Cerulean Pharma (CERU)

Initiating Coverage with an OUTPERFORM Rating and $12 PT: Nanopharmaceuticals Leading the Way to Better Oncology Therapies

- **Cerulean is a clinical-stage biotech developing CRLX101 and CRLX301, nanopharmaceutical formulations of camptothecin and docetaxel.** CRLX101 is in Phase I/II studies in advanced renal cell cancer, platinum-resistant ovarian cancer (both in combination with Avastin) and a neoadjuvant study in rectal cancer (in combination with radiation and capecitabine).
- **CERU's nanopharmaceutical technology takes advantage of the local tumor environment to preferentially target, accumulate and release chemotherapy directly to the tumor cells.** This capability has changed camptothecin from a drug that has been too toxic and difficult to dose to CRLX1010 that has been administered safely to over 200 patients, which compares well to currently approved cancer therapies.
- **CRLX101 in combination with Avastin appears to show a differentiated benefit in the relapsed renal cell carcinoma setting, with a 27% overall response rate (ORR), much better than the typical low-single-digit rate seen with approved therapies in the setting.** CRLX101 could be synergistic with VEGF inhibitors such as Avastin because CRLX101 inhibits hypoxia inducible factor-1α (HIF-1α), a protein that is upregulated in cancer cells in response to VEGF inhibition, and appears to cause resistance to the drug in tumor cells.
- **Similarly, CRLX101 as monotherapy generated a 14% ORR in platinum-resistant ovarian cancer patients, better than the 3% ORR topotecan (an approved camptothecin derivative) achieved in this setting.**
- **CRLX101 could have a relatively fast route to approval in neoadjuvant rectal cancer; if it can demonstrate improvements in the pathologic complete response rate, it could be a commercial product by late 2017.**
- **Initiating coverage with an OUTPERFORM rating and $12 price target.** Our $12 price target is derived from applying a 6 multiple to estimated 2020 sales of CRLX101, discounted back by 35%. We estimate approval in the renal cell carcinoma and ovarian cancer settings in the late 2018/early 2019 timeframe, and approval in rectal cancer in late 2017.

FYE Dec	2013A	2014E			2015E		
REV	ACTUAL	CURR.	PREV.	CONS.	CURR.	PREV.	CONS.
Q1 Mar	0.0A	0.0E		N/AE	0.0E		N/AE
Q2 Jun	0.0A	0.0E		N/AE	0.0E		N/AE
Q3 Sep	0.0A	0.0E		N/AE	0.0E		N/AE
Q4 Dec	0.0A	0.0E		N/AE	0.0E		N/AE
Year*	**0.0A**	**0.0E**		**N/AE**	**0.0E**		**N/AE**
Change	--	-100%			--		
	2013A	**2014E**			**2015E**		
EPS	**ACTUAL**	**CURR.**	**PREV.**	**CONS.**	**CURR.**	**PREV.**	**CONS.**
Q1 Mar	$0.00A	($0.21)E		--	($0.28)E		--
Q2 Jun	$0.00A	($0.30)E		--	($0.43)E		--
Q3 Sep	($0.96)A	($0.13)E		--	($0.45)E		--
Q4 Dec	($0.24)A	($0.18)E		--	($0.48)E		--
Year*	**($1.20)A**	**($0.82)E**		**--**	**($1.65)E**		**--**
P/E	--	--			--		
Change	--	31%			-100%		

Consensus estimates are from Thomson First Call.
** Numbers may not add up due to rounding.*

May 5, 2014

Price
$6.75

Rating
OUTPERFORM

12-Month Price Target
$12.00

David M. Nierengarten, Ph.D.
(415) 274-6862
david.nierengarten@wedbush.com

Gregory R. Wade, Ph.D.
(415) 274-6863
greg.wade@wedbush.com

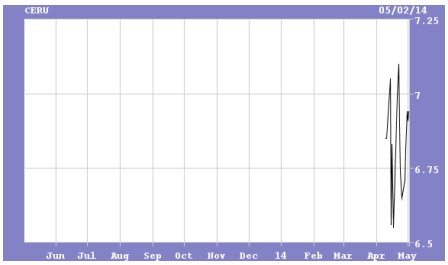
Christopher N. Marai, Ph.D.
(415) 274-6861
christopher.marai@wedbush.com

Company Information

Shares Outst (M)	20.3
Market Cap (M)	$137
52-Wk Range	$6.10 - $8.06
Book Value/sh	$-0.89
Cash/sh	$0.00
Enterprise Value (M)	$143.9
LT Debt/Cap %	-0.3
Cash Burn (M)	$14.8

Company Description

CERU is developing tumor-targeted nanopharmaceutical drug candidates for the treatment of cancer. The company's lead product candidate is CRLX101, a nanopharmaceutical of camptothecin in Phase II trials in multiple cancer indications.



Source: Thomson Reuters

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Investment Thesis

Cerulean Pharma (NASDAQ:CERU) is focused on developing dynamically tumor-targeted nanopharmaceuticals for the treatment of cancer. The company's lead product candidate, CRLX101, is a nanopharmaceutical formulation of camptothecin in Phase II development for multiple cancers, including renal cell carcinoma and ovarian cancer, and in the Phase I/II stage for neoadjuvant rectal cancer. CRLX101 is being developed as an add-on therapy in these lead indications, due to the synergistic effect the dual topoisomerase I and hypoxia inducible factor inhibitor has with VEGF inhibitors and radiotherapy. The company is also developing CRLX301, a nanopharmaceutical formulation of docetaxel that is expected to enter the clinic by the end of 2014.

Valuation

Our $12 price target is derived from applying a 6 multiple to 2020 sales of CRLX101 in the relapsed renal cell carcinoma (RCC), platinum-resistant ovarian cancer settings, and neoadjuvant rectal cancer settings, all discounted back by 35%. We estimate approval in the RCC and ovarian cancer settings in the late 2018/early 2019 timeframe, and approval in rectal cancer in late 2017. Our valuation does not take into account sales for CRLX101 in additional indications or for CRLX301, which would represent upsides to our target.

Risks

Risks to the achievement of our price target include failure to gain approval for CRLX101 in the ovarian, renal cell carcinoma and neoadjuvant rectal cancer settings, failure to achieve sales estimates for CRLX101 and failure to achieve earnings estimates.

Key points

- Cerulean (CERU) is developing nanopharmaceuticals that preferentially target tumor tissue and deliver chemotherapeutics over an extended time, allowing for safely increasing the effective dose and duration of the chemotherapy.
- Its lead product candidate, CRLX101, is a nanoparticle formulation of camptothecin that avoids the toxicity that prevented the agent from previously gaining approval (indeed, it appears to have a better safety profile than the approved camptothecin analogs, irinotecan and topotecan). CRLX101 has shown signs of efficacy in multiple cancer types, and appears that it could be synergistic with Avastin.
- CRLX101 also appears to inhibit hypoxia inducible factor-1α (HIF-1α), and could make it ideal for combining angiogenesis inhibitors and radiotherapy, both of which are known to up-regulate HIF-1α.
- While CRLX101 did not show a benefit compared to best supportive care in non-small-cell lung cancer patients in a Phase II trial, we believe that this failure is more a reflection of the challenging trial design than of CRLX101's efficacy profile, and think investors would be wise to focus instead on the safety and evidence of activity CRLX101 demonstrated in the study.
- CRLX101 in combination with Avastin appears to show a differentiated benefit in the relapsed renal cell carcinoma setting. In the ongoing Phase I/II study, the combination has demonstrated a 27% ORR rate, much better than the typical low-single-digit rate seen with approved therapies in the setting.
- In platinum-resistant ovarian cancer, CRLX101 monotherapy has generated a 14% ORR rate in an ongoing Phase II study, comparing favorably to the approved agent, topotecan (a camptothecin derivative), which achieved only a 3% ORR in the setting.
- In the relatively large rectal cancer market CRLX101 offers the potential to improve the success of neoadjuvant therapy (in combination with radiation and capecitabine), which can have a dramatic clinical and quality-of-life impact. We believe the quick time to data in the setting and potential accelerated approval based on surrogate endpoints can lead to sales by late 2017.
- CRLX301, the company's nanopharmaceutical formulation of docetaxel, has outperformed Taxotere (annual sales of >$1B prior to generic competition) in survival and inhibiting tumor growth in all preclinical animal tumor models tested. Although still early, we believe the preclinical data CRLX301 has generated is further validation of the company's nanoparticle platform.
- With a ~$70M enterprise value, and multiple near-term catalysts, we view CERU shares as having a favorable risk/reward profile. The company has developed a clinical program centered on CRLX101 in multiple indications with a high unmet need, and has a versatile platform that can deliver (and improve the therapeutic profile of) multiple drugs and therapeutic categories.

Cerulean Pharma Inc. Overview

Cerulean Pharma is based in Cambridge, Mass. and is focused on using its dynamic tumor targeted nanopharmaceutical platform to develop products for the treatment of cancer. Its lead product is in the Phase II stage to treat relapsed renal cell carcinoma, platinum-resistant ovarian cancer, gastric cancer and small cell lung cancer, and is in the Phase I/II stage to treat pre-operative rectal cancer. The company also has CRLX301, set to enter the clinic for solid tumors by year end.

Upcoming milestones

Mid:14	Updated data from initial monotherapy stage of Phase II trial of CRLX101 in ovarian cancer patients
H2:14	Completion of Phase Ib study of CRLX101 in combination with Xeloda plus radiation in neoadjuvant rectal cancer
H2:14	Initiation of randomized Phase II trial of CRLX101 in combination with Avastin in relapsed renal cell carcinoma
YE:14	Initiation of Phase I study of CRLX301 in advanced cancers
YE:14	Potential data from Phase II trial of CRLX101 in combination with Avastin in platinum refractory ovarian cancer
YE:14/Q1:15	Potential data from Phase I/II trial of CRLX101 in combination with chemoradiation in neoadjuvant rectal cancer
H1:15	Initiation of randomized Phase II trial of CRLX101 in combination with chemoradiation in neoadjuvant rectal cancer
Q1:15	Potential start of pivotal trial of CRLX101 in combination with Avastin in relapsed, platinum refractory ovarian cancer
YE:15	Potential data from Phase II trial of CRLX101 in combination with chemoradiation in neoadjuvant rectal cancer
YE:15	Potential data from Phase II trial of CRLX101 in combination with Avastin in relapsed clear cell renal cell carcinoma

Figure 1: Product Development Table

Product	Indication	Stage of Development
CRLX101	≥3rd line renal cell carcinoma (in combination with Avastin)	Phase II (start H2:14)
	≥2nd line platinum-resistant ovarian cancer (in combination with Avastin)	Phase II
	Neoadjuvant rectal cancer (in combination with Xeloda and radiotherapy)	Phase Ib/II
	Small-cell lung cancer	Phase II (investigator sponsored)
	HER-2 negative Gastric Cancer	Phase II (investigator sponsored)
CRLX301	Advanced solid tumors	Phase I (starting late 2014)

Source: Company data, Wedbush Securities

Nanopharmaceuticals

Nanopharmaceuticals are drug formulations consisting of particles whose size are in the nanoscale range (typically 1 to 100 nm). At this scale, drug particles adopt unique physical and biochemical properties which can enable improvements in drug delivery, pharmacokinetics, safety and receptor targeting. Because of their small size, nanoparticles can more readily penetrate cell membranes and are retained longer within cells, a characteristic referred to as the enhanced permeability and retention (EPR) effect. The high surface area-to-volume ratio for nanodrugs results in increased catalytic activity and solubility, and also enables the nanoparticles to carry relatively larger therapeutic payloads for increased drug volume per dosage unit. Since nanoparticles are also similar in size to antibodies and receptors, they can be readily linked to these molecules for enhanced targeting, which reduces nonspecific toxicity. The largest advancements for nanodrugs have been in the field of oncology, with the most notable successes so far being the approval of Doxil and Abraxane.

Figure 2: Select Nanopharmaceuticals Approved or in Development for Solid Tumors

Product	Composition	Company	Indication	Status
Doxil	Pegylated liposomal formulation of doxorubicin	JNJ	Multiple cancers	Approved (1995)
DaunoXome	Liposomal encapsulation of daunorubicin	Galen Ltd.	HIV-associated Kaposi's sarcoma	Approved (1996)
Abraxane	Albumin-bound paclitaxel	Celgene	Various solid tumors	Approved (2005)
MM-398	Liposome encapsulation of irinotecan	Merrimack	Pancreatic cancer and others	Phase III
NK-105	Polymeric nanoparticle containing paclitaxel	Nippon Kayaku	Breast cancer and stomach cancer	Phase III
NKTR-102	Pegylated conjugate of irinotecan	Nektar	Breast cancer and others	Phase III
Thermodox	Liposomal encapsulation of doxorubicin	Celsion	Liver, breast and pancreatic cancer	Phase III
BIND-014	Polymeric nanoparticle containing docetaxel	BIND	Prostate cancer and NSCLC	Phase II
CPX-1	Liposomal irinotecan	Celator	Colorectal cancer	Phase II
NC-6004	Polymeric nanoparticle formulation of cisplatin	NanoCarrier	Pancreatic cancer and NSCLC	Phase II
NK-012	Polymeric micelle of irinotecan	Nippon Kayaku	Breast cancer	Phase II
SP1049C	glycoprotein of doxorubicin	Supratek	Various solid tumors	Phase II
ALN-VSP	Lipid nanoparticle formulation of siRNA	Alnylam	Liver cancer	Phase I
NKTR-105	Pegylated conjugate of docetaxel	Nektar	Solid tumors	Phase I

Source: Wedbush Securities

Doxil (doxorubicin) was the first nanopharmaceutical approved by the FDA. Doxorubicin was one of the earliest anthracyclines discovered, but its use was limited due to its high cardiotoxicity. Doxil, which encapsulates doxorubicin within a liposome coated with polyethylene glycol (PEG), reduced this toxicity by altering the pharmacokinetics of doxorubicin, releasing it gradually from the liposomes. Similar safety concerns also limited the use of paclitaxel, which is insoluble and had to be delivered in a solvent (castor oil) that was associated with a number of adverse events. Abraxane is an alternative formulation of paclitaxel that lacks the toxic solvent of the original formulation as it uses albumin, a common blood protein, in nanoparticles to stabilize the drug.

The success of Doxil and Abraxane point to the promising approach of using nanopharmaceuticals to modify the way existing drugs are delivered and metabolized. This approach not only takes advantage of previously established clinical data, but can offer a shorter regulatory pathway via the 505(b)(2) standard. Both doxorubicin and paclitaxel lost patent-protection when they were reformulated and both were approved under the 505(b)(2) guidelines. Once approved, nanopharmaceuticals also have the benefit of stronger protection from generics due to the greater challenge in proving bioequivalence. For typical small molecules, bioequivalence for a generic is demonstrated by having similar pharmacokinetic measurements (including mean area under the plasma concentration curve and the maximum plasma concentration) to the branded drug. However for nanopharmaceuticals, the EPR effect and specific tissue targeting involved results in greater barriers to establishing bioequivalency. This barrier contributed to the near four-year delay of a generic competitor to Doxil following its patent expiration in 2009.

We believe CRLX301 could be approved under the 505(b)(2) pathway since the active ingredient, docetaxel, has already been approved in multiple cancer settings. CRLX101, however, will have to go through the traditional NDA process since camptothecin was never approved.

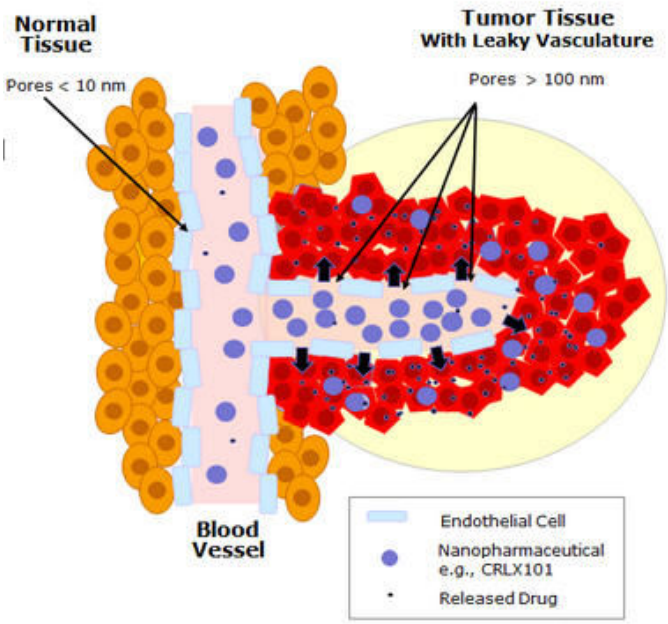
Cerulean's Platform

CERU has a proprietary dynamic tumor-targeting platform that generates polymer-based, covalently-bound nanoparticles that can accommodate small molecule anti-cancer payloads. The payload is connected by a glycine linker to linear cyclodextrin polymer, which consists of alternating subunits of cyclodextrin and polyethylene glycol (which contributes to avoiding clearance by the immune system). The polymer strands self-assemble into a nanoparticle of about 20 to 40nm in diameter, comprised of about five strands per nanoparticle. The nanoparticles are designed to be too large to enter into normal tissue, but small enough to be able to enter through the larger pores of porous tumor blood vessels, which have less densely lined endothelial cells (Fig. 3). From the tumor tissue the nanoparticles are transported into the tumor cells, and remain there as they are too large to be shuttled out by the tumor cell's efflux pumps. Coupled with reduced drainage from the tumor tissue, this gives the delivered drug molecules prolonged exposure within the tumor.

The nanopharmaceutical is designed to gradually release its therapeutic payload over time, with the glycine linker that attaches the payload to the particle's polymer backbone providing more continuous intra-tumor drug release. The covalent linker connection is cleaved primarily through hydrolysis, and the lower pH level in tumors (as compared to the bloodstream) slows the cleaving process and prolongs the release of the therapeutic payload. Once the cytotoxic payload is released, the nanoparticle backbone degrades into

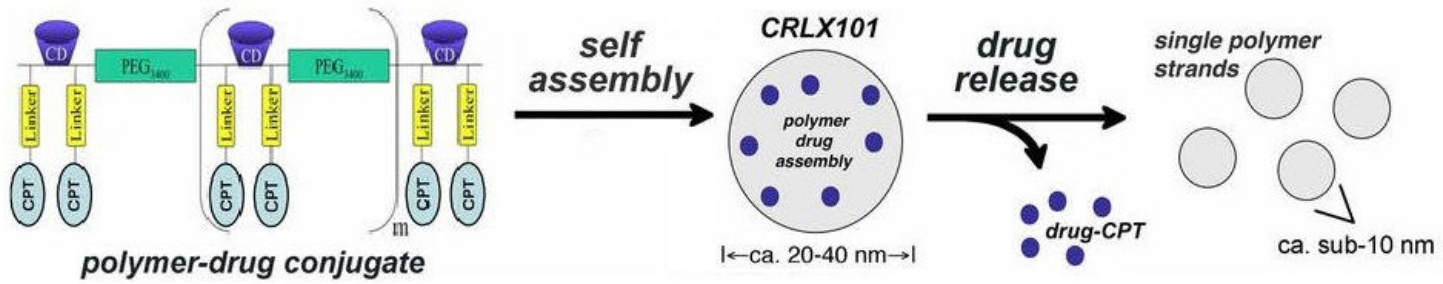
its component polymer strands, which are small enough to be excreted by the kidneys (Fig. 4). The presence of the linker separates CERU's products from other nanopharmaceuticals that deliver the drug in a polymer coating or inside a lipid capsule. By tailoring the chemistry of the linkers CERU is able to modulate the cleavage rate for optimal drug release.

Figure 3: Nanopharmaceutical Tumor Targeting



Source: Company data

Figure 4: Structure of CRLX101 and Schematic Diagram of Assembly and Disassembly



Source: Eliasof et al. *PNAS.*

CERU holds exclusive licenses from Calando Pharmaceuticals and the California Institute of Technology to IP covering cyclodextrin polymer (CDP) nanopharmaceutical technology and CDP-based product candidates, including CRLX101 and CRLX301. CERU also holds exclusive licenses from State University of New York to taxane-containing nanopharmaceuticals, such as CRLX301. Calando is eligible to receive $32.8M in milestones related to CRLX101 and ~$18M in milestones for CRLX301, in addition to low- to mid-single-digit royalties on worldwide sales for each candidate.

CERU also holds exclusive licenses from MIT to polymeric nanopharmaceutical (PNP) technology, which applies to the transport of large molecules (60 to 100nm in diameter) such as RNA. The company has conducted proof-of-concept studies that confirmed the platform can generate nanopharmaceuticals that can deliver RNA molecules like siRNA and mRNA which are metabolically unstable and have poor tumor uptake. The platform could also have applications in other indications, such as inflammation, where blood vessel leakiness occurs. With CERU focused on nanopharmaceuticals containing small molecule drug candidates for cancer, we expect the company to seek partners for any potential opportunities outside this area, including large molecule delivery or inflammatory applications.

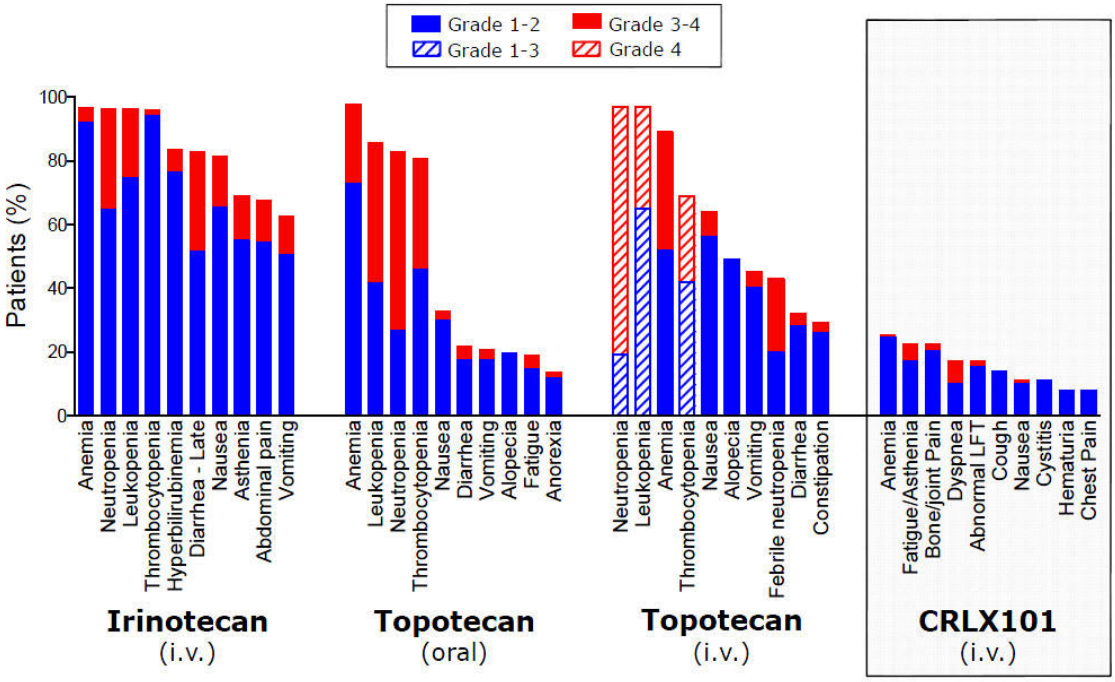
Since CRLX101 and CRLX301 are analogs, CERU is able to utilize a common supply chain and manufacturers for both programs. Manufacturing for the product candidates has been contracted out to cGMP-compliant third parties, and sufficient quantities of CRLX101 are currently available to support clinical testing through H1:15 (manufacturing of CRLX301 to support the Phase I/IIa trial is currently underway). The drug supply is set to be expanded this year and CERU management expects the current contract manufacturers to be capable of eventually producing commercial-level quantities.

CRLX101

CRLX101 is a nanopharmaceutical comprised of camptothecin covalently conjugated to a highly soluble cyclodextrin polymer that is administered intravenously. The plant alkaloid camptothecin inhibits topoisomerase I, an enzyme required for DNA replication and transcription that is essential for tumor cell growth. Camptothecin was one of the earliest chemotherapeutic agents discovered, but poor solubility and toxicity concerns prevented it from advancing to late-stage trials. Two less potent semisynthetic derivatives, irinotecan (Camptosar) and topotecan (Hycamtin), were later developed with reduced toxicity. In the 1990s, these two analogs received FDA approval for use against various solid tumors.

The toxicity of camptothecin was later attributed to the rapid conversion in human plasma of camptothecin from its active form to its inactive and toxic carboxylate form. The cyclodextrin polymer in CRLX101 prevents this rapid conversion by protecting the active camptothecin form from metabolism in the plasma, with the active form released only after delivery into the tumor cells. Patient data indicates that this targeted delivery gives CRLX101 a safety profile superior to that of the approved camptothecin derivatives. Supporting the improved safety profile, low systemic distribution of CRLX101, which has a volume of distribution ~2.4 liters compared to ~263 liters for Camptosar and ~130 liters for Hycamtin, indicating restricted distribution, limits exposure to healthy tissues. In addition, the slow cleaving process for the covalent linker creates a sustained camptothecin release resulting in durable drug exposure, with CRLX101 having a terminal half-life of ~28 hours compared to 2-3 hours for topotecan.

Figure 5: Safety Profile of CRLX101 versus Camptothecin Derivatives



* The label for IV topotecan categorizes non-hematological AEs as (a) grade 1-2 and (b) grade 3-4, but it categorizes hematological AEs as (a) grade 1-3 and (b) grade 4, so these AEs are shown with diagonal stripes.

Source: Company data

CRLX101 has been evaluated in over 200 patients, with little significant toxicity attributed to the drug. In addition to the Phase II trial in ovarian cancer and Phase I/II trials in RCC and rectal cancer, CRLX101 is also currently being evaluated as a single agent in two investigator-sponsored Phase II trials in small-cell lung cancer and HER-2 negative gastric cancer. The SCLC study is comparing CRLX101 to topotecan, the only approved second-line SCLC therapy. The gastric cancer study is a single-arm trial seeking to

establish the differentiated targeting of the nanodrug between tumor and adjacent healthy tissue. Biopsies collected 1-2 days post-treatment from an initial group of patients from the gastric cancer trial confirmed the targeted delivery of CRLX101, with camptothecin being predominantly present in tumor tissue, while only limited amounts of the drug were found in adjacent healthy tissue.

Prior Clinical Studies

An open-label, single-arm, dose-escalation Phase I/IIa trial in 62 heavily pre-treated (average 3.5 prior regimens) patients with advanced sold tumors was conducted from 2006 to 2011, with CERU taking over the study during the Phase I portion in 2009 from Calando. The Phase I portion established a MTD of 15 mg/m^2 for CRLX101 administered intravenously every two weeks, with toxicities at this dose being generally low-grade and reversible. The Phase II portion confirmed the sustained release (Tmax of 17.7-24.5 hours), long half-life (28 hours), slow clearance (91mL/hr) and low volume of distribution (2.4L) of CRLX101. The median PFS was 3.7 months, and the best overall response was stable disease in 64% (28/44) of patients treated at MTD. CRLX101 appeared to generate better results in a subset (n=22) of patients with NSCLC, with a median PFS of 4.4 months and 73% having stable disease.

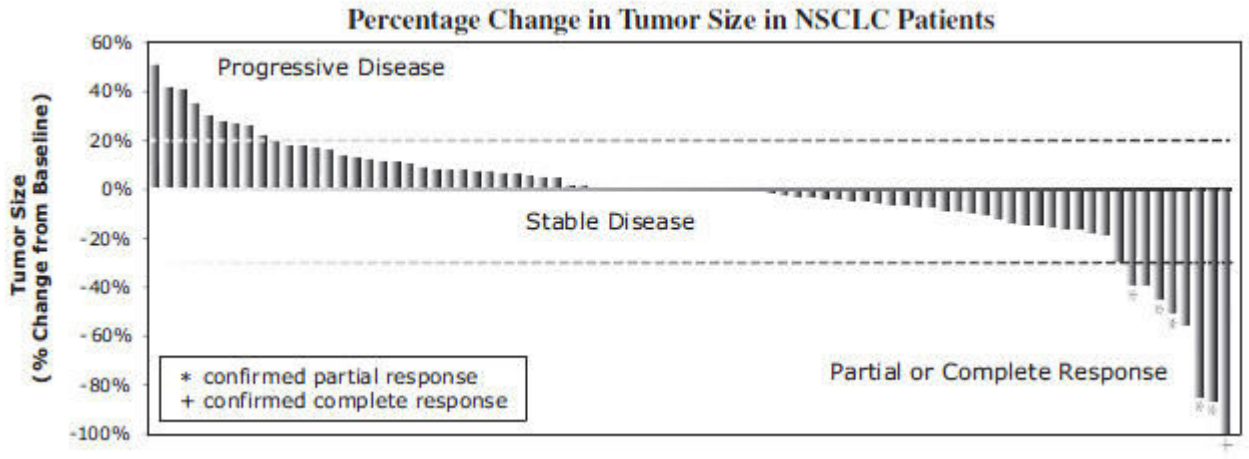
Phase II Trial in NSCLC

Based on the sensitivity of NSCLC tumors to topoisomerase I inhibitors, and the promising results seen in the NSCLC subset in the Phase I/IIa trial, CERU initiated a Phase II trial in the indication. In the trial, CRLX101 failed to meet the primary endpoint of improved overall survival (OS) compared to best supportive care (BSC). However, our view is that the outcome largely reflects the difficulty of conducting a trial of this design. The open-label trial enrolled 157 patients with second or third—line NSCLC in sites in Russia and Ukraine, with patients randomized 2:1 to single-agent CRLX101 (n=100) or BSC (n=57). Median OS for CRLX101 patients was 6.3 months, which is comparable to that of approved second- and third-line NSCLC agents, while median OS for patients in the BSC arm was 11.9 months. The latter figure was more than double that of previously established BSC benchmarks of 4.6-5.1 months, and higher than the median OS for approved, efficacious second- and third-line NSCLC agents such as Iressa (5.6 months), Tarceva (6.7 months) and docetaxel (7.5 months).

A post-trial analysis concluded that elements in the trial design helped skew survival in the BSC arm upwards. The open-label protocol resulted in selective patient withdrawal, with 16% of BSC patients vs. 5% of CRLX101 patients withdrawing prior to the completion of the first four-week treatment cycle. The patients who withdrew from the BSC arm had more rapid disease progression compared to the remaining patients in the arm, based on prognostic factors like time since initial diagnosis (323 vs. 480 days), time since relapse (25 vs. 81 days) and percentage of males (89% vs. 65%), who tend to have poorer survival than women. A time to treatment failure (TTF) analysis confirmed the impact of selective withdrawal, since median TTF for BSC was 1.7 months vs. 2.1 months for CRLX101 patients. Patients in the study also had access to post-treatment therapy, with 40% of BSC patients receiving post-trial treatment versus 28% of CRLX101 patients.

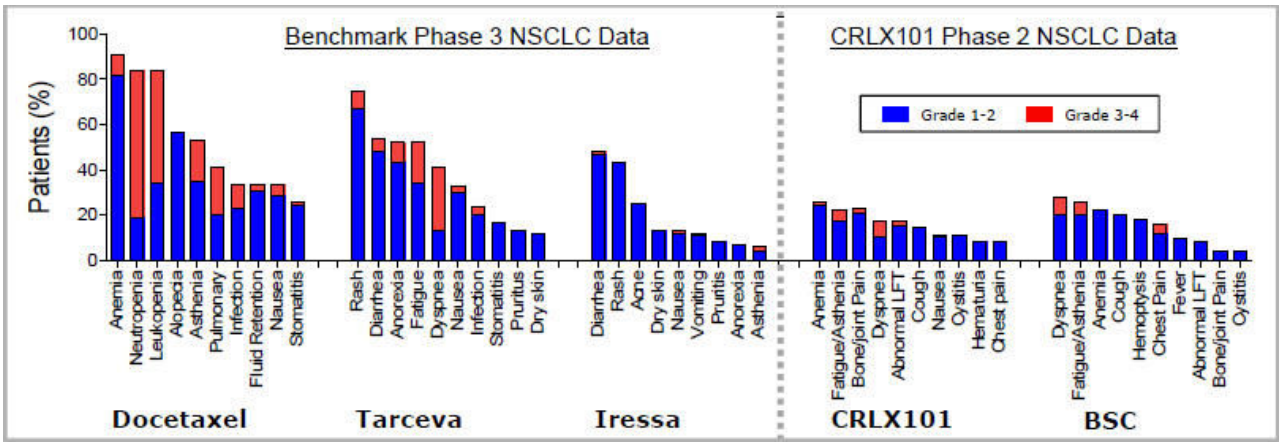
Despite not meeting the endpoint, CRLX101 demonstrated evidence of activity as measured by response (RECIST) criteria. Of the 81 NSCLC patients in the CRLX101 arm who received a CT scan following treatment, 89% achieved disease control and 43% achieved tumor shrinkage, including one complete response and five partial responses (Fig. 6). Patients receiving CRLX101 also had a comparable rate of adverse events to control, and the rates were significantly fewer than that associated with approved NSCLC agents (Fig. 7).

Figure 6: CRLX101 Activity in Refractory NSCLC Patients



Source: Company data

Figure 7: Safety Profile of CRLX101 in Refractory NSCLC compared to Best Supportive Care and Approved Agents

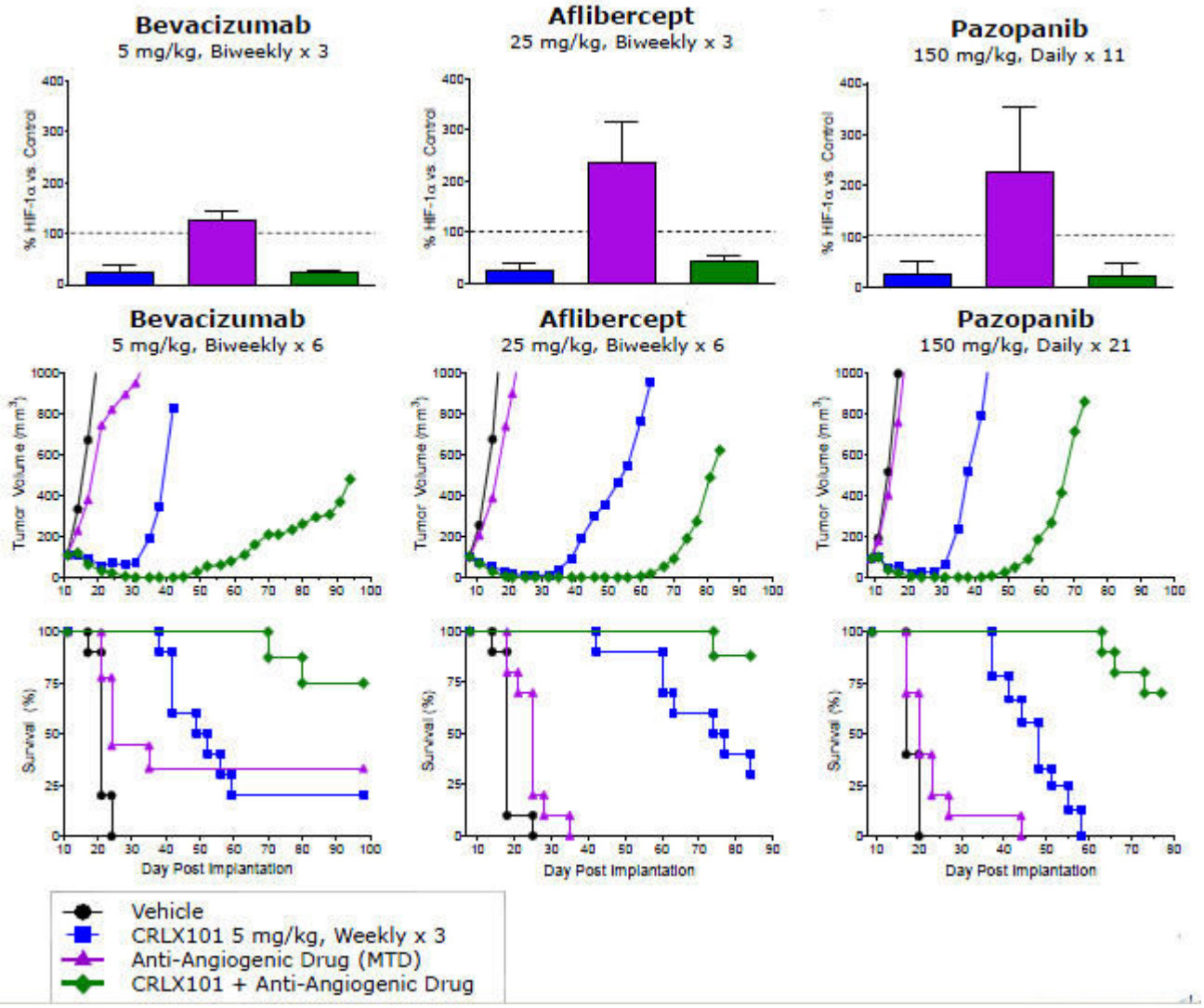


Source: Company data

Hypoxia Inducible Factor Inhibition

Following the results of the NSCLC trial, CERU concluded that CRLX101 was likely to show greater success as part of combination therapy and in settings requiring hypoxia inducible factor (HIF)-1α inhibition. HIF-1α is a protein activated by low oxygen levels, which is implicated in the promotion of tumor angiogenesis and metastasis. HIF-1α mediates resistance to anti-angiogenic therapy, since the latter induces hypoxia which concomitantly up-regulates HIF-1α. Camptothecin is an inhibitor of HIF-1α, but for durable inhibition to be maintained a metronomic dosing schedule of continuous low-dose camptothecin is required. The gradual, prolonged camptothecin release provided by the CERU's nanopharmaceutical platform makes CRLX101 the only durable HIF-1α inhibitor available, either commercially or in advanced clinical development. Research conducted by CERU confirmed that CRLX101 inhibited HIF-1α across multiple xenograft tumor models, and that the drug had a synergistic effect when combined with the anti-angiogenesis inhibitors Avastin (bevacizumab), Votrient (pazopanib) or Zaltrap (aflibercept). The combination therapy produced tumor growth inhibition and longer survival in animals, while counteracting the increased HIF-1α expression caused by the anti-angiogenics (Fig. 8). Irinotecan and topotecan also inhibit HIF-1α, but the effect is transient under a clinical dosing regimen, and metronomic dosing of the two agents results in unacceptable toxicity.

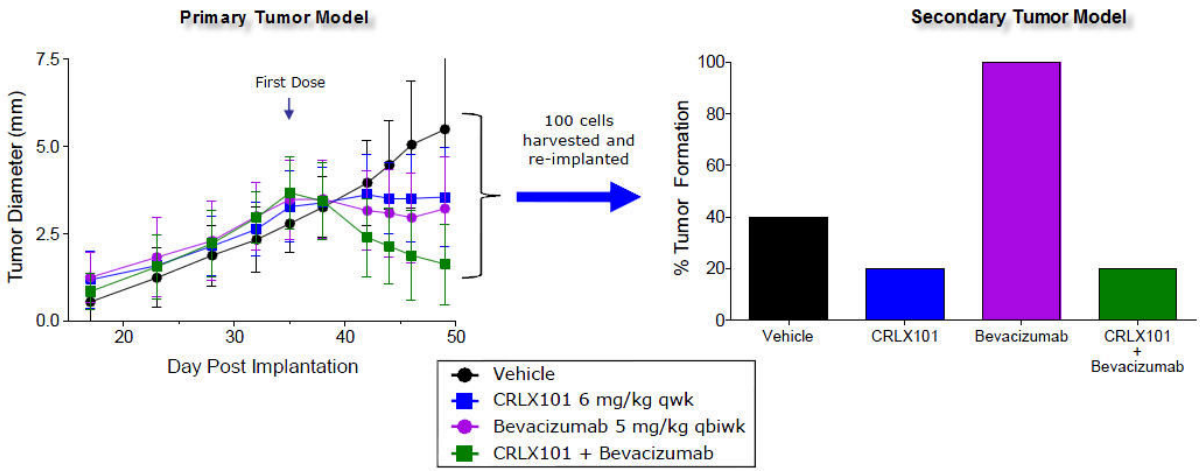
Figure 8: Single-Agent and Combination Effect of CRLX101 and Anti-angiogenics in Ovarian Xenograft Model



Source: Company data

The up-regulation of HIF-1α also triggers cancer stem cell formation, which regrows tumors that are more aggressive. In a preclinical study, tumor cells were taken from the tumors of nude mice that were treated with CRLX101 and Avastin and implanted into a new group of untreated healthy mice. At 90 days, the mice in the second group that received cells from the primary group treated with single-agent Avastin had the highest rate of tumor formation, indicating that Avastin treatment induced cancer stem cell growth. Mice in the secondary group that received the combination of CRLX101 with Avastin had a reduced rate of tumor formation, indicating that CRLX101 in combination prevented the Avastin-induced rise in cancer stem cells.

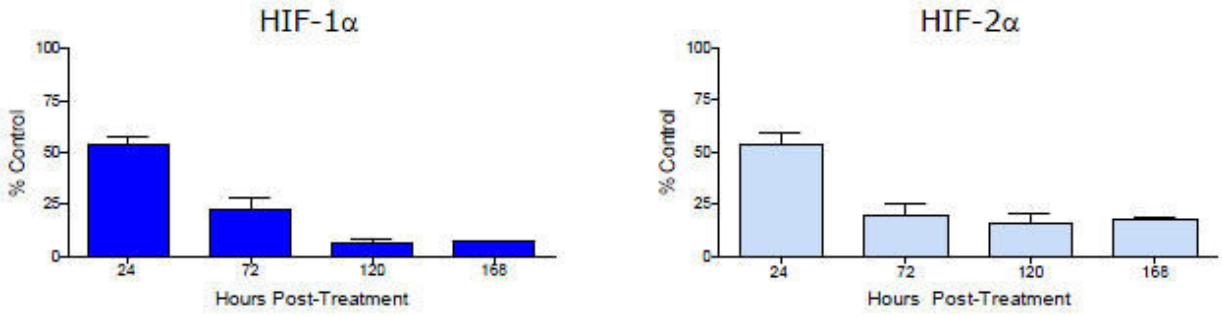
Figure 9: Inhibition of Avastin-Induced Cancer Stem Cell Growth in Xenograft Tumor Model



Source: Company data

In addition to HIF-1α, the closely related HIF-2α isoform was also inhibited by CRLX101. In a one week study in nude mouse xenograft tumor models, a single 6 mg/kg dose durably reduced HIF-1α by over 90% and HIF-2α by ~80% in tumor tissue compared to control.

Figure 10: HIF Expression in Xenograft Tumors After CRLX Treatment



Source: Company data

Renal Cell Carcinoma

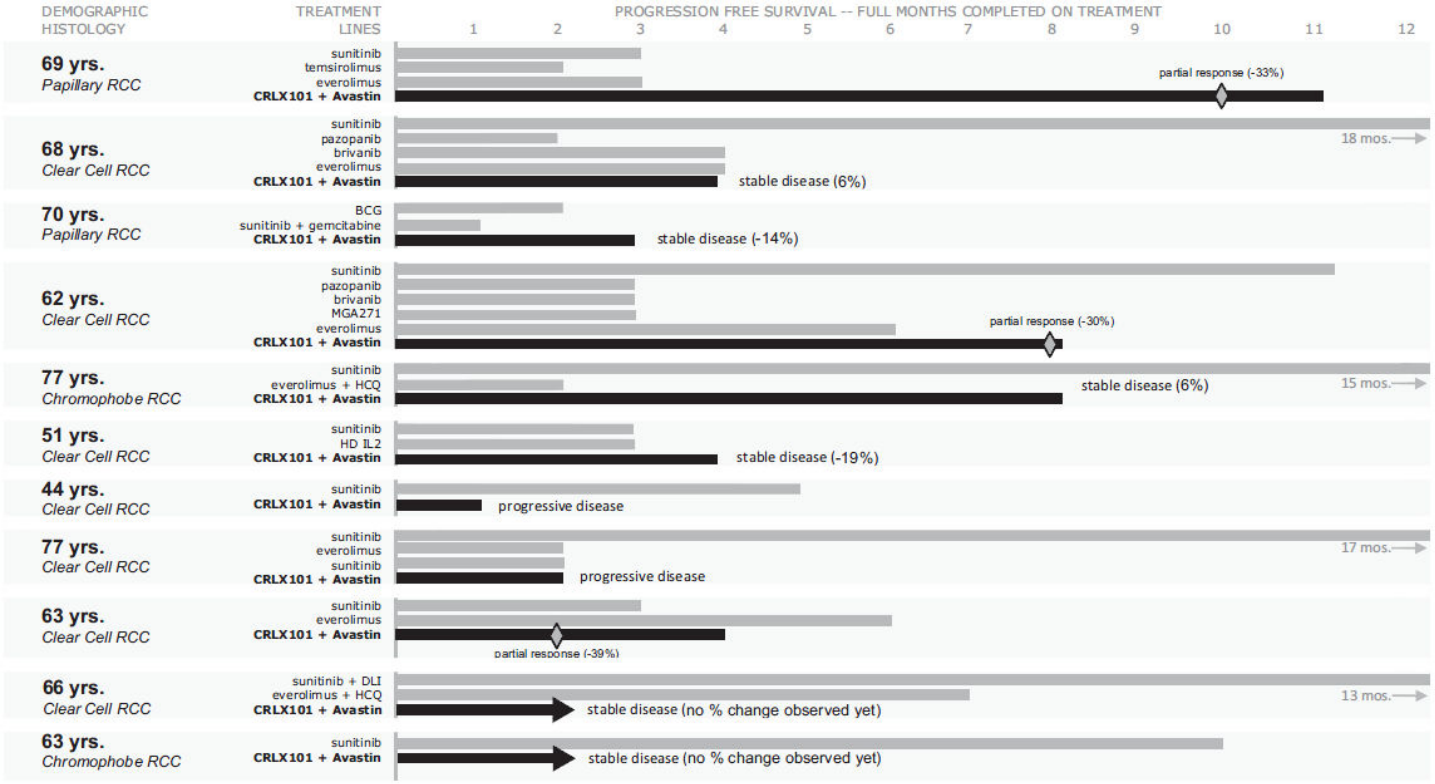
A form of cancer known for elevated levels of HIF factors is clear cell renal cell carcinoma, which is the most common subtype of RCC and accounts for ~85% of all cases. Clear cell RCC is characterized by mutations in the *VHL* tumor suppressor gene, which results in the intracytoplasmic accumulation of lipids that give the cytoplasm a clear appearance. The VHL complex normally targets HIF, but when *VHL* is mutated this leads to the accumulation of HIF-1a, HIF-2a and downstream proteins like VEGF. As a result, angiogenesis is an important early factor in the disease progression of RCC. Since the VEGF inhibitor Avastin is approved for the treatment of metastatic RCC, and CRLX101 has been shown to inhibit HIF (which drives Avastin resistance), the combination of the two agents is expected to provide a synergistic benefit in RCC, similar to that observed in preclinical testing. Avastin offers benefits over other VEGF inhibitors for combinability with CRLX101 since its side effect profile does not overlap and both drugs have a biweekly dosing schedule.

Clinical Program

An open-label investigator-sponsored Phase Ib/II trial of CRLX101 in combination with Avastin is currently being conducted in 22 RCC patients who have failed at least one prior molecularly targeted therapy. Patients in the study are administered treatment every two weeks, which consists of 12 or 15 mg/m^2 of IV CRLX101 and standard Avastin dosing of 10 mg/kg. The primary endpoint of the Phase Ib portion is to determine MTD, and primary endpoint of the Phase II portion is PFS at four months in a majority of the patients. The

combination appears to show a differentiated benefit, with three (27%) of the first 11 evaluable patients having partial responses (Fig. 11), a rate far higher than the low-single digit rate typically seen in RCC patients who have failed TKI treatment (Fig. 12).

Figure 11: Differentiated Benefit of CRLX101 with Avastin in Relapsed RCC



Source: Company data

In H2:14 CERU plans to begin a 1:1 randomized Phase II trial in advanced RCC patients assessing the combination of CRLX101 and Avastin to investigator's choice. The study will evaluate the combination of 15 mg/m^2 of CRLX101 and 10 mg/kg of Avastin in 80-120 third line RCC patients who have failed both VEGF inhibitors and mTOR inhibitors. The primary endpoints are ORR and PFS, and the study is 80% powered to detect a two-month improvement in median PFS. Data from the study is expected by end of 2015.

Market

There were an estimated 65,000 new cases of kidney cancer in the US, and RCC is the most common form, accounting for ~90% of kidney cancer cases. Although there are treatments approved for metastatic RCC, the majority of patients relapse eventually. Approved small molecule RCC treatments come from two mechanistic classes: tyrosine kinase inhibitors (TKI), including sunitinib (Sutent), Votrient, axitinib (Inlyta) and sorafenib (Nexavar); and mTOR inhibitors (mTORi), including everolimus (Afinitor) and temsirolimus (Torisel). Protein therapies include the anti-VEGF, Avastin and the immune stimulant interferon. Treatments used in front-line clear cell metastatic RCC include Sutent, Votrient and Avastin (with interferon), while second-line treatment regimens include Inlyta, Nexavar and Afinitor. Torisel is typically reserved for patients with non-clear RCC or poor-risk criteria. Every year about 11,000 patients progress to the third-line stage, for which the specific treatment used depends upon the sequence of prior therapies administered. Since the most common treatment sequence for clear cell RCC is Sutent followed by Inlyta, Afinitor is frequently prescribed for third-line therapy. If the patient has already failed on Afinitor, then Nexavar is frequently used.

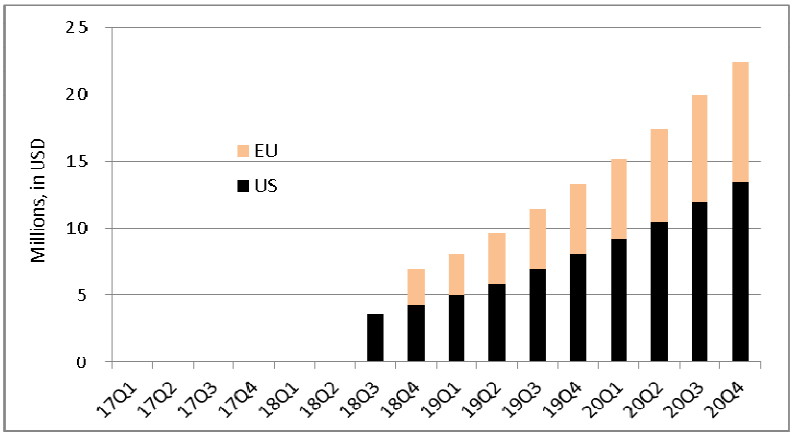
Figure 12: US Approved Treatments for Renal Cell Carcinoma

Product	Sutent (sunitinib)	Avastin (bevacizumab)	Votrient (pazopanib)	Inlyta (axitinib)	Nexavar (sorafenib)	Afinitor (everolimus)
Company	Pfizer	Roche	GSK	Pfizer	Bayer	Novartis
Description	Oral TKI	IV TKI	Oral TKI	Oral TKI	Oral TKI	Oral mTORi
Approved Label	Metastatic RCC	Metastatic RCC in combination with interferon	Metastatic RCC	Metastatic RCC after failure of systemic therapy	Metastatic RCC	Metastatic RCC after Sutent or Nexavar failure
Pivotal Trial (patients)	Phase III (n=750)	Phase III (n=649)	Phase III (n=435)	Phase III AXIS (n=723)	Phase III (n=769)	Phase III (n=416)
ORR	47%	31%	30%	23%	2%	2%
Median PFS	11 mo	10.2 mo	9.2 mo	6.7 mo	5.5 mo	4.9 mo
HR for OS	0.82 to interferon	0.86 to interferon (not stat sig)	0.73 to placebo (not stat sig)	0.97 to sorafenib (not stat sig)	0.72 to placebo (not stat sig)	0.87 to placebo (not stat sig)

Source: Wedbush Securities

We estimate a peak market share of 20% for CRLX101 in the third-line RCC setting. We expect CRLX101 to be priced at $10,000 per cycle. We expect approval in the US and Europe in H2:18, and forecast 2020 sales of $75M. Use of CRLX101 earlier in the treatment paradigm for RCC would represent an upside to our price target.

Figure 13: Forecasted Sales to 2020 in Relapsed RCC, by Quarter



Source: Wedbush Securities

Ovarian Cancer

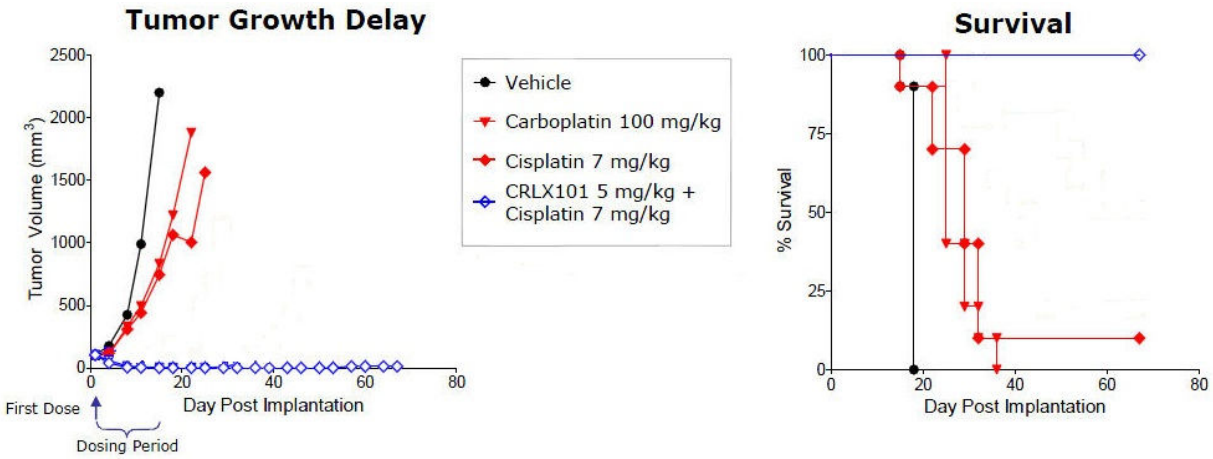
Ovarian cancer is the second most common gynecologic cancer, but the deadliest in absolute number, with about 22,000 new cases and 14,000 deaths per year in the US. The relatively poor prognosis of the cancer is due to the lack of early detection or screening test, which results in the majority of patients being in advanced stages at the time of diagnosis. Standard first-line treatment for ovarian cancer is tumor resection followed by platinum- and taxanes-based chemotherapy. For patients who show a response, the relapse rate is high, and subsequent therapy is dependent upon whether the patient is platinum-resistant (relapsed within six months) or platinum-sensitive (relapsed after six months). Platinum-sensitive patients typically receive another platinum-containing therapy, while platinum-resistant ovarian cancer (PROC) patients have fewer options and there is a high unmet need for new therapies.

Avastin, which is approved in the EU (not yet submitted for review in the US) for newly diagnosed and recurrent ovarian cancer, has shown success when combined with chemotherapy in improving PFS and ORR in PROC patients. The Phase III AURELIA study (sponsored by Roche) comparing single-agent chemotherapy (doxorubicin, paclitaxel or topotecan) with or without Avastin found that patients receiving the Avastin combination had substantial increases in PFS (6.7 vs. 3.4 months) and ORR (27.3 vs. 11.8%) compared to single-agent chemo alone. However, despite a positive trend, Avastin failed to produce a statistically significant improvement in OS.

Given that ovarian cancer has been identified as a HIF-overexpressing tumor type, which contributes to resistance to Avastin, the combination of CRLX101's HIF inhibition and Avastin could lead to a survival benefit in PROC patients.

When combined with Avastin, CRLX101 could perform better than the chemotherapeutic agents in AURELIA. Consider that in a mouse model of ovarian cancer, mice treated with CRLX101 monotherapy had greater tumor regression and higher survival rates compared to mice treated with carboplatin and cisplatin (Fig. 14). Recall also that the addition of CRLX101 to Avastin produced reductions in tumor volume and improvements in survival compared to Avastin alone in an ovarian xenograft model.

Figure 14: Comparison of CRLX101 and Platinum-Based Chemotherapy in Ovarian Xenograft Model

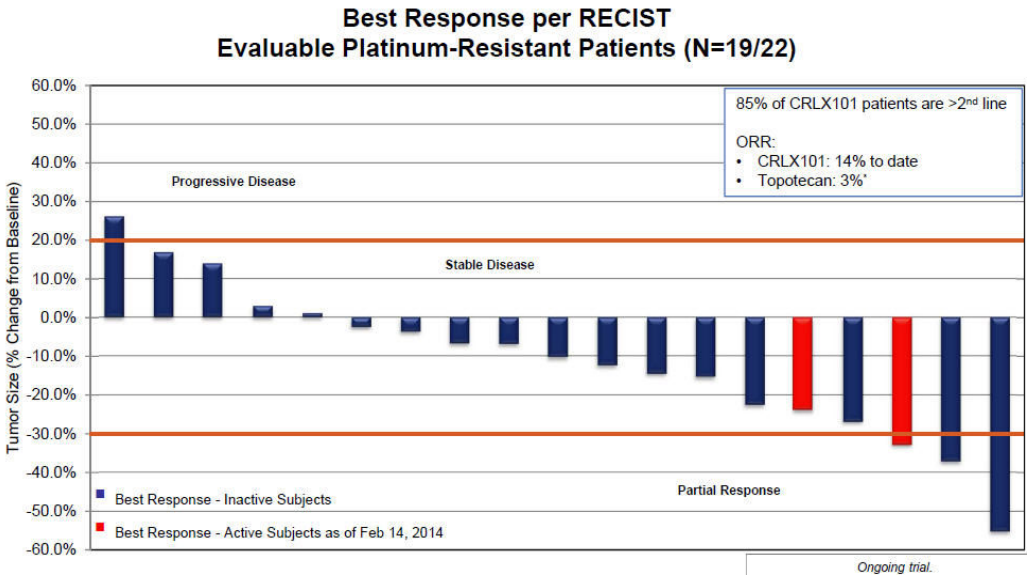


Source: Company data

Clinical Program

CRLX101 is currently being evaluated in a two-stage open-label, investigator-sponsored Phase II study in patients with relapsed ovarian cancer. The first stage evaluating 15 mg/m^2 CRLX101 as a single agent has met the PFS primary endpoint, with at least four patients (of 29 enrolled) having PFS of at least six months. Tumors shrunk in 15 patients, with four achieving partial responses. Of the 19 evaluable patients that were platinum resistant, 18 had stable disease or better, including three (14%) with a partial response. This response rate is impressive considering how challenging the setting is, with the approved agent topotecan showing only a 3% ORR.

Figure 15: Phase II Monotherapy Tumor Size Reductions



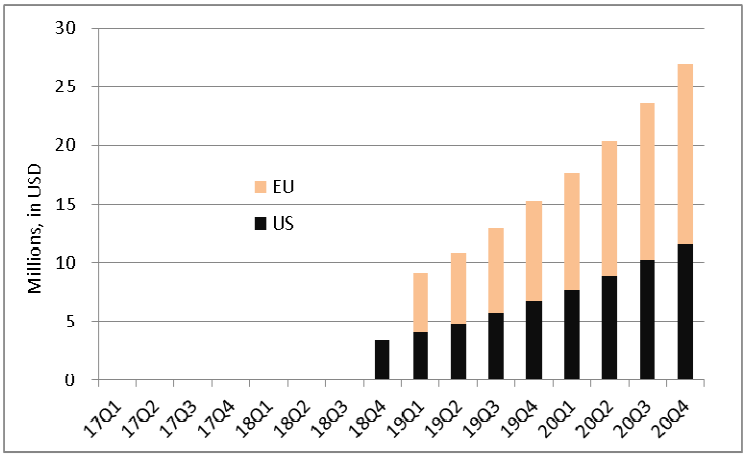
Source: Company data

The second stage of the trial is currently enrolling and will evaluate the combination of 15 mg/m^2 CRLX101 and 10 mg/kg Avastin (supplied by Roche) administered every two weeks in up to 43 second- and third-line platinum-resistant ovarian cancer patients. The primary endpoint is PFS at six months in at least eight patients. Assuming positive results (expected YE:14), including an objective response rate of at least 20%, CERU intends to begin a randomized pivotal trial of CRLX101 plus Avastin versus chemotherapy standard of care in relapsed PROC in early 2015.

Market

CERU estimates that 9,000 PROC patients become eligible for second-line and beyond treatment in the US each year. We believe EU figures are double that figure, and believe the combination could become approved for use in both territories in the late 2018/early 2019 timeframe. We believe CRLX101 could be priced at a premium to chemotherapy, like in RCC, and forecast 2020 sales of $88M.

Figure 16: Forecasted Sales to 2020 in Platinum-Resistant Ovarian Cancer, by Quarter



Source: Wedbush Securities

Given the superior performance of CRLX101 monotherapy versus platinum-based chemotherapy in ovarian xenograft models (Fig. 14), CERU could potentially seek earlier stage use for CRLX101 as a single-agent in combination with taxanes in front-line therapy for ovarian cancer. Another potential label expansion lies in the use of Avastin and CRLX101 as maintenance therapy. Sales in either of these settings would represent an upside to our price target.

Rectal Cancer

Colorectal cancer is the fourth most common cancer in the US among men and women with about 140,000 new cases each year, and rectal cancers account for about 30% of that figure. The curative treatment for rectal cancer is complete surgical resection of the tumor. In order to prevent tumor regrowth, surgeons aim to remove as much cancerous tissue as possible, which often requires the removal of the sphincter. Although this maximizes control over the cancer, sphincter removal results in fecal incontinence and a drastic lowering of quality of life. Preoperative chemoradiation, also referred to as neoadjuvant therapy, is currently the preferred option for advanced rectal cancers since it is associated with tumor regression and downstaging, resulting in a higher rate of sphincter preservation. Approximately 28,000 rectal cancer patients are diagnosed prior to the disease metastasizing beyond the lymph nodes, which makes them candidates for neoadjuvant therapy.

Xeloda (capecitabine) is an oral chemotherapeutic agent approved for rectal cancer, and the combination of Xeloda and radiotherapy is the current standard of care for rectal cancer. Rectal cancer patients who receive Xeloda in the neoadjuvant setting have a pathologic complete response (pCR) rate of 21% vs 18% for 5-fluorouracil (FU) infusion, the prior standard of care. A complete response following neoadjuvant therapy is indicative of improved long-term prognosis and sphincter preservation, since surgeons will often remove the sphincter if residual tumor remains following chemoradiation treatment.

The addition of CRLX101 to the standard of care regimen in neoadjuvant rectal cancer could lead to improvements in the response rate. The efficacy of radiotherapy is reduced by topoisomerase I, which can repair the DNA damage radiotherapy inflicts upon tumor cells. The XELERI regimen, which combines Xeloda with the topoisomerase inhibitor irinotecan, has produced pCR rates (21-38%) exceeding that of Xeloda alone. However, the addition of irinotecan introduces high levels of toxicity which limits adoption of the regimen. In addition, radiotherapy can also cause hypoxia in tumor regions, resulting in the up-regulation of HIF-1α. A dual topoisomerase I and HIF-1α inhibitor with a benign safety profile, like CRLX101, could act as an effective add-on therapy to chemoradiation in the neoadjuvant rectal cancer setting. Preclinical testing conducted by CERU showed CRLX101 to be an effective radiosensitizer in a head-and-neck xenograft model, with a synergistic effect noticed in both tumor volume and survival.

Clinical Program

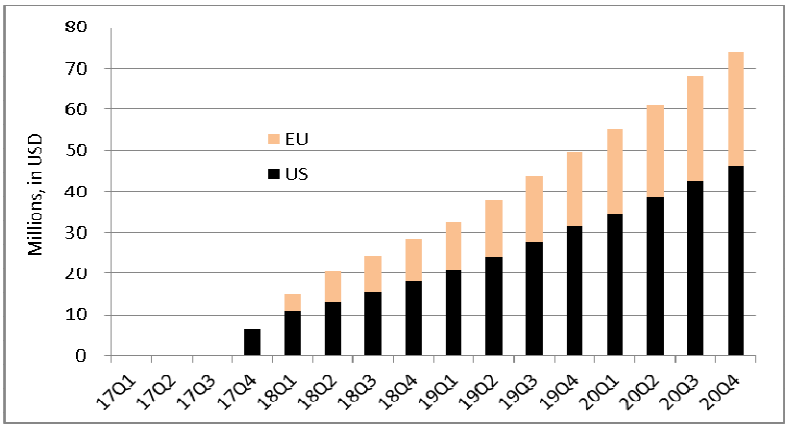
An open-label investigator-sponsored Phase Ib/II trial of CRLX101 in combination with Xeloda (capecitabine) and radiation therapy is currently enrolling up to 53 patients with rectal cancer. The Phase Ib dose-finding portion will identify the MTD of CRLX101 and Xeloda with radiotherapy, and the Phase II portion will seek to identify signs of efficacy. The primary endpoint is pathologic complete response, with secondary endpoints of disease free survival and OS.

Assuming positive results from this study, CERU will begin a 1:1 randomized Phase II trial comparing Xeloda and radiotherapy with or without CRLX101 in neoadjuvant rectal cancer in 80-120 patients in 2015. The co-primary endpoints to be measured at the time of surgery (~12 weeks after first dose) are pCR and sphincter preservation. Complete response data will be available by late 2015, and if positive CERU will likely seek an end of Phase II meeting with the FDA to discuss accelerated approval and the design for a Phase III study. It is possible that a randomized Phase III trial with a patient enrollment of 300-500 and endpoints of pCR and sphincter preservation could be sufficient to support accelerated approval, with the condition that confirmatory studies demonstrate superiority in disease-free survival for full approval.

Market

We estimate about 28,000 non-metastatic rectal cancer patients in the US became eligible for neoadjuvant treatment in 2013. We believe the patient numbers in Europe to be similar, based on incidence figures provided by the European Society for Medical Oncology. Assuming accelerated approval in the US, CRLX101 could launch in the US by late 2017. We expect pricing to at least match the $10,000 per course estimate assumed for the other indications. Given the relatively large patient population affected, we expect the rectal cancer indication to drive a majority of the value for CERU shares.

Figure 17: Forecasted Sales to 2020 in Neoadjuvant Rectal Cancer, by Quarter



Source: Wedbush Securities

CRLX301

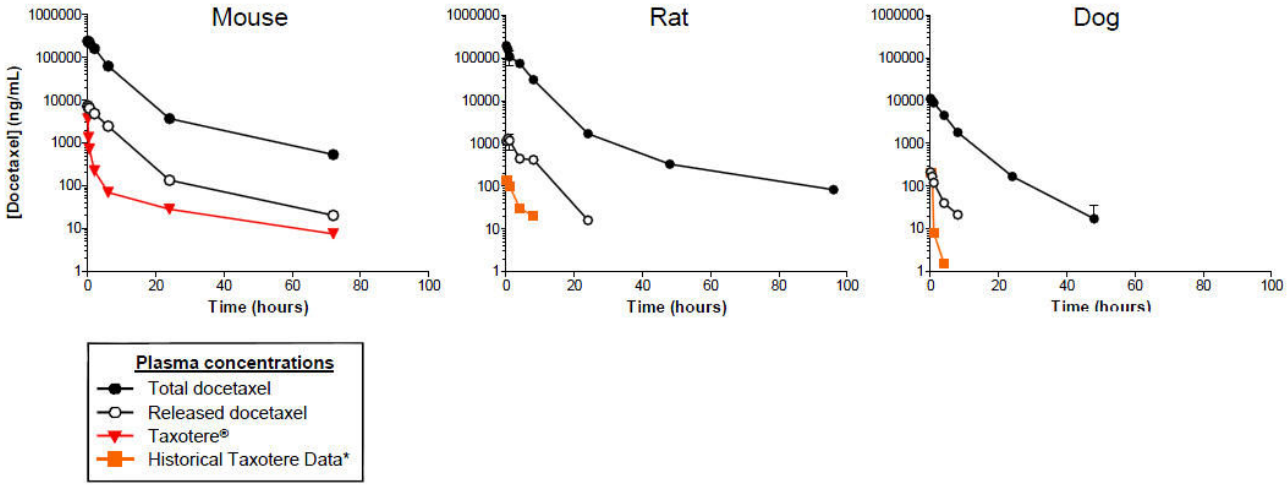
CRLX301 is a nanopharmaceutical analog of CRLX101 that carries the taxane docetaxel as its therapeutic payload. Docetaxel (Taxotere) is a potent chemotherapeutic that is a semi-synthetic analog of the taxane paclitaxel. Taxanes arrest cellular division by disrupting microtubule function through tubulin stabilization. Docetaxel and paclitaxel are similar in pharmacology and structure, but docetaxel appears to bind to tubulin with greater affinity and have a longer retention time within tumor cells. However, docetaxel is associated with more side effects, including neutropenia, fever and water retention. CRLX301 aims to use their nanoparticle technology to durably release docetaxel within tumors cells in order to increase the tolerability and reduce systemic exposure. The improved safety profile should also allow for CRLX301 to be combined with other cancer therapies that are not combinable with docetaxel today due to the toxicity.

Preclinical

Preclinical research in animal tumor models has demonstrated that CRLX301 improves upon the efficacy, safety and combinability of docetaxel. CRLX301 outperformed Taxotere in multiple efficacy models, and animals administered CRLX301 had a free docetaxel concentration within their tumors that is an order of magnitude larger than when administered Taxotere. In addition, CRLX301 was associated with better safety and a higher MTD, consistent with a decreased systemic exposure.

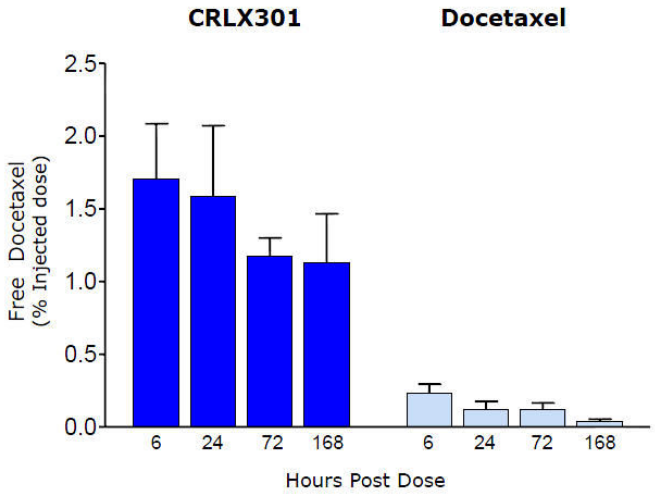
A PK study in 80 mice administered a single 15 mg/kg dose of either CRLX301 or docetaxel found that mice receiving CRLX301 had a more durable concentration of free docetaxel, including a ~500x increase in plasma exposure, compared to mice treated with Taxotere. Similar results were observed in rats receiving 10 mg/kg doses and dogs receiving 0.75 mg/kg doses of CRLX301 when compared with published data for the same Taxotere dose (Fig. 18). A separate PK study in a mouse melanoma model found that mice with tumors that were administered CRLX301 had approximately 10 times as much free docetaxel within their tumors compared to tumors from mice administered commercial docetaxel (Fig. 19). The mice were administered a single 15 mg/kg dose of either CRLX301 or commercial docetaxel and had their tumors extracted up to one week later for analysis.

Figure 18: Single-dose CRLX301 Plasma Pharmacokinetic Study



Source: Company data

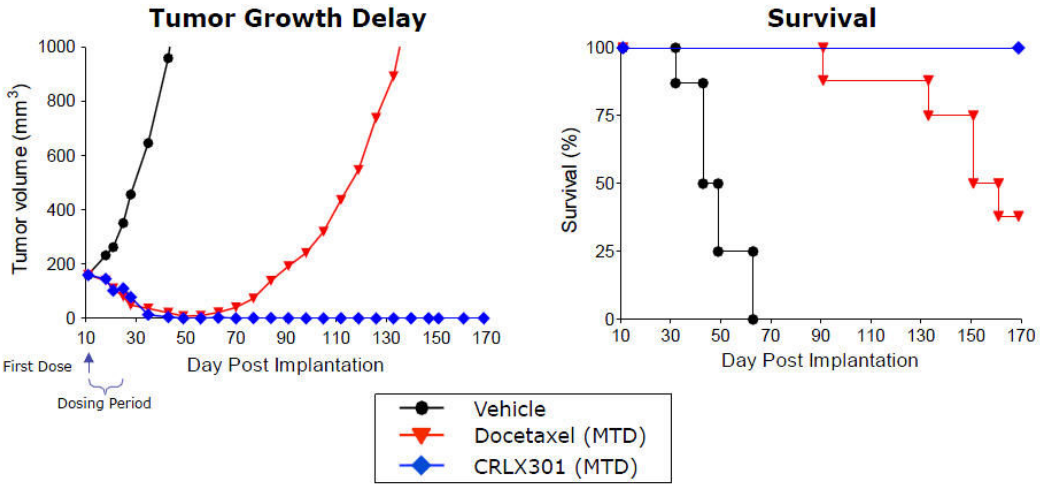
Figure 19: Single-dose CRLX301 Tumor Pharmacokinetic Study



Source: Company data

CRLX301 has been evaluated in multiple animal xenograft models, including prostate cancer, squamous and adenocarcinoma NSCLC, ovarian cancer (including multi-drug resistant type), triple-negative breast cancer and a syngeneic melanoma model, and in all models tested CRLX301 was non-inferior to docetaxel in survival rate, delaying tumor progression and/or complete response rate. In the prostate cancer model in nude mice, results of which are representative across all other animal xenograft models tested, mice treated with CRLX301 had complete tumor regression and a 100% tumor-free survival at study conclusion (Fig. 20). Toxicology studies determined that the MTD in dogs was ~20% higher for CRLX301 compared to published data for docetaxel, and in plasma PK studies the volume of distribution for CRLX301 was 50 times lower in rats and 138 times lower in dogs compared to published data.

Figure 20: Prostate Xenograft Study Comparing CRLX301 to Docetaxel and Saline Vehicle



Source: Company data

Phase I/IIa

The Phase I dose-escalation portion of a Phase I/IIa trial is set to begin in Australia by year end in patients with advanced solid tumors. Patients in the Phase I will be administered an IV infusion of CRLX301 once every three weeks until a safe MTD has been established. The start of the Phase I study will trigger a $250,000 milestone payable to Calando.

An IND is expected to be submitted to the FDA following start of the Australian study, allowing the Phase IIa portion of the trial to be conducted at sites in the US. CERU will evaluate the MTD of CRLX301 in 2 or 3 tumors of interest during the Phase IIa portion, or the company could progress to a randomized Phase II trial conducting a direct comparison between CRLX301 and the standard of care in a tumor of interest. We expect these possible tumor types to be ones for which docetaxel is already approved, such as breast cancer, gastric cancer, prostate cancer, NSCLC and head and neck cancer. Other possible tumor types of interest include ones where taxanes have demonstrated efficacy in or ones in which resistance to prior taxanes has been established, such as melanoma and ovarian cancer. We believe the clinical development risk of CRLX301 is lessened since docetaxel, unlike camptothecin, is already approved in humans, but due to its early status we are not including it in our valuation.

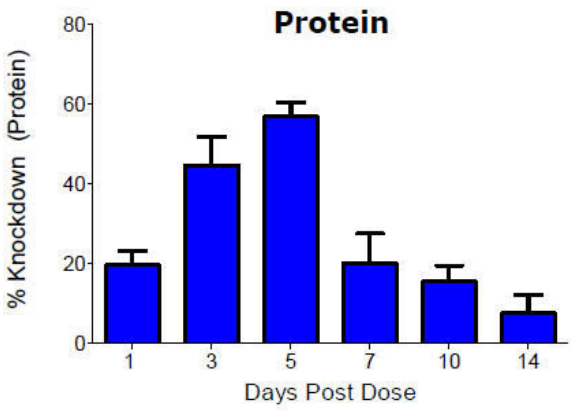
Other applications

Large Molecules

In addition to their cyclodextrin polymer-based candidates, CERU's drug platform can deliver polymeric nanoparticles carrying large molecules like nucleic acids. This opens up the potential for different treatment approaches, such as therapies based around RNA interference (RNAi). RNAi is a pathway through which RNA molecules like messenger RNA (mRNA), small interfering RNA (siRNA) and microRNA (miRNA) regulate gene expression. Therapeutic applications of RNAi include the silencing of genes that are upregulated in tumor cells or are involved in cellular division, but tumor uptake of RNA molecules is poor due to its large size and metabolic instability (leading to short circulation time). CERU's platform could have the potential to target RNA into tumor cells for durable release, which would be of interest to other firms developing RNAi-based therapies. The leading biotech firm in the RNAi space is Alnylam Pharmaceuticals (ALNY, Not covered), which is developing treatments for rare genetic disorders.

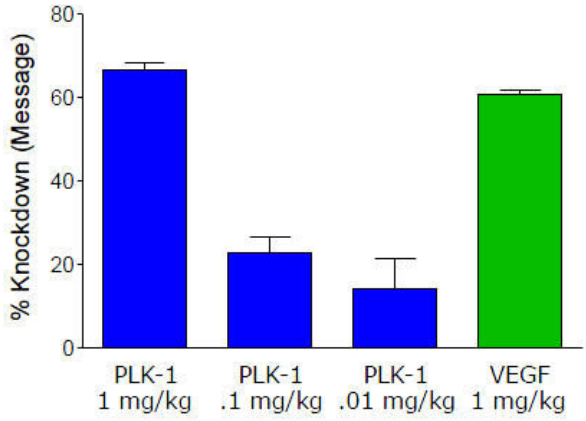
The technology was validated by CERU in four animal tumor types (breast, colorectal, hepatic and ovarian) which demonstrated tumor specific uptake of polymeric nanoparticles carrying siRNA led to significant and prolonged knockdown in tumors. In nude mice with tumors formed from subcutaneously implanted human breast cancer tumor cells expressing green-fluorescent protein (GFP), systemic administration of anti-GFP containing 3 mg/kg of siRNA polymer nanoparticles led to a one-week knockdown of the GFP protein. Knockdown peaked at ~60% five days after the single dose was administered (Fig. 21). In a separate study in mice with colorectal tumors, administration of polymer nanoparticles containing siRNA against the oncogene *PLK-1* or the angiogenic protein VEGF resulted in the knockdown of mRNA levels at 24 hours post-treatment. This included a 65% knockdown of *PLK-1* mRNA following three daily IV treatments of 1 mg/kg of siRNA polymer nanoparticles, with knockdown also observed for the 0.1 and 0.01 mg/kg doses (Fig. 22). The siRNA containing polymer nanoparticles appear safe, with no SAEs or cytokine response observed in any of the animal tumor models.

Figure 21: Green-Fluorescent Protein Xenograft Knockdown Study



Source: Company data

Figure 22: Colorectal Xenograft Knockdown Study



Source: Company data

CERU has indicated it is seeking to partner the RNA program since it is outside the company's focus, and as a result we are not including it in our valuation.

Inflammation

In addition to oncology, CERU's targeted nanopharmaceutical platform could have applications in certain inflammatory indications where vascular leakage occurs. Vascular permeability is a characteristic of acute inflammation, which can cause the endothelial cells of blood vessels to die or retract. Like with solid tumors, CERU's nanoparticles can take advantage of the endothelial gaps to gain entry and deliver treatment.

As with the RNA program, CERU has indicated interest in partnering the program with companies in the inflammation space since it is outside the company's focus. We speculate the technology would have the greatest appeal to companies developing treatments for autoimmune disorders. CERU has experimented with nanopharmaceuticals carrying the small molecules methotrexate and tofacitinib (Xeljanz) and found activity and tolerability improved when compared to the payload alone. Methotrexate is an anti-inflammatory drug used to treat rheumatoid arthritis and psoriasis. Xeljanz is approved in the US for rheumatoid arthritis, but was rejected in Europe over safety and efficacy concerns. Xeljanz, manufactured by Pfizer, is also in Phase III testing for psoriasis.

Management

Figure 23: Cerulean Management

Title	Biography
Oliver S. Fetzer, Ph.D. President and CEO	Dr. Fetzer has served as President and CEO since 2009. From 1993 to 2007, he served in multiple roles at Cubist Pharmaceuticals, including as Chief Business Officer and as SVP of Business Development, Corporate Development and R&D. Prior, he held various positions of increasing responsibility at Boston Consulting Group. Dr. Fetzer earned a B.S. in Biochemistry from the College of Charleston, a Ph.D. in Pharmaceutical Sciences from the Medical University of South Carolina and an M.B.A. from Carnegie Mellon University.
Edward G. Garmey, M.D. SVP and Chief Medical Officer	Dr. Garmey has served as SVP and CMO since 2011. He previously served as VP of Clinical Development at ArQule. Prior, he served as Medical Director at GPC Biotech. Dr. Garmey earned an A.B. from Harvard University and an M.D. from New York University.
Christopher D. T. Guiffre, J.D. SVP and Chief Business Officer	Mr. Guiffre has served as SVP and CBO since 2012. He previously served as President and CEO of Alvos Therapeutics from 2010 to 2012 and as CBO at Hydra Biosciences from 2008 to 2009. From 2001 to 2008 he served as a senior executive at Cubist Pharmaceuticals, most recently as SVP, General Counsel and Secretary. Mr. Guiffre earned a B.S. from Babson College and a J.D. and M.B.A. from Boston College.
Karen L. Roberts SVP of Finance and Administration	Ms. Roberts has served as SVP of Finance and Administration since 2010. She previously served as VP of Finance and Administration at Elixir Pharmaceuticals from 2001 to 2009. Prior, she served as Director of Finance at Dyax and as Corporate Controller and Director of Financial Administration at T Cell Sciences. Ms. Roberts earned a B.S. in Business Administration with a concentration in accounting from Salem State College.

Source: Company data, Wedbush Securities

Financial Model

CERU raised $61.5M in its April 10 IPO (including underwriter's option) after deducting commissions and expenses. We estimate the company will end Q2:14 with $65.3M in cash, sufficient, in our view, to last through 2015. Following the IPO and conversion of preferred stock, we estimate CERU currently has about 20.3M shares outstanding. Approximately 10.5M of these shares will become unlocked on October 7.

Figure 24: Financial Forecast through 2020

5/2/2014
Ticker: (CERU:Nasdaq)
Cerulean Pharma, Inc

Wedbush PacGrow Life Sciences
David M. Nierengarten, Ph.D.
415-274-6862

	2011	2012	2013	Q1	Q2	Q3	Q4	2014E	2015E	2016E	2017E	2018E	2019E	2020E
Revenues:														
US Product Sales	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$6,410	$69,227	$151,200	$245,284
ex-US sales	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$32,926	$103,235	$176,520
Licensing and other revenue	$305	$625	$6	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Total Revenues	**305**	**625**	**6**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**6,410**	**102,153**	**254,435**	**421,805**
Cost and Expenses:														
Cost of Sales	0	0	0	0	0	0	0	0	0	0	641	6,923	15,120	24,528
R&D	13,848	15,807	9,700	1,440	1,440	1,469	2,469	6,818	31,875	44,011	47,639	51,566	55,817	60,418
SG&A	5,335	6,393	6,166	1,607	4,480	1,639	1,671	9,396	7,027	7,419	9,517	53,472	101,089	126,809
Total Operating Expenses	**19,183**	**22,200**	**15,866**	**3,047**	**5,920**	**3,107**	**4,140**	**16,214**	**38,902**	**51,431**	**57,798**	**111,961**	**172,026**	**211,755**
Operating Income (Loss)	(18,878)	(21,575)	(15,860)	(3,047)	(5,920)	(3,107)	(4,140)	(16,214)	(38,902)	(51,431)	(51,387)	(9,808)	82,409	210,049
Net Interest Income (Expense)	(25)	(565)	(1,485)	(14)	(111)	441	431	747	1,597	1,795	1,862	2,450	2,584	4,870
Other non-operating Income (Expense)	(660)	(34)	202	0	0	0	0	0	0	0	0	0	0	0
Income Before Income Taxes	(19,563)	(22,174)	(17,143)	(3,060)	(6,031)	(2,666)	(3,709)	(15,467)	(37,304)	(49,635)	(49,525)	(7,359)	84,992	214,919
Provision for Income Taxes	0	0	0	0	0	0	0	0	0	0	0	652	33,147	83,818
Net Income (Loss)	(19,563)	(22,174)	(17,143)	(3,060)	(6,031)	(2,666)	(3,709)	(15,467)	(37,304)	(49,635)	(49,525)	(8,011)	51,845	131,101
Non-GAAP EPS	**(1.59)**	**(1.59)**	**(1.24)**	**(0.21)**	**(0.30)**	**(0.13)**	**(0.18)**	**(0.79)**	**(1.55)**	**(1.71)**	**(1.51)**	**(0.26)**	**1.53**	**3.90**
GAAP EPS	**(1.37)**	**(1.55)**	**(1.20)**	**(0.21)**	**(0.30)**	**(0.13)**	**(0.18)**	**(0.82)**	**(1.65)**	**(1.86)**	**(1.64)**	**(0.24)**	**1.55**	**3.92**
Total Shares Outstanding	14,305	14,305	14,305	14,305	20,290	20,315	20,340	20,340	24,440	29,440	33,440	33,440	33,440	33,440
Cash Burn	(18,590)	(18,590)	(7,840)	(1,697)	(5,920)	(3,171)	(4,048)	(14,836)	(40,637)	(50,401)	(51,925)	(15,754)	73,777	197,741
Cash Balance	16,707	16,707	5,488	12,277	66,115	62,385	57,768	57,768	54,805	75,949	81,654	67,351	110,289	228,362

Source: Wedbush Securities

Figure 25: CRLX101 Valuation Table

Indication	Territory	Patients	Peak Penetration Rate	Pricing per Cycle ($)	# of Cycles	2020 Sales (M)	Valuation per share (6x 2020, 35% discount)
3rd Line Renal Cell Carcinoma	US	11k	20%	10K	6	$45	$1.32
	EU	11k	20%	7.5K	6	$30	$0.87
2nd Line Platinum-Resistant Ovarian Cancer	US	9k	20%	10K	6	$38	$1.12
	EU	18k	20%	7.5K	6	$50	$1.47
Neoadjuvant Rectal Cancer	US	28k	35%	10K	3	$162	$4.75
	EU	25k	35%	7.5K	3	$97	$2.83
						Total	**$12.36**

Source: Wedbush Securities

Analyst Biography

David Nierengarten, Ph.D. is an Analyst covering stocks in the Biotechnology/Biopharmaceuticals/BioDefense sector. His prior sellside research experience at Robert W. Baird & Co. covered biotechnology companies of all market capitalizations, with a focus on oncology and rare diseases.
David received his B.S. (Biochemistry) from the University of Wisconsin-Madison and Ph.D. (Molecular and Cell Biology) from the University of California-Berkeley.
David's Edge: David's early stage venture capital investing experience gives him a balanced perspective on developmental-stage biotechnology companies and their ultimate risk/reward potential. His experience on the other side of that equation in a clinical-stage, venture backed biotechnology company provides him with insights into corporate operations. The combination of experiences creates a focus on value creation in this event-driven space.

Analyst Certification
I, David M. Nierengarten, Ph.D., Gregory R. Wade, Ph.D., Christopher N. Marai, Ph.D., certify that the views expressed in this report accurately reflect my personal opinion and that I have not and will not, directly or indirectly, receive compensation or other payments in connection with my specific recommendations or views contained in this report.

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Wedbush Equity Research Disclosures as of May 5, 2014

Company	Disclosure
Cerulean Pharma	1,3,5,7

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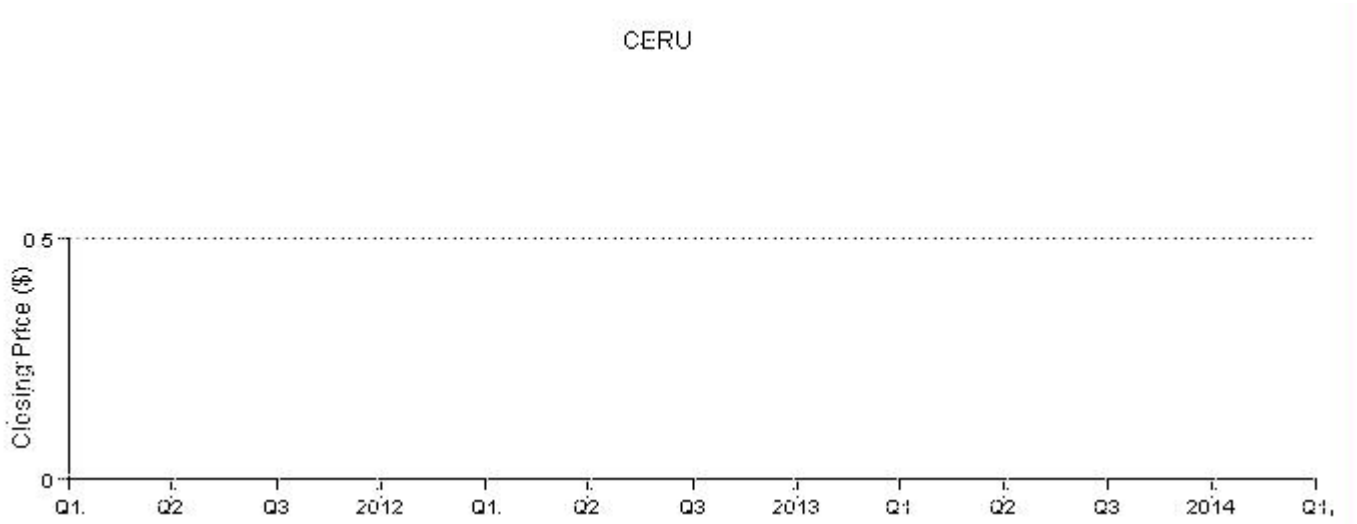

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OTHER DISCLOSURES

RESEARCH DEPT. * (213) 688-4505 * www.wedbush.com
EQUITY TRADING Los Angeles (213) 688-4470 / (800) 421-0178 * EQUITY SALES Los Angeles (800) 444-8076
CORPORATE HEADQUARTERS (213) 688-8000

WEDBUSH

EQUITY RESEARCH DEPARTMENT

(213) 688-4529

DIRECTOR OF RESEARCH
Mark D. Benson (213) 688-4435

MANAGER, RESEARCH OPERATIONS
Ellen Kang (213) 688-4529

RETAIL AND CONSUMER

Consumer Products
Rommel T. Dionisio (212) 938-9934
Alicia Reese (212) 938-9927

Footwear, Apparel and Accessories
Corinna Freedman (212) 668-9876

Healthy Lifestyles
Kurt M. Frederick, CFA CPA (415) 274-6822
Alicia Reese (212) 938-9927

Restaurants
Nick Setyan (213) 688-4519
Colin Radke (213) 688-6624

Specialty Retail: Hardlines
Joan L. Storms, CFA (213) 688-4537
John Garrett, CFA (213) 688-4523

Seth Basham, CFA (212) 938-9954

Specialty Retail: Softlines
Morry Brown (213) 688-4311
Taryn Kuida (213) 688-4505

RETAIL/CONSUMER MARKET RESEARCH

Gabriella Santaniello (213) 688-4557

INDUSTRIAL GROWTH TECHNOLOGY

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Andy Cheng (213) 688-4548

Enterprise Security
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Aaron Turner (213) 688-4429

Enterprise Software
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Nick McKay (213) 688-4343
Nick Citrin (213) 688-4495

Entertainment: Software
Michael Pachter (213) 688-4474
Nick McKay (213) 688-4343
Nick Citrin (213) 688-4495

Internet: Media and Gaming
Michael Pachter (213) 688-4474
Nick McKay (213) 688-4343
Nick Citrin (213) 688-4495

Internet: Social Media, Advertising & Technology
Shyam Patil, CFA (213) 688-8062
Andy Cheng (213) 688-4548

Media
James Dix, CFA (213) 688-4315

Movies and Entertainment
Michael Pachter (213) 688-4474
Nick McKay (213) 688-4343
Nick Citrin (213) 688-4495

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Ryan Jue, CFA (415) 263-6669

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CORPORATE HEADQUARTERS
1000 Wilshire Blvd., Los Angeles, CA 90017-2465
Tel: (213) 688-8000 www.wedbush.com