

## Therapeutic Antibody Development for Pharmaceutical and Biotech Companies



**Benjamin Doranz - CEO**

### **About Integral Molecular**

Integral Molecular is a research-driven biotechnology company creating innovative technologies and a pipeline of therapeutic antibodies for under-exploited membrane protein targets, including GPCRs, ion channels, and transporters. Its customers include all of the top pharmaceutical and biotechnology companies.

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

**CEOCFO: Mr. Doranz, what is the concept behind Integral Molecular?**

**Mr. Doranz:** Integral Molecular is a platform-based biotech company that develops antibodies against membrane proteins. Our core expertise focuses on membrane proteins such as GPCRs, ion channels and transporters. These complex membrane proteins are the targets for about 50 percent of the drugs on the market. They are difficult to work with, but are very important in the pharmaceutical industry.

**CEOCFO: What is it that your platform does that is not being done now? What do you understand about the platform and how have you come up with a solution?**

**Mr. Doranz:** Many scientists in the pharmaceutical industry run into technical problems. They are pursuing drug targets for diseases that are not yet cured and have no treatment, and it turns out that many of the underlying cellular and molecular targets for those diseases are very difficult to work on. Those are the kind of targets that we tackle. We supply the physical proteins for those targets and develop therapeutic antibodies against them. A customer, for instance, may come to us with a target for a disease that they have been trying to work on for months or sometimes years without success. We have the technologies, experience, and expertise to solve those difficult problems and get them to the next stage in the drug discovery process.

**CEOCFO: When someone comes to you at a certain point and says they need help, what is it that you would start to do? What kinds of testing might you run and where does the experience and intuitiveness come in?**

**Mr. Doranz:** We originally licensed technology out of the University of Pennsylvania where many in the company, including myself, came from educationally. We built the company based on that technology – now called the Lipoparticle. We have a fully equipped laboratory of about 10,000 square feet, and we have been doing this for over 10 years. When we receive a difficult target from a customer, we understand those challenges. We do not deal with the low-hanging fruit of the pharmaceutical industry - many of those have already been taken.

**CEOCFO: When you look at it, what kind of testing are you running? How do you start?**

**Mr. Doranz:** We usually start with a specific human membrane protein that is believed to cause a disease or contribute to a disease. What is needed is a drug - an antibody or a small molecule - that binds to that target and prevents that protein from causing the disease. What we do here is isolate those inhibitors against those membrane proteins targets, particularly antibodies. We will put a target through our platform, and we will isolate the antibodies that are specific to that target that have the functionality required. Those antibodies will bind to that target in cells, in an animal and in a person and prevent that protein target from causing the disease.

**CEOCFO: What is your technology able to look at that perhaps companies that have brought it to you do not know to look at or do not have the capability? What is it that your technology can evaluate that others cannot?**

**Mr. Doranz:** We basically take difficult protein targets and we make them easy to study. The targets that we work on are called membrane proteins, which are basically half inside a cell and half outside a cell. They sit in the membrane that surrounds all cells. Because they are in that position, they usually transmit information from one side of the cell to the other and play a vital role in cell health. However, also because they are that kind of protein that is half inside and half outside, physically they are actually very difficult to work with. You cannot just take them out of a cell, they misfold and turn into garbage if you simply strip them out of a cell membrane. Our technology simplifies that process and works with

them as if they are purified proteins, which makes the drug discovery process a lot easier than trying to deal with 1,000 proteins at a time. A typical project will involve taking a target and using our technology to concentrate the target and isolate antibodies against that protein. Those antibodies can then go into preclinical and clinical studies.

**CEOCFO: Are there competitive technologies and other companies or other systems that address that same issue?**

**Mr. Doranz:** Of course there are always different approaches to attacking problems, but what differentiates us is that we are very comfortable dealing with difficult problems. When we get to difficult scientific questions, difficult technical problems and these difficult proteins, we understand the types of strategies and effort that are required to come up with the solutions. We have developed a great deal of experience and expertise in house to be able to tackle those difficult questions and difficult targets. We work with many customers not because they do not have the scientific ability to learn those things, but because it takes time and effort. They can simply go to the experts in the field, us, who know the answers and know the tricks in dealing with those kinds of proteins.

**CEOCFO: Are there particular types of projects you prefer to work on given a choice?**

**Mr. Doranz:** We usually work on the difficult projects that have failed in other people's hands. Those are what we specialize in, but of course we never turn away easier projects as well. We have established our reputation by performing high quality scientific research and tackling difficult problems that other labs have not been able to address.

**CEOCFO: Do you hold patents for all your projects? Would you explain the business side here?**

**Mr. Doranz:** The original patents that we licensed are from the University of Pennsylvania, and we are the exclusive licensee of those patents. On top of that, we filed our own patents, so we have continued developing the technologies. We have also filed patents on the results of using the technology, the antibody therapeutics coming out of our pipeline.

**“We have established our reputation by performing high quality scientific research and tackling difficult problems that other labs have not been able to address... We engineer the target protein using our Shotgun Mutagenesis technology, concentrate it in our Lipoparticles, make antibodies against it using our MPS Discovery Engine, and make sure the antibodies cure the disease in animals and ultimately in humans... We stand out in our market because of the quality science, difficult targets and difficult problems we address.” - Benjamin Doranz**

**CEOCFO: Would you tell us about the products that you have available? Is that ancillary to the research part of the business?**

**Mr. Doranz:** We physically sell research products and services, as well as therapeutic products. Our research product is called the Lipoparticle, which are concentrated membrane proteins. We remove membrane proteins from the cellular environment, but keep them structurally intact. That means that the protein still looks like it does on the cell, but you no longer have the other unwanted proteins that are also in the cell. There are 5,000 different membrane proteins in the human genome, so customers could be interested in any one of those, or a variant. We also provide services where we want information about the protein, for example how strongly it binds or where the antibody binds to its target. That kind of information goes into patents, scientific manuscripts, and FDA filings for a new drug. Our Shotgun Mutagenesis technology allows us to understand how membrane proteins function and what they look like, and our MPS Discovery Engine technology allows us to isolate antibodies against membrane proteins.

**CEOCFO: How do you stay focused when it seems there are a lot of moving pieces?**

**Mr. Doranz:** For any company, focus is extremely important. You get too diverse and you do not necessarily do everything as well. The flip side, if you are too focused, you can take a lot more risk in developing only one product that may not have the expected market. It is always a balance, but in our company, what we do on a day-to-day basis is develop antibodies against membrane proteins. The specific membrane proteins can vary - there are about 5,000 in the human genome, and many of them are implicated in diseases. We develop targets essentially one at a time, but the process of getting from start to finish is pretty much the same for every target. We engineer the target protein using our Shotgun Mutagenesis technology, concentrate it in our Lipoparticles, make antibodies against it using our MPS Discovery Engine, and make sure the antibodies cure the disease in animals and ultimately in humans.

**CEOCFO: What has surprised you as the business has grown and developed?**

**Mr. Doranz:** Every day there are surprises - sometimes legal, sometimes technical, sometimes people and sometimes financial. I would say many times you cannot predict what customers are going to be interested in. In most cases, we have a pretty good sense of the science and the market, but in some cases our customers have taken roads that we

would never be able to predict. For example, different companies go after different targets. There's substantial risk for every target, but it could be the next blockbuster drug.

**CEOCFO: *Put it all together for our readers. Why take note of Integral Molecular?***

**Mr. Doranz:** We stand out in our market because of the quality science, difficult targets and difficult problems we address. We tackle challenging scientific problems that many others do not. In many cases, we go after the kinds of difficult questions asked in academic labs, whereas many companies shy away from those kinds of problems because they take a lot of time, effort and expertise to answer. But those are the kinds of problems that we like. When customers ask difficult questions, instead of learning the whole process themselves, they come to us for the answers. That is what we are all about.

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**BIO:** Ben Doranz is President and CEO of Integral Molecular. Dr. Doranz co-founded the company in 2001 and has led all aspects of the company's growth since its inception, bringing three different technologies from research to market and growing the company into a profitable commercial entity. He is an inventor on six of the company's patents, the principal investigator on over 20 NIH grants, and an author on over 50 publications, including articles published in *Cell*, *Science*, and *Nature*. Dr. Doranz is an established life science entrepreneur previously responsible for directing the biotechnology program at the Port of Technology business incubator in Philadelphia and helping create startups at the Center for Technology Transfer at the University of Pennsylvania. Dr. Doranz earned a Ph.D. in Cellular and Molecular Biology from the University of Pennsylvania where he was involved in the discovery the coreceptor for HIV (CCR5), an MBA at the Wharton School of Business where we won the business plan competition, and a B.A. at Cornell University.

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