



**Creating New Drugs Based on Safe Existing Compounds Using a Systems Biology Based, Computationally Driven Pharmacometric Platform with Current Programs in Inflammatory Diseases such as Atopic Dermatitis and Psoriasis**



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**- Bruce W. Kovacs, MD**

**CEOCFO: Dr. Kovacs, would you tell us about Afecta Pharmaceuticals?**

**Dr. Kovacs:** Afecta Pharmaceuticals is focused developing our pipeline of next generation immune-modulators to treat inflammatory disorders. Our lead drugs were created by identifying and improving on existing, safe molecules, and then developing them into new medicines. Starting with these “de-risked” drug-like compounds enables us to have a shorter and more cost effective path to regulatory approval. Our emphasis is to create novel lead drugs that simultaneously modulate multiple targets in key newly discovered disease process pathways.

**CEOCFO: How do you know what to consider?**

**Dr. Kovacs:** We have developed a computationally driven, systems biology based platform called PharmetRx. With this platform we test compounds for their biological activity profile across a broad spectrum of cell types, disease models and relevant pathways. Using that data we are able to characterize the physical-chemical properties and the range of biological activities of the molecules in these model systems. We call this a pharmacometric “fingerprint”. We are also able to identify key molecular differences between the disease and normal cells and map that information to specific disease processes and pathways and correlate that to specific compounds or groups of compounds. With this information we are able to determine what specific disease pathways the molecule affects and what particular characteristics of the molecule are the responsible factors for having that affect. The compound’s fingerprint gives us a broad understanding of what the compound is capable of such as: molecular targets it capable of interacting with, specific disease related processes it is likely to affect and so on. This enables us to identify potential lead compounds targeted to specific disease processes and patient types. Importantly, the “fingerprint” also gives us information about the chemical characteristics of the compound that can be modified to improve specific activity or reduce side effects. We have used this technology to identify and develop new drugs for inflammatory disorders, but it also has broad applicability in most other types of disease as well.

**CEOCFO: Would you give us an example on what you would find and how it is different?**

**Dr. Kovacs:** The vast amount of data we produce for each compound reveals the spectrum of pharmacological activity potential for the compound. This includes not only disease specific therapeutic potentials but also for side effects, toxicity, metabolism etc. Since the pharmacologic activity profile is directly correlated to the chemical composition and structure of the compound and because this data is digital it enables us to compare a given compound with other compounds, either existing compounds or those created by computers entirely in silico. This enables us to create focused, intelligently

designed new compounds based on the prototype compound profile that are likely to have improved pharmacologic properties. We have, for example, designed potential therapies for cancer based on antibiotic drugs.

**CEOFO: *What are you working on now?***

**Dr. Kovacs:** We are focused on late stage pre-clinical development of our novel immuno-modulatory drugs. Currently, we are targeting immune mediated skin diseases such as Atopic Dermatitis, Psoriasis, and several related orphan disorders.

**CEOFO: *Why the decision to look in that direction?***

**Dr. Kovacs:** Inflammation is one of the key physiological processes of the human organism in health and disease; it occurs in every organ system. Diseases with an inflammatory basis are among the most common and complex conditions, affecting millions of people. Current treatments for these disorders are limited, have significant side-effects and are expensive. We have chosen dermatologic disorders because there is a large unmet need. Our pipeline drugs modulate key disease relevant pathways and affect multiple targets in those pathways, thus they have great potential use in these particular disorders, in which there is a dynamic interplay of various cell types and inflammatory mediators.

**CEOFO: *Is it well accepted that inflammation is a factor in much of the disease?***

**Dr. Kovacs:** Yes, it is a concept that is particularly in the mainstream now and has been increasing so over the last few years. Inflammation and immunity underlie a number of disorders almost regardless of the type of the disorder. For example in head trauma we know that there is an associated inflammation that occurs with central nervous system trauma and that process makes the injury worse, increases the extent of the injury and produces chronic dysfunction. Similarly in heart disease, we now know that chronic low-grade inflammation is intimately involved in all stages of atherosclerosis, the process that leads to cholesterol-clogged arteries. This means that inflammation sets the stage for heart attacks, and most strokes. Over the last ten years there has been a large and growing understanding that inflammation underlies many diseases that we thought had nothing to do with inflammation even those that are influenced by environment such as obesity and diabetes.

**CEOFO: *What is in the pipeline?***

**Dr. Kovacs:** Afecta has three lead candidate drugs AFX-372, AFX-272 and AFX-210 that are being advanced to begin proof of concept trials in humans for specific patient groups with inflammatory skin disorders. Each of these drugs affects a different key inflammatory disease process pathway particularly involved in atopic dermatitis, psoriasis and other related conditions. These will be first of their kind small molecules to inhibit these important disease-related processes.

**CEOFO: *Your site shows “Patient Inspired, Physician Driven.” Would you explain that philosophy?***

**Dr. Kovacs:** Afecta has a “bottom-up” approach to drug discovery and development. We focus on filling specific therapeutic niches defined by patient driven needs. Historically, large pharma companies have had a “top-down...one size fits all” approach that defines their drug development programs by identifying the largest markets. We were founded in 2002 by a group of university based physicians in different specialty areas of medicine each focused on better understanding the chronic disorders that affected our patients and finding better therapies for them. By first identifying the needs that our patients tell us they have we are better able to hone in on key elements of disorders that are not being met by existing therapies. To some extent this is empowered by discovering how individual genetic differences in patients, can be leveraged to develop new therapies. Initially, Afecta focused on particular sub-sets of patients with neuro-development disorders. We discovered two neuro-modulator drugs that act in the central nervous system to simultaneously modulate multiple pathways that we identified to be abnormal in these patients. We were successful in licensing these lead drugs out for late stage clinical development. The most advanced of these is now in a pivotal Phase III trial for impulsive aggression in specific sub-sets of children with behavioral disorders and was given FDA fast tract status. More recently, we have now turned our attention from neuro-modulators to drugs that suppress inflammatory processes, also by modulation of multiple pathways.

**CEOFO: *Is the strategy to license what you find?***

**Dr. Kovacs:** Afecta intends to continue to out-license our drug candidates to partners. In each case we want to move these candidates further and further along in development process before establishing co-development partners for the final stages of development, regulatory approval and eventual marketing. This maximizes our return on investment by not duplicating the resources of our partners. At this time, our goal is not to become a traditional, fully integrated pharmaceutical company; that conducts the all human testing and eventual marketing. We consider ourselves more of a late-stage drug development company with rich pipeline of late stage drug candidates, as well as a unique and powerful platform.

**CEOCFO: *What is funding like for you today? Does the investment community understand your approach?***

**Dr. Kovacs:** We have not had external investment yet. Rather we have used licensing and milestone revenue to fund our operations. Overall, I think there has been a lull in biotech investment and there has been a particular reluctance in the investment community over the last several years to invest in pharmaceuticals for a variety of reasons. Going forward, the current investment climate is becoming more favorable for companies like Afecta that can apply computational and personalization strategies to create a faster, less expensive drug development track. Currently, from the investment perspective we have seen a considerable amount of interest both from the standpoint of non-diluted capital, vis-a-vis partnering our development programs, as well as from the traditional investment community. There is a growing appreciation that our approach mitigates development risks and is an attractive business model.

**CEOCFO: *What surprised you as Afecta has grown and evolved?***

**Dr. Kovacs:** One thing that surprised me as a physician is just how difficult it is in this day and age to get a new drug onto the market. The regulatory hurdles have increased remarkably in recent years. The other thing that surprised me is the number of people that it takes to do drug development, someone told me not long ago that the greatest team sport in the world is coming up with a new drug, it requires many people with diverse areas of expertise all acting in concert for one purpose. This is why it is such a difficult task and why it takes so long. That is one of the reasons we chose a more focused development model that represents a faster, less risky path to approval.

**CEOCFO: *Do you see the need to bring in new people or license your platform as opposed to something you have actually developed?***

**Dr. Kovacs:** We are in discussions to offer our discovery platform and capabilities to others. Afecta has advanced to a stage where we want to focus on internal drug development projects, rather than discovery projects. Therefore, we have an unused capacity in our PharmetRx drug discovery platform. We are in discussions now for partnering with other companies who might like to leverage our platform and core expertise to come up with new drug candidates for other diseases. Insofar as new additions to our team, we are looking for experienced professionals to direct our internal drug development programs.

**CEOCFO: *What does the next six months to a year look like for Afecta?***

**Dr. Kovacs:** In that time period Afecta is going to continue to accumulate what we need to have for our pre IND meeting with the FDA to present our target product concepts for atopic dermatitis, as well as continue to gather the data that we would need to be able to file a full IND for the drugs. In addition, we plan to implement the collaborative strategy that I mentioned earlier which is focused on leveraging the use of our PharmetRx platform as a service.

**CEOCFO: *As you have been working on the atopic dermatitis, has it proceeded the way you expected?***

**Dr. Kovacs:** Yes it did. The traditional thinking in medicine for a long time has been the “magic bullet approach”. Meaning that you need a magic bullet drug to hit a single specific target very precisely to cure the disease. Our approach now in complex disorders such as atopic dermatitis and other inflammatory disorders is that one must be able to hit multiple targets simultaneously in order to achieve the optimal therapeutic effect that one seeks. That has been one of the big lessons of modern systems biology and one of the things that we have directed our attention to from the beginning. We are focused on creating drugs that simultaneously affect key pathways and multiple targets in given disease process rather than finding a drug that hits just one target. The thinking here is that nature is clever and has built in redundant systems so that if you knock out one specific target in a disease process, there is always a work-around that lead to treatment resistance and failures. The lesson here is, you need to hit multiple targets simultaneously if you really want to shut down the disease process.

**CEOCFO: *Why pay attention to Afecta pharmaceuticals and why are your concepts and theories important?***

**Dr. Kovacs:** I think our company is important because we are leading the way in developing small molecule drugs that that engage multiple targets in key disease pathways involved chronic complex disorders. This is a somewhat revolutionary new approach and we have a unique and powerful platform that empowers us to achieve success. Secondly, modifying and improving existing proven safe molecules that can be brought into the market much faster and which we can subsequently be improved to create the next better version of the drug is a cost effective, risk mitigated business model.

**CEOCFO: *Final thoughts?***

**Dr. Kovacs:** Afecta’s pipeline of new immune-modulators, novel discovery platform and product focused business model fits perfectly into the new paradigm of twenty first century medicine; that is to find ways to develop more effective and personalized drugs to treat patients at lower costs and with shorter timelines. Our previous successes are testament to our ability to achieve that goal.



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