THE WALL STREET TRANSCRIPT
Connecting Market Leaders with Investors

Critical Outcome Technologies, Inc. (CVE:COT)

ALISON SILVA, M.A., is the President and Chief Executive Officer and a Director of Critical Outcome Technologies, Inc. Previously, she was a Co-Founder, Executive Vice President and Chief Operating Officer at Synlogic, Inc., where she led the regulatory strategy, drug development and operational aspects of the company's focus on the discovery and development of engineered therapeutic probiotics. Ms. Silva is also a Co-Founder of The Orphan Group, a specialty consulting company focused on assisting companies with developing and implementing their orphan drug strategy and product lifecycle management. Ms. Silva previously held the position of Chief Operating Officer at SLA Pharma, a GI oncology-focused biotech company, where she was responsible for heading up U.S. corporate and clinical operations for their pipeline of orphan drug candidates. Prior to joining SLA Pharma, Ms. Silva was Vice President of Drug Development at Marina Biotech through its acquisition of Cequent Pharmaceuticals in 2010, where she held the same role since 2007. Ms. Silva began her career in drug development in clinical operations with various positions at Pfizer, Massachusetts General Hospital and the University of Massachusetts. Ms. Silva holds a bachelor's degree from Clark University, and a master's degree from Clark University and UMass Medical Center.

SECTOR — PHARMACEUTICALS

TWST: What is Critical Outcome Technologies today?

Ms. Silva: We are a clinical-stage biotech company that uses a proprietary technology platform to identify drugs to treat cancer and other unmet medical needs. We are a public company that is traded on the venture arm of the TSX in Canada and on the OTC market in the U.S. We have two offices: one in Boston, Massachusetts, and one in London, Ontario. Our first drug candidate, COTI-2, is an oral, small molecule intended to treat gynecologic malignancies via a p53-dependent mechanism of action. We initiated a Phase I clinical trial at MD Anderson Cancer Center in Houston, Texas, in February 2016, and added a second site, Northwestern University's Lurie Cancer Center, in Chicago, Illinois, in June 2016.

At the heart of our organization, we are a technology platform company that has built a solid pipeline of development candidates via a technology called CHEMSAS®. CHEMSAS is a computational platform technology that is based on a hybrid of machine learning and proprietary algorithms that allows us to predict biological activity based upon a compound's molecular structure. We currently program up to 300 or so input parameters that analyze 3D structures and produce unique data patterns that provide markers of potential toxicity and efficacy.

TWST: So that platform that you just mentioned, CHEMSAS, would enable you to have a better idea of which potential molecules to go forward with?

Ms. Silva: Yes, absolutely. It's our mechanism for in silico high-throughput screening of extensive libraries of potential compounds. We analyze different structures to gauge binding affinities, predict bioavailability and drug interactions, and flag potential markers of toxicity. This process allows us to narrow down the number of compounds advancing into the traditional drug development process, allowing us to quicken the pace of early discovery efforts.

TWST: Your platform technology, are you intending at all to license it or to provide it as a service to other companies, or are you holding on to it at this point to use it for your own internally developed compounds?

Ms. Silva: We are using CHEMSAS for the discovery of our own compounds and are not pursuing any fee-for-service or licensing agreements. We intend to build our pipeline internally and advance our drugs into the clinic, through different increasing value proposition and de-risking phases of development. We could potentially license CHEMSAS opportunistically with the appropriate partner in the future.

TWST: Talk about that lead asset in terms of where it is in the pipeline and also the science behind it, and then why you chose the particular lead indication you chose for it.

Ms. Silva: Our lead asset, COTI-2, is an activator of p53 function. p53 has been widely regarded as an undruggable target of interest for about 50 years and has been dubbed "the guardian of the genome." In healthy patients, p53 protein functions by inducing apoptotic cell death,

suppressing tumor growth and cellular proliferation, thereby fending off disease. When the normal p53 function is lost, which is the case in the mutated form of the p53 gene, the body loses its defensive ability against disease progression, and patients experience a state of hyperproliferation, uncontrolled cellular growth and tumor development.

The p53 mutation rate is something that is of particular interest within our company. Industry and academic research cites p53 mutation rates ranging from 38% to about 96% of all cancers. COTI-2 induces a wild-type-like conformational change in the misfolded protein, enabling the protein to regain its function. It restores the sequence-specific transcriptional activity, allowing the protein to induce apoptosis, cellular growth arrest and senescence.

Our COTI-2 program is currently in a Phase Ib/IIa in the U.S. at two sites, MD Anderson Cancer Center and Northwestern University. It is presently directed at the target population of gynecological malignancies, which includes ovarian cancer, endometrial cancer and cervical cancer. We were granted FDA orphan drug designation for ovarian cancer, so likely a drug label in the future would be directed at that specific population of p53-mutated gynecological cancers.

COTI-2 is in the dose-escalation phase of the current trial, specifically in the fourth dosing cohort. This is a very standard 3+3 study design, with an initial 28-day surveillance period followed by dose-level escalation after the cohort has safely tolerated the therapy for the surveillance period. As I mentioned, we currently are dosing patients in cohort 4, which is a dose of 1.7 mg/kg. Cohort 1 started at a dose level of 0.25 mg/kg, with cohort by cohort increases to 0.5 mg/kg, cohort 2; 1.0 mg/kg, cohort 3; and now at 1.7 mg/kg.

The trial is progressing very well. We are authorized to dose up to cohort 6, which would escalate the dose level up to 3.5 mg/kg. We will escalate to that dosing level, reach a maximum tolerated dose, or MTD, prior to that, or we could reach a dose that shows biomarker and radiological therapeutic activity prior to the conclusion of the standard dose-escalation phase. The 3+3 study design allows us to expand each cohort to take a closer look at the data and its significance.

TWST: If this were to be successful, is there a companion diagnostic you would need?

Ms. Silva: p53 is a gene that most cancer patients are routinely screened for, so we don't need a companion diagnostic. When patients undergo genomic screening, p53 is one of the first genes analyzed, so we would easily know this going into the trial. Also, this is a standard-of-care laboratory test that is covered by insurance, so this inclusion criteria would be readily available to us with standard screening.

TWST: You talked about the orphan designation and your interactions with the FDA that could help expedite the development of COTI-2. When is the earliest you might see COTI-2 in the marketplace if you did get positive results?

Ms. Silva: Our earliest publicly stated projections for commercialization would be approximately 2021, and that is if all stars aligned from clinical and regulatory standards. The first time COTI-2 was ever introduced to patients was one year ago. We are ensuring we run a sound Phase I trial, with the primary objective being safety and tolerability. If we observe signs of efficacy in this current trial, in addition to definitive safety, there are real benefits to patients and the company based upon our orphan drug strategy.

Orphan drug status usually comes with an expedited review process, smaller-sized clinical trials, early entry into the patient population, an extended patent life, access to funding, all essentially translating into a more manageable development process for small biotech companies. The combination of our preclinical data and unmet medical need supported our entry into the ovarian cancer population as our "first in man" trial — and are the assumptions associated with the earliest predicted commercial availability of COTI-2 in 2021.

TWST: Do you have all the financing that you need to get to the next set of milestones, and are you looking for any additional financing or partnerships at this time?

Ms. Silva: We have publicly stated that we are financed until about the third or fourth quarter of 2017. That will get us through this next milestone readout, which is the completion of the dose-escalation phase expected at the end of the second quarter. That will be a key time period for us as we identify the MTD, which will be the dose that will carry forward into the two expansion cohorts.

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After we complete the dose-escalation phase, we will initiate two expansion phases that have already received regulatory authorization: one for ovarian cancer patients, and one for head and neck cancer patients. Preclinically, we have demonstrated that COTI-2 is incredibly active in a head and neck cancer xenograft mouse model, both as a monotherapy and in combination with radiotherapy. Additionally, head and neck cancer patients exhibit a very high p53 mutation rate, so this was a natural second indication to pursue with COTI-2.

TWST: Was the reason that you chose ovarian based upon early tests demonstrating the potential for efficacy?

Ms. Silva: The selection was based upon preclinical efficacy, molecule screening as well as the target profiling patient population and development competition.

In addition to this key data, which will be used to advance our program, we are looking at safety and tolerability as the primary endpoints of the trial. We are also looking at biomarker and radiology endpoints, which include pre- and post-dose CA 125 levels and imaging to assess any potential benefit. The readouts occurring in the middle of the year will be a very interesting period of news flow for us.

We are currently looking at partnership opportunities. That is a never-ending campaign of any small biotech. We have conversations with a few pharma companies every quarter or so to update them on our progress. They continue to be interested in our progress, not only

of our COTI-2 program in the clinic but also in our growing pipeline. We are currently running certain preclinical studies at the request of large pharma to look at additional indications, combination therapies and specific animal models. At some point before the third quarter, likely, we will be looking at additional financing, and this could be in the form of a partnership leading to a nondilutive capital or a traditional financing raise.

TWST: I want to make sure we cover the company's other assets. You have another technology called ROSALIND™ as well as a small cell lung cancer library. Can you talk about some of the other assets and what you are doing with them at the moment?

Ms. Silva: Sure, let me discuss ROSALIND first. ROSALIND is not our parent technology, but it really is a complement to the oncology portfolio we are building. ROSALIND is a smart data technology for realizing this promise of personalized medicine that we hear a lot about for cancer patients. ROSALIND is a programmable computer simulation of cellular patterns, in which we are able to look at the causal relationships between genetic mutations and cell-signaling abnormalities in cancer cells. The program generates a readout of the best mono or combination therapies for patients. We've also used ROSALIND to evaluate the effectiveness of our own assets in combination with other therapies.

The initial utility of the ROSALIND platform is to look at existing therapies and be able to help oncologists prescribe the most effective drug combinations for their patient's particular gene mutation(s). Right now, a lot of patients with a wide variety of cancers are receiving first-line therapies that are considered standard of care and can have minimal to moderate activity for that specific tumor type. The promise of our technology is to be able to provide a more personalized and hopefully less toxic list of suggested therapies for oncologists.

The KRAS gene functions by providing your body with instructions for making the KRAS protein, which plays a role in signaling a number of cellular pathways that regulate healthy cell growth and proliferation. When this protein is in its overactive state and unable to be regulated, you have hyperprolific cell growth and proliferation. COTI-219 preclinically has demonstrated the ability to inactivate the production of KRAS in this state and dampen that response that carries with it overactive tumor cell growth.

The interesting thing about KRAS is it is a mutation that is found in so many cancers. You mentioned small cell lung cancer; KRAS is prevalent in about 35% of these cases, in about 45% of colorectal cancer and also in about 90% of pancreatic cancers. Additionally, patients presenting with KRAS mutations have clinically been observed as being poor responders to first-line therapies, further highlighting the transformational nature of an oral targeted therapy that could block the function of the mutant KRAS protein.

We announced COTI-219 as our second clinical candidate in October of 2016. Right now, we are progressing through IND-enabling studies, scale up and manufacturing in order to advance this clinical candidate with the IND filing anticipated by the end of 2017. The trial will likely focus on a rare form of leukemia that we have identified as having a 100% rate of KRAS mutation.

TWST: Further to the library of molecules I believe that you have, would you extend this repository to others at this stage, and or is it for internal pipeline development?

Ms. Silva: That library is a group of small molecules that we have identified via CHEMSAS, and we are working on their best utility, where they fit best into our oncology portfolio. The development of these discovery and preclinical assets depends largely on the generation of

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We want to acknowledge the pure numbers challenge behind this art. If you take the number of FDA-approved oncology drugs and look at unique mono and combination therapy possibilities — for up to three combinations therapies — an oncologist is facing over half a billion potential drug combinations to assess for their patients. Our platform is designed to simplify this process and to help the medical community better treat their patients. ROSALIND is presently in a validation study of 100 patients. We are running the retrospective study out of our offices and providing the data output from ROSALIND to oncologists who are interested in incorporating the readout into their patient-care decisions.

In terms of our other assets, COTI-2 leads our pipeline. We announced our second clinical candidate, COTI-219, last year, which is another oral small molecule. This was again discovered by our CHEMSAS platform. COTI-219 targets the mutant form of KRAS. Similar to COTI-2's broad-reaching potential as targeting a tumor suppressor gene, KRAS belongs to another important family of genes implicated in the development of cancers known as oncogenes.

funds over the next few years. While we focus on advancement of COTI-2 and COTI-219, we would be open to various partnerships for these assets that are in earlier stages of development. We also would look at regional and co-development deals with all of our molecules.

TWST: If COTI-2 was successful and you were able to bring that to market for ovarian cancer in the U.S., then what would be your next step? Would you then try to go to other countries for that indication, or would you try to commercialize it in another gynecological cancer in the U.S.?

Ms. Silva: We plan to take COTI-2, intended for the treatment of ovarian cancer, to registration in the U.S. As mentioned, we would be open to regional or co-development deals, with the main driver being to expand COTI-2's reach in oncology. That said, independently or with a partner, there are a number of other orphan diseases we could target with COTI-2, including head and neck cancer, cervical cancer and endometrial cancer. We would like to pursue these other indications, as well as combination therapies with COTI-2, which may be an ideal area of potential partnerships.

We observe preclinically that COTI-2, in combination with low-grade radiation therapy, has a significant additive effect in eradicating tumors compared to radiotherapy alone. Additionally, combination therapy with cisplatin has demonstrated a synergistic combination profile at low doses, potentially allowing patients to escape some drug-limiting toxicities they previously experienced with higher concentrations of their chemotherapeutic. Both of the above scenarios would lend themselves nicely to a partner with relevant in-kind expertise.

TWST: Just for readers who don't know, how many patients are in ovarian cancer for the U.S.?

Ms. Silva: In the U.S., there are about 180,000 ovarian cancer patients.

TWST: OK. And the standard of care right now is?

Ms. Silva: The standard of care is usually the combination of a platinum compound, such as cisplatin or carboplatin, and a taxane, such as paclitaxel, or Taxol, or docetaxel, or Taxotere. There are several p53 targeted therapies in development. We differentiate ourselves in three areas: We offer an oral route of administration versus intravenous dosing, we specifically target just the mutant form of the protein resulting from the genetic defect, and those prior two points allow us to dose at levels that are orders of magnitude less concentrated, potentially leading to increased efficacy at doses with a superior safety profile.

TWST: What significant management or operational changes might be taking place in the company in the next 12 to 24 months? And if they are happening, why would they be happening?

Ms. Silva: We do not anticipate any managerial changes over this time frame. I joined the company as President in July of last year, and was appointed as CEO and President on January 1 of this year. We are also in good shape for planned operational changes. We opened our Boston office six months ago, which was a big corporate change for us. So we will be running all of our science and computational work out of the London, Ontario, office and running most of the corporate and clinical operations out of our Boston office. Those changes have been implemented and will continue to evolve over the next 18 to 24 months.

In terms of corporate growth, we would love to uplift to one of the U.S. securities boards as well as the main board on the TSX. Currently, we are on the venture arm of the TSX in Canada and the OTC in the U.S. market. This type of corporate repositioning is predicated upon perceived corporate valuation, funding, capital structure and stock performance, driven by our clinical results, the strength of our pipeline and underlying technologies.

TWST: What do you want a potential investor in Critical Outcome Technologies to know today?

Ms. Silva: The company has developed a portfolio of oncology technologies and development-stage assets dedicated to improving personalized patient care. Both CHEMSAS and ROSALIND focus on the identification of ideal novel or existing therapies to provide the most targeted approach to treating cancers. This is truly transformational and disruptive.

On the molecule-creation side, we are a company that is able to both design and develop new clinical candidates via the CHEMSAS engine, allowing us to build a pipeline at an almost unlimited cadence. We have chosen a strategic path from a development standpoint that will give us a principal proof of concept in patients as early as possible, via the orphan drug designation, and that will be our strategy moving forward with all of our front-line candidates. The traditional bench-to-bedside approach to drug development with standard, long-established timelines does not apply to us. We hope this strategy combined with our novel technology platforms and team of computational experts provides a unique opportunity to bring safe and effective products to patients in need.

TWST: Is there anything else you wanted to mention that we haven't covered already?

Ms. Silva: No, I think that is a lot of information, thank you.

TWST: Thank you. (KJL)

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