

THE WALL STREET TRANSCRIPT

Connecting Market Leaders with Investors

Moleculin Biotech, Inc. (NASDAQ:MBRX)



WALTER V. KLEMP is President, Chief Executive Officer and Chairman of Moleculin Biotech, Inc. Mr. Klemp has been Moleculin Biotech's Co-Founder, Chairman and CEO since 2007. Mr. Klemp has 32 years of experience in startup and high growth companies, the past 15 of which have been spent developing FDA-approved dermatology therapy devices and topical compounds, as well as cancer therapeutics. Mr. Klemp was also President and CEO of Zeno Corporation from 2004 to 2010, where he successfully developed and marketed a number of dermatology devices and drugs from concept through FDA approval. Previously, Mr. Klemp served as Founder, CEO and Chairman of Drypers Corporation, a publicly traded multinational consumer products company, from 1987 to 2000. At Drypers, Mr. Klemp developed growth strategies, orchestrated mergers and acquisitions, and grew the company from startup to \$400 million in annualized sales and to a number-one ranking on the INC 500. Notably, he has overseen nearly \$750 million in public and private financings throughout his career.

SECTOR — PHARMACEUTICALS

TWST: What are Moleculin Biotech's core technologies?

Mr. Klemp: Moleculin has really three core technologies. The best way to characterize the three, without going too deeply into the science, is to say, one is a somewhat familiar chemotherapy approach that focuses on destroying the DNA of rapidly replicating tumor cells. That is a drug that we have named Annamycin that is being tested for AML — acute myeloid leukemia. It avoids several of the major pitfalls of the current chemotherapies available for leukemia patients.

We then have two portfolios of small molecules, with one of them named by the lead molecule, so it is the WP1066 portfolio. It is a collection of molecules that focus on the cell signaling that makes tumor progression possible. Instead of directly trying to poison the DNA of a tumor cell, the 1066 portfolio works toward affecting the aberrant cell-signaling activities that make tumors possible and allows them to flourish.

The third technology is another portfolio that goes by its lead molecule name, which is WP1122, and its focus is to cut off the fuel supply of tumors. It has long been known that tumors are hyperconsumers of glucose. Effectively, for many years, it was believed that if we could feed tumors essentially a nonconvertible form of glucose — we call them glucose decoys — that we might be able to starve them to death. It is sort of like starving them to death by feeding them junk food.

But the problem has been that most of those glucose decoys are very rapidly metabolized and have trouble crossing the blood-brain barrier. We have a collection of molecules that are capable of crossing the blood-brain barrier, and we think there will be therapeutic quantities that have a much longer half-life. They stay in the system long enough to

hopefully have an effect. Those are the three core technologies, with one focused on poisoning the DNA of tumor cells, another one focused on cell signaling, and the third one focused on tumor metabolism.

TWST: Are they all at either the Phase I or II stage?

Mr. Klemp: Annamycin is in two Phase I/II trials right now. However, it is important to distinguish that this drug has actually moved through a prior developer and a number of prior clinical trials, so we have some basis to form our expectations for what we think we are going to see in the clinic. For 1066, we just started a Phase I physicians-sponsored clinical trial at MD Anderson Cancer Center for the treatment of brain tumors. In the case of 1122, the metabolic inhibitor portfolio, we aren't there yet. We are in the process of preparing the package that you would present to the FDA for approval to do a clinical trial, but that has not been completed yet.

TWST: You also have a candidate called 1732 in the pipeline that is being developed in Australia? What is this?

Mr. Klemp: 1732 is built on the same chemical backbone as 1066. It really falls into that 1066 cell-signaling category. One of the things that we discovered in working with 1066 over the years is that it is not very soluble in water, and that lack of solubility tends to limit it to certain routes of administration. For example, 1066 is being delivered orally because it is much more difficult to put a nonsoluble chemical into, let's say, an IV solution. We have long believed that it would be beneficial if we could come up with a soluble version of that molecule that we could use for other routes of administration, like intravenous delivery.

This candidate was recently discovered and licensed from MD Anderson, and because we wanted to put it on a very fast track for development, we took advantage of a pretty aggressive R&D program

that exists in Australia. The government there provides a tax credit to develop the drug there whereby it can reduce up to 43.5% of your total research and development costs. That is a huge economic incentive for us. Also, the contractors there are in a position to move very quickly. That is the reason that we opened a subsidiary in Australia so that we could take advantage of this incentive program and follow a path that we think may be a faster pathway to IND — investigational new drug — approval of 1732.

TWST: Regarding that agreement in Australia, does it require you to commercialize the drug first in Australia?

Mr. Klemp: It does not. The only requirement that they place is that the subsidiary — and it is wholly owned by Moleculin — exist in Australia, and at a minimum, there has to be intellectual property rights for the territory of Australia. What that means is we create a sublicense to our subsidiary, and therefore, our Moleculin Australia subsidiary has the right to market the drug that is eventually produced in the country of Australia. It is very understandable why they do that because, eventually, they want you to become a taxpayer in Australia so that they can point to their constituency and explain how this R&D program not only brought research and development activity but also brought future tax revenues to the country as well. It is only with regard to the country of Australia, and there are no other geographic rights.

TWST: On your relationship with the MD Anderson Cancer Center from which you are licensing technology, is it exclusive?

Mr. Klemp: Correct. Yes, absolutely, and that's true for all three of our core technologies.

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TWST: Which of these areas are ones that other companies are not working as aggressively in as far as mechanisms of action?

Mr. Klemp: Literally all three areas are ones that we have a unique footprint in. Let me explain. In the case of Annamycin, chemotherapy agents tend to be thought of as old school. You have seen lots of interesting articles about CAR-T cells and targeted therapies and personalized medicine, and this is all fabulous, but in my experience, in the biotech industry, the flow of attention and, therefore, funding tends to go in waves and follows trends or sometimes even fads. The current trend is all about immunotherapy, as in CAR-T cells and targeted medicine and personalized medicine, so that is where the attention and the funding has flowed.

As a consequence, very few people are paying any attention to improving the bedrock foundational treatment mechanisms like chemotherapy. They are just not focused on it. It is understandable because that is not where the grant dollars are and where Wall Street is focusing its attention. But the fact is, and I will use acute myeloid leukemia as an example, the foundational induction therapy for AML, if God forbid you have it, would be to get you a bone marrow transplant because, through it, you have got an 80% chance of beating your leukemia, which is phenomenal. The problem is, you have only got about

a 20% or 25% chance of actually responding adequately to the induction therapy to ever get to that bone marrow transplant, and that is why so many AML patients cannot defeat the disease. They cannot ever get to that bone marrow transplant.

So that induction therapy has not changed in the last 40 years, or not until very recently when there was a minor improvement of a drug called Vyxeos by a company called Celator that Jazz Pharmaceuticals paid \$1.5 billion for. It is a tremendous development. The reality is, Vyxeos extends some patients' life span by about three and a half months, but it doesn't fundamentally change the outcome for the vast majority of AML patients, and that's what we think we can do with Annamycin. It is a perfect example of where we don't see anybody else in the sector focusing on how to dramatically improve the fundamental induction therapy, meaning the chemotherapy that enables people to get to a bone marrow transplant.

Why is because it is not popular and there is not a lot of focus on it. But the reason that induction therapies fail in the vast majority of AML patients is a couple of things. One reason is multidrug resistance, so the mechanisms in the cells essentially recognize the chemotherapy as poison and pump it out as fast as we can pump it in. We can pump more into you, but another problem is that all of the existing approved chemotherapies for induction therapy are high in cardiotoxicity. So, if we increase the dosage beyond the specified maximum limit, we are going to kill you by stopping your heart.

They are all in a box right now in that they cannot move and improve from where they are. That is what is so different about

Annamycin. One, it avoids those mechanisms that result in multidrug resistance. This ability has been independently verified in peer-reviewed journal articles. Second, it appears to have little to no cardiotoxicity, and that has also been anecdotally observed because it has already been in 114 patients without any indications of cardiotoxicity.

So essentially, Annamycin avoids the two pitfalls that prevent induction therapies from working appropriately in the majority of patients because it has already done so in clinical trials. Although it is not statistically significant, we have patient data that suggests to us that we may be able to more than double the number of patients who qualify for a bone marrow transplant. So, we believe Annamycin has the ability to immediately begin saving lives. To us, it is super exciting and even more exciting because it is also pretty far along its pathway.

TWST: Depending on the indication, is this a monotherapy or combination therapy? In some cases, for some indications you are or may go after, are you proposing that you just use your drug or others as well?

Mr. Klemp: It is an indication of the level of confidence that we have based on prior evidence that it functions as a monotherapy. We would not go down that path if we didn't think the drug had a pretty solid chance of performing on that basis.

TWST: Can you comment on the uniqueness of 1066 relative to its competing drug candidates?

Mr. Klemp: With regard to 1066, the cell-signaling portfolio, I have to be careful in that I tend to be a bit over-exuberant. So STAT3 has been a long-established target and a sought-after one because it is implicated in a very wide range of tumors. It is more highly activated in some of the worst tumors out there, like pancreatic cancer, head and neck tumors, and stomach cancer, as well as acute myeloid leukemia. For a couple of decades, it has been considered a holy grail kind of target. The problem is that no one has been able to consistently and directly inhibit the activation of STAT3 because the signaling mechanisms that enable it are so vast and broad.

I'll give you an example. Pfizer had a JAK3 inhibitor that they claimed was really the drug to target STAT3. Well, STAT3 can be activated by JAK3, which is upstream in the cell-signaling pathway. Essentially, they created a receptor inhibitor that blocks the activation of JAK3, which in turn would indirectly block the activation of STAT3. But the problem is, STAT3 can be activated by any one of half a dozen upstream effectors. Just blocking JAK3 doesn't really get the job done.

So another Big Pharma was developing a JAK2 inhibitor, which is one of the other pathways. They have the same problem. They could see some reduction in STAT3 but not enough to have a therapeutic effect. Eventually what people started to realize is that they would have to combine a JAK2 inhibitor and a JAK3 inhibitor and a SARC inhibitor and on and on. But if we did, guess what, we are going to kill the patient because all of those receptors are needed for normal healthy cell function, and if you block them all, you will literally kill someone.

“1066 is an analogue of caffeic acid, but what the discoverer did was he spent years isolating and understanding what made bee pollen, a fairly commonly understood anti-inflammatory. All of that research ultimately pointed to caffeic acid, and they were off to the races in terms of generating these analogues.”

Effectively, the industry came up against a brick wall in that it just couldn't find a way to more directly inhibit STAT3 without regard to the upstream effectors. That is what 1066 does. It is the subject of over 50 peer-reviewed journal articles. The animal data supports our assertions and has been validated by multiple separate institutions. In the case of 1066, others have independently confirmed the presence of all of the properties that we are describing. There is a good pedigree here on the ability to inhibit the activated form of STAT3 that has been now linked to reduction of tumor activity in animal models.

So all of the building blocks are there, but as you probably know, just because you can cure a tumor in a mouse or a dog or whatever does not mean you are going to cure a human. The next step for 1066 is getting into humans, and that has literally just begun. I feel fairly comfortable in saying there is really no one else out there that we know of that is this far along with a compound that is well-documented to be a significant inhibitor of the activated form of STAT3.

Now, the second aspect of 1066 is that it also appears to be an immune stimulator, so in animal models, it has shown to actually upregulate STAT1, which is considered to have tumor-suppressive characteristics. The way it does that is by reducing regulatory T cells, and if you've heard anything about what they are calling TRegs, or

regulatory T cells, is that they are essentially the traffic cops of the immune system. Sometimes if you have a situation in which a tumor is active and your normal T-cell activity would go attack that tumor, the TRegs come to rescue that tumor cell by stopping the immune system from attacking the tumor. 1066 not only has the ability to downregulate STAT3, which is linked with increased cell survival, increased proliferation and increased angiogenesis, but it is upregulating STAT1, which in animal models is directly linked to reducing TRegs to allow the immune system to go after the tumor on its own.

In terms of the anti-angiogenesis and anti-proliferation, you can stop the co-opting of the vasculature by a tumor and the misdirection of the immune system and metastasis, which are all of the bad things that we don't want a tumor to be able to do. STAT3 activation enables this. We have never seen anything in the literature to suggest anybody else has a technology that has these capabilities. Normally, you would use multiple drugs to try to bring about these effects. If I had to pick a drug where the science is more captivating and enticing to research clinicians around the world, it would have to be 1066 because there is nothing out there like it at all.

TWST: What type of molecule is this? Is it in any way a biologic?

Mr. Klemp: No, it is not a biologic but rather an analogue of a naturally occurring compound. It is fairly common for a researcher to look at nature to see what seems to have some therapeutic effect. In folk medicines, we have tried to isolate, distill and amplify those capabilities from nature. So in this case, it is a derivative of bee pollen. The chemical name is called caffeic acid.

1066 is an analogue of caffeic acid, but what the discoverer did was he spent years isolating and understanding what made bee pollen, a fairly commonly understood anti-inflammatory. All of that research ultimately pointed to caffeic acid, and they were off to the races in terms of generating these analogues. 1066 is the most exciting of about 700 analogues in this portfolio.

TWST: I don't want to put you on the spot, but what do you think is one of the most compelling data points that you've seen come out of studies to date? Would it be too far to say that 1066 could both address tumors and potentially prevent new tumor growth?

Mr. Klemp: We would pull up short of calling it a preventative measure because that has all kinds of other connotations, including that you might take the drug even if you didn't have a tumor, right? We are not ready to go there at all. We don't have data to support that claim, but what I would say is, to us, the most compelling data are that, one, in our own animal models where we have transplanted human tumors into animals, we can simultaneously show three things: that STAT3 activation goes down, STAT1 is upregulated and tumors recede.

The reason we all go into the clinic eventually is to ensure that what we saw in animals does actually translate into humans, so we still have to check that box, but that information alone is

hugely compelling. It is because it is so difficult to find anything that's capable of directly inhibiting STAT3. Like I mentioned, those findings have been validated in multiple independent institutions. In our public disclosures, we have announced previously that, for example, the Mayo Clinic and Emory University have proposed to collaborate with us on their own animal studies. To me, that is the most compelling science to date.

TWST: Also, you were going to distinguish 1122?

Mr. Klemp: 1122 is the least mature technology in our pipeline, but whenever we meet with scientists, it is probably the most intriguing to everybody because so little has ever been done in the field of essentially dialing back the metabolism of tumors. There was one major effort about a decade ago to try to use a compound called 2-Deoxy-D-glucose to treat tumors, but the trial failed, and after a post-trial assessment, the real problem was 2-Deoxy-D-glucose did not have a long enough half-life. It is rapidly metabolized in patients, and it has a lot of trouble getting across the blood-brain barrier. Essentially, the industry just sort of hit that roadblock, stopped and didn't advance.

Our inventor found a way to increase the half-life with a mechanism that would also allow it to cross the blood-brain barrier. What inspired this is the difference between morphine and heroin. Most people don't realize that heroin is literally morphine with a prodrug attached to it. A prodrug will do things like extend half-life or facilitate a transfer across the blood-brain barrier. So morphine is a great painkiller because it tends to not cross the blood-brain barrier, so it can reduce severe pain without impairing the mental capability of the patient too drastically.

What a chemist did to create heroin was to attach two acetyl groups to make a diacetyl prodrug version of morphine so that now it rapidly crosses the blood-brain barrier where enzymes cleave off those acetyl groups, and you end up with morphine inside the brain. Because those acetyl groups are gone, it cannot get back out. It rapidly accumulates, which is why heroin is so effective as a hallucinogenic and is so addictive, or partly why.

Our inventor basically said, "I think I can put that same diacetyl group on 2-Deoxy-D-glucose, and I should have something that will cross the blood-brain barrier and then accumulate in the brain once it's in." It turns out it is true, at least it is true in mice.

You probably know that the standard of care for the first-line treatment for brain tumor glioblastoma is temozolomide, or a drug called Temodar. We compared 1122 in a head-to-head comparison against Temodar in what we call mouse xenograft models whereby human brain tumors were transplanted into the brains of mice. 1122 outperforms Temodar, and when you combine the two, you get an even better synergistic effect. So it is probably the coolest technology for people to talk about because so little has been done here. In the case of 1066, lots of people have tried and failed, and so what makes 1066 so exciting is it looks like we finally found a way to achieve this holy grail targeting effect.

TWST: What did you want to tell potential investors or current investors today about Moleculin Biotech? As you do so, can you give us a quick update on your financing status?

Mr. Klemp: To me, the most important message to investors is that we have three distinctly different technologies. When you look at companies with our market cap in biotech, basically almost all of them have one technology with possibly some ancillary ones, but it is usually just an add-on or a different route of administration or a different indication for the technology. In the case of Moleculin, these technologies are as different as night and day from one another. We legitimately have multiple shots on goal, to abuse a hockey term. So effectively, any one of these drugs could become a blockbuster in their own right, and yet none is dependent on the other.

Strangely, they may have combination opportunities because, let's face it, the notion of combination drugs is now popular. It used to be a kind of a dirty word in that it might indicate that your technology was a failure because it couldn't perform as a standalone, but nowadays, it is normal course to consider combination therapies. The characteristics of those three core technologies I just described could be synergistic with one another. So it is not just three shots on goal, but three plus the combination of those three along the way. That is probably the most important message I could get to people.

The second message would be, with regard to Annamycin, there is a history of activity in patients that suggests we have something here beyond just animal data. Because of that, people should pay attention to the fact that in the relatively near term, let's say in the next one to two years, we could be reporting data that is literally game-changing in the AML space. To me, in a nutshell, that is what I would have people focus on. But don't underestimate the other two technologies just because Annamycin is a little farther along.

With regard to finance, we follow a pattern of making sure we always have nine to 12 months' worth of cash run rate in front of us. We have been consistent with that. We are certainly in that position today. But we always have had access to additional capital when it was called for, and I don't see that changing for us right now. It looks like we have a strong following of people who get the story. Obviously, nobody is in this, or nobody should be in this, to find \$0.50 on a \$1.60 share or whatever. This is about what this company is worth if just one of these drugs does what we think it can do.

TWST: Thank you. (KJL)

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