

**Validating POL 1 and CK2 Inhibitors as Targets in Cancer, and Demonstrating their Small Molecule CX-5461 Drug's Ability to Selectively Kill Cancer Cells but Not Normal Cells Separates Cylene Pharmaceuticals, Inc. from Other Pharma Companies**

**Healthcare  
Biotechnology  
(Private)**

**Cylene Pharmaceuticals, Inc.**

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**William G. Rice, Ph.D.  
President and CEO**

**BIO:**

Dr. Rice serves as Cylene's President and CEO and as a Director. He brings more than 20 years of know-how from diverse leadership roles and industry experience, during which he received numerous biotech achievement awards, delivered multiple first-in-class agents, negotiated various business relationships, executed a series of corporate financings, and was a finalist for Ernst & Young's

Entrepreneur of the Year Award. Dr. Rice joined Cylene from Achillion Pharmaceuticals, where he was founder, President, CEO and Director. Prior to Achillion, Dr. Rice was Senior Scientist and Head of the Drug Mechanism Laboratory at the National Cancer Institute-Frederick Research Center, where he received the Scientific Achievement Award and Outstanding Performance Award, and he identified novel agents and published in Science, Nature and other prestigious journals. Dr. Rice was an academic professor of Pediatric Hematology and Oncology at Emory University School of Medicine, he served as a Post-doctoral Trainee in the Department of Internal Medicine at the University of Michigan Medical Center, and he holds a Ph.D. in biochemistry from Emory University.

**Company Profile:**

Cylene Pharmaceuticals is a clinical stage private company developing small molecule drugs against newly validated cancer targets. Cylene's leadership in exploiting CK2 pathways enables rational drug combinations for improved treatment outcomes against many cancer indications. Cylene's Pol I Inhibitor program created CX-5461 as a small molecule, non-genotoxic drug to selectively kill cancer cells by activating the p53 tumor suppressor in malignant but not normal cells. Cylene's unique approaches deliver innovative cancer agents that can enable pharmaceutical companies to expand their portfolios and extend the efficacy, lifecycle and reach of current cancer therapeutics.

**Interview conducted by:  
Lynn Fosse, Senior Editor  
CEOCFO Magazine**

**CEOCFO:** Dr. Rice, what is the vision and focus at Cylene Pharmaceuticals?

**Dr. Rice:** Currently, we are a private company, focused exclusively in the oncology space. We discover and develop small molecule inhibitors of newly validated targets for cancer therapy, so that we can deliver impactful and life-saving drugs to cancer patients.

**CEOCFO:** Many companies are broadly doing the same thing. What is your niche and what perspective do you have that is a bit different?

**Dr. Rice:** One of the major items of difference is the types of targets that we go after. There is a concept YAKI (Yet Another Kinase Inhibitor). If you look around, so many companies are going after small molecules or various inhibitors of Kinases that are mutated. These various companies believe they can come up with an inhibitor of those and target a specific type of cancer. We took a little bit of a different approach. For instance, the RNA Polymerase 1 (POL 1) is a target that we have gone after. It is a target that people have known about for decades. It is known to be over expressed in cancer and everyone believed it might be a target. However, it is also important in normal cells. Therefore, people thought if you inhibit POL 1 then you would affect both cancer cells and normal cells. Many scientists out there would not go after POL 1. However, we believed that the biology indicated if you selectively target POL 1 in cancer cells you

can selectively kill cancer cells and not normal cells. That was a belief we had based on data. We were willing to go after new molecular targets, take the time and expense to validate those targets, then create new inhibitors of those targets and advance the new drugs to the clinic. In the case of POL 1, it is the target we just validated and that is presented in the *Cancer Cell* article. We developed a first in class molecule and now we are taking that to the clinic within a matter of months. In another technology, in this case, we were going after a Kinase, but one that is not mutated in cancer cells. Many people saw it as a housekeeping protein. However, we saw that it is over expressed in cancer and we validated it as essential in cancer. The target, called CK2, is a protein Kinase. We demonstrated that we can develop small molecule inhibitors of CK2 and drive those molecules to the clinic. In each of these cases, we set our sights on novel targets, ones that are typically not mutated. Scientists have seen that POL 1 and CK2 are important in cancer, but they had not been validated as targets. We validate both of these targets, create first in class molecules against each target and then advanced these innovative drugs to the clinic. That represents, in many ways, how we are different. We approach very different types of molecular targets that we feel are going to be essential in cancer, but that others have either overlooked or have been unable to target.

**CEOFCO:** What is it about you and your team that gives you the confidence to take an approach shielded away from by others?

**Dr. Rice:** Above all, we follow the science. When it comes to the targets, you first determine what types of indications or cancers would you want to treat, and ask is there a market to sell a drug in those cancers? If we wish to develop a particular type of drug, we ask if we can actually afford to develop it, can we commercialize it, and is there an unmet medical need? Then you go back and investigate the hardcore science and not just conjecture or people's beliefs or idealism. It is pragmatism. You look at the

molecular level and try to gain understanding of whether it can be a target. For instance, I was Head of the Drug Mechanism Lab at The National Cancer Institute before I went into biotechnology, and I have a strong background in understanding new molecular mechanisms of drugs. I brought that mindset into the company. Separately, Daniel Von Hoff, M.D., the founder of our company, is a world leading clinical oncologist who has taken more drugs into Phase 1 than any other person on the planet. He understands that if you are going to develop a new drug that delivers a major clinical impact, then the drug needs to be against a new molecular target. That is how you are really going to have an impact on the disease and help the patients. He had been developing other people's drugs for years. Therefore, he founded this company to go after new molecular targets to develop new classes of drugs, and that is what we have done.

**Cylene's Pol I Inhibitor program created CX-5461 as a small molecule, non-genotoxic drug to selectively kill cancer cells by activating the p53 tumor suppressor in malignant but not normal cells. - William G. Rice, Ph.D.**

It was originally in his DNA and then I brought my DNA into the mix. We do not want to do the same thing over and over and just make a better mouse trap. We want to create new technologies, new targets and new classes of drugs. You will see, when you read the *Cancer Cell* paper that we just published, this represents an entirely new molecular approach to cancer therapy. It truly is a major advancement.

**CEOFCO:** Has the medical community been paying attention?

**Dr. Rice:** We have not been out there talking about this concept because if you come out and you say you are going after a new target, then everybody says, "Yeah, yeah, come back when it is validated." Therefore, we validated it. If you go out with a validated target but no drug, they say, "Come back when you have a drug." Then if we do that, they say, "Come back when you are in the clinic". Therefore, we waited and completed

the process of identifying the target, validating it and creating a first-in-class drug known as CX-5461. Then we even identified genetic markers that tell us which tumors are the most sensitive so we can select the patients most likely to benefit from the drug. That is personalized medicine, and we utilized pharmacogenomics to guide which patients could best be served by CX-5461. Now we have the drug and it is going into the clinic in just a couple of months. We have been quiet and kept this program off the radar screen. However, I can tell you that the people who work with us and know about CX-5461 are extremely excited because scientists and clinicians have long sought a drug to selectively activate p53 in cancer cells. These include Dan Von Hoff who is the founder of Cylene, Brian Druker, who is an advisor to the company, and also the clinicians who will be performing the Phase 1 study in Australia. The medical community is embracing POL 1 as a target and CX-5461 as a drug as they learn about them. However, most people are not yet aware of the technology.

**CEOFCO:** Why Australia for your trial?

**Dr. Rice:** As we began working in POL 1, we believed in this target, we went after it; we created this new drug, CX-5461. As we began to develop CX-5461, it became clear we did not fully understand all the mechanistic steps of how it can selectively kill a cancer cell. Therefore, we looked around the world and said "who are the world leaders in POL 1," and that is the group at Peter MacCallum (Peter Mac) Cancer Centre in Australia. Ross Hannon and Grant MacArthur are experts in POL 1, and we began interacting with them. They are the ones who then validated POL 1 as a target. We collaborated to show that the drug selectively killed cancer cells in animal models of cancer and spared the normal cells. Then, our collaborative group received a grant from the Australian government to support the Phase 1, which will be performed at the Peter Mac in Australia.

**CEO CFO:** What is the timetable on that?

**Dr. Rice:** The clinical trial begins during the second half of this year. In just a matter of a couple of months, the trial will be up and running and accruing patients. That typically requires eighteen months to perform the dose escalation phase of Phase 1.

**CEO CFO:** Are you funded for the immediate future or are you looking for funds?

**Dr. Rice:** Every biotech company is always raising funds, because that is what we do just to stay alive. Thus far, we have been funded by exceptional venture capitalists either the corporate investors such as Novartis and Lilly, or the traditional venture capitalists, including Sanderling, HBM, BioVentures, Mitsui and others. We have great investors. They have supported development of all these technologies and all of these first-in-class molecules, so they can bring new drugs to patients. At this point, we are always in the process of raising money. Therefore, we are going to take advantage of momentum and plan to raise more capital to continue to support the clinical trials going forward. We perform staged financings that allow us to achieve sequential stages of development.

**CEO CFO:** Where are you on some of the other projects at Cylene?

**Dr. Rice:** The first one that I discussed is CX-5461 and it is just now entering Phase 1. We have very high expectations for that one. Also, our first CK2 inhibitor, called CX-4945, has completed Phase 1 studies in both solid tumors and multiple myeloma and now it is poised to move into Phase II drug combination studies. We also have our next generation CK2 inhibitor that is at the preclinical stage, poised to move into formulation and manufacturing studies so we can prepare it for an IND submission within the next twelve to eighteen months. We have our plate full with many technologies and molecules and first-in-class agents.

**CEO CFO:** Are you always looking for new ideas?

**Dr. Rice:** We always interested in new ideas and new targets. However, at this point we literally cannot finance additional programs. We have at least three molecules now to advance. One is going into Phase II, another one is going into Phase 1 and another one is going into preclinical development. Our plate is very full and to finance additional programs is something we just cannot do at this point. We also have molecules from which we can select a next generation POL 1 inhibitor, but we just do not have the cash to move all of those molecules forward.

**CEO CFO:** Do you have patents?

**Dr. Rice:** Oh yes! We have a very strong patent portfolio, both around CK2 and POL 1 programs. We are the only company to make inroads into those targets today.

**CEO CFO:** It must be very exciting for you!

**Dr. Rice:** It is exciting to be able to create an entirely new molecular approach to cancer and to develop drugs that are going to move into cancer patients and may save lives.

**CEO CFO:** What should investors remember most about Cylene Pharmaceuticals?

**Dr. Rice:** We tackle new and high quality molecular targets, we create entirely new approaches to treating cancer and we design and develop completely new types of drugs. Those are the drugs that are going to have impact for the patients and in the market place. For investors, our approach can deliver a substantial return on investment while still being altruistic and making sure that this industry is fueled so that we can develop new drugs for patients into the future.

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C Y L E N E  
P h a r m a c e u t i c a l s

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