CERULEAN

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Dear Stockholders,

The Cerulean team is targeting cancer cells through known, active pathways, and a reduction of the off-tissue toxicity that limits the application of therapies against these pathways, with our nanoparticle-drug conjugates (NDCs). This is a strategy that has yielded clinical and commercial success in many areas of oncology, including many recent examples, and we believe our engineered approach to designing anti-cancer therapies has the potential to deliver even better outcomes.

In 2015 and early 2016, we made a number of key advances. We presented important clinical data for our lead program, CRLX101, in kidney and ovarian cancers. We secured collaborations with the GOG Foundation Inc., AstraZeneca and the National Cancer Institute (NCI). We were awarded fast track designation in kidney cancer as well as orphan drug designation in ovarian cancer. We also presented and published clinical evidence showing how CRLX101 preferentially accumulates in the tumor while sparing healthy tissue. We strengthened the Board of Directors, the management team, and our balance sheet.

Our first platform-generated NDC is CRLX101, and its lead indication is kidney cancer, known as renal cell carcinoma (RCC). The RCC treatment paradigm is changing rapidly as many companies rush to address a pronounced unmet medical need. Recent and imminent approvals are giving patients better options in first and second line metastatic RCC. We believe these improvements will lead to a reordering of the standard of care, with immunotherapies as the preferred initial treatment option and new TKIs as the preferred second line option. We also believe that later lines of treatment represent an attractive opportunity for CRLX101, as RCC patients will benefit from the new treatment options in first and second line, thus growing the market in third and fourth line. Here, as in earlier lines of treatment, we believe combination therapies will be the key to unlocking greater benefit for patients.

To that end, in March 2015, we announced positive Phase 1b/2 data of CRLX101 in combination with Avastin® (bevacizumab) for the treatment of relapsed RCC. Avastin is approved for use in RCC, and is among the most successful cancer products. The investigator-sponsored trial achieved its primary endpoint of safety and tolerability. The trial also achieved at least 50% of patients reaching four months or more of progression-free survival (PFS). Median PFS among all patients in the trial receiving the combination was 9.9 months, a multifold improvement over historical comparators, which, in the third and fourth line setting, show approximately 3.5 months of PFS.

These data led us to run our ongoing randomized Phase 2 clinical trial in third and fourth line RCC. This fully enrolled, 115 patient trial compares CRLX101 plus Avastin to investigator's choice of standard of care in RCC patients who have received two or three prior lines of therapy. The trial is sized to show a 2.3 month improvement over an expected 3.5 month median PFS for standard of care, or a 40% improvement in PFS over available third and fourth line treatments.

Beyond RCC, we are exploring the combination of CRLX101 and anti-cancer agents in other cancers with significant unmet medical need. Among these are two trials in relapsed ovarian cancer, including a second Avastin combination Phase 2 trial sponsored by Massachusetts General Hospital and another trial being conducted in collaboration with the GOG Foundation, which is assessing CRLX101 in combination with paclitaxel. We are also collaborating with AstraZeneca and the NCI to evaluate CRLX101 with LYNPARZA™ (olaparib), a PARP inhibitor, in the treatment of solid tumors. Further, we are researching CRLX101 preclinically in combination with immuno-oncology agents.

Our second platform-generated NDC is CRLX301. We are currently studying CRLX301 in a Phase 1/2a trial in solid tumors. In the Phase 1 portion of the trial, we established the maximum tolerated dose in a once every three weeks dosing regimen and we currently are treating another cohort with a weekly dosing regimen.

None of this progress could have been achieved without the hard work of the dedicated team here at Cerulean, the support of collaborators in our industry and the medical community, or the loyalty of our investors. The potential opportunities for CRLX101, CRLX301 and our platform are exciting. I thank you for your continued support, and look forward to reporting on our progress as we continue to focus on building value for all our constituents.

Very truly yours,

Christopher D. T. Guiffre
President & Chief Executive Officer