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PTM Therapeutics – Taking a Novel Approach to Treating Inflammatory Bowel Disease and Colon Cancer Using Monoclonal Antibody Technology to Target PTMs Found on Proteins



Jennifer C. Cheng PhD JD
CEO/Co-Founder

PTM Therapeutics
<https://www.ptmthera.com/>

Contact:
jennifer@ptmthera.com

Interview conducted by:
Lynn Fosse, Senior Editor
CEOCFO Magazine

CEOCFO: *Dr. Cheng, what is the vision behind PTM Therapeutics?*

Dr. Cheng: We are developing drugs against post-translational modification (PTM) targets which are expressed on diseased cells. We think that these targets can make great therapeutics and the biology and the science behind post-translational modifications are not well known and therefore have been neglected as far as looking for potential therapeutic targets.

CEOCFO: *What are post-translational modifications?*

Dr. Cheng: These are modifications that a cell will put on proteins before they are finished. Think of it as when you are making a birthday cake; it is the frosting, the sprinkles, and the design that you put on the cake before the cake is ready to be presented. For some proteins, these PTMs can modify their functions.

CEOCFO: *Is it working directly on proteins that are in the body?*

Dr. Cheng: These PTMs are routine things that are put on proteins to affect their functions and maybe expression. They are epigenetic in origin and are secondary modifications that are put on after the protein is made but before the proteins are totally finished. There are situations when these PTMs are aberrantly present on proteins that correlate with disease/disease progression.

CEOCFO: *What is happening in the body and how do you get something to target the protein after it is expressed but before it is circulated?*

Dr. Cheng: We are using monoclonal antibody technology to target these PTMs that are put onto proteins that correlate with disease. We found that we can make monoclonal antibodies that bind to these PTMs. Some of the post-translational modifications are only found on disease cells.

In our case, we have found a sugar target that is only present on proteins that are on sites of inflammation. We have one program in inflammatory bowel disease, so we are looking at inflamed intestinal mucosa that happens when you have either Crohn's colitis or ulcerative colitis.

Our second program is about targeting cancer cells. We are looking at colon cancer cells and we found that there is also the sugar moiety that is only expressed on proteins on cancer cells. Specifically, we are looking at treating metastatic

colon cancer. Colon cancer is the second most common cancer in the US associated with cancer deaths. Even with our standard of care treatment of a cocktail of chemotherapeutics, the 5-year survival rate of a patient with metastatic colon cancer is around 13%. This is shockingly low.

CEOCFO: *It sounds sensible to me that if you can catch the protein before it does great damage; why has the medical community not thought of doing this or not found a way?*

Dr. Cheng: One of the problems is that this field of science has not matured and we are just beginning to understand why cells do this. Historically, this area of research has been a little bit neglected and we are just beginning to understand that some of these PTMs correlate with disease. Hopefully, it is being worked on more and we will gain more insight in the future.

CEOCFO: *What made you decide it was worth founding a company to look into this arena?*

Dr. Cheng: I first got into this when I was looking at some data with my academic collaborator and we began with our first program in inflammatory bowel disease. Although this affects over 3 million Americans, it is not a disease that is talked about and it is not a disease that is well understood. Even though this is a large population of a lot of Americans that suffer from it, and a lot of approved drugs are addressing it, I think we are only addressing half of the disease. There is an immune component where you have immune dysregulation and your immune system is past the lining of your digestive tract. For Crohn's patients it is anywhere along the digestive tract, and for ulcerative colitis it is located in the colon.

"The investment community should be looking at companies that have novel ideas, but taking thoughtful, reasonable steps to develop therapeutics and investing in them and taking that risk. We are excited about novelty, but I feel that that novel equals risk in so many of the VC's heads, and they tend to be risk averse. This is my shout-out for taking more risks and taking risks on companies that are trying to do something new." Jennifer C. Cheng PhD JD

All of the approved drugs out there right now are mainly focused on immune dysregulation. They try to control the out-of-control immune system to help the patient feel fewer symptoms. What is completely unaddressed right now is the damage that is happening to the intestinal tract from the dysregulation. Our antibody drug will help the intestinal tract heal and restore function. I thought that this was a novel way to help the patients and it is a new way for the IBD field to look at therapy.

CEOCFO: *Where are you today in development?*

Dr. Cheng: We started right before the pandemic and right now we have generated proof-of-concept efficacy data in mice. We have efficacy and disease-relevant mouse models. Therefore, we are looking to raise a Series-A Round, to fund the company through Phase 1 clinical trials.

CEOCFO: *Where do Crohn's disease and ulcerative colitis stand in the pecking order of what investors might look at and how do you get investors to pay attention?*

Dr. Cheng: It is not one of those sexy diseases as you might imagine, although investors are paying attention because last year, we had two large acquisitions or transactions happen in the IBD world. That always attracts attention when there are large amounts of money changing hands.

Historically it is a tough space in that there has been a lot of failure in the clinic but we are taking a different and novel approach. We have a different mechanism of action that we are focused on as opposed to what had come before. We are excited about that and hopefully, investors will be also.

CEOCFO: *Condition Target Discovery Platforms is the title I see on your site for what you are doing. Would you tell us about that and how the words explain what you are doing with this particular indication and how you can do it for others?*

Dr. Cheng: That is our discovery platform. It is based on a simple idea of how we are looking for things that we can target with an antibody therapeutic that is highly expressed on disease cells and not there on normal cells. That is how we get to specificity and also can derisk potential safety issues.

Our research discovery platform is focused on this idea. It is not new but we have found a way through companies that we have been with and experienced, to hone in on those diamonds and look at things that are just expressed on disease cells and also potential therapeutic targets that are novel with interesting functions and profiles that we want.

CEO CFO: *How will get into the body?*

Dr. Cheng: The technology we use is antibody therapeutics so it is biologics. There are a lot of different antibody therapeutics out there for everything from cancer to chronic diseases and mostly they have been administered through either an IV in a clinic through infusion or large molecule medications like insulin which have been administered through a pen needle so that you can do it at home through injection.

CEO CFO: *How costly will it be at the end of the day?*

Dr. Cheng: On the whole scheme of things because of the biologics, it is formulated for injection and the manufacturing is using recombinant methods. It is going to be at a higher price compared to small molecule drugs. I envision it would be on par with other biologic therapies. 75% of IBD patients do not have a good treatment regimen and there are so many drugs out on the market for that. That tells me that yes there are options for patients but they are not very good options. The majority of these patients are not finding exactly what they need or they are not finding therapies that meet their needs and they do not work well enough for them. We think that because we are taking a different approach to treating this disease, this may offer a segment of the patient population an alternative to something they find does not work well for them.

I think that is a life-changing thing. I feel that for patients with chronic diseases, we do not understand the patient experience or we do not appreciate the patient experience. Chronic diseases are just that, once you get diagnosed with it you are going to have it for the rest of your life. A lot of the diagnoses for IBD come when patients are in their late teens like 18 or 19 years old to early 20s. That could mean 60 more years of living with the disease. Because of the symptoms and what the patients are experiencing, if they do not have good control over their disease, it affects everyday life. Not only does it affect everyday life for the patient but it affects everyday life for their families, their friends, and their support system.

Patients report that they do not want to leave the house or they cannot hold down a job because they are insecure. If we can offer some of these patients something that works better than the options they have now, I think that is life-changing on all levels. If you can find a way to price this so that it is reasonable and on par with other therapies of its kind, I think that is a home run.

CEO CFO: *I think that insurance providers are recognizing more and more the importance of dealing with things so that it is easier on the patient and ultimately patients do not end up needing as much care/money through the insurance carrier.*

Dr. Cheng: Getting a patient into remission and having not only a better quality of life, it means less chance of hospitalization and less chance of surgery. In our country, the cost of hospitalizations in the year is in the billions of dollars. If we can save on that, it is a home run, not only for the patient, but for our healthcare system as a whole.

CEO CFO: *What if anything might people in the medical community and people in the investment community not understand or recognize about what you are doing at PTM Therapeutics?*

Dr. Cheng: What I want to emphasize is supporting the whole ecosystem. We are an early-stage startup and we are looking for funding. We want to get into the clinic because the proof is safety and efficacy in patients. We think that we have something that can game-changer. I think that the financial and investment climate currently is uncertain, but I want to appeal to the investment community to take risks. This is what I think investments should be made in, these novel ideas that are not a me-too or three.

The investment community should be looking at companies that have novel ideas, but taking thoughtful, reasonable steps to develop therapeutics and investing in them and taking that risk. We are excited about novelty, but I feel that that novel equals risk in so many of the VC's heads, and they tend to be risk averse. This is my shout-out for taking more risks and taking risks on companies that are trying to do something new.