EDISON

Cerulean Pharma

Initiation of coverage

Multiple price inflections on clinical pipeline

Pharma & biotech

Cerulean is on track to announce critical Phase II trial results for CRLX101 in metastatic renal cancer (mRCC) in H116 following encouraging preliminary efficacy data in a Phase IIa readout presented at ASCO in 2015. Additionally, interim Phase Ib/II results are due for CRLX101 in ovarian and rectal cancers in H215 and Phase I data for CRLX301 in 2015 in solid tumors. If positive, these results should renew confidence in Cerulean's pipeline and its differentiated nanoparticle drug conjugate technology (NDC). We value Cerulean at $273m ($10.0 per share).

Year end	Revenue ($m)	PBT* ($m)	EPS* (c)	DPS (c)	P/E (x)	Yield (%)
12/13	0.0	(17.3)	(25.35)	0.0	N/A	N/A
12/14	0.0	(21.4)	(1.64)	0.0	N/A	N/A
12/15e	0.0	(39.3)	(1.57)	0.0	N/A	N/A
12/16e	0.0	(40.5)	(1.57)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding intangible amortisation, exceptional items and share-based payments.

Few treatment options for late-stage mRCC patients

The ongoing Phase II randomized trial for CRLX101 – with its slow release of payload camptothecin – in mRCC follows impressive Phase IIa interim results, showing median progression-free survival of 9.9 months vs standard of care at 3.5 months. If successful, CRLX101 will launch as a new mechanism of action into a large market (>10,000 patients) in third- and fourth-line mRCC where there are limited viable treatment options. Designated FDA Fast Track status, we currently forecast peak sales of $490m for CRLX101 in combination with Avastin in mRCC (and $340m and $770m respectively in follow-on indications of ovarian and rectal cancers).

Technology platform has potential across indications

Cerulean's nanoparticle-drug conjugation enables the delivery of potent but relatively toxic well-known and commercialized drug treatments to selectively target tumor cells while sparing the body's normal cells, thereby improving the safety and efficacy of treatment. Results for Cerulean's second NDC, CRLX301 – with payload docetaxel – are expected by year end, while the technology holds the potential for numerous NDC combinations with other currently marketed drugs.

Valuation: $273m ($10.0 per share)

Our value for Cerulean of $273m or $10.0 per share reflects our NPV-based methodology, to which we apply Edison's standard 12.5% discount rate. Following a successful fund-raising grossing $40.3m in April, Cerulean reported cash holdings of $85.5m on 20 June, a runway that should extend into 2017. With ~80% of its current market capitalization underpinned by cash, the shares seem overlooked by the market, particularly given strong early data, established proof of principle and a positive safety profile for its lead drug candidate, CRLX101. We expect multiple upcoming data readouts, if positive, to re-rate the shares.

10 September 2015

Price	**US$4.7**
Market cap	**US$128m**

Net debt ($m) at end June 2015	71.0
Shares in issue	27.3m
Free float	62%
Code	CERU
Primary exchange	NASDAQ
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	18.0	(2.1)	14.5
Rel (local)	26.3	4.9	17.3
52-week high/low	US$10.7		US$3.3

Business description

Cerulean is a US-based oncology company with a proprietary platform utilizing nanoparticle-drug conjugates (NDCs). Lead product CRLX101 combined with Avastin is in Phase II clinical trials in third- and fourth-line RCC and second- and third-line ovarian cancer. CRLX101 in combination with chemotherapy is also in Phase Ib/IIa in neoadjuvant rectal cancer.

Next events

CRLX301 in solid tumors	Q415
CRLX101 interim Phase I/IIa ovarian and rectal cancers	H215
CRLX101 Phase II RCC	H116
Q3 results	November 2015

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Edison profile page

Investment summary

Company description: Proprietary NDCs

Cerulean was established in 2005 for the development of its nanotechnology for therapeutics, focusing primarily on oncology through its proprietary Dynamic Tumor Targeting Platform. Its lead candidate, CRLX101, is in development for metastatic renal cell carcinoma (mRCC), ovarian and rectal cancers, and we anticipate multiple data readouts in these indications over the next year. Cerulean completed an IPO in April 2014 and the following May (2014) raised additional public equity, which together netted $59.9m. In total the company has raised $224.6m, including funds of $40m via a public offer in April 2015. It currently employs 45 people and is headquartered in Cambridge, Massachusetts. Originally established under the name Tempo Pharmaceuticals, the name was changed to Cerulean Pharma in 2008.

Valuation: Upside on upcoming key data points

We value Cerulean at $273m or $10.0 per share based on a risk-adjusted net present value of cash flows for CRLX101 and CRLX301 and their associated costs, applying our standard 12.5% discount rate. Given Cerulean's plans to self-commercialize its cancer pipeline in the US, we include considerable future expenses related to R&D and sales and marketing, also modelling the significant financial upside related to direct market access. Outside the US, Cerulean is looking to partner. Cerulean's share price has languished in recent months despite encouraging early efficacy data for its lead candidate CRLX101 in mRCC and we point to several data points in the coming quarters, which should lead to increasing market recognition of the company's intrinsic value. We believe the potential of its pipeline is considerably underappreciated by investors, particularly when considering its current market capitalization of $128m ($4.7 per share) vis-à-vis a net cash balance of $71.0m at end June 2015.

Financials: Ample cash runway

Cerulean presented second quarter 2015 results on 6 August, reporting a net loss of $9.9m for the three months versus a loss of $7.4m in Q214. R&D increased to $6.7m in Q215 vs $2.7m in Q215, primarily due to a step-up in costs associated with clinical trials, while SG&A expenses of $2.7m in Q215 were up from $2.0m to support a growing corporate infrastructure. Following its successful fund-raising in April, grossing proceeds of $40.3m, Cerulean ended June 2015 with cash of $85.5m and net debt of $71.1m), which we anticipate should be sufficient to fund planned clinical trials into 2017. Thereafter, we expect Cerulean will require an estimated $80m for its growing clinical development portfolio, with the amount required dependent on the final trial design of key pivotal clinical development programs. On our forecasts, the company will reach profitability in 2020 based on a successful first launch of CRLX101 in mRCC in 2019.

Sensitivities: Company at a critical juncture

Now in the midst of critical proof-of-concept trials for its lead drug candidates, Cerulean is subject to the risks typically associated with an early- to mid-stage drug development company, including the possibility of unfavourable outcomes in clinical trials, regulatory changes and the success of competitors. Additionally, as Cerulean looks to retain marketing rights for its treatment candidates in the US, additional funding will be required to complete its clinical trial programs in currently pursued indications and for the resources needed for full commercialization, including marketing and salesforce costs. The company is nearing a critical juncture in its development program, with key efficacy data for CRLX101's lead indication in mRCC expected in the first half of the coming year. We maintain that the solid Phase I/IIa results in mRCC reported in mid-2015, including impressive initial efficacy and strong safety data, help to de-risk this upcoming event.

Differentiated platform offers multi-treatment potential

Drug conjugation and the HIF survival pathway

Cerulean's pipeline is advancing through critical efficacy studies, with key data points expected in the coming quarters. CRLX101, with a payload of camptothecin, is in Phase II trials in its lead indication, relapsed renal cell carcinoma, Phase I/b and Phase II studies in relapsed ovarian and Phase I/IIb in non-metastatic rectal cancers. Phase I results from its Phase I/IIa trial for a second nanoparticle-drug conjugate, CRLX301 (with a docetaxel payload) in solid tumors are expected by the end of this year, and we believe another drug candidate is likely to be announced in 2016.

The company's drug conjugation platform looks to have the capability for the creation of many more drug candidates in oncology, targeting numerous tumor types in additional combinations, constrained only by the necessary funding for follow on development. Cerulean also has the potential to exploit its technology in other diseases areas, including anti-inflammatory pathways, possibly through strategic partnering.

Exhibit 1: Cerulean pipeline

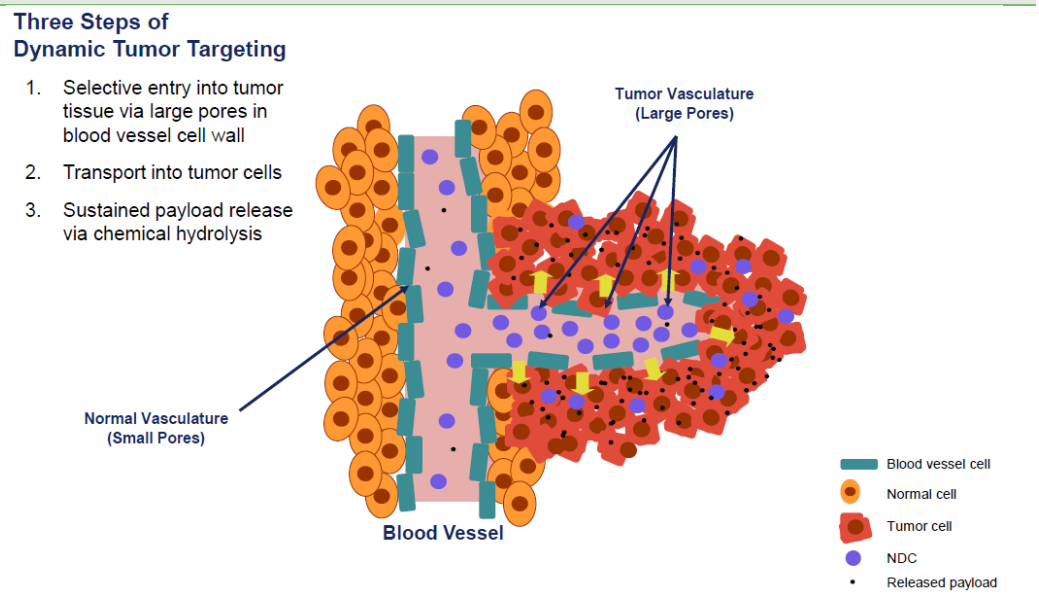
NDC	Indication	Combination	Stage of development	Newsflow 2015-16
CRLX101 payload camptothecin	Relapsed renal cell carcinoma	Avastin	Phase II	Phase II primary (PFS) and secondary (ORR) endpoint data mRCC Q216.
				Final RCC IST data in peer-reviewed journal end 2015.
				Initiate Phase III 2016.
CRLX101 payload camptothecin	Relapsed ovarian cancer	Paclitaxel	Phase Ib	Phase Ib conducted with GOG safety and efficacy. Data in H116.
CRLX101 payload camptothecin	Relapsed ovarian cancer	Avastin	Phase II	Ongoing interim IST conducted by MGH and Avastin provided by Genentech.
CRLX101 payload camptothecin	Non-metastatic rectal cancer	Chemo-radiotherapy	Phase Ib/II	Interim Phase Ib/II IST data H215.
CRLX301 payload docetaxel	Solid tumors		Phase I	Phase I safety and efficacy data in solid tumors Q415.
				Initiating Phase IIa solid tumors H116, Phase II H117.

Source: Edison Investment Research

Cerulean's research is focused on oncology through its proprietary Dynamic Tumor Targeting Platform (originally developed at MIT and Caltech), which utilizes nanoparticle-drug conjugates (NDCs). These NDCs, made of proprietary cyclodextrin-based polymers, are covalently linked to various anti-cancer therapeutics, or payloads. Cerulean believes its technology is differentiated from other companies with drug conjugate technology through a preferential delivery of its anti-cancer payloads through its linker technology. The technology is thought to work through the leakiness of new blood vessels in tumors, which provides an entry point for payload into tumor tissue, where it then undergoes a sustained release via chemical hydrolysis inside the tumor cells. The nanoparticle drug conjugation enables the delivery of potent and relatively non-toxic drug treatments to selectively target tumor cells while sparing the body's normal cells.

Nanotechnology, or the delivery of drugs to specific cells using nanoparticles, is not unique to drug development. Two nanopharmaceutical oncology treatments are approved by the FDA and are commercially available: Celgene's Abraxane (2014 sales $848m), a nanoparticle albumin-bound paclitaxel to treat breast cancer, non-small cell lung cancer and pancreatic cancer, and the recently launched Spectrum Pharmaceutical's Marqibo, a vincristine sulfate liposome injection for relapsed Philadelphia chromosome-negative acute lymphoblastic leukemia.

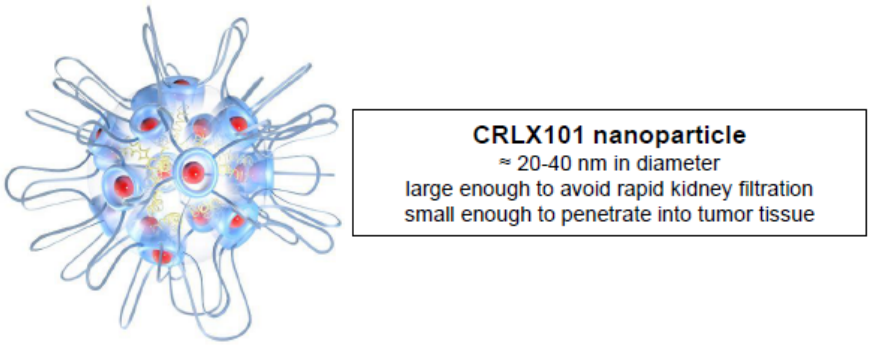
Exhibit 2: Cerulean's Dynamic Tumor Targeting offers sustained release of anti-cancer payload inside tumor cells



Source: Cerulean Pharma company presentation

In 2013, Cerulean reported trial results in a 157-patient, open-label lung cancer study comparing CRLX101 against standard of care in Russia and the Ukraine. The study did not reach its ambitious primary endpoint of overall survival (OS) – typically progression-free survival (PFS) is an FDA-approvable endpoint and often used in initial proof-of-concept studies. While efficacy for CRLX101 alone was somewhat below expectations, on review the company believes the comparative numbers in the study were likely heavily distorted by a high drop-out rate, as well as a portion of patients thought to have received additive chemotherapy treatments in addition to best supportive care in the comparator arm. However, the trial served to establish a strong safety profile for CRLX101, improving the odds of its success in combination with other treatments and targeting alternative cancers. The trial also gave rise to the theory that CRLX101's inhibition of hypoxia inducible factor (HIF) protein could counteract the build-up of HIF caused by VEGF inhibitors that are thought to aid the survival of cancer cells and resist drugs. Cerulean was rebuilt with a new strategic plan and a $15m bridge loan in 2013, eventually completing a successful IPO in April 2014. Today, it is focused on three types of cancer that are known to rely on the HIF survival pathway to overcome drugs and has two NDCs in clinical development in cancer indications.

Exhibit 3: CRLX101 nanoparticle



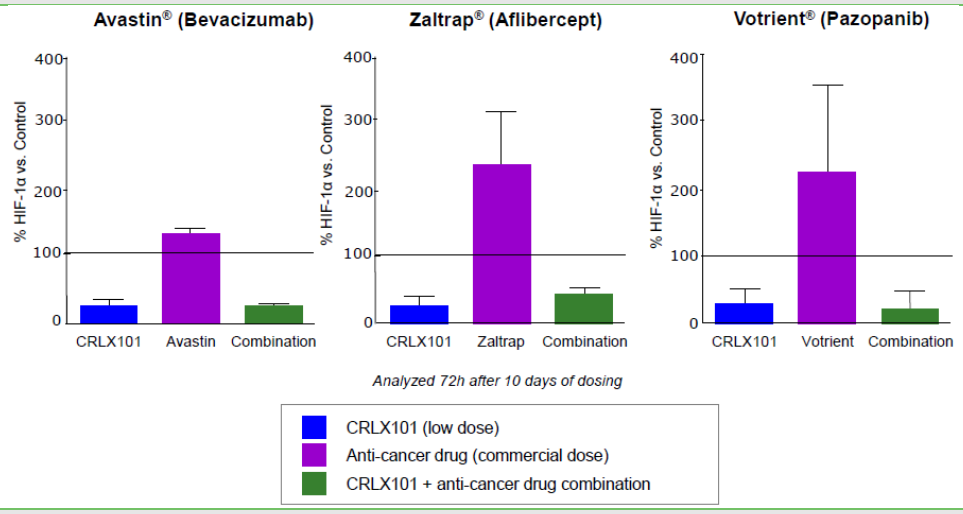
Source: Cerulean Pharma

Pipeline – a big year

CRLX101 greatly reduces toxicity

CRLX101 is a nano-particle drug conjugate with a payload of camptothecin, a dual inhibitor of topoisomerase 1 (topo1), involved in cellular replication, and hypoxia inducible factor (HIF). HIF's subunit, HIF-1α, which looks to build up under hypoxic (oxygen starved) conditions in tumors, is thought to be a master regulator of cancer cell survival mechanisms. It is postulated that HIF-1α triggers cancer cell survival pathways including angiogenesis, drug resistance and metastasis. To date there are no marketed cancer products that durably inhibit HIF-1α. CRLX101 has been dosed in more than 300 patients across various indications. As a monotherapy, the treatment has been shown to be generally well tolerated and its toxicity profile defined by low-grade adverse events and no treatment-related trial deaths.

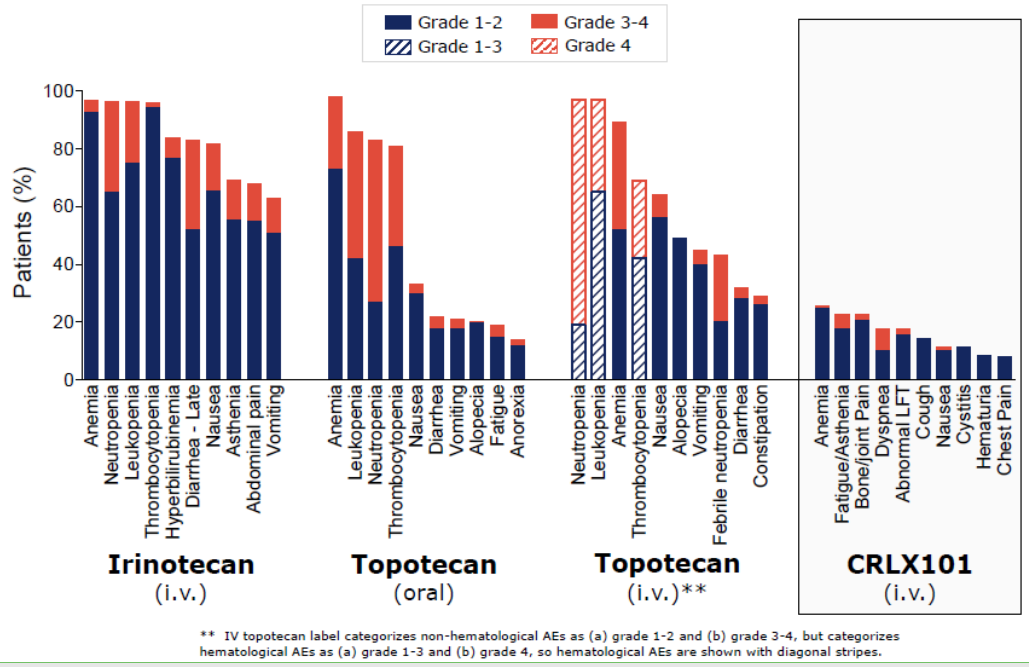
Exhibit 4: CRLX101 in ovarian cancer model prevents HIF-1α increases by other treatments



Source: Clinical Cancer Research 2015, 21:808

Camptothecin analogs have been marketed as irinotecan (Pfizer's Camptosar with peak sales of $970m) and topotecan (GSK's Hycamtin with peak sales of $204m) and used in numerous tumor types. Neither has exhibited activity against HIF-1α, possibly due to dosing constraints and method of delivery. Topotecan is approved for ovarian, cervical and non-small cell lung cancer and irinotecan for metastatic colorectal cancer. While potent, their use thus far has been limited by high toxicity and cannot specifically target tumors. CRLX101, as a nanoparticle-drug conjugate (NDC) is designed to concentrate its camptothecin payload in tumors with a slow sustained release into tumor cells, thereby significantly reducing toxic effects and potentially proving more efficacious. It looks to have the potential to be combined with numerous cancer treatments, having shown preclinical activity when combined with Avastin (bevacizumab) and chemoradiotherapy, while early research data also indicate synergy and potential combinability with additional anti-cancer agents including Zaltrap (antineoplastic and VEGF) and Votrient (tyrosine kinase inhibitor). Thus far CRLX101's development program encompasses company- and investigator-sponsored (ISTs) trials. Clinical studies are ongoing in relapsed renal cell carcinoma (with Avastin), relapsed ovarian (with Avastin and paclitaxel) and neoadjuvant rectal cancer (with chemoradiotherapy), as detailed in Exhibit 1 above.

Exhibit 5: Top adverse events – CRLX101 and approved chemotherapies in the same class



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

Source: Cerulean Pharma. Data not from comparative trial. Note: Irinotecan (FDA label); Topetecan (FDA label), CRLX101 at 15mg/m^2 MTD (Phase II NSCLC trial: 100 patients).

In May 2015 the FDA granted CRLX101 Orphan Drug designation for the treatment of ovarian cancer and in April 2105 awarded Fast Track designation for CRLX101 in combination with Avastin in third- and fourth-line metastatic RCC, paving the way for a potential future accelerated approval process.

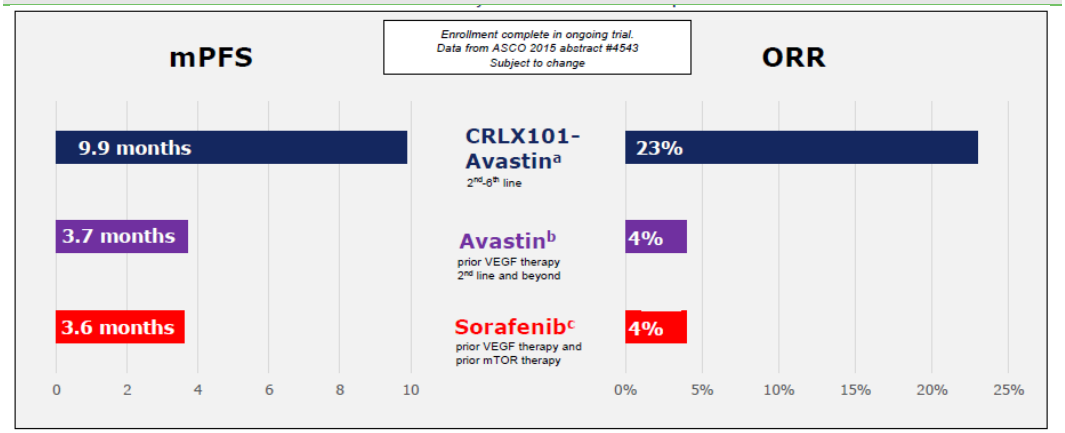
Substantial potential for CRLX101 in unmet need of third/fourth-line rRCC

CRLX101's potential is significant in rRCC, a cancer where an estimated 30% of patients will experience disease recurrence, according to the American Cancer Society. Current standard of care in front-line therapy is normally a tyrosine kinase inhibitor (TKI) and/or mammalian target of rapamycin inhibitor (mTORI), of which there is a number of each on the market. There are next to no viable treatment options for third- and fourth-line use and little in development. CRLX101, with its differentiated mechanism of action to existing treatments, represents a new approach to advanced RCC patients.

The ongoing Phase II randomized trial for CRLX101 in mRCC follows highly encouraging top-line interim results from an investigator-led, 22-patient Phase Ib/II trial in second- to sixth-line mRCC of CRLX101 in combination with Avastin. As presented at ASCO in June 2015, data showed a median PFS of 9.9 months (11.2 months among four of the second-line patients and 7.6 months for the 18 patients in third- to sixth-line). This compares favourably with the PFS of the standard of care in this setting of approximately 3.5 months. The RECIST[1] among all patients was 23%, whereas several studies in relapsed RCC have suggested RECIST response rates of between just 2% and 4%, including one study on Avastin alone. While the trial was a small and single-arm study, it served to demonstrate CRLX101's noteworthy potential potency. Final data are being submitted to a peer-reviewed journal for publication later this year.

[1] Response Evaluation Criteria in Solid Tumours (RECIST) is a set of published rules that define when tumors in cancer patients improve, stay the same or worsen during treatment.

Exhibit 6: Phase Ib/II in relapsed RCC



Source: Cerulean Pharma. Note: Selective data not from comparative trial (a) CRLX101+ Avastin –Dr Keefe's ASCO 2015 abstract #4543 (b) Clinical Genitourinary Cancer, 15 September 2013;116(18): 4256-65.

CRLX101 in combination with Avastin is currently in a randomized Phase II proof-of-concept trial (the RCC trial) investigating its use in third- and fourth-line RCC vs the current standard of care. Patient enrolment in 38 centers in the US and five in South Korea is expected to be complete in the fall of this year. The primary endpoint of the trial aims to show a 3.5- to 5.8-month median PFS in 90 clear cell RCC patients treated with CRLX101 plus Avastin with a hazard ratio of 0.6 and at 80% statistical power (20 patients with non-clear cell will be evaluated independently). Secondary/ exploratory endpoints include overall survival, ORR, safety, pharmacokinetics and plasma biomarkers. Top line primary endpoint and overall response data from the trial is anticipated in Q216.

Metastatic renal cell carcinoma (RCC) treatment protocol

Kidney cancer is among the 10 most commonly diagnosed cancers in men and women in the US. Approximately 64,000 new cases of RCC are expected in the US in 2015 (of which 80% are clear cell RCC and 20% non-clear cell RCC).[2] RCC is one of the most resistant tumors to chemotherapy, radiotherapy and hormonal therapy. If detected early, five-year survival for RCC is high, although in late-stage metastatic RCC the rate of five-year survival is less than 10%.[3] Deaths resulting from RCC are expected to reach up to 14,000 this year, signaling the high recurrence and need for improved therapies. The addressable market in third- and fourth-line mRCC in the US and Europe is approximately 25,000 patients pa[4] for a market opportunity estimated at $1.8bn.

Until the advent of targeted therapies about a decade ago, treatment of mRCC generally consisted of cytokine therapy (eg interleukin-2 and interferon). Approved drugs used in first- and second-line mRCC are now primarily limited to two targeted approaches: VEGF receptors – mainly TKIs such as sunitinib, sorafenib and axitinib – and mTORS (mammalian target of rapamycin) such as everolimus and temsirolimus. In July, BMS discontinued its CheckMate-025 trial after an independent data monitoring committee concluded that its checkpoint inhibitor, nivolumab (Opdivo), demonstrated superior OS compared to everolimus in a Phase III trial in mRCC. Checkpoint inhibitors are a relatively newer class of drug that block PD-1, activating the immune system to attack tumors. Given evidence of efficacy in trials to date, we believe that immune checkpoint inhibitors like Opdivo have the potential for use as a front-line treatment in RCC.Also in July 2015 two companies announced Phase III results that are likely to have an effect on first- and second-line RCC treatment options. Exelixis announced that its TKI, cabozantinib (cabo), showed

[2] Siegel R, Maishadham D, Jemal A. Cancer statistics, 2012. CA Cancer j Clin. 2012; 62:10-29.

[3] http://www.cancer.org/cancer/kidneycancer/detailedguide/kidney-cancer-adult-surivival-rates.

[4] Cancer Statistics, 2015. Cancer J Clin. 2015 Jan-Feb;65(1):5-29.

statistically significant PFS benefit and an interim trend towards an OS benefit versus mTOR everolimus.

Currently, the standard of care in later-stage treatment is a TKI not already used in front line treatment. However, these have historically shown little differentiation in terms of efficacy, demonstrating only modest PFS benefit in patients. The RCC pipeline includes drugs in various classes including immune checkpoint inhibitors, vaccines and novel angiogenesis inhibitors, most of which are targeting earlier line treatment.

Exhibit 7: Select Phase II/III trials in RCC

Company	Product	Therapy Class	Status	target/est enrollment	administration	Notes
Argos Therapeutics, Inc.	AGS-003	Second-generation RNA-loaded autologous dendritic cell immunotherapy	Completed Phase III enrollment	~450	8 injections year 1 then quarterly boosters	Open-label ADAPTR trial comparing AGS-03 plus Sutent vs. Sutenet alone
Exelixis, Inc.	Cometriq (cabozantinib)	Spectrum-selective kinase inhibitor of VEGF rec 2 and c-Met receptor tyrosine kinase ene)	Encouraging Phase III data	658	daily oral	METEOR is an open-label, event-driven trial of cabozantinib vs. everolimus with primary endpoint PFS
BMS/Ono Pharmaceutical Co.	Opdivo (nivolumab)	Human IgG4 mAb against PD-1	Phase III stopped ahead of schedule on positive data	821	bi-weekly IV or daily oral	Check-Mate trial, an open ended study vs. everolimus stopped in July as met its endpoint of OS.
Acceleron Pharma, Inc.	ACE-041 (dalantercept)	Angiogenesis inhibitor that binds to TGF beta preventing signaling through activin receptor-like kinase 1	Phase II part 2	130	twice-daily oral	DART trial dalantercept plus Inlyta vs Inlyta alone in patients who progressed following 1 VEGF receptor TKI
Boehringer Ingelheim GmbH	Vargatef (nintedanib)	Inhibitor of multiple pro-angiogenic kinases, including VEGF, PDGFR and FGF	Phase II	99	twice-daily oral	Open-label trial comparing efficacy and tolerablity of nintedanib vs sunitinib in untreated RCC patients
Eisai Co. Ltd.	E7080 Lenvima (lenvatinib)	Inhibitor of multiple VEGF receptor tyrosine kinases	Phase Ib/II	150	daily oral	Open label trial with everolimus in unresectable advanced or mRCC following VEGF treatment
Tracon Pharmaceuticals, Inc.	TRC105	Human chimeric mAb against endoglin	Phase Ib/II	168	IV	In combination with Inlyta axitinib following 1 VEGF inhibitor

Source: Biocentury, clinicaltrials.gov

Two investigator-led trials progressing in relapsed ovarian cancer

CRLX101 received Orphan Drug designation in May 2015 in relapsed ovarian cancer following positive data in a monotherapy trial, which met its primary endpoint showing four of 29 patients achieving ≥ six-month PFS. CRLX101 plus Avastin is being evaluated in an investigator-sponsored trial IST Phase II in second/third-line recurrent platinum-resistant ovarian cancer as monotherapy and in combination with Avastin. The primary endpoint of the trial is PFS at six months and secondary assessments include ORR and toxicity. Updated results from the trial are expected in the course of 2015. Cerulean has also announced the first patient dosing of a Phase Ib trial, conducted together with the GOG Foundation[5] evaluating CRLX101 in combination with weekly paclitaxel in relapsed ovarian cancer. The open-label, dose-escalation study will enroll up to 18 patients with recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer and will also evaluate preliminary evidence of efficacy. Clinical results are anticipated in H116. The addressable market in second- and third-line ovarian cancer in the US and Europe is approximately 24,000 patients pa[6] for a market opportunity estimated at $1.6bn.

[5] The GOG Foundation is an independent international non-profit organization conducting clinical trials for patients with a variety of gynecological malignancies.

[6] Cancer Statistics, 2015. Cancer J Clin. 2015 Jan-Feb;65(1):5-29.

Neoadjuvant rectal cancer

A Phase Ib/II trial is underway at three US centers evaluating CRLX101 with chemoradiotherapy (CRT) as neoadjuvant[7] treatment of newly diagnosed rectal cancer. Objectives of the trial include rate of pathological complete response (pCR), disease-free survival (DFS) and OS, safety and tolerability and analysis of plasma biomarkers. Initial results in the Phase I portion of the study reported in January have established a maximum dose of 15 mg/m^2 of CRLX101 where no serious adverse events have been reported from the maximum tested dose. Efficacy as of March is encouraging, with seven of eight patients achieving an AJCC/UICC tumor regression score of 0 to 1 (scale of 0 to 3, with 3 the worst). Two of the eight patients showed a pCR, a measure associated with long-term survival, with the current SOC achieving a 10-20% pCR.[8] Cerulean plans to announce updated results by year end 2015. The addressable market in neoadjuvant rectal cancer in the US and Europe is approximately 24,000 patients pa[9] for a market opportunity estimated at more than $5bn.

CRLX301

Like CRLX101, CRLX301 is an NDC with a slow and concentrated release inside tumor cells. Preclinical studies have shown that its payload, docetaxel, delivers up to a 10x greater dose into tumors vs administration of commercially available docetaxel with lower toxicity. CRLX301 showed a similar or improved benefit in all of the seven animal models and statistically improved survival in five of the seven models. First clinical data in Phase I are expected before year end in solid tumors and the second stage of the trial, Phase IIa, is scheduled to commence in H117.

Comprehensive patent estate

With patent extension, the central composition-of-matter patent for CRLX101 expires in 2029 and the dosing patent runs to 2030 for CRLX101. Cerulean also has an extensive patent estate worldwide on its product and technology in three categories: those related to covalent linkage of therapeutics to the cyclodextrin polymer or CDP (CRLX 101 and CRLX301), association of a therapeutic to a polymer and polymeric nanoparticles

Sensitivities

Cerulean is subject to the risks typically associated with an earlier-stage drug development company, including the possibility of unfavourable outcomes in clinical trials, regulatory changes, success of competitors and commercial decisions by partners or potential partners. Additionally, as Cerulean looks to retain marketing rights for its treatment candidates in the US, it will need to secure additional funding to complete its clinical trial programs in currently pursued indications and for commercialization expenses, including marketing and salesforce costs. In the current year, Cerulean has made significant progress in the advancement of its lead treatment candidates through clinical trials. It is moving towards a critical juncture in its development program with key proof-of-concept data for CRLX101's lead indication in mRCC expected in the first half of the coming year. We believe the solid Phase I/IIa data presented as ASCO this year in mRCC should have contributed to a de-risking of the CRLX101 program and note that the current share price does not look to reflect this risk mitigation.

[7] Neoadjuvant therapy aims to reduce the size or extent of the cancer before using radical treatment intervention, making procedures easier/more likely to succeed and reducing the consequences of a more extensive treatment technique.

[8] Br J Surg. 2012 Jul;99(7):918-28.

[9] Cancer Statistics, 2015. Cancer J Clin. 2015 Jan-Feb;65(1):5-29.

Valuation

We value Cerulean at $273m or $10.0 per share on a risk-adjusted net present value basis. We believe the potential of its pipeline is considerably underappreciated by investors pointing to the company's current market capitalization of $128m ($4.7 per share) vis-à-vis a net cash balance at end June 2015 of $71.0m. We model risk-adjusted cash flow for CRLX101 in its three targeted indications of mRCC and ovarian and rectal cancers through to expected loss of market exclusivity in 2029, and include a nominal valuation for CRLX301 which is in a Phase I safety study. We also forecast operational costs for Cerulean, including a significant step-up in R&D as candidates progress through clinical trials.

- We remain conservative in our forecasting, including latter lines of therapy only for CRLX101 as targeted in current studies. Our valuation assumes CRLX101 is used as third- and fourth-line only in mRCC, in second- and third-line in ovarian cancer and as a treatment in neoadjuvant rectal cancer only. We believe that if proven effective in pivotal trials, CRLX101 could also have an opportunity as a treatment in front line settings and possibly in combination with other treatments. The total addressable market for CRLX101 could therefore be more than doubled.
- As addressed earlier, we maintain relatively low penetration rates for CRLX101, eg 25% in mRCC in the US and 20% in Europe, allowing for additional share price upside from our baseline forecasts.
- We include expected milestones of $32.8m and low to mid-single digit royalty payments to licensors of the drug technology platform.
- We include a financing need of $40m in each of 2017 and 2018 in our forecasts as illustrative long-term debt, which we anticipate will be needed to fund future pivotal trials in RCC, ovarian and rectal cancers.

Exhibit 8: Valuation

Product	Launch	Peak sales ($m)	NPV ($m)	Risk adjustment	rNPV ($m)	rNPV/share ($)	Key assumptions
CRLX101 mRCC	2019	490	288	35%	101	3.69	Assumes market of 10,000 patients US (15k EU) in third- and fourth-line, penetration 25% US and 20% EU.
CRLX101 ovarian	2021	340	141	20%	28	1.03	Assumes market of 9,000 patients US (15K EU) in third- and fourth-line, penetration 20% US and 15% EU.
CRLX101 rectal	2021	770	347	15%	52	1.90	Assumes market of 28,000 patients (47k EU) in third- and fourth-line, penetration 15% US and 10% EU.
CRLX301	2023	550	210	10%	21	0.77	Indicative peak sales of $550m.
Net cash (end Q215)					71	2.60	
Overall valuation					273	10.00	

Source: Edison Investment Research

Financials

Cerulean is currently adequately capitalized. Following its successful fund-raising in April, which grossed proceeds of $40.3m, Cerulean ended June 2015 with cash of $85.5m and net debt of $71.1m), which we anticipate should be sufficient to fund planned clinical trials into 2017. The company borrowed $15m in January 2015 on the first tranche of a loan agreement with Hercules and holds options to draw down an additional $11m. From 2017 we expect Cerulean will look to source additional funding for its growing clinical trial program. We include $40m in illustrative long-term debt in our model in each of 2017 and 2018, mainly to cover expected R&D costs. However, we note amounts remain heavily dependent on the final trial design of key pivotal programs for

CRLX101 and CRLX301. On our forecasts, the company will reach profitability in 2020 based on the successful first launch of CRLX101 in mRCC.

The company reported second quarter 2015 results on 6 August. A net loss of $9.9m was reported, compared with a loss of $7.4m in Q214. R&D increased to $6.7m in Q115 vs $2.7m in Q214, primarily due to costs associated with clinical trials for CRLX101 of $5.0m in Q215 vs $1.9m in the previous year, which are mainly related to the expense of the ongoing RCC trial. SG&A expenses were $2.7m in Q215, up from $2.0m to support a growing corporate infrastructure.

Exhibit 9: Financial summary

$000s	2013	2014	2015e	2016e	2017e
Year-end 31 December	US GAAP	US GAAP	US GAAP	US GAAP	US GAAP
PROFIT & LOSS					
Revenue	6	80	0	0	0
Cost of Sales	0	0	0	0	0
Gross Profit	6	80	0	0	0
Research and development	(9,700)	(11,772)	(25,699)	(27,500)	(28,500)
General & administrative	(6,166)	(8,587)	(11,398)	(12,538)	(13,792)
EBITDA	(16,057)	(20,405)	(37,180)	(40,247)	(42,572)
Operating Profit (before GW and except.)	(15,860)	(20,279)	(37,097)	(40,038)	(42,292)
Intangible Amortisation	0	0	0	0	0
Exceptionals/Other	0	0	0	0	0
Operating Profit	(15,860)	(20,279)	(37,097)	(40,038)	(42,292)
Net Interest	(1,485)	(1,074)	(2,214)	(438)	(446)
Other (includes change in fair value of warrants)	202	(1,989)	(8)	0	0
Profit Before Tax (norm)	(17,345)	(21,353)	(39,311)	(40,476)	(42,738)
Profit Before Tax (FRS 3)	(17,143)	(23,342)	(39,319)	(40,476)	(42,738)
Tax	0	0	0	0	0
Deferred tax	0	0	0	0	0
Profit After Tax (norm)	(17,345)	(21,353)	(39,311)	(40,476)	(42,738)
Profit After Tax (FRS 3)	(17,143)	(23,342)	(39,319)	(40,476)	(42,738)
Average Number of Shares Outstanding (m)	0.7	14.5	25.0	25.8	26.5
EPS - normalised fully diluted ($)	(25.35)	(1.64)	(1.57)	(1.57)	(1.61)
EPS - FRS 3 ($)	(25.35)	(1.64)	(1.57)	(1.57)	(1.61)
Dividend per share ($)	0.0	0.0	0.0	0.0	0.0
BALANCE SHEET					
Fixed Assets	380	557	1,350	1,589	1,768
Intangible Assets	0	0	0	0	0
Tangible Assets	245	342	697	936	1,115
Other	135	215	653	653	653
Current Assets	6,447	52,836	66,748	27,753	26,589
Stocks	0	0	0	0	0
Debtors	959	1,662	1,609	1,609	1,609
Cash	5,488	51,174	65,139	26,144	24,980
Other	0	0	0	0	0
Current Liabilities	(15,146)	(8,061)	(7,845)	(7,845)	(7,845)
Creditors	(12,012)	(4,937)	(5,191)	(5,191)	(5,191)
Short term borrowings	(3,134)	(3,124)	(2,654)	(2,654)	(2,654)
Long Term Liabilities	(85,980)	(7)	(12,387)	(12,534)	(52,682)
Long term borrowings	(3,124)	0	(12,163)	(12,310)	(52,458)
Other long term liabilities	(82,856)	(7)	(224)	(224)	(224)
Net Assets	(94,299)	45,325	47,865	8,963	(32,169)
CASH FLOW					
Operating Cash Flow	(17,202)	(19,477)	(36,536)	(38,546)	(40,704)
Net Interest	588	416	1,791	445	449
Tax	0	0	0	0	0
Capex	(7)	(225)	(438)	(449)	(460)
Acquisitions/disposals	0	40	0	0	0
Equity Financing	35	60,002	39,657	0	0
Dividends	0	0	0	0	0
Other	8,236	8,064	(2,203)	(870)	0
Net Cash Flow	(8,350)	48,820	2,272	(39,419)	(40,714)
Opening net debt/(cash)	(7,580)	770	(48,050)	(50,322)	(11,180)
HP finance leases initiated	0	0	0	0	0
Exchange rate movements	0	0	0	0	0
Other	0	0	0	278	0
Closing net debt/(cash)	770	(48,050)	(50,322)	(11,180)	29,534

Source: Edison Investment Research, company accounts

Contact details	Revenue by geography
840 Memorial Drive 5th Floor Cambridge, MA 02139 Cambridge, MA 617-551-9600 ceruleanrx.com	N/A

Management team

Christopher Guiffre: President and CEO	Adrian Senderowicz: CMO
Before taking on the role of president and CEO of Cerulean in March 2015, Mr Guiffre served as COO and senior VP and chief business officer. Previously, he held executive positions with biotechnology firms that included Alvos Therapeutics, Hydra Biosciences and Cubist Pharmaceuticals.	Dr Senderowicz joined Cerulean in September 2015. Previously, he was CMO and senior VP of clinical development and regulatory affairs at Ignyta, VP of global regulatory oncology at Sanofi, CMO at Tokai Pharmaceuticals and senior medical director of oncology clinical development at Astra Zeneca.
Gregg Beloff: Interim CFO	
Interim CFO since May 2015, Mr Beloff is a member of Danforth Advisors, specializing in financial and strategic support to life sciences companies. Previously, he served as CFO at two public and three private companies. In his roles he has managed finance, accounting, corporate communications, human resources, legal, IT and business development.	

Principal shareholders	(%)
Polaris Venture Partners	17.30
Fidelity Management & Research	14.39
Venrock Partners	11.04
CVF	9.49
Lilly Ventures	8.63
Lux Capital Management	3.31

Companies named in this report

Argos Therapeutics, Exelixis, BMS, Ono Pharmaceutical Company, Acceleron Pharma, Boehringer Ingelheim

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