

Standardized Platform for Molecular Diagnostic Testing



Dr. Jeffrey Miller, Ph.D.
Founder, CSO & CEO

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CEOCFO: Dr. Miller, would you tell us the concept behind Invivoscribe?

Dr. Miller: Going back twenty years, I wanted to create a standardized platform, a company, both on the GMP manufacturing and later on the clinical testing side, that could provide internationally harmonized molecular diagnostic testing. It started because with the reference lab I was with at the time, I saw that the tests they performed were home-brewed, or laboratory developed tests, which are standard in the industry still today. However, there was real heterogeneity between the tests they did and tests done by some of the other partners or even the labs within the organization. I saw that discordant results could potentially occur because of that. I thought that we could also get better control of things like our reagents. I was looking toward the future and now it is nice to see that more and more groups are embracing this vision.

CEOCFO: Why is Invivoscribe Technologies a noteworthy company?

Dr. Miller: The number of people afflicted with hematologic malignancies is growing as the population gets older and that is the area of our focus. There are now some twenty thousand patients per year in the US afflicted with acute myeloid leukemia, AML. When you have targeted therapies and pharma is developing targeted therapies, in order to enroll sufficient patients to power clinical studies you need an international reach for enrollment in clinical trials. When you do clinical studies around targeted therapies, precise stratification of the patients is critically important so that you can show the efficacy of the drug as quickly as possible. You want to make sure that if you test for the presence of a biomarker for inclusion in the trial, you do not miscall and inappropriately enroll a patient, especially if the biomarker test is semi-quantitative. For example, if you set a limit of detection or allelic threshold for a biomarker mutation for inclusion in a trial, and different tests generate different results at the enrollment sites in Asia, Europe and the US, then you chance categorizing and enrolling patients inappropriately because you

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have not stratified your patients in a coherent way. Since we are all supposed to keep our eye on the ball and provide a service for optimizing patient care, if you are not looking to embrace processes that bring therapeutics to patients most quickly and efficiently, then you are really hurting the patient population that you are obligated to serve as your primary customer.

Invivoscribe has internationally harmonized testing and that is critical for enrollment of patients in clinical trials. A number of key opinion leaders have come out with studies that show that *FLT3*-targeted drugs work with a certain cutoff on the *FLT3* allelic burden or signal ratio. In testing to stratify patients for *FLT3*-targeted clinical trials it is important that testing gives you a ratio that is internationally consistent no matter where the testing is done, so when a patient gets tested in Europe or the USA or Asia that same test cutoff and ratio can apply. This is critical so patients can be included in a clinical trial in a way that allows the drug to have the best chance of demonstrating efficacy so it can get through the regulatory authorities as quickly as possible. Also, to avoid the expensive and time consuming delay of having to conduct bridging studies of the test itself, the companion diagnostic, which is now required for approval of virtually all biomarker stratified drugs, the test also needs to get through the regulatory authorities as quickly as possible. So our goal is for the drug to have the best chance of showing efficacy and getting approved as rapidly and cost effectively as possible because getting a life saving drug or therapy to market more quickly is where we can best serve the patient's interests. That is and should be our goal.

CEOCFO: *With all of the government regulation, how has that been overlooked?*

Dr. Miller: I would not say it has been overlooked. I think the regulatory authority is quite good. It is kind of bifurcated between the medical device or FDA side and the CLIA- CAP- clinical laboratory testing side. I am one of the few CEOs that embrace regulation and I see it as a benefit to the patients. People have to remember that is whom we serve. Sometimes the perception is that it is overreaching. I am not suggesting it is very efficient, but I think there is nobody on the regulatory side whether in CLIA, CAP, the FDA or European or Asian regulatory groups who are in there to do anything but their best to make regulation least burdensome. Their vision is the vision of the community as a whole and that is to provide the best quality tests for patient outcome so test results are clinically actionable and helpful for the physicians and healthcare providers and ultimately for the patient.

CEOCFO: *What is a typical day for you?*

Dr. Miller: When I walk in and I think I have this agenda or series of tasks in front of me for the day, it will certainly change and be entirely different from what I expected. We have over 500 institutional partners around the world in fifty plus countries and those partners are using our testing reagents and controls, so we have to accommodate requests for everything from RUO assays for a lot of research labs, ASR products for sale to high complexity labs here in the US, and CE-marked IVD products for sale outside North America. We have been extremely successful with the entire range of our products, including our NGS bioinformatics software. So, the day starts with communication with our offices and partners in Europe and ends in the evening with communication with partners in Asia. I have a very good executive team

here that helps me manage the workflow, prioritize projects and manage the business. It is a combination of the ISO 15189 clinical labs, which we have started in strategic locations around the world and will continue to expand internationally, and then the reagent and test business, the manufacturing business, which is the ISO 13485 compliant, GMP manufacturing side.

CEOCFO: *What is better about your reagents?*

Dr. Miller: I would say we really put a lot of emphasis on quality, which is our differentiator - along with the fact that we have been in this space for twenty years and we understand the clonality market better than anybody else. We made the transition from Southern blot testing, to PCR-based gel detection, to capillary electrophoresis and now to NGS, and we now have the best bioinformatics software to go with these testing products. I would say quality is our differentiator and we are proud of our team and what they work for. For example, NASA really got its act together after the fire on Apollo 1. After that tragedy they did a complete reorganization and they said now we are going to have a situation where anybody can call out and say that if they do not feel comfortable we cannot go forward because there is a problem here. Well, we have had that mentality for at least a decade, so if anyone on the team feels that a product is not ready, they can say something; actually, they are encouraged and obliged to say something. These products are being developed under ISO 13485 design control, this includes our software. We feel that we are doing the DOE experiments and doing slow and careful development work. We make sure there is no hiccup or a dropped ball when you move from development to manufacturing because we have manufacturing actually make a lot of reagents for doing a lot of the later stage development activities. We do things right and we do things better than many of the bigger companies out there.

CEOCFO: *How do you know you are bringing the right people into the company to join the team?*

Dr. Miller: The best advertisement for new employees is our reputation in the marketplace. There are very few people in our space who are not aware of us and aware of the fact that we stand for quality. I think that they come in to interview knowing what we stand for and that is why they come in. It is gratifying that even prospective employees are coming in with excitement and expectations around our vision.

CEOCFO: *Are you surprised that quality is a differentiator in your industry when life and death could potentially revolve around what you are doing?*

Dr. Miller: Some of it is just experience. For example, many of the test centers that are doing LDTs would not even acknowledge that they are manufacturers. If you do not understand that you are a manufacturer when you are making test reagents and controls for the clinical tests you are running in your center, then you just don't get it. We know from two decades of work how critical it is to lock down even the most basic of reagents. We audit critical vendors and take this seriously. Again, many of the labs that produce LDTs would not even characterize themselves as manufacturers. We have seen differences in performance between LDT lots when we do collaborative studies and that is why when we do collaborative studies with top cancer centers we harmonize and provide

reagents for the parallel studies. We think that is important for reproducibility and precision and to ensure concordance in test results.

CEOCFO: *You have several companies in lots of locations. Why is it set up the way it is under several different names?*

Dr. Miller: We have now started our seventh company, LabPMM Japan. It was never my intention to start a company other than Invivoscribe. However, when the only logical and coherent way forward that allows you to be able to control, standardize, harmonize, and maintain the vision I have for consistency and quality of testing, the only way to do that is to start another company. You cannot do that by acquisition. We see no company out there we could acquire that is as serious as we are about building in quality from the ground up. Acquisition is about marrying cultures, so you really put your organization at risk if your new entity does not take QSR as seriously as you do.

CEOCFO: *What is your strategy for reaching out?*

Dr. Miller: It is very collaborative. We certainly listen to our partners and we have partnerships that we have had for two decades around the world. However, the majority of our decisions come from simply knowing the field ourselves, not really in response to what customers are asking for. I'll borrow an oft-used quote: "If Henry Ford had asked his customers what they wanted they would have said a faster horse." Our process is to identify from the literature and from the most up-to-date work that is being done, both by us, and by people around the world. What tests and technologies are going to have an impact and be clinically necessary and important and will help our customers in eighteen months to three years over the horizon? That is the development time line that you need to launch your products.

CEOCFO: *What surprised you as you watched the company evolve?*

Dr. Miller: I think my intention was to run a small company that did things correctly, maintained the focus on quality, harmonized SOPs, and GMP reagents. I just have been very pleasantly surprised at the growth of our companies and the ability to hold it together in the sense of not losing that focus - even with the expansions and with the multiple international subsidiaries. I have been gratified and fortunate to identify good colleagues to help me manage and run these companies. Looking back, I cannot believe what we have accomplished but it has been a result of taking a very coherent and logical series of baby steps in the right direction.

CEOCFO: *Are there geographic areas where you would like to have a stronger presence?*

Dr. Miller: We would like to expand but in a logical coherent way. One of the reasons we have been successful is that we manage our growth so that we do not get into territories that just make no economic sense or where there is not a driving need to be there yet or where we have not figured out some of the difficulties managing businesses in those areas. We are moving more internationally and we will have an increasing worldwide presence, it is just that we do it in a measured way. Much of our growth has been driven by accommodation for our partners. Our pharma partners assist us in developing capabilities in countries where we would not on our own have ventured in at this point. Often, when you have a good partner, then it makes economic sense.