biotechnology company focused on developing novel therapeutics to treat pain and inflammation. Its lead product candidate is CR845, a best-in-class peripherally selective kappa-opioid receptor-based molecule for the treatment of acute and chronic pain as well as neuropathic and inflammatory pain.

CARA has completed two phase II trials in pain relief following soft- (laparoscopic hysterectomy) and hard-tissue (bunionectomy) surgical procedures. In the soft tissue trial, both the primary and secondary endpoints were met. In the hard tissue trial, topline data showed that the primary endpoint of reduction in pain over 24 hours was met, as was the secondary endpoint of reduction in pain intensity over the entire 48-hour dosing period. CARA is currently planning three phase III clinical trials with the FDA with an anticipated start of enrollment in 1H15.

CARA also has developed both a capsule and tablet oral formulation of CR845. The capsule formulation successfully completed a proof-of-concept phase 1 trial in April 2012 looking at bioavailability, safety, and efficacy. The tablet formulation just completed phase 1a/1b trials last week, with a phase IIa proof-of-concept trial in acute pain expected to start during the first half of 2015.

Figure 3. Kappa-opioid Receptor



Source: Wu et al., Nature 485 (7398)327-32

CR845 — KAPPA-OPIOID RECEPTOR AGONIST

Kappa- vs. Mu-Opioid Receptors

Kappa-opioid receptors are one of the three classic opioid receptors primarily located on the neural synapse of the brain and pain neurons in the central nervous system (CNS). There are three classic opioid receptors: mu, delta, and kappa. These receptors are responsible for the release of dopamine, which is associated with stimulating the brain's reward and pleasure centers. The most commonly known of these receptors is the mu receptor, which is activated by opioids such as morphine and can cause pain relief, sedation, and euphoria. Though opioids are highly effective analgesics, they often have serious side effects such as nausea, vomiting, respiratory depression, and reduction in

gastrointestinal motility. Due to their ability to cause a state of euphoria, drugs that stimulate mu-opioid receptors also tend to cause physical and physiological dependence that leads to addiction.

Lead product candidate CR845 is a peripherally acting kappa-opioid-receptor agonist for the treatment of both chronic and acute pain. It is designed to treat pain via activation of the peripheral kappa-opioid receptors without triggering mu-opioid receptors. By not triggering the mu-opioid receptors, CR845 bypasses the unwanted opioid-related side effects, such as nausea and vomiting and, more importantly, respiratory depression and potential addiction.

Not Your Typical Kappa

- No interaction with the central nervous system: Early on, neurobiologists considered the idea of kappa-opioid receptors as possible targets for pain. However, they soon discovered that due to the activation of kappa-opioid receptors in the CNS, several serious side effects were observed. These included acute psychiatric disorders, dysphoria, depression, and hallucinations. CR845, however, is unique. CR845 is designed with specific chemical characteristics that restrict it from entering the blood/brain barrier and CNS. Therefore, CR845 only acts on those nerve receptors outside of the brain and spinal cord. This peripheral action allows CR845 to be a powerful analgesic without the unwanted CNS side effects.

- Reduction in standard mu-opioid-related side effects: Morphine and the morphine derivatives OxyContin and Vicodin are the most commonly prescribed mu-opioids for both acute and chronic pain. These strong mu-opioid analgesics have been associated with post-operative opioid-induced respiratory depression (POIRD) and post-operative nausea and vomiting (PONV), as well as opioid-induced bowel dysfunctional (OBD). As CR845 is a highly selective kappa receptor, it has shown statistically significant reduction of opioid-related adverse effects such as POIRD and PONV

- Abuse potential is limited with CR845: Current mu-opioid treatments are known to cause feelings of euphoria, which has shown an increased potential for abuse and addiction. In fact, studies have shown a rapidly growing problem of abuse, with an 81% increase in abuse of prescription pain drugs (primarily from OxyContin and Vicodin) from 1992-2003. Activation of kappa receptors does not cause euphoria, which makes CR845 less likely to be abused. CR845 demonstrated positive abuse liability study data in October 2014 showing lower “likeability” vs. IV pentazocine ($p<0.0001$). CARA management plans to ask the FDA that, if approved, CR845 be either Schedule V or an unscheduled pain reliever. This would offer a significant competitive advantage over other scheduled drugs.

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- Safer drug-drug interaction profile: Another benefit of CR845 is that it is a peptide composed of four non-natural D-amino acids that are not metabolized in the liver. This means it will not interact with liver enzymes that are responsible for the metabolism of some of the most commonly used drugs like statins, ACE inhibitors, and some beta-blockers.

- IV to oral step down: CARA is developing CR845 in at least two formulations — intravenous (IV) and tablet form. CARA intends to have the IV formulation in the acute or hospital setting to be used pre- and post-operatively. With the IV phase II trials indicating 24 hours of statistically significant pain relief after the post-operative pain therapies dissipate, CARA can perpetuate the use of CR845 by offering a tablet form. Once patients no longer need the IV formulation for pain, they can "step down" to the oral formulation upon discharge from the hospital. The tablet form also expands the marketplace for CR845, as it can be given for chronic pain.

Intravenous CR845 and Acute Pain

By definition, acute pain occurs suddenly, often as a result of illness, trauma or surgery. Though onset of acute pain is rapid and may resolve over the short term, it may also last for days or weeks depending on the severity of the injury or illness and how rapidly the patient recovers and heals**.**

Pain and surgery tend to go hand in hand, and postoperative pain is a substantial market of the overall pain marketplace. A recent study indicated that there are more than 46 million inpatient and 53 million outpatient surgeries performed in the US annually. According to the updated practice guidelines developed by the American Society of Anesthesiologists, the current standard for surgical pain management is a multimodal approach. This would consist of administration of two or more drugs that act on different pain mechanisms. Post-surgical pain is usually administered via IV and is usually a product containing mu-opioids such as oxycodone, oxymorphone, and hydrocodone. There are ~300 million intravenous anesthetic units dosed per year in the US.

Phase IIb Clinical Trials

Laparoscopic Hysterectomy (CLIN2002)

In June 2012 CARA completed a multicenter, double-randomized, double-blind, placebo-controlled phase IIb trial consisting of 203 patients at 22 sites in the US. Patients were administered either placebo or 0.04 mg/kg IV CR845 preoperatively and post-surgery; if they had a pain intensity score of ≥40 on a 100-point scale, they were randomized to receive either placebo or one dose of 0.04 mg/kg IV CR845. Efficacy was measured using time-specific 24-hour pain intensity difference. In summary, there were four measureable cohorts: placebo/placebo, CR845/placebo, placebo/CR845 and CR845/CR845.

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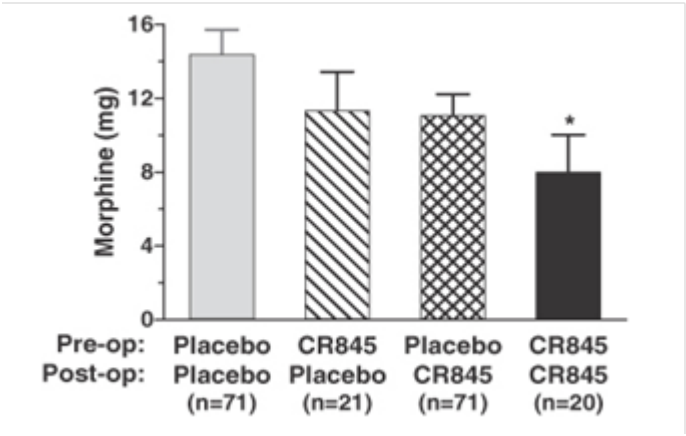
The primary endpoint of reduction in total rescue morphine consumption in the first 24 hours post-surgery met statistical significance, with the CR845/ CR845 group using approximately 33% less morphine than those in the placebo/placebo group.

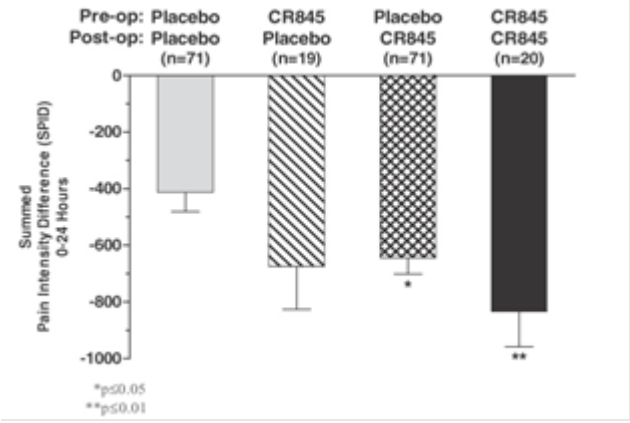
Figure 4. Rescue Morphine Use



Source: Company Documents

For the secondary endpoint of efficacy compared to placebo in pain reduction up to 24 hours, the CR845/CR845 group exhibited a statistically significant reduction of pain over a 24-hour time period as indicated by an improvement in 0-24 hour mean summed pain intensity difference (SPID). Pain intensity difference (PID) in the CR845/CR845 group also exhibited statistically significant improvements in pain over 0-4, 0-8, and 0-16 hour time intervals.

Figure 5. Phase IIb SPID from 0-24 Hours



Source: Company Documents

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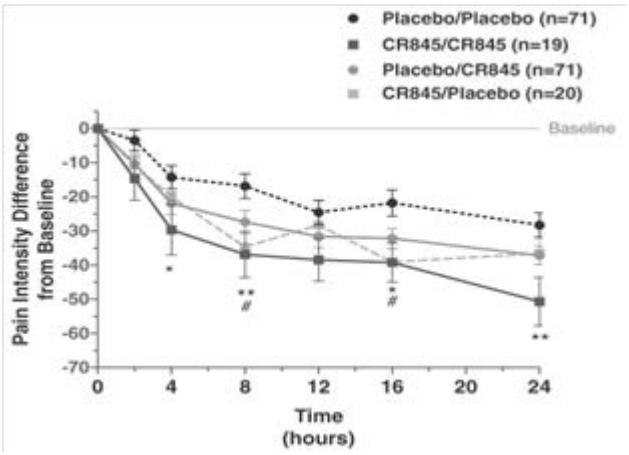
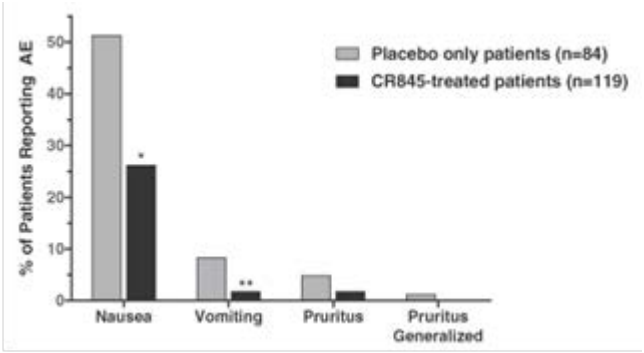
Figure 6. Phase IIb PID at Specific Time Intervals



Source: Company Documents

With the reduced use of rescue morphine, there was also a reduction in opioid-related side effects such as nausea, vomiting, and pruritus. Also important to note, there were no CNS-related effects seen with centrally acting kappa opioid agonists.

Figure 7. Incidence of Opioid-Related AEs



Source: Company Documents

**p≤0.001 **p≤0.05*

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Figure 8. Phase IIb Laparoscopic Hysterectomy Trial

CLIN 2002 - Phase 2b Laparoscopic Hysterectomy Trial	
Aim	Determine if CR845 is effective in treating pain associated with laparoscopic hysterectomy
Design	Multi-center, double-randomized, double-blind, placebo controlled - one preemptive IV dose and one postoperative IV dose, rescue morphine allowed
Dosing	CR845 0.04 mg/kg single IV dose administered pre-op and post-op for pain compared to IV placebo1*: 1) IV CR845 both pre- and post-op (CR845/CR845) 2) Placebo pre-op and IV CR845 post-op (Placebo/CR845) 3) IV CR845 pre-op and Placebo post-op (CR845/Placebo) 4) Placebo pre-op and Placebo post-op (Placebo/Placebo)
Endpoints	1*: Total morphine consumption in the first 24 hours in patients who are re-randomized in post-op period - 24 hours 2*: To evaluate the efficacy of CR845 compared to placebo for reducing pain following laparoscopic hysterectomy - up to 24 hours 2*: To evaluate the effect of CR845 compared to placebo on the use of opioid analgesics during post-op period - UP to 24 hours
Patients	N = 203
Safety	Nausea 26.1% CR845 vs. 51.2% placebo, Vomiting 1.7% CR845 vs. 8.3% placebo, also decreased pruritus
Results - 6/11/12	Patients given pre & post op CR845 resulted in stat. signif. reduction (~33%) in rescue morphine use over 24 hrs post-surgery. Patient group exhibited ~ 2X or (~100%) increase in their calculated 24-hr PID (p=0.002) and SPID (p=0.003)value compared to placebo. Signif24-hr analgesic seen in single post-op dose of CR845 where SPID value (p=0.014) increased by more htan 50% when compared to placebo.

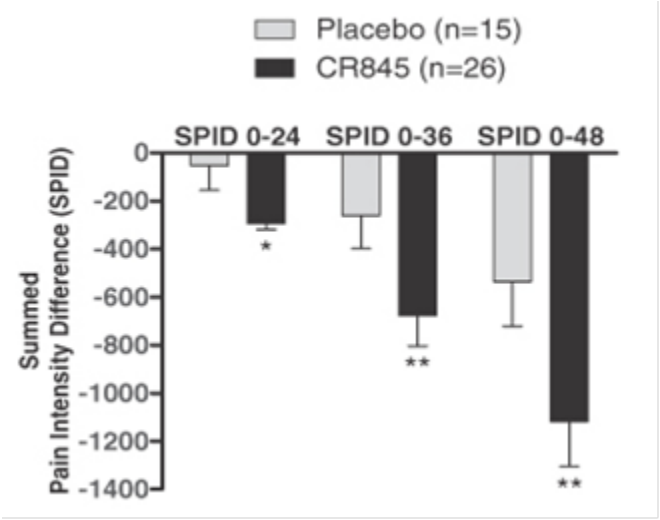
Source: Company Documents

Bunionectomy (CLIN2003)

In October 2013 CARA completed a randomized, double-blind, placebo-controlled trial consisting of 51 patients in the US. Patients received an initial bolus dose of CR845 or placebo at randomization and again at patient's request, 30-60 minutes later and thereafter as needed up to every eight hours over a 48-hour dosing period. Fentanyl was available as a "rescue" medication for patients not reporting adequate pain relief.

In the completer analysis, the CR845 treatment arm met the primary endpoint of statistically significant (p=<0.05) reduction in pain intensity as measured by the SPID score over the initial 24-hour period compared to placebo. The CR845 arm also met the secondary endpoint of a statistical (p=<0.025) reduction in pain intensity over the entire 48-hour dosing period.

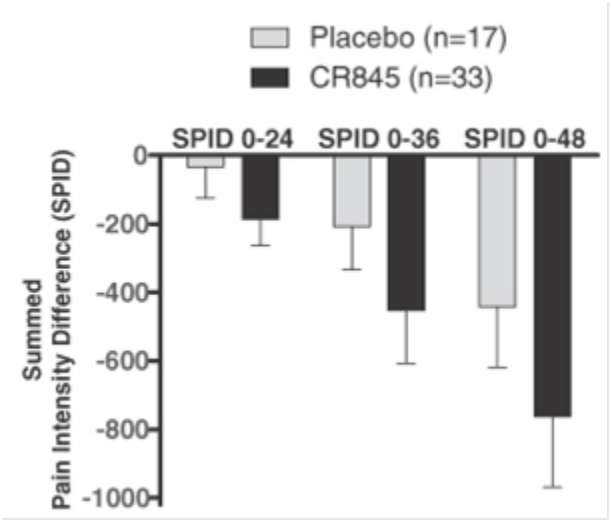
Figure 9. SPID 0-24 Hours, 0-36 Hours, 0-48 Hours in Completer Population



Source: Company Documents

**p≤0.05 **p≤0.03*

Figure 10. SPID 0-24 Hours, 0-36 Hours, 0-48 Hours in mITT Population (Completers + Non-Completers)



Source: Company Documents

In addition, the CR845 treatment resulted in a statistically significant reduction in the incidence of opioid-related adverse events of nausea and vomiting (by 60% and 80%, respectively; $p<0.05$) compared to placebo during the 48-hour period of treatment. Though there was no observed difference in the overall mean fentanyl use between the placebo and CR845 treatment groups, CARA believes the ability of CR845 to reduce nausea and vomiting despite fentanyl

use is due to a direct anti-vomiting or anti-nausea effect resulting from its kappa-opioid-agonist mechanism of action.

Figure 11. Phase II Bunionectomy Trial

CLIN2003 - Phase 2 Bunionectomy Trial	
Aim	Determine the analgesic efficiacy as well as safety and tolerability of CR845 after a bunionectomy
Design	Single-center, randomized, double-blind, placebo controlled parallel group proof of concept study
Dosing	CR845 0.04mg/kg initial dose followed by prn dosing
Endpoints	1': 24 hour summed pain intensity differences (SPID24) 2': Evaluate the efficacy of CR845 compared to placebo inreducing pain following bunionectomy (up to 48 hours) 2': Evaluate the effect of CR845 compared to placebo on the use of rescue opioids (fentanyl) during the post-op period (up to 48 hours)
Patients	N = 51
Safety	Safe & well tolerated, stat. signif reduction in incidence of opioid-related AE of nausea and vomiting (by 60% and 80%)
Results - 10/29/2013	Primary endpoint met: stat. signif. reduction in pain intensity as measured by SPID over initial 24 hours v. placebo ($p<0.05$). Seconday endpoint met: stat. signif. reduction in pain intensity over entier 48-hour dosing period $p<0.025$). CR845 also resulted in a stat. signif. reduction in the incidence of opioid-related adverse events of nausea (by 60%) and vomiting (by 80%) at $p<0.05$ compared to placebo over the 48 hours of treatment.

Phase 3 Clinical Development Plan for IV CR845

With the success of the phase IIb trials in both hard- and soft-tissue surgeries, CARA is currently planning its phase III clinical program for management of acute pain in a hospital setting. Current assumptions are that CARA will be required to complete two phase III trials, one with pain resulting from a soft-tissue surgery and one in patients with pain resulting from a hard-tissue surgery.

- Potential phase III trial (CLIN3001): CLIN3001 is a randomized, double-blind, placebo-controlled trial with ~400 female patients with postoperative pain after laparoscopic hysterectomy. Patients will be assigned one of three doses or placebo. The primary endpoint is expected to be the SPID at 24 hours with secondary endpoints of rescue morphine use, SPID at other time points, and occurrence of nausea and vomiting.

- Potential phase III trial (CLIN3002): CLIN3002 is a randomized, double-blind, placebo controlled trial with ~400 male or female patients with postoperative pain after bunionectomy. Patients will be assigned one of three doses or placebo. The primary endpoint is expected to be the SPID at 48 hours with secondary endpoints of rescue morphine use, SPID at other time points, and occurrence of nausea and vomiting.

- Potential phase III trial (CLIN3003): CLIN3003 is an adaptive trial design of 500-600 patients with postoperative pain following either laparoscopic hysterectomy or bunionectomy surgery. This trial is looking at efficacy of IV CR845 when dosed pre- and post-surgery as compared with IV CR845 only post-surgery. This will be a three-arm trial — CR845 pre- and post-surgery, post-surgery only, or just placebo. Primary endpoints are expected to be at either SPID at 24 or 48 hours

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with secondary endpoints of rescue morphine use, SPID at other time points, TOPAR at 24 and 48 hours, and occurrence of nausea and vomiting.

Oral CR845 and Chronic Pain

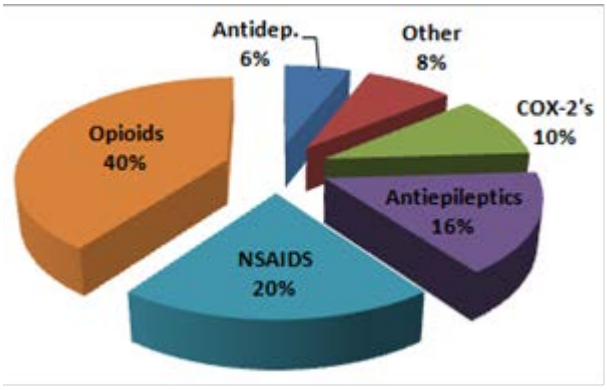
Chronic pain can be progressive, arising from conditions such as systemic inflammation and musculoskeletal problems, the most common of which is lower back pain. Chronic pain is defined as any pain that lasts longer than three to six months. Co-morbidities associated with chronic pain include cancer, rheumatoid arthritis, and fibromyalgia or nerve damage from diabetes.

Current non-opioids: Generally, mild to moderate pain is treated with over-the-counter products such as aspirin, acetaminophen, and naproxen sodium. Non-opioid therapies can be limiting due to their limited efficacy and side effects such as liver toxicity, bleeding, serious GI complications (including ulcers and kidney damage), and even more serious cardiovascular thrombotic events such as stroke and heart attack. Treatments for chronic pain are dependent on severity.

Opioids: Opioids are the most commonly prescribed drug for both acute and chronic pain, with mu-opioids at the front of the pack. Morphine and the morphine derivatives OxyContin and Vicodin are all commonly used. Though powerful in their pain relief, opioids have safety and tolerability issues. Chronic opioid users can develop a tolerance for the opioid, which results in the need for a higher dose. Also, due to their CNS activity, mu-opioids can produce feelings of euphoria that can lead to abuse and addiction.

Yet even with these risks, opioids remain the most prescribed pain medication with ~40% of the $20.6B global pain market in 2011. According to IMS Health, in 2012 the US market for opioid painkillers reached $9.4B.

Figure 12. 2011 Total Market Sales — $20.6B



Source: Decision Rsrcs, Chronic Pain Study, Nov. 2011

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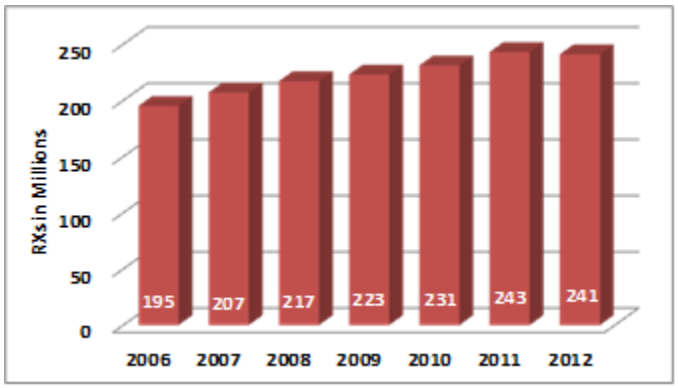
Figure 13. Annual US Prescriptions of Opioid Painkillers



Source: IMS Health

Phase Ia Clinical Trial

In April 2012 CARA completed a first-in-man phase 1 clinical trial of an oral formulation of CR845. The trial was a single-center, double-blind, placebo-controlled study to evaluate the pharmacokinetics (PK), safety, and pharmacodynamics of CR845 in 50 healthy patients. Patients were randomized and received either placebo or one of four single ascending doses of the capsule of CR845. The study demonstrated a mean oral bioavailability of 16% across all groups, under fast with peak and total exposures proportional to each dose.

Phase Ib Clinical Development Plan for Oral CR845

CARA conducted both a single ascending- and multiple ascending-dose trial in the first half of 2014, which read out positive data just last week. The company plans to initiate a phase IIa proof-of-concept trial in acute pain in the first half of 2015.

- The single ascending-dose study: This study included six tablet strengths from 0.1 mg to 10 mg and demonstrated a mean oral bioavailability of 10% across all dose groups under fasting conditions, with a range of maximum plasma concentrations of CR845 bracketing the concentrations seen in previously successful phase II trials with IV CR845. All tested dose strengths were also shown to be active at the kappa opioid receptor, as assessed by statistically significant ($p < 0.0001$) acute changes in blood measurements of an established neuroendocrine biomarker.

- The multiple ascending-dose study: This study used repeat-doses of the 0.1 mg, 1 mg, and 5 mg tablets administered twice a day for one week. All tablet doses were well tolerated with no serious adverse events (SAEs) reported and all adverse events (AEs) were mild and generally similar to those reported with IV CR845. Clinical safety laboratory measurements were normal across all tablet strengths after single or repeat dosing.

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Potential "Blockbuster" Opportunity in Uremic Pruritus as Well

In August 2014 CARA initiated a proof-of-concept phase II trial for IV CR845 for the treatment of uremic pruritus (UP), a systemic condition with high prevalence in dialysis patients for which there are no approved therapeutics in the US. We anticipate topline dose-ranging pharmacokinetic (PK) and safety data from this trial in December 2014, with topline efficacy results anticipated in 2Q15.

According to the Journal of the European Academy of Dermatology and Venereology, UP is present in 40-50% of adults with chronic kidney disease (CKD), demonstrating that UP remains an important clinical symptom and health issue in the estimated 20 million US patients with CKD (Centers for Disease Control).

In some patients UP occurs intermittently and lasts only several minutes, but other patients suffer from prolonged periods of severe pruritus, which can occur throughout the day and night. The occurrence, duration, and intensity of UP can change over time and the itching is usually worst at night. The areas most commonly affected by UP are the back, limbs, chest, and head, but 20-50% of patients experience generalized pruritus. External heat, sweat, and stress can aggravate UP, and cold or hot showers can alleviate symptoms.

UP has a substantial effect on quality of life, as it causes serious discomfort, anxiety, depression, and sleeping disorders. Sleeping disorders cause chronic fatigue, are associated with disturbance of day and night rhythm, and have a negative influence on mental and physical capacity. UP is increasingly recognized as an indicator of excess mortality risk in patients with CKD.

While there are no approved therapeutics in the US for CKD, this systemic condition is found to be highly prevalent amongst dialysis patients. Measures to control UP in patients on dialysis include optimization of dialysis efficacy, use of biocompatible dialysis membranes, and improvement of the nutritional status of the patient. Adequate control of plasma levels of calcium and phosphorus and the concomitant treatment of secondary hyperparathyroidism can ameliorate pruritus symptoms in some cases. In patients with CKD, cases of pruritus caused by liver diseases (e.g. hepatitis), primary skin diseases (e.g. atopic dermatitis, contact dermatitis, psoriasis, and urticaria), and endocrine disorders (e.g. Graves disease, hypothyroidism, and diabetes mellitus) require specific treatments. Available treatment options for UP include both topical and systemic therapies.

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Major Risks

Exogenous events could impact our outlook. We believe pharmaceutical companies have the least control over competitive, political, and regulatory risks. Although we have incorporated competitive assumptions into our forecasts, there may be other risks beyond the scope of our analysis. Changes in the drug reimbursement system, as well as any political or regulatory amendments, may significantly influence the earnings power of these companies.

Actual clinical results and the FDA's conclusions may deviate from expectations. Many of our assumptions are based on a review of incomplete clinical trial data available in the public domain. Often our conclusions are drawn from early stage data, which may not be reflected by pivotal studies. Furthermore, the FDA's conclusions may not coincide with our own, materially changing our revenue and earnings assumptions.

Compliance issues, product recalls, and other mandates by regulatory authorities could materially change our expectations. Regulatory compliance issues, ranging from accounting irregularities to defective manufacturing practices, could materially change our assumptions and earnings outlook. Unanticipated product recalls and labeling changes could also have adverse consequences on our earnings assumptions.

Legal risks could lead to additional liabilities and revenue loss. In addition to the expenses incurred by patent challenges, product liability and other legal suits could occur and lead to additional liabilities and revenue loss, which could substantially change our financial assumptions.

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MANAGEMENT

Derek Chalmers, PhD, CEO, President and Director: Dr. Chalmers has 17 years' experience in the biotechnology industry with increasing levels of corporate and business responsibilities. Dr. Chalmers served as a principal investigator at Neurocrine Biosciences prior to co-founding Arena Pharmaceuticals in 1997. He served as vice president and executive director of ARNA until May 2004, prior to co-founding CARA. Dr. Chalmers has extensive corporate financing experience, having led both private and IPO roadshow teams. Dr. Chalmers is an inventor or co-inventor on more than 50 issued or pending US patents.

Michael Lewis, PhD, Chief Scientific Officer: Dr. Lewis has had extensive experience in the biopharmaceutical industry, and prior to that, about five years of experience in opioid research at the National Institutes of Health and the University of Michigan. After establishing and directing a molecular pharmacology lab at DuPont, Dr. Lewis co-founded Cephalon, Inc., serving as director of pharmacology and senior director of scientific affairs. He participated in pre- and post-IPO road shows in Japan and the US as well as presentations to obtain corporate partners, including Schering-Plough and Kyowa Hakko. Dr. Lewis later co-founded and served as chief scientific advisor to Adolor Corporation and also participated on the company's analgesics development team and assisted in pre-IPO financing and corporate partnering presentations. Dr. Lewis was subsequently invited by Dr. Chalmers to co-found ARNA, and he served as a pre-IPO director and chief scientific advisor to ARNA. Dr. Lewis is presently a director of PolyMedix, Inc., a privately held biotechnology company that is developing antimicrobial agents based on a novel computational chemistry platform. Dr. Lewis is an inventor or co-inventor on 15 issued US patents and is an author or co-author of more than 40 publications on opioids, including journal articles, invited reviews, and book chapters.

Josef Schoell, Chief Financial Officer: Mr. Schoell has more than 20 years of financial and accounting experience, including 10 years in the biotechnology industry. From 2003 until joining the company, Mr. Schoell was a consultant with Robert Half Management Resources. From 1995 to 2002 he served as the chief financial officer and vice president-finance of the American Biogenetic Sciences Inc. and controller from 1992 to 1995. From 1988 until joining American Biogenetic Sciences Inc., Mr. Schoell was an independent consultant providing financial accounting and computer services. From 1978 until 1988, Mr. Schoell served in various financial and accounting positions with JP Stevens. Mr. Schoell is a graduate of New York University Stern School of Business, is a certified public accountant in New York State and a member of

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the New York State Society of Certified Public Accountants, American Institute of Certified Public Accountants, and Financial Executives International.

Joseph Stauffer, Chief Medical Officer: Dr. Stauffer brings to CARA more than 15 years of pain development and regulatory experience, having served as chief medical officer at numerous specialty pharmaceutical companies, including Ikaria, Inc. and Alpharma. While at Alpharma, prior to the company's acquisition by King Pharmaceuticals, he led the clinical development program for EMBEDA, the first abuse-deterrent long-acting opioid analgesic approved by the FDA. Prior to getting his industry start as the global medical director for pain therapeutics at Abbott Laboratories (ABT-$45.71-NR), Dr. Stauffer served as a medical review officer in the FDA's Anti-inflammatory and Analgesic Division of the Center for Drug Evaluation and Research, where he reviewed regulatory filings for a variety of pain and anti-inflammatory compounds. Dr. Stauffer has also been a founding member of several FDA, industry, and academic working groups, including the Analgesic Clinical Trial Translations, Innovations, Opportunities and Networks (ACTTION) and the Initiative on Methods, Measurement and Pain Assessment in Clinical Trials (IMMPACT).

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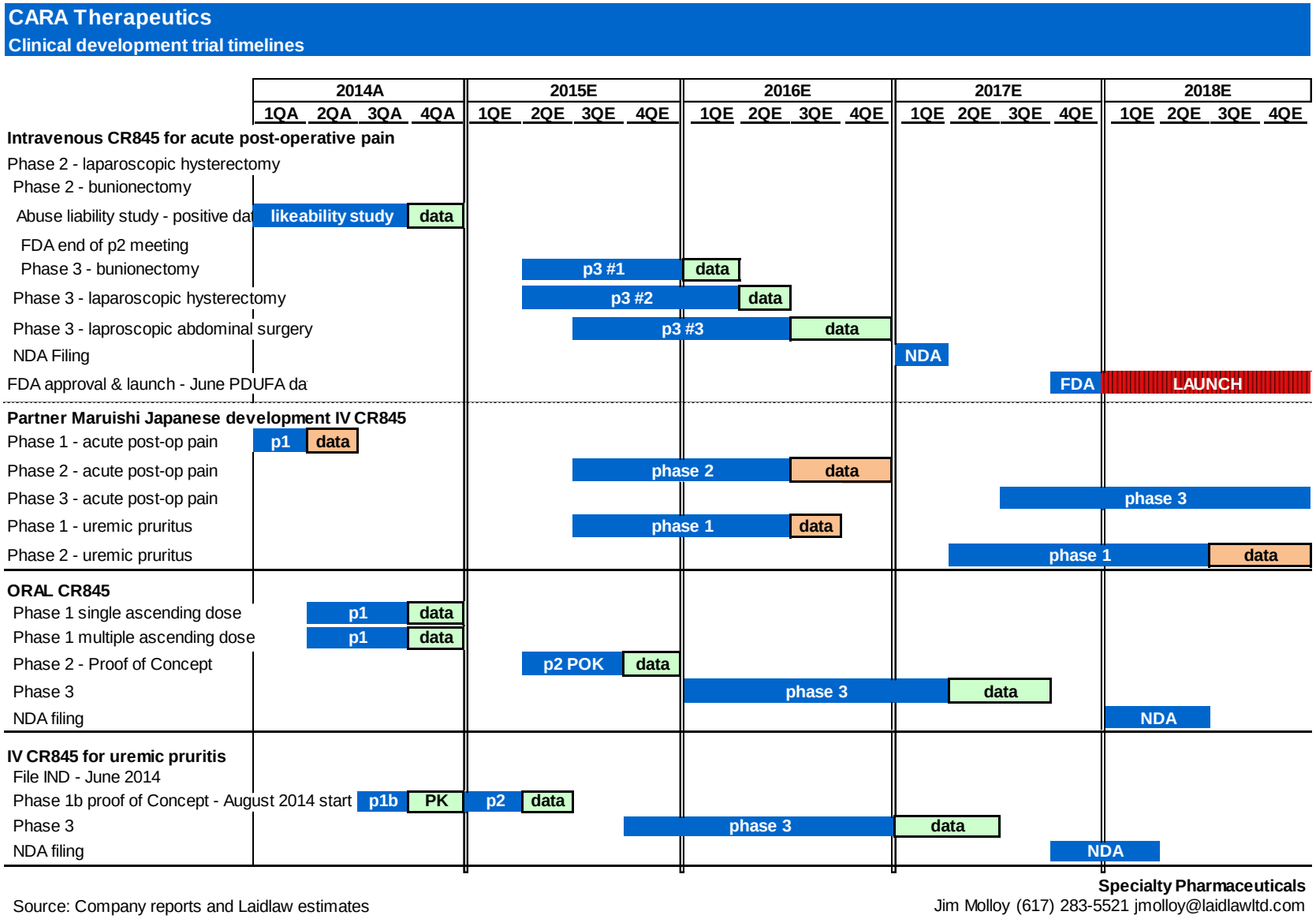
Figure 1: Potential Clinical Trial Timelines



Source: Company reports and Laidlaw estimates

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Source: Company reports; Laidlaw & Company estimates

Figure 2: Quarterly Income Statement

CARA Therapeutics
Quarterly income statement

($000 except per share)	2014A 1QA	2014A 2QA	2014A 3QA	2014A 4QA	2014A Year	2015E 1QE	2015E 2QE	2015E 3QE	2015E 4QE	2015E Year
Revenues										
License & milestones		$302			$302					
Collaborative revenues	$178	658	$1,125	$914	2,875	$1,000	$1,000	$1,000	$1,000	$4,000
Total Revenue	**$178**	**$960**	**$1,125**	**$914**	**$3,177**	**$1,000**	**$1,000**	**$1,000**	**$1,000**	**$4,000**
Expenses:										
Cost of Revenue (COGS)	-	-	-	-	-	-	-	-	-	-
Gross Margin	**178**	**960**	**1,125**	**914**	**3,177**	**1,000**	**1,000**	**1,000**	**1,000**	**4,000**
Research and development	2,201	3,200	6,208	3,459	15,068	7,500	7,500	8,000	8,000	31,000
General and administrative	1,398	1,472	1,250	1,791	6,181	1,750	2,000	2,000	2,250	8,000
Total operating expenses	3,599	4,672	7,458	5,250	21,249	9,250	9,500	10,000	10,250	39,000
Income (loss) from Operations	**(3,421)**	**(3,712)**	**(6,333)**	**(4,336)**	**(18,072)**	**(8,250)**	**(8,500)**	**(9,000)**	**(9,250)**	**(35,000)**
Interest income (expense), net	22	56	26	22	126	25	25	25	25	100
Other (exp) gain, net										
Income (loss) before taxes	**(3,399)**	**(3,656)**	**(6,307)**	**(4,314)**	**(17,946)**	**(8,225)**	**(8,475)**	**(8,975)**	**(9,225)**	**(34,900)**
Income tax exp (benefit)	(16)	(11)	(32)	(142)	(201)					
Net income (Loss)	**(3,383)**	**(3,645)**	**(6,275)**	**(4,172)**	**(17,745)**	**(8,225)**	**(8,475)**	**(8,975)**	**(9,225)**	**(34,900)**
Net income to common										
Earning per Share (EPS)	**($0.22)**	**($0.16)**	**($0.28)**	**($0.18)**	**($0.85)**	**($0.36)**	**($0.29)**	**($0.30)**	**($0.31)**	**($1.25)**
Adj EPS ex-1x & non-cash items										
Weighted avg. shares (000)	15,654	22,608	22,713	22,791	20,966	23,041	29,291	29,541	29,791	27,916
Fully diluted shares (000)	16,551	23,686	23,677	24,038	21,988	25,791	32,041	32,291	32,541	30,666

Source: Company reports and Laidlaw estimates

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Figure 2: Annual Income Statement

CARA Therapeutics
Annual income statement

($000 except per share)	2013A	2014A	2015E	2016E	2017E	2018E	Comments
Revenues							
CR845 - IV version						$96,948	Launch 1Q18
CR845 - oral version						-	2019 launch
License & milestones	$9,637	$302	-	-	-	-	
Collaborative revenues	2,327	2,875	$4,000	$4,000	$4,000	4,000	
Total Revenue	**$11,964**	**$3,177**	**$4,000**	**$4,000**	**$4,000**	**$100,948**	
Expenses:							
Cost of Revenue (COGS)	-	-	-	-	-	14,542	
Gross Margin	**11,964**	**3,177**	**4,000**	**4,000**	**4,000**	**86,406**	
R&D	8,685	15,068	31,000	33,000	34,500	28,500	
G&A	3,516	6,181	8,000	9,000	9,500	26,250	
Total op exp	12,201	21,249	39,000	42,000	44,000	54,750	
Inc/(loss) from Ops	**(237)**	**(18,072)**	**(35,000)**	**(38,000)**	**(40,000)**	**31,656**	
Int income (exp), net	(3,756)	126	100	100	100	100	
Other expenses, net	-	-	-	-	-	-	
Inc/(loss) before taxes	**(3,993)**	**(17,946)**	**(34,900)**	**(37,900)**	**(39,900)**	**31,756**	
Income tax exp (benefit)	(3)	(201)	-	-	-	-	
Net income (Loss)	**($3,990)**	**($17,745)**	**($34,900)**	**($37,900)**	**($39,900)**	**$31,756**	
Net income to common	**($3,072)**						
Earning per Share	**($0.74)**	**($0.85)**	**($1.25)**	**($1.30)**	**($1.30)**	**$0.85**	
Weighted avg. shares (000)	4,133	20,966	27,916	29,166	30,666	32,167	
Fully diluted shares (000)	17,197	21,988	30,666	32,166	34,166	37,167	

Source: Company reports and Laidlaw estimates

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Figure 1: Balance Sheet

CARA Therapeutics
Balance sheet

($000's except per share)	2013A	1Q14A	2Q14A	3Q14A	2014A	2015E	2016E	2017E	2018E
ASSETS:									
Current assets									
Cash and cash equivalents	$12,357	$67,038	$62,812	$58,393	$52,663	$90,532	$55,407	$21,033	$73,641
Income tax receivable	61	46	57	89	200	70	70	70	70
Prepaid expenses and other	2,140	1,142	2,186	928	287	500	750	750	750
Total current assets	**14,558**	**68,226**	**65,055**	**59,410**	**53,150**	**91,102**	**56,227**	**21,853**	**74,461**
PP&E	2,825	2,629	2,439	2,262	2,084	3,500	3,750	4,250	4,750
Restricted cash	700	700	700	700	700	700	700	700	700
Total Assets	**18,083**	**71,555**	**68,194**	**62,372**	**55,934**	**95,302**	**60,677**	**26,803**	**79,911**
LIABILITIES									
Total current liabilities	**5,433**	**5,753**	**5,617**	**6,093**	**3,398**	**7,000**	**7,500**	**10,000**	**30,000**
Total liabilities	**6,572**	**6,827**	**6,626**	**7,037**	**4,272**	**7,874**	**8,374**	**10,874**	**30,874**
Shareholders Equity									
Convertible preferred share	65,586								
Beneficial conversion feature									
Common stock	4	23	23	23	23	23	23	23	23
Additional paid-in-capital	8,377	130,544	131,029	131,341	131,840	202,506	205,281	208,807	210,159
Accumulated deficit	(62,456)	(65,839)	(69,484)	(76,029)	(80,201)	(115,101)	(153,001)	(192,901)	(161,145)
Total shareholders' equity	**11,511**	**64,728**	**61,568**	**55,335**	**51,662**	**87,428**	**52,303**	**15,929**	**49,037**
Total liabilites & net worth	**18,083**	**71,555**	**68,194**	**62,372**	**55,934**	**95,302**	**60,677**	**26,803**	**79,911**

Source: Company reports; Laidlaw & Company estimates

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Figure 2: Cash flow Statement

CARA Therapeutics
Balance sheet

($000's except per share)	2013A	1Q14A	2Q14A	3Q14A	2014A	2015E	2016E	2017E	2018E
ASSETS:									
Current assets									
Cash and cash equivalents	$12,357	$67,038	$62,812	$58,393	$52,663	$90,532	$55,407	$21,033	$73,641
Income tax receivable	61	46	57	89	200	70	70	70	70
Prepaid expenses and other	2,140	1,142	2,186	928	287	500	750	750	750
Total current assets	**14,558**	**68,226**	**65,055**	**59,410**	**53,150**	**91,102**	**56,227**	**21,853**	**74,461**
PP&E	2,825	2,629	2,439	2,262	2,084	3,500	3,750	4,250	4,750
Restricted cash	700	700	700	700	700	700	700	700	700
Total Assets	**18,083**	**71,555**	**68,194**	**62,372**	**55,934**	**95,302**	**60,677**	**26,803**	**79,911**
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Shareholders Equity									
Convertible preferred share	65,586								
Beneficial conversion feature									
Common stock	4	23	23	23	23	23	23	23	23
Additional paid-in-capital	8,377	130,544	131,029	131,341	131,840	202,506	205,281	208,807	210,159
Accumulated deficit	(62,456)	(65,839)	(69,484)	(76,029)	(80,201)	(115,101)	(153,001)	(192,901)	(161,145)
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Source: Company reports and Laidlaw estimates

Source: Company reports; Laidlaw & Company estimates

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DISCLOSURES:

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Additional information available upon request.

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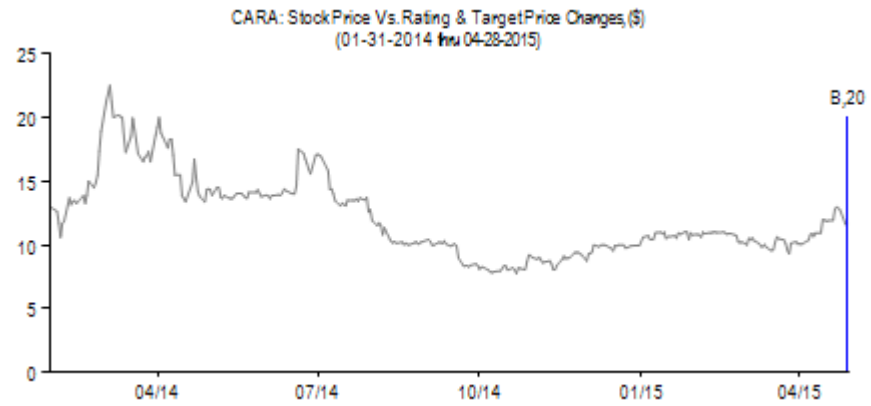
Rating and Price Target Change History



3 Year Rating Change History

Date	Rating	Closing Price ($)
04/28/2015	Buy (B)	11.62*

3 Year Price Change History

Date	Target Price ($)	Closing Price, ($)
04/28/2015	20.00	11.62*

** Previous Close4/27/2015*

Source: Laidlaw & Company **Created by: Blue-Compass.net**

Laidlaw & Company Rating System*		% of Companies Under Coverage With This Rating	% of Companies for which Laidlaw & Company has performed services for in the last 12 months	
			Investment Banking	Brokerage
Strong Buy (SB)	Expected to significantly outperform the sector over 12 months.	0.00%	0.00%	0.00%
Buy (B)	Expected to outperform the sector average over 12 months.	72.00%	32.00%	8.00%
Hold (H)	Expected returns to be in line with the sector average over 12 months.	4.00%	0.00%	0.00%
Sell (S)	Returns expected to significantly underperform the sector average over 12 months.	0.00%	0.00%	0.00%

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NOTES: