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Cost Efficient Production for RNA for Topical Application of RNAi in Agriculture for Uses in Insect and Weed Control with Potential to Replace Genetic Modification

Dr. John Killmer - *CEO*

CEOCFO: ***Dr. Killmer, what is the concept behind APSE today?***
Dr. Killmer: APSE is a company that is focused on two things: the cost efficient production of RNA (ribonucleic acid) for topical applications of RNAi (RNA interference) in broad acre agriculture as well as the development of an APSE RNAi product portfolio.

CEOCFO: ***How is this used in agriculture?***
Dr. Killmer: It is not used yet because it is very new technology--certainly the topical applications. There are some applications of RNAi that will be used in genetically modified plants. However, our approach is through topical applications which have nothing to do with genetic modification and are themselves not GMO.

CEOCFO: ***What are they? What is the purpose?***
Dr. Killmer: Basically, RNAi, properly developed, can be used for almost all current applications in crop protection or in the seeds and traits components of agriculture.

CEOCFO: ***What will this be replacing or how will this enhance what is happening now?***
Dr. Killmer: People often think of new technologies as replacing many of the old technologies and that could be the case here. However, the normal process usually is that new technologies become a component in the portfolio of things that farmers use for production. Topical RNAi in particular can be used to control insects. It can be used to reverse insect resistance to insecticides. It can be used to reverse the resistance that certain weeds have built up to herbicides. The biggest potential use for RNAi will be to replace genetic modification with topical applications of RNA. The RNAi technology is not GMO technology. RNAi technology affects the template between DNA and the proteins that are formed. By affecting that template it exerts its effect, but it does not change the DNA of the organism that is treated and thus it is not inherited in the progeny of that plant or organism.

CEOCFO: ***Although people complain about GMO, isn't it to have something internal instead of an addition?***
Dr. Killmer: It depends. It is easier to just have it in the plant, but it is quite a bit more expensive and more time consuming to develop the in plant technology. Also, I use this example quite often; while genetic modification is fairly common in North America and South America, there are many, many places in the world where genetic modification will not be used. That is often due to a number of reasons, but most often it is public perception or government regulations related to public perception. For example, in the United States most of the corn is genetically modified and some in South America. However, when you look at corn globally only about thirty percent of the corn, globally, is genetically modified. Farmers, where genetic modification is not accepted, do not have any way to do certain things that the GMO crops provide and there is a possibility of doing some of those things with RNAi. The most common example that is used would be to have a topical RNAi that could be sprayed on plants to increase draught tolerance. However, you would not have to do this until you actually knew that there was a draught and therefore it gives you a lot of flexibility.

CEOCFO: ***How are you able to manufacture or grow at low rates? What is the process and how is it competitive?***
Dr. Killmer: The RNA that provides the RNAi affect is usually just a little snippet of RNA. It is a small amount or a small sequence of RNA that binds with another RNA inside the insect or the plant to exert the effect. However, many researchers will say that the first RNA that they purchased was in the range of maybe one hundred thousand dollars a gram. More recently, the lowest number that we have heard, other than our number, is about fifty dollars a gram. The use rates for topical applications of RNAi are anticipated to be in the one gram to five grams per acre rate. Obviously at fifty dollars a gram that is not economic for any farmer. Therefore, this was the challenge that APSE took on. Our current target for producing RNA is two dollars a gram. We believe that at a cost of two dollars a gram and a use rate of maybe one to five grams per acre RNAi could be used in many applications and it would economic.

CEOCFO: ***What does the industry think? Are people on board? Are they skeptical? Are they paying attention?***
Dr. Killmer: Everyone is paying attention but I think that the industry, per se, tends to be very, very cautious in talking about the research that they are doing; in particular talking about new areas such as RNAi. However, if you look at the patent literature there is a tremendous amount of patents that have been filed for applications of RNAi in agriculture and each and every one of the big six agricultural companies have filed many, many patents in this area. The one area where there are very few, if any, patents is in the actual production of the RNA, which is an area in which we specialize.

CEOCFO: ***How did you figure out how to do it the right way?***
Dr. Killmer: We had an inventor in the company that figured this out. Normally, when you are producing a complex biological molecule, you are usually better served by letting biology do the production. For instance, complex biological molecules such as insulin are produced in microbes. These are genetically engineered microbes that are specifically focused to produce things like insulin. This is not just the case with insulin, but it is the case with many, many complex proteins that are used in health therapy and that sort of thing. Since RNA is a really complex molecule it was obvious to look at a biological mechanism for producing it. APSE determined that we could genetically engineer or transform kind of a workhorse microbe in the laboratory and use it to make RNA. This was not really the innovation. Others have been able to do that. However, the production of RNA is just a common mechanism in life and it is a common mechanism in microbes. The normal procedure that a cell uses is that it produces RNA, the RNA is used as a template to produce a protein and then the RNA is destroyed. It is degraded inside the cell so that its components can be recycled and used for the next template, which might be different. It is that recycling or the degradation of the RNA that makes it difficult to accumulate much of the RNA that you are interested in, inside the cell. The APSE innovation was to transform the cell, not just to make the RNA, but also to make a small protein shell that captures the RNA as it is being produced and it protects the target RNA from that degradation. That allows this target RNA to accumulate inside the cell and ultimately be extracted and used in RNAi applications.

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CEOCFO: ***What is happening today? Where are you? What is the business strategy?***
Dr. Killmer: Our business strategy has morphed a little bit in the last year. The original concept, since it is a very small startup company, was to develop production technology for producing RNA in large volumes at low cost and then to license this technology to various strategic players in the agriculture industry. That is still part of our business model. We view that part as necessary, but not necessarily sufficient to be a vibrant business. In order to be a vibrant business we determined that we had to have our own products. It makes sense because if you have great production technology for new molecules and a new technology that can be implemented in the marketplace then why not have your own products! Therefore, basically our business model now is to develop technology, to license the technology with an up front fee and a downstream royalty, but also to develop our own products. The way that we manage the value capture for the technology is to very narrowly license the technology or production. That means that when we provide a license to a licensee then that license will be for only one unique RNA sequence. As this technology evolves and progresses in agriculture there will be literally thousands of unique sequences that will be used. Therefore, we believe that that is a viable business model. Licensing probably will be the place where APSE will be able to have its initial revenues. We believe that we might be able to license the technology within even a couple of years. The APSE product, per se, will take a little bit longer. The initial product of a forthcoming APSE product portfolio will be an RNA product that will control ants; in particular fire ants and household ants in a very environmentally benign way. While RNA is a complex biological molecule it really does not have very much in the way of environmental consequences. RNA is in all living things and it is estimated that we consume about a gram of RNA per day. So, in summary, the APSE business model is to license the technology it develops and also to use that technology to produce a portfolio of APSE own products.

CEOCFO: ***What do you and your team understand about the business side of developing products and marketing products in addition to the scientific knowledge you have?***
Dr. Killmer: Actually, this is one of the reasons that I was recruited to join the company. I basically have about thirty years of experience in the industry. I started in agriculture at Monsanto with a PhD doing technology. I have spent maybe about half of my career in technology development and about half of my career in business. Most of my career, twenty five years or so, was spent at Monsanto. Around the last five years of that time I ran the business for Monsanto in China. This was not a technology job; it was a P&L job. In the thirty years of my career about fifteen years was spent outside of the

country. The whole focus in my career has been to take technology, develop it, turn it into products and then sell those products.

CEOCFO: ***Are you seeking investment? Are you funded for your next steps?***
Dr. Killmer: The company has, until now, been funded primarily by angels and accelerators. We are in the state of Missouri and there is a state entity here called The Missouri Technology Corporation. That state entity will match various investments from qualified investors. Therefore, using angels and accelerators and a match from the Missouri Technology Corporation we raised about seven hundred and fifty thousand dollars last year and we look to start a new raise in probably the third quarter of this year. We suspect that at that point we will be looking at venture capital and we are looking to raise three million dollars.

CEOCFO: ***Why is APSE important? Why should people care about the company as well as the opportunity?***
Dr. Killmer: APSE is important because we are providing ways to facilitate the commercialization of a very new technology that is an environmentally benign and a non-GMO tool that can be used in many areas of agriculture. That technology will be particularly important as another product in the portfolio that farmers can use, even in those areas where GMOs are prevalent. However, it will be particularly important in areas where GMOs are not possible. It also allows you to do things that simply could not be done before. Beneficial insects are very, very important in agriculture, but as soon as you spray an insecticide you loose the benefit. That is because you could kill all the insects. RNAi will allow you to control only the harmful insects. That is just something that cannot be done with normal technology. Over the years' insects have built up resistance to insecticides and there are aspects of RNAi technology that can be used to change that, to make insects susceptible to just the smell of the insecticide that formally they had become completely resistant to. RNAi technology not only will help farmers but it is also environmentally benign, so it will be good for the environment long term. APSE's discoveries and innovations will help drive this technology into commercial utilization.

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