So I will be talking today about a problem that faces society and in the street, which is where the new medicine is coming from. And it sort of sums it up in this: you read in the newspapers about the remarkable new drug discoveries, curing cancer, and we can cure a mouse. According to the newspapers, we are curing cancer everyday, but anybody who has had a family member go through it, we know it’s just not true.

So we spend about 100 billion dollars a year in University research and pharmaceutical and biotech industries spend about a 100 billion dollars themselves in research. And it’s been going for the past decades. So why? What’s the fundamental problem? Is it because we’re not investing enough? Probably not. Is it because we’re funding dumb people? Definitely not, I hope. We’re discovering stuff everyday.

So where is the disconnect? We’re paying for it, we’re funding the smart people, they’re discovering stuff – but there are no cures. So in order to sort of grasp the scenario, we really have to understand how medicines are made. And we automatically assume drug discovery – large pharma does it. And that’s just not true. It’s neither true scientifically, nor economically.

So if we’re to think of the classical way that we think drugs are made - from a generation of an idea to a product - it involves the academic sector and the circles or the size of the money invested. Biotech and pharma, and then the health care system. So this is the eco system, as it were, in which an idea, for treating cancer, gets initiated in the lab, the early stage science is done, somebody decides that it might be a product, the regulatory stuff, and then the physicians, nurses and patients that contribute to the process.

So look at the size of the circle. If medicines aren’t getting developed it’s not fair to say, “that’s the problem.” It’s as much our problem as citizens and scientists, as it is an industry problem. Now its an industry problem because it’s their economic return that’s at stake. We obviously want to help, they can’t do it alone. So we need to take responsibility.

So how is this eco system doing? [Referring to presentation slide] People may have seen these graphs in many guises, but here’s 1963, heres 2008. This is the amount of money. Here is the amount of money invested in RMP. This includes both sectors. This is the amount of new drugs the FDA approves each year. So you can see we're investing more and more money and we're making the same number of medicines, so therefore the productivity of the sector is going down. Making and flipping hamburgers, productivity is going up every year. Making cars, productivity is going up every year. This is probably the only sector, where the more money we pull in, the products aren't coming out. So there's some fundamental problem in this.

So why is it so unproductive? What's happening is that, how a drug is invented, is first you have an idea. You have an idea in the lab: in this cancer, this part of the cancer, this protein in the cancer is hyperactive. It's got the foot on the accelerator. We need to stop it. Fantastic. So off you go to your laboratory, you make the foot on the accelerator and you try to find a log jam. That's your starting point. Then you've got to make sure it works in animals. Then you've got to make sure it doesn't kill anybody. Then you finally - this is after about 8 years and maybe 40 million dollars - you're testing it in actual cancer patients, a small number of patients. And then if it looks good, then you finally test it in a larger number. That's a 10-12 year process. It probably costs between half a billion to a billion dollars. Just to check it. And what's the discouraging thing, is that despite all the brainiacs that work on it, when you finally test a new idea in people that actually have the disease, at least 9 out of 10 times it doesn't work.

So you can have a room full of Nobel prize winners saying, "That's the accelerator we should block, it's working in animals, it's looking fantastic," and then you get to man - a "proof of concept" they call it - does this idea really work in people? No. And so, that is the biggest problem in drug discovery. It's not: Can I make a molecule? It's not whether we patent or not. It's not about the regulatory process. We do not understand enough about human biology to predict, that by inhibiting this protein, it will cure the patient. 95 out of 100 times, we get it wrong. That is not a science, that's not a business. That is a lottery.

So it is interesting to unpack why that happens. So we can do fine; we can make a molecule, we can get it safe in people, but when we test it in human beings, it doesn't work. And those are the costs that are associated with each of those steps.

So, what are the economic consequences of this business lottery? First, economically, the U.S. has seen the closure of 1800 locations of large pharma. The EU has seen 14. Canada had many - we had Merck in Montreal, Berner-England in Montreal - now we have none. So the CEOs of the companies, very wise, they say: If we don't understand what's going on, what is the point of doing these pre-clinical studies, if we know 9.5 out of 10 times, research is a waste of money? We should fund other stuff, and let the academics do the research. And these are really wise business decisions. Why would you spend more money on lottery tickets? It makes perfect business sense. And 100,000 pharma employees get let go in the last 5 years. This is an interesting stat, because when I was in school, it was risky to go to University, but if you went to pharma, that was a job for life. Well that's not the case anymore.

So that is a really high level, quick, probably incomprehensible view of how medicines are invented. But the conclusion has to be, that every system we put in place is not working. To approve 20 new drugs in a year, the world spends 200 billion dollars on bio-medical research. They're shutting down research sites. Many pharmaceuticals view Alzheimer's and say "I'm not doing it." We're going to have an aging population in Canada - all the Western countries, the demographics are all moving to aging. Chronic disease of cancer, Alzheimer's, and other neurodegenerative diseases are going to increase, and the pharmaceutical companies, which are partners in inventing medicine, they go "Not for me. We don't know how Alzheimer's works. What's the point in trying?" So Novartis - out of it. Glaxosmithkline - we're not doing it anymore. This is serious for society, because part of the ecosystem has said it isn't worth it.

So there's still no good medicine, and for my children, there's no end in sight, there's no pot at the end of the rainbow. It's definitely a shrinking of this establishment, and health care costs, of course, march up. So within the system it's really hard.

So I'm going to talk today about our attempts to change the system, because to me that's the only solution. And the first problem is: look in the mirror. In 2001 the human genome was sequenced. Blair and Clinton shaking hands and saying, "This is changing life on the planet." But it didn't.

But it did do something. What the genome does is the sequence of all our genes. And from looking at the sequence of our DNA, we can say we have 20,000 genes in us. And what a gene does, a gene is a like an architect's drawing for a machine called a protein. So there's 20,000 proteins. And proteins are drug targets. So if we figure out what each of those 20,000 do, we will be able to explain human biology, and when they go wrong, we will be able to understand disease. Pretty clear. That's it. That's our universe of biology. It's not like chemistry, where we can make a million molecules. It's not like astronomy, where it goes on and on and on. This is a real box. Explain that, we've got the human condition explained. For the first time, in any scientific endeavour, on this planet.

And it's quite a remarkable achievement, but it isn't having an impact. And to demonstrate that, what I did was, I said, well let's look at a few of these genes. So there's a family of proteins in humans. These genes all sort of look and do the same thing - they're called protein kinases. They are drug targets. And every one of them has a name. So you can go on the Internet and say "How many people have published a paper on Kinase number 1?" And it'll spit back a list. "How many people have published a paper on Kinase number 2?" And it'll spit back a list. You can do it for all 518 kinases, and what you get is this graph [referring to presentation slide]: 518 of them, they all have a name, and the number of papers per kinase in these bars. And it doesn't take a scientist to figure out: wow, what are you guys doing? You're all working on the same kinases. And my mom's a grade 1 teacher, the smartest in our family, said "I thought you scientists like to explore stuff." Not really, Mom. So you think, wow, the scientists in the system, they're important. Yes they are. But if you start doing experiments that don't ask "Is this one important?", tell me the ones that are important. So you can do experiments that are less biased, you get answers like these - every time you see a little bar, somebody did an experiment and said "That kinase is kind of cool." And this one - sequencing cancers to find which ones might be cancer targets.

So you have a huge disconnect - you have the scientific establishment - myopia, focusing on a little area, and the data saying hey guys, there's cool stuff out there.

So why is this happening? And for those that don't know how science works, and how science funding works, it's peer review. So how do we as professors get our recognition? Is it money? Not really. I mean money's nice, we all get paid well. But that's not why we got into this. We're curious. But if we're just curious, we just think ourselves curious, that's not good enough. We have to have our friends tell us we're good. That's the cool thing for us. So how do you get your friends to tell you you're good? You work in an area where there's other people. And you do good stuff. And therefore you've got this peer pressure to work in the same area. And then we write grants to get funding, it gets reviewed by 10 people. They all work on a certain area, you better darn well write something in your grant that relates to them, or you're not going to get funded. If you want a fund on a kinase that's never been worked on, and you say "I'd like to study kinase 351 because nobody knows anything about it", you will not get your grant because we don't get funded to explore.

We get funded because we tell good stories. We get funded based on how elegant the idea is. It can't be elegant about 351. You can be darn elegant about this because there's lots of data and you can make hypotheses and you can be apparently smart. The other thing is if you want to get invited to Barcelona or Oshawa to do talks. Don't work down here [referring to unstudied kinases] - who's going to invite you? These are the organizing committee members, they're the editors of the journals - the whole system forces us to be able to work on areas where other people work. And in reality, if the University of Toronto, indeed, if all of Canada got blown up by a neutron bomb, it wouldn't affect the planet one bit. The scientific progress would be exactly the same. Because I can guarantee you that every scientific experiment that we are doing is being done elsewhere. Because how funders fund money is they don't give it to the best idea in the world, they give it to the best in Canada.

Well I read the same literatures as my friends in Germany, we're going to write the same grants, because no one is smarter than anybody else, they'll get funded, I'll get funded - by definition we've created a community, by definition we've created a community that is competitive, and by definition nobody's working out here [referring to unstudied kinases]. It's a bizarre system but that's how it works.

Why now, do I say when we're doing a phase 2 clinical trial on a new cancer drug, "Trust me, it's going to work. I know a lot about biology"? How? Two thirds of the proteins in us, we don't even know what they do. We may pretend and convince ourselves we know a lot about 10 of them, and we can create a nice story, and have the Harvard bow tie to prove it, and I can walk in and be the key opinion leader and tell everybody, but the reality is the best way to know if you've got the answer right is if you can predict what happens - and we can't.

So this is the problem in drug discovery. It's not that other stuff. So the question becomes "how do we fix this?" Well first, is it getting any better? No. [Referring to presentation slide] So if you look at pre-the-human-genome and 2002, and after the human genome when life was supposed to change, and you plot papers on this axis and kinases ordered pre-genome in their 'cool-ometer', you can see that most of the papers are still on chestnuts. 65% of the papers in 2009 were on the 50 kinases that were hot in 1993.

As one example, here's 2 kinases that are mutated in skin cancers, that's melanoma, identified by Genomix. Fantastic. Ones down there, 40 years after Nixon's war on cancer, why didn't we know about it? Because we were all studying these ones. These are not unimportant - but do we have the balance right? And the idea from the drug discovery perspective is no, because every time we going into a human with a new drug, it doesn't work. 1 out of 20 does.

So we need to change. But industry, of course, is a data-driven industry. So what I do is you plot the patents from industry and overlay them over the academic research, and 1) you learn that basic science counts, because industry does follow basic science, but 2) if we don't do a good job in basic science, they have no choice but to follow us into that myopic little ring of doom that we can't get out of.

So if you go to your vice-president of oncology and say "I want to start a new program" - that's a 10 million dollar bet, if you're just starting. On kinase 351, show me the data. There aren't any. Then you have key opinion leader from Harvard with the bow tie come in and talk about number 20, where the mice do funny things and the cancer's shrunk - well oh, that's exciting. You've got the Harvard guy with the bow time who you went to school with telling you to work number 20, and if there's lots of scientific literature, it's a no brainer where you put your money. But think about it. That same key opinion leader is going to Bayer, Pfizer, and they're going to tell him the same thing. And what happens? You get industry doing the exact same thing.

So we have a weird system, right? We have the genome, we have the way to understand human biology, but the way professors work isn't there, and the way industry works isn't there - so how do you circle that square? We have a societal problem. These guys (scientists) are supposed to fix it, and we're not doing a good job. We're doing a disservice to our children. So something has to change.

No one is doing anything wrong - industry is science-driven, they're following the best literature. If I was a young scientist now, I'd work right here. It's the way to get advances, it's the way to get promotion, it's the way to get tenure, it's the way to become well known. If you work out here you might be out of a job in 5 years because nobody thinks you're doing anything important. So the actors are acting logically. It's just the system that's messed up.

The way in which we reward scientists is the main issue. And industry relies on us for innovation. One of the interesting and kind of distressing things is that it actually gets worse. This is a chart that I got from a guy who heads up our lab in Oxford, and he just writes it in a different way. This is the same graph that I showed you before, the professor thinks of a new accelerator, that's the way to cure the cancer, industry works to fund an inhibitor, you say this is the one we're going to think it's a drug, we make sure it's not going to make any people sick, we take it into phase 1 and make sure people's hair doesn't fall out, we test it in the proof of concept and trial and that's a 50 million dollar bet. The trouble is, you know what really happens? Every new target, because they got the same literature, the same key opinion leaders, the same scientists group think, this is what happens.

So I can name you probably every cancer target, or every Alzheimer's target when they were still doing it, is the same thing. Hundreds of parallel programs, 20 different companies, doing 10 different trials each. So, you know what the success rates are - this is going to hurt you. But now imagine how it really works. Let's imagine we're Aurora Kinase, and you have 20 companies trying to make a drug to Aurora Kinase to best treat cancer. It stops cells dividing and cancer cells divide quickly. It should work. So now they're hustling and racing to market, and lets say Merck gets there first. Merck runs its pivotal phase 2 proof of concept studies. It's a therapeutic window. It makes people sick before it makes them better. The therapeutic window is too low. We're dropping this one. The FDA knows it, but they're not telling anybody. Merck knows it, but they're not telling anybody. Now it could be an effective compound or it could be just that the target's bad. So the next one does the same thing. Now we're convinced that Aurora Kinase is a dumb idea. But is anyone telling the ladies who are in their last months of life now? You only warn people of these investigative drugs when you've failed the current treatment.

So we have incredibly sick people, their families are desperate for cures, they're starting to take medicines that will not work. It's going to make them sicker in their last months of life. This is seriously stupid. All the actors are playing exactly appropriately. You can find reasons why you can rationalize it, but no one would invent this system from scratch. It's just dumb. It's a waste of money, it's a waste of really smart people, it puts patients at risk, and it doesn't actually make any cancer drugs at the end of the day. And industry's downsizing and we're leaving Alzheimer's. It's not a happy story.

So why aren't there enough new medicines? My answer is simple: we don't know enough about human biology. If we had a comprehensive understanding of human biology, we'd make medicines, industry would be profitable, we'd have medicines for our kids. Can we do anything about it? This is where, I think, for Canada, for smaller institutions there's an enormous opportunity.

The system is the system. Well why don't we let those guys play in their sandbox over here. Why don't we start to figure out, why don't we work on the proteins that nobody else works on. The system will conspire against it, reviewers of papers won't like it, but if I had 10 dollars to spend, and I want to get my biggest ROI for the world and for Canada, it wouldn't be the hundredth person to work on the same old chestnut that everyone's working on. My 10 bucks is going to be the first 10 bucks on 5 different things down here. It's an enormous economic opportunity for Canada and it's the right science.

Now I don't see it's going to happen, but if I were God, this is what I would do, and I were a smaller institution, I would support my scientists to go that way because, Toronto, we're all here. We're part of the feeding frenzy, we want to be big and famous and sexy, and down here, there's so much opportunity for smaller places and smaller countries, because really, Canada is a small country to compete. This is why I started the SGC 10 years ago. I saw that unless we can figure out a way to get resources on that side, we are not going to be able to have medicines, we're not going to have economic prosperity, we're going to do good science.

So we're a public private partnership. The head office is in London, and we fund research at 2 places: the University of Toronto and the University of Oxford. We're funded by 8 and soon 9 pharmaceutical companies who donate, participate, and collaborate, they give us about 8 million dollars over 4 years each. It's the largest public-private partnership in early stage science on the planet. We have over 200 scientists, we never file for IP, and that enables us because it's about the science - because the problem is not "can I make a molecule, can I take it forward", it's "to what target should I take it forward." And figuring that out is best in an open sharing environment. So we've declared, no matter what we've discovered, we'll never file for patent. We give stuff away. We have no legal agreements. You can use it and have fun. And we make purified proteins, which are the output of genes, we do bio-chemical assays, we solve the 3-dimensional shapes of the structures, we create chemical inhibitors to give away - and all for human protein set up; the potential to be drug targets. We do about 15% of the world's human protein structures every year. It's quite a Canadian success story.

So how are we going to get people to work out here? And this is when my friend Tim at GSK spoke from his experience. So this is another 48 genes in the human genome. They all code proteins that sort of look the same, slightly different so they do different things. One binds the hormone estrogen, and does estrogen activities, that's the estrogen receptor. Another one is endosterone, progesterone, glucorticoid. So these are pretty important proteins. And in the 1990s, biochemists had discovered how estrogen works and got this estrogen receptor and there were 6 known on the planet. Every single one is a drug target. So in the mid 1990s companies were sequencing the human genome, and we found 42 new ones. So Glaxosmith loved it. We'll pay you 10 million dollars, you tell us the secret codes for these, and we'll start researching them internally and trying to make drugs to them. But we don't know what they do, so they called it reverse endocrinology. We'll make the drug and then we'll start giving it to animals and you know what happens to the animal, and then infer. That's what this thing must do. So they did that. And it worked for 5, 10 years. Fantastic science. They made the drug and they couldn't figure out what disease, they couldn't figure out what to do. So then they thought, well you know what we're going to do, we're going to identify 3 key opinion leaders and give them the molecule, accompanied by a legal agreement, but that wasn't enough. So then they said, how in the world are we going to find out what this drug target does? What happens if we give this molecule away? Now they hadn't patented it, so they weren't risking that much, but even at that point in time it was a risk to give out the chemistry. But they did it. And people started to use it.

Now let's look at the sociology of how science works. [Referring to presentation slide] This is the graph, ordered, before all this activity, pre 1995. And then in 2009. There's a difference isn't there? It's not like the kinases. Something's caused people to shift. There's only one thing that relates to those loci of research activity, where professors have decided I'm going to start working on these and publishing. Those are the only 8 molecules that Glaxo Wellcome made and gave away, so that nobody had to sign anything, you just order it from a catalogue and use it in your lab. And look how much of an effect this had - same order; these are not ordered by coolness, they are not ordered by genetic link to disease, they're not ordered by when they were discovered, they're not ordered by anything except Can I do the experiment with the molecule, and Can I not do the experiment. [Referring to presentation slide] That's mutated and mature onset diabetes, there's Parkinson's ones out there. What causes professors to work? The chemical probe. This was the insight.

Tim and I thought, wow, you can't tell a professor to work on anything, because frankly we're "too smart" to be told by any of you guys what to work on, but what happens if you give a professor a tool compound, you don't have to tell them, like flies, they start to work. So how do you use this behaviour of scientists to our own end? What if we make tool compounds, this time, before we do all that work internally, and right as we get it, give them away.

The hypothesis is, that professors all around the world - we don't have to pay them, we don't have to ask them, we don't have to do anything - will go, oh thank you and start doing experiments on kidneys, on brains, on skin, on all sorts of systems, for free. So yeah, it's a way to use the behaviour of scientists, the sociology of scientists, to our nefarious end. Interestingly, the evidence suggests that research tools drive research into areas more than biological importance or relevance or the story. If I can do the experiment, I'll do it. But, the data are, unless they are freely available, no one will use them. There are some tools and some receptors you have to write a way for patents and get a material transfer agreement, and evidence shows, people don't use them. They'll use them if they can order them, not tell anybody what they're doing, from a catalogue, and do the experiment. But here is the problem. The best chemists to make these tools are in the pharmaceutical industry. Most of the research in pharma takes place in other places in the world.

So how do we get these guys? Because most pharma aren't as enlightened as Tim, who realizes, you give away a little, and we get back a lot in return. So this started our convincing of the Glaxosmith senior management, why not do something a little bit different. Why don't we think about combining the SGC, which internally we had all these research capabilities, we know how to solve structures, and structures solve inhibitors, we've got all the assays, we've got all the proteins, we spent about 2 million dollars getting this trove ready. And we said, pharma, why don't you the chemists to the cost. Now they freaked out a little, cuz chemists are their inner sanctum. What do you mean, sell chemists? But over the long run, they thought, well if we give one molecule away, just one, it won't really hurt us because we'll have so much in the background. So they agreed.

So the idea was we'll form a partnership where we use our strengths and their strengths, their money and our money combined, and we would throw molecules into the public domain for professors. And the hypothesis was they'd start using them. And they'd start doing experiments and publishing papers, and the GSK scientists would sit at the side, watching the scientific literature, and then internally making their own decisions, there's enough known about that protein that they're going to start working on it in secret, going to find their own proprietary program.

So use a little bit of chemistry to open new areas of science where they can capitalize with speed and their real expertise. If you give a pharmaceutical company a target, they will make the medicine. Whether it's the right target, that's the key question. This helps them get there. And so we decided to focus this project, it had to be a big thematic project on a neuroscience called epigenetics. Epigenetics refers to things on top of the genome. So that and that are the same genome, but somehow the DNA is read differently at two different times, and that's not changing in the gene sequences - the code is the same - it's actually chemical marks that are put on top of the DNA. Little on/off switches, methyl groups, and the DNA is wrapped around protein, and these proteins have little sign posts on them - a chemical marker on the cetyl group, the methyl group - and it's the combination of all these little marks that turn genes on and off, and make a caterpillar into a butterfly. What happens in cancer, is sometimes the cell forgets it's a skin cell and starts to go backwards and starts to divide like crazy like it used to divide when it was a baby. It's forgotten it's supposed to be a mature skin cell, and it's possible - we don't know - that epigenetics - proteins that regulate the turning on and off of genes might be drug targets. It's a huge risk, it's a cool area of science, we thought it was a fantastic place for us to collaborate. Interestingly, there's 400 proteins in the human genome that regulate this process. They fall into families like the kinases, and look at the patterns. The patterns are exactly the same. [Referring to presentation slide] And if we don't do anything, it's going to do the same things as the kinases [research].

So the idea was, why don't we start selecting some of these lesser known ones, make tools, and throw them out there. And so it went from just Glaxo, to now eight companies have joined under the exact same terms. Together we work on a lot of projects. The deal is the company has to give one fantastic molecule to public domain. The molecule, what they create, it can't just be something in their pocket, it costs about 5 million dollars to make in total. They have to have a very strict criteria of utility, they have to go in and hit the protein alone - they can't hit other ones, and they have to go inside cells and work inside cells.

And so this is not easy science, but when you're working with the experts you can. So this collaboration now includes Yansen, Bayer, Berner-Inglehinde. It's a large organization and it's fun to do this out of Canada because with GSK we work from a lab in England. Feli and Illy we work from their lab in Indianapolis. With Novartis we work in two labs - Cambridge, Massachusetts and Bausel. In Pfizer it's San Diego and Cambridge. Abbots in Chicago. We have academic chemists in Boston and North Carolina and in London. Takeida is out of Tokyo. Berner-Inglehinde and Bayer are out of Germany. These are where their hot beds of science are and those are the guys we work with.

So then what happens is because we're giving it away, we can walk to any professor and say I've got this cool compound, do you want to use it? Here's the deal though - you can't patent it. And then they go "bring it on", because what they're thinking is how do I get my fastest paper. They have the first inhibitor of the coolest target and they're the ones who get to use it.

So we have hundreds of labs to collaborate with us. It doesn't cost us anything. We get the best scientists on the planet to work for the Project, as it were, all donating their ideas into the public domain. And it's been a lot of fun.

I'm going to take one anecdotal example of what can happen and I'm going to talk about a class of proteins called bromodomains. And these are proteins that sort of look like a cylinder with a hole in the middle. And remember I told you DNA is wrapped around these things. There's 21 metres of DNA in each of our cells - how does it fit? Well it's wrapped around and around these things. And these things are chemically modified. And these bromodomains come and only when this is acetylate, bind it. And that binding brings other proteins to this area and says turn this gene on. So the bromodomain is the first part. And it's a protein and it only binds when it's acetylate. We started to work on one of these bromodomains that's involved in a really rare cancer called NUT midline carcinoma. Nobody really knows where the cells come from - it appears in adolescence, early adulthood. It's fatal - 6 months, you're dead. What happens is, you know we have chromosomes. Well in these patients what happens is one chromosome breaks and joins to another. And right where they fuse they create a monster protein that causes the cancer. And it fuses one of these bromodomain proteins to another protein called NUT. So NUT br80 fusion causes the cancer. The hypothesis was, if we block this bromodomain from working, this monster protein will die, there's nothing to accelerate the cancer, the cancer will go away. That was the idea. It turned out being true. We collaborated with a doctor at Harvard and this is the chemical compound that we invented. We were given a big hint by Glaxosmithkline. And so we called it JQ1. We made it available, unlike pharma. We solved it's code crystal structure to find out exactly how it fit into bromodomain 4 and we published a paper and sure enough, if you inhibit it the cancers die. So you think, okay, Glaxo is going to be really excited now because now we've linked a molecule with a disease. But they weren't too excited.

Remember our original hypothesis though. If you make these tool compounds, we hypothesized that by giving them away, people will start to work on them. That didn't have to be true. There's lots of examples in biology where they make mice with genes knocked out and 20 years ago if we created a collection of these mice with each gene knocked out, people would by crying for them - but nobody used them.

So this was a hypothesis at the time, but look what happened. Here what we're doing is we're plotting research papers on bromodomains from 1990 going forward. And you can see this is usually tracking with NIH funding legs - more people doing science, the more papers you're going to get. And then something happened here. That's when our tool paper was published. And for the first three of our chemical probe papers, it's the top cited paper on that target since its publication in the world.

So these papers and these molecules are having a profound impact in skewing biomedical research to work on these things. And the bromodomain story is really interesting. So JQ1, which is the molecule we made, was started when Glaxo told us there's a patent by Mitsubishi. Patents aren't evil. Patents are a great way to disclose knowledge. If we didn't have patents, everyone would have their secret sauce and it wouldn't be shared. The real issue is the appropriate use of patents.

So Mitsubishi filed a patent on the molecule that inhibited a bromodomain. It was all in Japanese - we wouldn't have found it. So Glaxo said, hey look here. So we started that publication that worked with Oxford and Jay at Harvard, and as I said, we published the paper. At the same time, Glaxo had an internal molecule that looked a little bit different that they pursued and they published back to back with us. They were pursuing this one for sepsis and why, it turns out they were so free with the information, they'd stopped their program.

This happens often in industry. One information group starts to work on a protein target, they get to a certain point, the risk gets too great and they figure it might fail and they 'park it' - they just put the compound aside and say we're not working on that anymore. And they move on to something else. So this molecule, that GSK published, I bet, was parked. Glaxo said bromodomains isn't for us. But we gave JQ1 away, they didn't. We gave it to hundreds of labs, and you know what, other people took that compound and said hey that bromodomain is not only just for that rare cancer, it's for AML, multiple myeloma, large cancers, it's for HIV. Then Glaxo got excited. They have a compound that's almost clinic ready. They had parked it. They didn't know what to do. Around the world, the availability of the compound, people were saying we have an idea. And Glaxo went into the clinic.

For those who are in drug discovery, this is surreal timelines from first disclosure to patent literature to first in man. And they've expanded the studies now. So what did GSK get from donating us their chemistry? From telling us their idea? There are still people in GSK that say that was a mistake, competitor disadvantage, we gave it away. But the wise ones would say, my lord, we're in the clinic, 3 years before we would've been. You can monetize that. If that makes a drug, that's billions of dollars in revenue. For giving away one molecule, it's a pretty good deal.

And this is going to happen more and more. And what's astounding is, let's take a parallel universe, which is the development of Gleevec, which is a cancer drug. The same biochemical story - there's a chromosome, it breaks. This time its two proteins called BCR and Able that get fused. Able is one of those kinases. A precursor to Novartis had a compound. In 1992 they said I think it's a drug. They started to work with an American hospital to try and get the clinical trial done.

And it hit lawyers. And one year went by. And 2 years went by. And they couldn't come to an agreement. And then the university did a deal with another company saying that anything we work on in this area of science belongs to you. This wasn't in that package. The professor had to leave. He went to Oregon. He did the pivotal trial. He won all the awards. And it took 6 years. 2 years of that was lawyers talking to lawyers. 2 years of people dying. And look what happened.

Now this isn't all due to peace and love and sharing, but certainly the acceleration of timelines from discovery to first in man - it's mostly going to fail 95% of the time - but nevertheless, the acceleration of this time, I think is a dramatic example of how open access and sharing when science is the driver can really help people. And it's helping our industry partners. And it's helping science. But unfortunately, there are 23 companies now working on that protein. Much like I described before, the hot papers, we're giving consulting to everybody. So we're really contributing to this larger problem now. Whereas everybody at Glaxo has not said one word about it's year and a half old clinical trial. We don't know what's happening to those patients. Glaxo thinks it's their competitive advantage of course, because they know all the pharmacology internally. Eventually some of it might get published. But it's how the system works. You can't blame them. But that's what we've contributed to.

So I think that we should ask a bigger question. I've got the industry to share chemistry - that's a pretty profound change in how it works. Why do we have to have 20 companies and universities and biotechs pursuing the same idea? Nobody would think that's rational. You could take the same amount of money and pursue 20 ideas. And you do them well and in the open, and that would bring far more opportunities to industry to make money, there would be far more areas to compete, and actually do what they do well, which is develop and sell drugs. And what if we shared progress all the way through? So when we think we're inventing a new medicine for dermatitis, it actually turns out to be a lupus drug. And if we find that out in real time, not sequentially, which is how it works. I just don't think this is a dumb idea. It would change the end of research to the proof of concept trial. The 95% failure rate where the lottery ends and where real drug discovery and pharma begins.

I think that we could really think about sharing progress all the way through. It would make money for industry. They're losing money now so it can't be any worse. So we actually came up with an idea to try this. The idea is to form a public-private partnership and just through this early chemistry, but to take these completely wild targets all the way through to proof of concept in the open. Create a clinical candidate that you share. Do the clinical trial open. Share all the data. Pool the resources of all the industries to do this so that we can put a lot more research on that side of the unknown curve. And if we test the ideas, then we won't have this distressing thing where patients are getting dosed with molecules that somebody knows are going to be poisons.

Now industry is looking for someone to lead. And here's another example. Why not us? We're known around the world. We're a small country. But we are trusted. And this is a kind of endeavour where trust is a very key differentiator. So we managed to convince the Canadian Institute for Health Research, the agency in Canada that funds research, to put some money on the table and say to industry, if you come in and match it, we'll run a project all the way from beginning to end in the open, in the neurosciences. It's probably going to be schizophrenia because it's a huge need and nobody knows what to do. And it'll be a proof of concept of the concept of doing open access drug discovery. The probability of course is that the molecule that we choose to test the idea will not be a drug, because the first molecule is almost never a drug. But we'll learn so much that industry can compete in the wave after, finding out what's wrong with it, what are the warts, what are the target effects, how to fix them, come up with better dosing - plenty of room to compete. But at least they'll be competing on a target that they know works as opposed to competing for the lottery ticket, where it's unguided.

And the more opportunities we bring like that to pharma, the more medicines we're going to get. I'm absolutely convinced of that. We're starting to coordinate - we've got 3 companies in already, and the Canadian company. Canada is leading on this. And I think it's a pretty exciting part because this is going to have a tremendous impact on the way that medicines are developed. Because there is an inherent pressure for all the other jurisdictions to play here. Let them.