

Using a Capital Efficient Business Model, Melior Discover Inc. has Created a Cost-Effective, Time Effective Way of Discovering New Therapeutics – Using their *theraTRACE*® Indications Discovery Platform



**MELIOR
DISCOVERY**

**Healthcare
Drug Development - Diabetes
(Private)**



**Andrew G. Reaume, PhD, MBA
Co-Founder, President and CEO**

BIO:

Dr. Reaume was previously a Senior Business Analyst at Pfizer, Inc. in the department of Genomics and Pro-

teomic Sciences. There he spearheaded an initiative to create a platform for comprehensively characterizing (phenotyping) genetically modified mice and ran the collaboration involving a third party partnership to build it. This effort involved working closely with scientists throughout the global Pfizer organization, business development professionals, information technology specialists as well as the scientists and business development professionals at the partner company.

From 1993 to 1999, Dr. Reaume worked as a research scientist at Cephalon where he was principally involved in creating animal models of neurodegenerative disease. During this time Dr. Reaume worked closely on a number of projects with Dr. Saporito, co-founder of Melior. In addition to Dr. Reaume's research activities at Cephalon, he identified and helped coordinate three in-licensing opportunities.

In 2003, he received his MBA from the Wharton School where he graduated with honors in Entrepreneurial Management. He received his PhD in genetics from the University of Connecticut in 1990.

Company Profile:

Melior Discover Inc (Exton, PA) has pioneered a unique, optimized, high throughput pharmacology platform that is able to systematically identify novel indications for pre-clinical and development stage drug candidates. Melior also applies this expertise to the provision of a range of essential pre-clinical and discovery services for clients in the pharmaceutical and biopharmaceutical industries, including

pharmacokinetic evaluations, efficacy models and bioanalytical testing.

Melior's *theraTRACE*® indications discovery platform allows for known drug-like compounds to be comprehensively screened using a battery of in vivo assays spanning multiple therapeutic areas. Currently, over 40 validated animal models are represented in the platform spanning a broad range of therapeutic areas including inflammation, immunology, diabetes & metabolic syndrome, dermatology, cardiovascular, gastrointestinal, psychiatric, neurological and neurodegenerative disorders. In most cases, Melior's *theraTRACE*® system is able to provide a complete pharmacological profile of a compound in 10 weeks. *theraTRACE*® has found particular utility in facilitating the crucial "go/no go" development decisions routinely faced by pharmaceutical and biopharmaceutical companies.

In addition to the *theraTRACE*® indications discovery platform, Melior is able to extend its high throughput pharmacology approach to customized in vivo efficacy evaluations in other focused therapeutic areas. Melior has established expertise in the following major areas:

- Central Nervous System (including Neurodegenerative diseases and Psychiatry)
- Inflammation
- Acute and chronic pain
- Metabolic diseases
- Gastrointestinal and urology
- Cardiovascular diseases
- Dermatology

Melior's management has combined experience of more than 120 years in

pharmacology and drug discovery applications and has evaluated more than 250 compounds for novel indications in just 5 years. The company has long-term collaborations with Pfizer, Merck, AstraZeneca, Johnson and Johnson, amongst others major partners.

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

CEOFCO: Dr. Reaume, what was the vision when you founded Melior and where are you today?

Dr. Reaume: The vision was essentially that there is a lot of untapped value in drug candidates that are discontinued at clinical stages for reasons other than safety. They were brought through for a particular therapeutic indication, but may not be sufficiently effective in that indication. However, there is a lot of potential in repositioning those types of product candidates into other therapeutic areas. When we started up there was a lot of anecdotal evidence of drugs that were pursued for one indication, but serendipitously ended up being used for another indication. There are many examples of this, but the one everyone refers to is Viagra, developed originally for hypertension and as we know ended up being used for erectile dysfunction. The mission of the company then was to set out and make this happen more systematically as a very time-effective, cost-effective, way of bringing new therapeutic product opportunities to the market.

CEOFCO: How does Melior Discovery decide what has potential?

Dr. Reaume: That gets to the essence of what is special and unique about Melior Discovery. We have platform technology that is designed to take appropriate discontinued compounds, and identify which ones have new therapeutic potential and for what indications. This platform technology comes out of a know-how that I had developed in an initiative that I spearheaded while at Pfizer, prior to starting Melior, that we spun out and built the company around.

Then there is the criteria we use to identify the best candidates to enter into that platform. They involve small molecules, clinical stage product candidates that were previously discontinued for reasons other than safety. Therefore, they are beautiful drug-like compounds that are well-tolerated in humans and biologically active. They just were not quite effective in the clinical trials for the original indication.

CEOFCO: Melior evaluated more than 100 compounds; is it all science or is there some intuition or gut-feeling involved as well?

Dr. Reaume: I do not think that I could answer that it is all science insofar as the type of work that we do. It is very much a non-hypothesis approach. In that respect, it does not follow the dogma that otherwise is traditionally used to bring candidates to the clinic. Briefly said, it involves an assembly of disease models rep-

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resenting very a broad spectrum of therapeutic areas. So, for example, models of neurodegenerative disease, models of dermatology, inflammatory diseases and so on, are assembled together and that we then use in a completely unbiased way. We screen for where the alternative therapeutic activity of these compounds may lie. That aspect of it is not science driven.

If the question was in terms of choosing the substrates, yes, I suppose there is a bit of a mix of rote criteria. Some of the ones that I listed previously: small, drug like molecules, with good safety features in the clinic and so on.

In addition to that, the part that is sort of, to use your term, "gut-feel", would be the contribution that is brought to this process by a key member of our scientific team Chris Lipinski. Chris is probably the most recognized name in the field of medicinal chemistry. He is an individual who can look at a molecular structure and, just as a pa-

thologist who has decades of experience in deciphering between healthy tissue and disease tissue, Chris can look at a molecular structure and say whether this is more likely to be a drug-like compound with favorable attributes from a drug-like perspective or not.

CEOFCO: What are some of the main drugs and indications that Melior has reviewed?

Dr. Reaume: Our lead program is a molecule that was originally brought up through Phase II clinical studies for gastric ulcers. However, as I have described in our prototypical example, it was discontinued because it was not quite effective in gastric ulcers. It was otherwise well-tolerated in the 187 patients that it has been exposed to, and at relatively high doses at that. We took the molecule, entered it into the platform and what emerged was activity around metabolic disease including obesity and diabetes. What

we really focused on was that aspect in diabetes. At this juncture we have shown, and published, that it is quite effective in multiple models, really all the available preclinical models in diabetes. We show that it is, or more, effective than the existing therapies that are available. Most importantly, it fits what some in the field have described as the Holy Grail of what is needed in diabetes right now. If you follow the field at all you might know that there has been the disappearance of a major class of diabetes therapeutics. These are the things referred to as TZDs, or PPAR-gamma activators as insulin sensitizers. Only one still remains on the market. In 2008, Avandia, which is rosiglitazone, was shown to have some significant cardiovascular liabilities and so that class of drugs has essentially disappeared. They were the only example of insulin sensitizers. So, what the key opinion leaders in the field have said now is that the Holy Grail would be a next generation insulin sensitizer that does not have this PPAR-gamma activity. In other words, lacking the liabilities that are associated with that type of insulin sensitizer. That is exactly what Melior has shown that it has uncovered. It is a next generation

insulin sensitizer that does not work through this PPAR mechanism. So this is what we are excited about.

CEO CFO: Are you doing these tests in partnership with other companies; how does the revenue model work?

Dr. Reaume: Our work with this diabetes candidate does not currently involve a partnership. However, we do form partnerships that leverage our core competence of animal model testing. What is truly unique about Melior is the way that we multiplexed 40 or so animal models to form a proprietary platform technology. We partner with pharmaceutical companies allowing them access to this platform. Beyond that, we do a lot of this animal model testing; what is referred to as preclinical in vivo pharmacology. That is really our core expertise. The revenue model is that we take that core capability and partner with companies, be they small biotech companies or pharmaceutical companies, on a fee-for-service basis allowing us to drive a cost-effective, capital-efficient, way of doing our own drug discovery.

CEO CFO: Are you referring to the *theraTRACE*®?

Dr. Reaume: The platform where all these models are coupled to one another is *theraTRACE*®.

CEO CFO: What exactly is the *theraTRACE* platform doing that others cannot do?

Dr. Reaume: Normally you have an animal model where you are testing a

group of animals on maybe several different doses of the compound together with, some placebo and positive controls. All together that group of animals forms a cohort that is entered into the test. If we are just thinking of it in terms of a single animal model, that cohort serves that animal model. The idea of *theraTRACE*® and multiplexing, is the notion that you can take that same cohort of animals and have them perform double, triple, quadruple or more duty. To use a very trivial example, we might have an animal model of high fat diet, animals on a western diet, to see changes in obesity over time. A simplistic example would be to have that same cohort of animals to look at aspects of analgesia, in a simple hot plate model that is well recognized in the field. The key here when you start embarking on that kind of an effort is to ensure that when you put these together that the one model is not influencing the other and vice versa. That is what we spent a lot of time figuring out. We have determined what models go together and what sequence to put them in. This is something we rigorously validated.

CEO CFO: As you go forward, will you be pursuing more on your own like in the diabetes?

Dr. Reaume: It will be more sort of business as usual. Since we brought the lead program to mature stage, it has been spun out now into a separate corporate entity that we expect will soon be autonomous from Melior Discovery. That is, we have created

the separate entity called Melior Pharmaceuticals I. We are just in the process of forming Melior Pharmaceuticals II, which is a spun-off entity that has a collection of three independent assets; therapeutic candidates for atopic dermatitis. We can envision continuing to do that where each of these entities forms independent exits for investors and continue to do it in a capital efficient way by continuing to bring in revenue through fee-for-service.

CEO CFO: Why should Melior stand out to investors?

Dr. Reaume: What we have created is a cost-effective, time-effective way of discovering new therapeutics. Therefore, for those investors looking in the biotech field, this is very efficient way of bringing new products to the market. Here I am referring to the drug repositioning approach in particular, and layered on top of that is a capital efficiency derived from the business model that we have developed.



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**Melior Discover Inc.
860 Springdale Drive
Exton, PA 19341
Phone: 610-280-0633
www.meliordiscovery.com**