Stanford eCorner

History of Surromed

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Ringold talks about Surromed's goals: 1) To improve the use of existing drugs and diagnostics 2) Right medicine for the right patient in the right dose at the right time. Ringold talks in detail about the limitations of diagnostic techniques and drug use today and how Surromed tries to find a solution to some of the problems. He shares a report by McKinsey which summarizes the status of drug discovery.

Transcript

The second company was Surromed. And Surromed really came out of an analysis that led to the mission that you see here, which is ultimately to enable the precise diagnosis and personalized treatment of disease. And this is an approach that has been started from a basis of genetic differences among individuals with response to the form of their disease as well as the response to drugs. But, I think it's much broader than that in many ways. And the goals, really, in the end are two: one, to improve the use of existing drugs. Most of you in this room probably don't go to doctors that often or get diagnosed, or treated, or prescribed drugs. Those of us who are a little older will have experienced that or have parents who have experienced that. And when you really stop to think about it, doctors are at a significant disadvantage. And the patient is essentially an individual experiment almost all the time. When you walk in and say, "I'm feeling pain," well, we'll give you something to take care of the pain.

We're probably going to diagnose what it is. There are no good doctors that say, "Gee, you have pain because X is happening and we know how to treat that." You walk in and say, "Gee, I'm depressed. Well, let's try Prozac. Well, how long do I need to try it? Well, try it for a month or two and then we'll see how you're doing. Not doing so well? Let's try a different anti-depressant." Rheumatoid arthritis, "Oh, my joints are really sore. Well let's try a little Methotrexate. Let's see how you do, then we'll try a little disinhibitor. Now, we'll put you on an expensive medication like Enbrel which is a TNF inhibitor, costs $15-20,000 a year. And we'll do the experiment, we'll see if you respond to this drug, which is a pretty expensive experiment to do. And if it doesn't work, What's going on? Your disease is getting worse and worse and worse, week after week after week.

It's not the doctor's fault. We don't have the diagnostic wherewithal that the doctor can use to prescribe and to diagnose and to predict the course of your disease. And therapeutic intervention has to be based on more knowledge if we're going to be really effective about it. It's kind of crazy to think when you send your blood or urine sample out to a clinical lab, that the number of things that are being measured, maybe 15 or 20 different analytes that are being measured, is about 10% of what is measured in the oil of the transmission of your car when you take it in to have it analyzed for what's going wrong with your car. That's the state of technology in the medical-clinical industry. And why is that? Well, because most of the things that we've measured have been discovered over a very long period of time to be validated as tests that are informative. Usually, it has happened in the academic community. I'll give you two good examples. Blood pressure, high blood pressure and high cholesterol. These are two surrogate markers of disease, right? And Surromed actually came from the concept of discovering new surrogate markers useful in medicine.

So, where do these surrogate markers come from? They come typically by happenstance brought academic research over long periods of time. The notion that elevated cholesterol was a clear risk factor for developing atherosclerotic disease took 30-40 years of very slow, methodical and non-directed effort in the academic community. And so we said at Surromed is why don't we set out to develop technology that instead of measuring 10 or 20 things from a tube of blood, we can measure a thousand things or 2,000 things or 5,000 things and then use informatics technology to sort out what things are changing in people who have disease A versus disease B, who respond to drug A versus those who don't respond to drug A and the biological questions, but essentially an intent to discover surrogate markers. The technology didn't exist though. So this is a Type A company. Here is the problem, how we actually going to build the technology or the capability to go looking for these new surrogate markers, diagnostic markers, bio markers, or a lot of names being used for more or less the same principle. The second reason was my experience at Syntex and Glaxo led me and others to recognize that one of the reasons that drug development and drug discovery is so inefficient and failure rates are so high is that the models, the animal models we use of human disease are not often very close to the human disease. What we call a disease is often a syndrome of a constellation of several different diseases. Rheumatoid arthritis is not one disease. Joint degenerations, stiffness, inflammation are common hallmarks of Rheumatoid arthritis.

But the underlying cause and pathology can be subcategorized into at least five or six different very clear diseases. And why should we think that any particular therapeutic approach if it's going to be particularly well-targeted is going to be equivalently good for all five forms of Rheumatoid arthritis. But we don't have a diagnostic test today that says you've got RA Type 1 versus RA Type 2, 3, 4 or 5. Depression, even on the classical scale that psychiatrists use, is categorized into nine different forms of depression. So again, why would we think that a new concept, that takes 12 years and $700 million to develop a new drug, is going to work for all nine forms of depression? It's a nonsensical concept when you really think about it. And so, a lot of drugs enter the clinic and maybe they do work for one or two out of the nine forms of depression. But, in the early clinical trials, that drug will statistically fail because we can't enroll. We don't have a test that says we only are enrolling Type 2 and Type 7, which are the responsive types, to this therapeutic approach. We're enrolling all nine. And seven out of the nine can't possibly respond because they don't have the mechanism for which that drug is actually directed.

Now there are lots of other reasons drugs fail, but if you take the standard, the average... So, here's my motto, "The right medicine to the right patient at the right dose and at the right time." Now, if we could do that, we'd improve medicine and healthcare dramatically. This is a study done by MacKenzie and Lehman Brothers that kind of summarizes the status of drug discovery and the woeful inadequacies in the success rate that we see. So, in the lower bar, the traditional model that, really over in the last 10-15 years in a mid to large-size pharmaceutical company, they might be investigating 50 targets, meaning proteins, enzymes, pathways for intervention and disease. And out of that, maybe four to five molecules would actually enter into clinical trials. Meaning, it's going to go into people to be tested. And out of those four to five, only one will make it all the way through and be approved as a drug. Now, for those of you on the business side here, even a smaller proportion than one out of four or five ever even pay back the investment made in developing them, okay? So if you take that, how many baseball players, if you're batting average on your team was 100, how long would you stay as manger of that team? Not long. And so, fundamental dynamic would be, "Hey, let's get to 2 out of 10 successes, instead of 1 out of 10." Now, you've fundamentally changed the financial dynamics of the industry. We're not talking about getting to 80% success; we're talking to getting 20% success from 10.

Now it's actually happening with Genomics, all these new targets from the sequencing of the genome, is that the companies are now going after 200 or more targets because they're available. "Oh, I thought there were two serotonins receptors, now there's 12 serotonin receptors. So, let's start working on 12 serotonin receptors even though we have no clue which one of them is associated with any particular pathology. They're less validated targets." A second consequence which just kind of eats at me, is that this huge amount of money that's being invested across the industry and R&Dhas traditionally and continues to go disproportionately to meet two compounds and formulation extensions of existing compounds. Warner Lambert was bought by Pfizer in a "merger of equals." It was an unfriendly take over. The story was if Pfizer said, "No, this is a merger of equals. In fact, we'll use a combined name. We're going to use P-F-I-Z from Pfizer and E-R from Warner. And we're going to call it Pfizer." Okay? Now they're doing it with Pharmacia. And they said, "We're going to use the P from Pharmacia and the F-I-Z-E-R from Pfizer, and we're going to call it Pfizer again." And so, any company that has a letter in the word Pfizer be careful, you know.

But, that drug is a cholesterol-lowering drug that this year 2003 will become the first $10 billion pharmaceutical product, single molecule. Now, I ask myself, that's great, it's a huge market, Pfizer's doing well. But, it's like a third or fourth generation statin for lowering cholesterol. And healthcare, meaning lowered risk of atherosclerotic disease, has not been improved dramatically by having a third generation statin. Any one of two or three other statins that are out there are more or less the same. You could argue for slight differences. But, we don't have anything to treat Alzheimer's disease. We don't have anything to treat pancreatic cancer. We don't have anything to treat Coulomb's disease. There are a lot of diseases out there that are costing the healthcare system a ton of money in which much less money is being invested in discovering drugs.

And the reason is, why? Be interactive. Why is no money going into those or a disproportionately lower amount of money going into those? Because the market is too small to recoup the cost of development. Many answer, "The market is too small to recoup the cost of development." That's true in a very small, select cases. I mean, I would argue, if you had a good effective treatment for lung cancer, you have a multi-billion dollar product. So there's another reason. The market's rewarding me-too drugs and that seems to be the long hanging truth so that's what people are putting more money into. Yeah. The failure rate on unproven concepts being a leader in this industry that come up with the first drug to something new as a true therapeutic breakthrough, the proportion of success there goes way down to maybe 1 in 20. And so, the reason that it's even 1 in 4-5 is that that's weighted by, "Well, I'll make another Statin, I know it's going to low cholesterol." So, it's already there. It's an established market, the mechanisms established.

All I have to do is create a molecule that has some very modest marketing hook to get a small piece or a significant piece of a very large established market. But when you really think about improving healthcare, there's kind of a skewed perspective there. I mean, we ought to be investing more money on creating breakthrough drugs, not on rewarding me-too products. And, I don't know how you get around it because the economics say if you only work on breakthrough drugs, you're not going to survive because the hit rate, the success rate is too low. So what we need to do as an industry, and that's what we as biotech companies or entrepreneurial companies need to do, is to try to come up with ways to help solve that problem. Whether it's incrementally or radically, will depend on how successful you are. So anyway that's the basis. And so going from large numbers of patients in clinical trials, very subjective endpoints, think about how you would do a test for a new Alzheimer's disease drug. How would you actually test whether your drug is working? Somebody else. Design your Alzheimer's trial of your new drug.

Anybody? You take a bunch of old people who have already lost a significant part of cognitive ability, you stratify half of them to not get the drug, half of them get the drug for a minimum of 12-18 months and you give them a psychometric cognitive test 18 months later and say that this group will lose their memory slower than this other group. I mean what a nightmare. I mean, that is a terrible end point to have to use to make a $500 million investment on a new concept, okay. We don't have a blood test that says Gee you've got Alzheimer's disease. Or, another imaging test, an MRI that says, "Gee, your brain function has improved!" Right? We have these silly cognitive evaluation tests. It's not that they can't work, but imagine you have five new concepts to treat Alzheimer's disease. And you want to do a quick study to figure out which of these five have the highest probability of succeeding. And so you want an answer in two months. You can't do it today. There is no way of doing it.

You'll have to roll the dice, spend hundreds of millions of dollars getting to that very long subjective endpoint to figure out whether you chose the good one or the wrong one. And most of the time you're going to pick the wrong one. It's just the way it is today because we don't' have enough information. So we need to change the paradigm. Basically what you want to do is to have fewer patients, much better characterized, are they Alzheimer's Type 1, 2, 3 or 4. And we do a short study and say, "Geez, the Type 2s are getting much better than the Type 1, 3 and 4." And we have a test that tells us which are the Type 2s. And now we do a much larger study but only with Type 2 patients rather than Types 1, 3, and 4. And guess what? The likelihood of success is going to go up dramatically, right? So where do these biomarkers come from? So I'm not going to spend a lot of the time on the technology per se. Just believe me. We have technology now where we can take a tube of blood and measure 5,000 things, okay? And what that required was integrating engineering skills, chemistry skills, biology skills and very importantly database and informatics skills in order to be able to reduce the data, interrogate the data, and be able to make sense of vast amounts of data from small amounts of a biological fluid.