Transcript

Station:	**MELBOURNE CONFERENCE UNIT**	Date:	**03/06/2015**
Program:	**CONFERENCE**	Time:	**08:00 AM**
Compere:		Summary ID:	**M00061970042**
Item:	**AUDIO SUPPLIED BY CLIENT**		

Audience:	Male 16+	Female 16+	All people
	N/A	N/A	N/A

VOICE OVER: Today at the National Press Club, Professor Ashok Saluja. Professor Saluja is this year's Australian Society for Medical Research Medallist. Educated in India and the United States, he is internationally renowned for his work on pancreatic cancer. Professor Ashok Saluja with today's National Press Club address.

LAURIE WILSON: Ladies and gentlemen, welcome once again to the National Press Club for today's Westpac address. This has been a big week for us here, an eminent week - a week of eminent speakers, I should say. We started with the Secretary-General of Amnesty International, Salil Shetty; Australian of the Year and domestic violence campaigner, Rosie Batty, and we end on an equally high note. It's our pleasure to welcome Professor Ashok Saluja, the winner of the Australian Society for Medical Research Medal for 2015 for his contribution to medical science.

After many decades of research, Professor Saluja has developed a drug called Minnelide, which is showing tremendous potential for treating pancreatic cancer. Around a quarter of a million people around the world

die each year; five Australians every week die from this disease. It's claimed the lives recently of such well known people as Apple founder Steven Jobs, and indeed my colleague and good friend, one of the most prominent journalists in this country, Peter Harvey from the Nine Network.

Before we hear from our speaker though, I would like to invite Federal Liberal MP, Andrew Southcott, to formally - well, say a few words and formally present Dr Saluja with his award. Would you please welcome Andrew Southcott?

[Applause]

ANDREW SOUTHCOTT: Well thank you very much, Laurie Wilson, President of the National Press Club. To Stephen Jones, Shadow Assistant Minister for Health, Professor Ashok Saluja, and Mrs Saluja, welcome. Dr Phoebe Phillips, the President of ASMR, Dr Sarah Meachem, the President-elect of ASMR, and Dr Daniel Johnstone, the Executive Director or ASMR, ladies and gentlemen, good evening.

I am very pleased to be here to represent the Minister for Health, the Honourable Sussan Ley. We're in the company tonight of some of Australia's most brilliant and dedicated health and medical researchers, including ASMR's executive members. You and your colleagues around the country are engaged in one of the highest levels of public service. Every day you're working hard to bring us closer to better treatments, methods of prevention, and cures for conditions that cause ill health and take away lives much too soon.

Your service to this country is deeply valued by all Australians, and especially by the Australian Government.

Now tonight's event is a highlight of Medical Research Week. Tonight we celebrate the achievements of the 2015 ASMR Medallist. This year there's a special connection between the ASMR Medallist and the ASMR because I understand that the President of the ASMR, Dr Phoebe Phillips, worked with Professor Saluja in both Boston and in Minnesota during her first post-doctoral position in 2005.

The ASMR have certainly made an excellent choice from an outstanding national and international field. The Medallist this year is Professor Ashok Saluja. Professor Saluja is a professor and vice-chair of the University of Minnesota Department of Surgery. He's achieved international renown for his research into pancreatitis and pancreatic cancer. Significantly, he and his team have found that pancreatic tumour cells overexpress heat shock protein 70.

They identified a compound derived from a plant called the thunder god vine that successfully inhibits this protein, and has been shown in mouse models to shrink pancreatic cancer tumours, even in cases where the cancer is at an advanced stage.

Now what does that mean? Well, for 50 years, pancreatic cancer has had one of the lowest survival rates of any cancer, and it hasn't really changed over that time. The median survival for someone diagnosed

with pancreatic cancer is six months. So this is a breakthrough which offers the possibility of an improvement for people with pancreatic cancer.

At the moment, the five-year survival rate is around 5 per cent. It does require radical surgery, which is only an option for a small subset of pancreatic cancer patients. So the drug is currently nearing the end of a three-year long Phase 1 clinical trial. Professor Saluja will be up here shortly to tell you more about his research, and perhaps share some details about how that trial is progressing.

On behalf of the Health Minister, it's my great privilege to present Professor Saluja with the - as the ASMR Medallist.

[Applause]

LAURIE WILSON: There's no need to resume your seat, Professor Saluja, because it's now time for me to hand over to you. So would you please welcome our guest today, the winner of the ASMR Medal for 2015, Professor Ashok Saluja.

[Applause]

ASHOK SALUJA: Thank you. Thank you so much. This is an amazing moment in my life. Honourable Dr Andrew Southcott, representing the Minister for Health; Dr Phoebe Phillips, President of ASMR; Mr Laurie Wilson, President of National Press Club; fellow scientists, members of the press, and dear colleagues, it is a

singular honour to be here today to receive the Medal of the Australian Society of Medical Research.

When I was growing up in India I could never have imagined that my life would lead to this lectern where I stand before you. Even recently when I received an email telling me that I was under consideration for this medal, my first thought was that someone must be playing a joke on me, or that there had been some serious mistake. However, now that I standing here before you, I can safely put those thoughts aside.

I was always interested in science, and after finishing my initial education in India I found myself headed to the United States to continue my doctoral duty. While I studied plants for my PhD, I was more intrigued in human diseases and medical research, so I changed my path and started my research in pancreatic diseases at Harvard Medical School.

While I was star struck by the glamour of medical research, I don't think that's the usual way most people hold. But I am reasonably sure that the most people consider medical research to be important. What is not generally realised, however, is that focus of medical research changes constantly because of the changes in the set of diseases confronting humanity at any given time.

It was a changing terrain, even before 1928 when Alexander Fleming noticed that a bacteria would not grow on a culture medium accidentally contaminated with mould. But this observation, which would lead to

the discovery of penicillin, has revolutionised our ability to treat diseases caused by bacteria, which were previously a major cause of death, where cities and states would be wiped out with this.

We have made great strides since then, eradicating diseases that once thought were impossible to treat. Dr Salk developed first polio vaccine in the early 50s. We have since gone to develop successful vaccines for, among others, measles, Rubella, mumps, and yellow fever, and of course, the HPV vaccine developed right here in Australia at the University of Queensland.

At the University of Minnesota, where I am from, Walt Lillehei pioneered open-heart surgery, and then went to partner with Earl Bakken to develop the pacemaker. Achievements that could not be imagined 100 years back are now reality. These advances are only possible with considerable financial support. In the US alone, $117 billion is spent annually on medical research. Of this, nearly a third comes from the National Institute of Health, a federal government agency. However, public funding in the US has not kept up with inflation for the last 10 years or so, just like in Australia.

The good news is that there is a light at the end of the tunnel. The US congress is currently considering act which is appropriately named as 21st Century Cures Act which will significantly increase funding for biomedical research for the next five years. They are going to add 4.6 per cent increase every year for the next three years, and additional separate budget

appropriation of US$2 billion (*) a year for the next five years. That will certainly make a big difference.

We have further to go. Tax to research, people in the US and in Australia and many other developed countries in the world are living nearly 30 years longer than they did just a hundred years back. When an aged population and our modern lifestyle, we are facing a new set of issues. According to WHO non-communicable diseases were responsible for 68 per cent of deaths globally, up from 60 per cent just 15 years back in 2000. That means 38 million more people are suffering from these diseases.

The four main causes of deaths today are cardiovascular disease, cancer, diabetes and chronic lung diseases. Now that we have turned our focus on these diseases we are starting to see the progress being made. Take for example HIV-AIDS. If somebody had told me just 30 years back, just 30 years back that newly infected 20-something could expect to live well into their 70s, I would have doubted that person's sanity. But today there are 34 million people living with HIV worldwide, while we are still looking for a cure. We have therapies that are giving people long and relatively healthy lives, despite their HIV-positive status.

Things have changed to the point that today an HIV-positive person is more likely to die of heart disease or cancer than of AIDS. Likewise, breast cancer. I remember very well the day my mother was given a suspected diagnosis of breast cancer. I was 12 years

old. A pale of mourning settled over our house. It was as though we had already been bereaved. Fortunately the biopsy came back negative and she lived to be 85.

Consider our feeling of defeat and emotionally surrendering of our mother merely on the suspicion of breast cancer, and contrast that with the situation today. When a five year survival rate for somebody diagnosed during early stages is well over 90 per cent for breast cancer. There are 2.9 million woman survivors alive in the US today, which is significant given that there are approximately 300,000 cases diagnosed each year.

Breast cancer death rates have fallen an amazing 34 per cent in the last 25 years. Research is now moving towards targeted therapies, something that has been encouraged by activists and survivors because it means less severe side-effects. As you can see, the treatment of both of these diseases have made significant progress over the last 30 years. They both have a passionate base of advocates, and this results in funding. An extraordinary amount of money has been focused on these diseases and simply put, funding equals success.

Beginning in the mid-1980s the US government steadily funded AIDS research, starting with mere US$20 million in 1985, to over US$1 billion a year currently. Within 12 years of initial funding the AIDS related death rate had dropped by nearly 50 per cent. Half - 50 per cent. The US government and several foundations have continued to steadily fund this research over the

last 30 years to a level of more than US$2 billion a year. Resulting in over a hundred new drugs being approved by FDA, which have improved patient survival and quality of life for AIDS patients.

The funding is even more impressive - and rightly so - for breast cancer. According to the Susan G Komen Foundation the federal government spent US$30 million on breast cancer research and the treatment and prevention in 1982. It now spends over US$850 million per year on breast cancer research. Foundations play a big role as well. Komen Foundation themselves have funded over US$800 million in research since 1982. They have also funded more than US$1.7 billion for screening, education and treatment.

But while the National Cancer Institute - which is part of NIH in US - funding works out to be about US$13,452 for every breast cancer death. It is spending significantly less. Less than one-sixth of the amount per person for pancreatic cancer. The Department of Defense in the US funds breast and prostate cancers research heavily. But there is no dedicated funding for pancreatic cancer.

There are few foundations dedicated to pancreatic cancer research - very few. Despite its lethality, pancreatic cancer remains an often - and at best - a very poor cousin in medical research. I understand funding for pancreatic cancer research in Australia is even less, while more than 2000 Australian lives are lost every year to this cancer.

This brings me to my work on pancreatic cancer. I have a comparison I use to put it in perspective. If pancreatic cancer diagnosis is worse than getting the death sentence even in the state of Texas. For those of you who don't know about Texas and its propensity for death penalty, Texas executes - unfortunately - more prisoners than the rest of the country combined. Fortunately Australia does not believe in death sentence. However, even in Texas it is an average of six years between the sentence and execution of the prisoner.

But for patients of pancreatic cancer their median survival time is not six years. Not even one year. It is just six months. Put it another way, half of the people who are diagnosed with pancreatic cancer today will not be around for next Christmas. It is the only cancer that has a single digit five-year survival rate. This year nearly 50,000 Americans will be diagnosed with pancreatic cancer, and unfortunately most will succumb within a year. This translates to more than a quarter of a million people worldwide.

So what is it about pancreatic cancer that has stumped the doctors and scientists? Surely it's no more difficult to understand as other cancers that have better prognosis. But it is differentiated from them by several problems that begin with the fact that early detection is basically impossible for this disease at this time. Most people are diagnosed in the later stages of disease when it is too late to operate or offer much more than palliative care. Even if we could diagnose the cancer early, what can we do about it? The current

chemotherapy drugs add on an average about three months to these patients' lives and these are the best drugs which are available today. These prognoses are dismal. A better treatment is certainly needed.

This brings me to my life's work, Minnelide. I had been working on pancreatitis and other disease closely related to pancreatic cancer for nearly 30 years and during that time found that the protein HSP70, which stands for heat shock protein, was protective and increased the survival of pancreatic cells in pancreatitis.

We know that a large amount of HSP70 occurs in pancreatic cancer cells. Also we knew from the literature that Quercetin inhibits HSP70 which would cause pancreatic cancer cells to die. Quercetin is a bioflavonoid found in wine, red wine in particular, apples, kale and grapes.

Though it might initially be great fun most people don't want or cannot drink 50 glasses of wine a day or eat a bushel of kale. For this reason we searched for another inhibitor of HSP70 in cancer cells. We are fortunate to discover with the help of a smart, hardworking and dedicated postdoc from Australia that triptolide, which comes from a plant in China known as Thunder God Vine, this killed pancreatic cancer cells at much lower doses than Quercetin.

However, triptolide sadly was not water-soluble, a factor that limited its clinical use. We therefore altered the molecules to create Minnelide, named after the

University of Minnesota, and this compound is water-soluble, injectable, testable in animals and eventually in human beings.

After extensive pre-clinical testing in animals with very promising results we are in the process of completing a Phase 1 clinical trial for Minnelide. It took us a long time to get FDA approval for these human studies and while many have jokes about how FDA runs as fast as the fastest snail, their caution is well-founded, at least most of the time. However, we now have a clinical trial underway on Minnelide and the initial results are very encouraging. We presented these findings at a large cancer meeting in Philadelphia last month and we are cautiously very optimistic.

I often hear people throw around the term “discover the cure for cancer” as though it is something that someone will find someday on a pleasant summer's evening walk.

Speaking from our experience from Minnelide I can say with complete honesty that this one drug, for this one particular type of cancer, is the result of 20 years of research by many people and expenditures of millions of dollars. We are fortunate to have received money from NIH, my own institution the University of Minnesota, philanthropic support as well as industrial support to bring it to clinical trial.

Sometimes young researchers tell me that all easy diseases have been cured and now they have these really tough nuts to crack. In a technical sense that's

true. We need far more sophisticated technology to answer the questions that face us today. However, in terms of hard work, ingenuity and even adversity nothing has changed.

But that sophisticated technology translates directly into more expensive equipment and supplies. The Tufts Center for the Study of Drug Development estimates that it costs about $1.4 billion to bring a drug to market, an amount that is greater than the budget of many small nations.

If you look at the countless number of diseases out there waiting for a cure it becomes clear that no one source of funding, no one country alone can solve this problem. The statement, it takes a village has never been more apt.

Thus it's important to have a variety of funding sources to look at health care issues. Industry has an important role in funding research but industry is inherently self-serving. It must answer to shareholders and boards. This is not a criticism but it's the nature of things that industry is profit driven. It is not looking to serve the common good first.

Companies have also become more risk averse as costs mount. They would rather licence a promising treatment at clinical trial stage than fund lab research from early stages. The Government has a substantial interest in providing health care funding. Certainly it has a responsibility to fund things that are useful for the common good but are not necessarily profitable.

It is estimated that for every dollar the NIH spends in research it creates $2.21 of spending on respectable, stable jobs and businesses in local community. Government has to be the driving force behind public health research.

Studies to improve the quality and value of patient care, comparison of approved drugs or screening and prevention tools as well as bench research are ultimately responsibilities of a civilised society and government of the civilised society.

In a *New York Times* opinion piece last month, Newt Gingrich argued that funding for NIH should be doubled in the next five years. Now, as a strong liberal I never thought I would live to see a day when I would agree with former Speaker of the House Gingrich, much less quote him on health care.

But on this topic I agree with him wholeheartedly. The Federal Government in the US funds a very respectable chunk of medical research but it is on hook for the rising cost of treating diseases. Mr Gingrich cited the example of Alzheimer's where the total cost of care is expect to exceed $20 trillion - not billion, $20 trillion over the next four decades, and that is a lifetime still for many of us.

This includes a 420 per cent increase in costs to Medicare and 330 per cent increase in cost to Medicaid. However, delaying the average onset by just five years, just five years delay would reduce the

number of Americans with Alzheimer's in 2050 by 42 per cent and cut the cost by one third.

That is just the direct benefit. It does not count the toll Alzheimer's takes on the caregivers who are often the family members, their wellbeing and the economic productivity, yet the NIH is spending only about half a billion dollars a year on this research. This is less than one per cent of what these conditions will cost to Medicare and Medicaid [indistinct].

As health care activist Mary Lasker said, if you think research is expensive, try disease. In the US we are fortunate to have strong philanthropic support, especially in medical research. This is primarily unique to the United States and one of the things that make me very proud to be an American.

We have a culture of giving at every level of economic success. Some examples are the Ford Foundation, the Robert Wood Johnson Foundation and of course most well-known of all, the Bill and Melinda Gates Foundation. Mr and Mrs Gates have set the example by giving over $10 billion for global public health.

In a recent interview, Francis Collins, the director of NIH, acknowledged that philanthropists were terrifically important for filling gaps and taking advantage of new opportunities. The science, he emphasised, has never been at a more exciting moment. Indeed, people are taking notice. According to an MIT study, roughly 30 per cent of research money is coming from philanthropic sources at the leading

universities in the US. Something Australia and the rest of the world need to follow.

The first large scale success funded by philanthropy came with cystic fibrosis. Around the year 2000, a surge of wealthy donors began making large contributions to Cystic Fibrosis Foundation. Tom and Ginny Hughes of Connecticut, who had two daughters with the disease cystic fibrosis, and gave millions of dollars. Mr Hughes, a banker, helped the charity develop strategies to expand its fundraising. Year after year, the Foundation held galas, hikes, runs, golf tournaments. They eventually raised more than $250 million. This Foundation used the money to establish partnerships across industry and academia, breaking through walls typically found around research teams. In little over 10 years, this resulted in first treatment for an underlying cause of cystic fibrosis.

This is a story of personal adversity and inspiring philanthropy. Soon, other people with personal connections or experience with disease put their money into research. Jonathan Gray, an executive at Blackstone Group, a private equity firm, gave the University of Pennsylvania $25 million to set up a centre to study female cancers, after his sister-in-law died from ovarian cancer at the age of 44.

The chairman and co-founder of Nike Shoes, Phil Knight, was so pleased with the progress resulting from his $100 million gift to Oregon Health & Science University in 2008 that he last year pledged another $500 million donation to the Knight Cancer Centre, if

they could match that money through fundraising, and I know they are very successful in doing that.

My own group has benefitted from personal philanthropy. Many who have had family members with pancreatic cancer are anxious to hear about our progress and contribute in any way they can. We have had people hold fundraisers in somebody's honour, with hundreds of people and hours of work put into raise $7000 to all the way up to donors who can pledge millions of dollars.

The cynics might say that we blew through that $7000 with just one or two failed experiments. But to them I would only say - as I'm sure Thomas Edison would have said - there's no such thing as a failed experiment. Those $7000 showed us where we were wrong, and took us one or two steps closer to the right experiment. So every bit helps. To anyone who can give just $20 to us, I would say thank you, you brought us a bit closer to our goal of winning a war against pancreatic cancer. And it is a war.

And now, on a personal note, about my own very pleasant connection with Australia. Back in 2005, a young post-doctoral fellow from Australia joined my group. She was an extraordinarily cheerful and hard worker and did very good work on pancreatic cancer. I had no doubt that she would go far - and she has. Her name is Dr Phoebe Phillips, and she is here as President of ASMR. Congratulations, Phoebe. To see a young competent person's career develop and blossom is one of my life's greatest joy.

I would like to end with the mantra of my life, and with a plea. First for my plea. To the Health Minister of Australia. You are the one who can do the most to keep the torch of Sir Macfarlane Burnet, Lord Howard Florey and Dr Barry Marshall burning bright. The fuel for this flame is funding. My plea to you is, to do all you can for funding Australian medical research.

I appeal to the Australian Government, and all other governments of the developed world, to invest just two per cent, just two per cent of their healthcare budget in research. And it's an investment. And if you do that, I assure you it will result in not only decreased human suffering, but also in a significant decrease in your healthcare costs.

As for my mantra, it is inspired by John Lennon's *Imagine*. In the last one hour, the time that we have been together here, 50 more people have lost their lives to pancreatic cancer in the last one hour. Today, 1000 human beings will be lost to pancreatic cancer. Imagine, that one day, we will have conquered this dragon. Imagine, that these 1000 people could be going about their lives just now. And I imagine that that day will dawn in my lifetime. Just imagine.

Thank you. Thank you so much, from the bottom of my pancreas, thank you.

LAURIE WILSON: Professor Saluja, thank you very much for your comments and congratulations again on your award, on that recognition. Let's move now to a period of question time. We're going to have a number of

questions. I'm joined on the panel by Simon Grose who's the editor of Canberra IQ, formerly a quite prominent science and technology journalist but now he spreads his wings more widely to other areas but still very knowledgeable in that space so he's going to assist me initially for a bit of a discussion with the professor and then we'll - we've got a couple of journalists joining us - a number of journalists in the audience but as I think we indicated earlier, we'd certainly like to be able to open this up to questions from around the audience. So, I'll get an indication a little later of who'd like a question but we'll move on now.

You're at that phase one trial stage, in terms of the the drug. For - particularly for our viewers, but I mean, I guess also obviously for people in this room, what's the process and realistically, if that optimism - you've said you're cautiously optimistic, if that optimism proves well founded, realistically, what are we looking at in terms of - if there are no major hurdles, in terms of a drug like this potentially - well, coming to market and becoming available?

ASHOK SALUJA: I think first of all, let me just explain a little bit about phase one trials. The phase one trials are other name for damage dose escalation trials. The primary aim of phase one trial is to try what is the most tolerable dose of the drug which does not cause serious adverse [indistinct] and serious side effects. As you know, any cancer chemotherapy will eventually have a serious - adverse events and side effects. So, that's the primary goal that we want to see where we go with that.

And of course, in the process, we also learn about the efficacy of the drug, many times, and in this case we are really fortunate that early trial. So far we have done 27 patients so far in the last about two years and out of those 27 patients, you know, I could see that that - about - maybe - at least 60, 70 per cent had their tumour really regressed and some where tumour was stable and there were a few with the tumour still continue to increase. So, I am - after this phase one trial which should be over in next few months - maybe four to six months we're expecting, and we are already working on the next stage which we call phase two trial. And in the phase two trial, that's where we really look at very stringent efficacy of the drug that it is really working.

Although, for most drugs, you have to have phase three after that which is - takes many years to complete and hundreds of millions of dollars, but the writing recently FDA has changed their rules a little bit. If there's a cancer drug which looks in phase two trial, very promising, then that gets given approval without phase three trial so that you can do actually - it's not that you don't do phase three, that phase three continues while you are treating patients in large number, quote, unquote, marketing the drug. So, I am very optimist that after we do our phase two trial that if these results holds, which so far are, that we will get approval within the next two to three years.

LAURIE WILSON: And that commercial support is there. I mean, as you mentioned during your address, typically it takes well in excess of a billion to get a drug to market.

ASHOK SALUJA: Absolutely, absolutely. I - again, it cost a billion but it cost, you know, it was steadily. It's not that you need to have $1 billion today so so far we have about - I can tell you that we have spent about $20 million on phase one trial and I am very fortunate that we have some investors - actually there's one investor right now who's so dedicated and so convinced that he has put in $20 million of his own money and is the co-founder and co-chair of the company which is doing this trial and - but I think if the phase one is successful the way it looks like, I don't see for this drug that we - that the drug will not go to market for lack of money because I think there's a large amount of interest in this right now.

LAURIE WILSON: Simon?

SIMON GROSE: Yes, I'm interested in the - how you target the heat shock protein 70. Pancreatic cancer cells over express this protein, you target then you kill them. But I also understand that these proteins have good functions in a healthy body - maintaining a healthy body, and I was just wondering if you could outline what those functions are, what are the good things that Hsp70 does and therefore, what are the potential side effects of your treatment?

ASHOK SALUJA: Great question. So, heat shock proteins are very ubiquitous, that is they are there in every cell as you mention. Every cell in plants, humans, bacteria, animals and all of our cells have the capability of producing Hsp70. I - other Hsps, 70 is just one of those Hsps. Their function is - they're basically chaperones. They

transport things within our cells. However, there are two different kinds of Hsps. One which are present in every cell in small amounts are known as constitutive Hsps. And that's what they do, they are chaperones and they do these things, whereas the protein which is there in cancer cells, that is known as inducible Hsp70. That is induced, it's over expressed when there is a danger, when there is a need for that protein. So, the cancer cells are always under threat in our body. They really don't belong there so they are under threat so they produce - in order to protect themself, they synthesize large quantities of this protein. So, this is inducible protein. So, the drug we have, Minnelide, is targeting that inducible protein. So, that's why it is not - it's less likely - I shouldn't - there's nothing black and white in medical research, that it's less likely to affect the normal cells. And our data suggests that because we did the experiments in mice where we had mice where we induced pancreatic cancer and the ones that were not treated - was treated with just a water of saline, those mice as expected died in 45 days. All of them were dead in 44 days whereas the ones where we gave Minnelide, they lived their normal life of more than - for 400-500 days. So, if it was so [indistinct] if it was so - you know, if - hurting the other cells then these mice would not live. However, I want to caution here, that humans are not mice.

SIMON GROSE: Yeah.

ASHOK SALUJA: Well, I guess we know that right?

[Laughter]

LAURIE WILSON: Astute observation..

[Laughter]

SIMON GROSE: And I'd like to also just drill down to the Eureka moment. You said that the active ingredient was discovered by a - by Postdoc. I just wondered if you give us the - some details of that. I - was it virtual modelling of lots of compounds or physical sampling or did someone have a bright idea?

ASHOK SALUJA: I think it's really what we call in US, brute hard work. It was not modelling, we were looking for many different compounds. Fortunately, our goal was to find something which inhibits Hsp70 in pancreatic cancer cells. We have lots of cell lines, that was not a problem, these are very easily available to quantitate that, to see if Hsp70 is there or not there. That is whether it's inhibited or not, is a relatively easy test. We call [indistinct] but it's just a very easy way doing that. One can do that in a couple of days that part. And Phoebe could do it one day because she didn't go home at night so she could finish it in one day rather than two days.

So, we were looking at many different compounds. We probably tested hundreds of compounds and they were all educated guesses. It's not that we just randomly picked something from the street and check it because we knew that this drug, the parent compound Triptolide in China, is used for many different things. It's known for hundreds of years and they have thousands of publications on this and it does

effect their reports, not systematic studies, there's no clinical trials or anything, but there are reports that it does affect some cancers. Not pancreatic cancer at that time but no one really knew how it works so we were the first one to show that it is really inhibiting Hsp70 and that's what - and that was just - I would somewhat say is luck and hard work.

SIMON GROSE: One last question from me, I note that the incidence of pancreatic cancer is higher in males than females but some of the data I've seen from Australia is that the female proportion is coming up a bit. Can you - do you have any insights into that difference?

ASHOK SALUJA: I think realistically there's no difference in them, I think the propensity is very very same. I think this is one of the few non-discriminatory things in life. Women are not discriminated unfortunately for this, I wish they were but they are not. But more specifically, to answer your question, which may not be very relevant for this trivia, maybe not, but I was in a meeting in India and someone was presenting what you are suggesting. They were telling us that the women get much less pancreatic cancer than men. And I strongly disagree because I think the fact was that most of the time, unfortunately, in most of the societies - I hope it's not in Australia - that women are not diagnosed properly and not treated properly. They live in small village, small place, they get stomach ache, that's the beginning of, you know, diarrhoea or something, you just go and do some simple remedies and you are never diagnosed. Whereas, the male members of these societies are the first ones to be diagnosed. So, that is

my feeling. I don't have a data to prove to you, but that's what I think.

QUESTION: Well, gender bias, in other words then…

ASHOK SALUJA: It's gender bias.

QUESTION: Just - before I go to the floor, just one quick question, is there any research being done, you mentioned the fact that often by the time you're diagnosed, you're not that far away from your final hours anyway. Is there any research being done on earlier diagnosis?

ASHOK SALUJA: I think right now, yes. I think there is a lot of effort. We just had a meeting for American Pancreatic Cancer Association, which is one of the largest organisation to work on pancreatic diseases, and we had a full day discussion on earlier diagnosis, so there are groups who are working on that. It's very difficult not to crack. How do we analyse millions and millions of people? How do we decide who to test for early diagnosis?

LAURIE WILSON: I mean, as a layman, it occurs to me that the earlier you're diagnosed, once you've got an effective drug, the more effective drug- that drug potentially could be.

ASHOK SALUJA: Absolutely. But the problem is like in US we have 300 million people. Where do we start testing people? Although I think now we are getting some ideas from research that about two to five per cent of pancreatic cancer is genetics. So to that- and I just saw a case that this 50-year-old man all of a sudden developed what

we call stage three pancreatic cancer. And when I looked at the history, his mother died from pancreatic cancer when she was 50, his two aunts died from different cancers in their very young age. So I think that there is some link, and these are the people we need to start - so we will immediately start looking for two kids of this person.

LAURIE WILSON: Let me go to the floor, question now from Dr Jon Millard.

JON MILLARD: Professor Saluja, Jon Millard from ArtSound FM, Professor Saluja, Minnelide has its effect by suppressing heat shock protein 70, which is produced by the cancer cells to the pancreas. [Indistinct] apoptosis and cell death. My question is, is it- Hsp70, that protein found in any other tissues of the body, particularly in other carcinomas, and if so, is there the possibility for the - if you're - drug are effective, that they could be effective against other cells, particularly adenocarcinomas like most pancreatic cancers are?

ASHOK SALUJA: Great question. And the answer is absolutely yes, that it is - first of all our trial, which we are doing - phase one trial - is not for pancreatic cancer alone. It's for all GI - gastrointestinal cancers, which incudes liver cancer, gastric cancer, colon cancer and actually, in our phase one, one of the best responses in gastric cancer. We do have some good pancreatic cancer response, but the best one, where we have seen up to 50 per cent reduction in tumour burden within three, four months of treatment was a gastric cancer patient. So right now there are many different groups in our

university and other places - and actually there's someone in Sydney and they wrote to me that they want to get Minnelide to try in the cancer test group studies. So I think - I'm very optimistic that it's going to be effective in many different cancers. Prostate cancer is another example, we just presented our data and our papers in the review, that we think that it's going to be more effective in very hard to treat prostate cancer, which is oestrogen [indistinct] and all those kind of things. So I think that's where there is more hope.

But I want to come back to another part, that why we are so excited about Minnelide. Although our initial work was, initial thought when Phoebe was there, that it is effective in - its inhibitor of Hsp70, but now we are studying that how it inhibits Hsp70, so looking at the events which are upstream. And it turns out that Minnelide is really blocking NF-kappa B and SP-1, others even. So other cellular components which are pro-survival. So it has really in many ways, Minnelide is one drug with multiple beneficial effects. It is a combination of drugs in itself. And that's what excites us most in this.

LAURIE WILSON: Next question,[indistinct]. Before I ask [indistinct] to ask you a question, might get a bit of an indication, who around the audience might actually like a question, do we have any people who actually would like to ask a question, you're all very shy at the moment, obviously. Okay, there's one over there, well I'll take one from Mark and they'll come back, Maurice [indistinct] will come to you.

QUESTION: You've spoken about the challenge of getting enough medical research funding, I was intrigued to read today actually, there's a big debate going on at the *New England Journal of Medicine*, which I believe previously has been super scrupulous about not publishing researchers whose work had been funded by the pharmaceutical industry, there is now apparently signs that they might be moving away from that and this is causing quite a lot of debate among the research community. What's your view about pharmaceutical company sponsored research, and do you have any views on the sorts of issues raised by the *New England Journal of Medicine*?

ASHOK SALUJA: First of all, I always supported the policy of *New England Journal of Medicine* which by the way was in the next building where I spent 20 years in Boston. So, I think this practice of pharmaceutical companies, you know, supporting their research and publishing has been grossly misused over the years. There are many studies which are published which are not only funded by pharmaceutical companies, these are the manuscripts which were analysed, written and just you put a famous investigators name on that, famous scientist, professors name of that and publish that, I think that kind of practice is absolutely wrong and it should not be tolerated.

However, things have really changed in US. No journal - forget New England Journal, no one would want to publish these kinds of things anymore. In my own university, it is very stringent thing. Actually in Minnesota, a drug company cannot even buy me a cup

of coffee. It's prohibited. So, it's - so we have a very clear - that does not mean that these pharmaceutical companies does not support research. Actually my research - about one third of my research is supported by pharmaceutical companies. As long as we declare it upfront, every talk I give, every slide - last night I gave a talk in Sydney so I had a slide where I disclose that where my funding is, what my financial interests are. As long as that's clear, I think this is - it's reasonable to publish these studies. So, I think the drug companies, has to go - has to partner with academia otherwise we cannot do that. Actually, as I proposed in my last part of my talk that I think we need to spend two per cent of our health care budget for medical research. By the same token, I think the drug companies need to spend two per cent of their revenue to support basic research. If we don't support basic and translational research in academic institutions, that's where it's going to take place, one way or the other, our future will be dark.

LAURIE WILSON: Question on my right.

ROBERT RAMSEY: Robert Ramsey from the National Association for Research Fellows. So, Professor Saluja, you were rightly celebrating young researchers like Phoebe and Dan who were 10 years ago in your laboratory making these similar discoveries and fostering the next wave of discovery. I observe across Australia, at the moment, a crisis in the future for the mid-career researchers and I'm wondering are you experiencing the same thing in the United States and what's the response to the

security and the future development of our young and bright researchers?

ASHOK SALUJA: Thank you. I think it's a serious concern. I mean more and more I learnt in doing this trip in Australia and before, I think it's a serious issue which the Australian society at large, the health ministry and [indistinct] has to come around to do something, otherwise there is going to be a very major problem for medical research. You can always wash you hand and say why do we need it. Well, maybe you don't want very much [indistinct] who showed us the importance of gastric cultures. Those of you who don't know very much of this work, before you showed that the answers are simply an infection of [indistinct] bacteria and simple penicillin or antibiotics and you spend $5 and you cured that. Before that thousands of surgeons made their living, their life time was treating these ulcers by surgical approach which never worked but we still did that. So that's the contribution of Australia. So that's the contribution of the young smart and some not so young, people in Australia which will make difference.

So right now your system is that you give them three, four, five years of appointments like Phoebe and Dan and others have. I mean how long are they going to continue like that? Eventually you get tired, that all of us need some safety in our life. I think you need to have them prove for sure, you don't want to just give a job or give resources to someone who's not proven. I'm not for that. But once someone is proven, five years, ten years, fifteen years, after that they have to have some basic safety. You don't want Phoebe

Phillips, people like her and Dan where you have spent two, three, five million dollars already in training them and now all of a sudden that one year their fellowship is denied - which happens all the time, this is no big deal. You know the scientists such that some times you have a dry period and some not, and so what do they do then? Should they start doing now what? Market drug, become a drug representative or start selling real estate, what should they do? I think you have trained them, you have invested millions of dollars, don't waste that.

LAURIE WILSON: [Indistinct]

QUESTION: Thanks Laurie. A couple of questions if I may. This is a very aggressive cancer and I'm wondering what impacts that really has for human trials if the average life span of someone who attracts this is six months, I wonder how you manage that compared to other sort of live human trials. I'll ask that first then I'll come back to you.

ASHOK SALUJA: So I think - we hope and we pray that these patients will be diagnosed a little bit quickly, but we want to [indistinct] therapies and hopefully Minnelide is one of those. I don't think Minnelide is the only answer [indistinct] cure our cancers, all pancreatic cancer, I don't expect that over a quarter of a million patients which are going to be diagnosed this year with pancreatic cancer and we give them Minnelide and it's going to be a magic bullet. That's not going to happen. But, we need many more developments like that. Just imagine - and that's what I do, that even if it makes a

difference, in half, maybe just 10 per cent, that is 25,000 human lives every year. So we need that. So I think - and it's going to save a tremendous amount of resources on the society. So I think it's a win win for everyone to invest in this and hopefully with Minnelide we'll be able to treat. If not Minnelide, there should be other things and that's why we need to do research.

QUESTION: My second question is the prevalence of pancreatic cancer, is it more a western disease? Is there any data to support that it's more likely to be in western countries rather than in Asian countries and is the research coming from more America or Asia?

ASHOK SALUJA: Well I - first of all I'll take the example of Australia, that's where we are. So you can compare Australia with US. I think the prevalence is almost similar, I mean one can quibble about some numbers. There are 2000 cases by the year - more than 2000, and the population of Australia is about what, one-fifteenth of US give or take some, so you multiply 2000 by 15 is 30-plus thousand and in US it's about 40-plus thousand. So it could be some - just in a similar [indistinct]. And it's true for most other countries same. The problem with developing countries, I mean you can't compare the data from [indistinct], from India, from China and other places where [indistinct] there's lots and you go to some big centres and they have lines of people with pancreatic cancer there, but there's not even good data. So you cannot compare that. I think it's to a large proportion and I know from India because I'm from there, most of the time it's not diagnosed.

LAURIE WILSON: I'll take one more question from the audience behind you there Morris and we'll finish with a question from Simon.

QUESTION: Thank you Dr Saluja, and I'm one of the Indian scientists as well who came from India to Australia [indistinct]. Just one curious question is do we know the motive action, how does it work, like if the active compound, it suppresses [indistinct] protein, but what's the motive action is it apoptotic or is it immune response because some of the drugs we are seeing recently, the TVAC (*) especially is more of an autoimmune response kind of response.

ASHOK SALUJA: I think that's a great question I think - and we spend a lot of effort in our group. We have 25 young scientists working and about half of them really study the mechanism because mechanism is very important component of any drug development. And what we are finding out more and more is it does both. It certainly is causing apoptosis that's what our initial work was, but now we are finding out that it's not directly affecting HSP70 it's a transcriptional inhibitor, so its way upstream from HSP70 and HSP70's downstream. So it inhibits HSP70, it causes apoptosis but since it also affects the immune response by effecting [indistinct] and other transcription factor. So I think it has multiple effects but that's the beauty of this component that it can affect several different arms which are pro-survival. And the aim pro-survival for cancer cells so if you can inhibit those arms, then you have multiple effects.

LAURIE WILSON: Simon I'll let you wrap up.

QUESTION: I just want to ask you how you manage your IP, what have you been able to patent and who owns the patent?

ASHOK SALUJA: Great question and that is - I have - University of Minnesota and most other places in US are very, very stringent about what we call conflict of interest management so we - anytime we have some discovery we have to file for a patent and we have a big office in the university which manages that portfolio and once we have a patent - and it's pretty elaborate process as you might know it takes several years before you get a patent on this, but once you have patent then that - so university owns the patent but the inventors have a stake in that. Once it's a successful patent, if the money, profits come from that, that's shared file with the inventor and also in the research lab, so you get money for doing further research. And if it's licenced like in my case, this is licenced to a company which I helped co-found. So I'm a co-founder of a company named Minneamrita Therapeutics which is doing the clinical trials for this and this company has licenced this drug, this compound from the university.

So there is a very, very stringent process by which the university manages this conflict of interest. Actually it's a little too strict, we have four attorneys whose job is really to manage conflict of interest and I have spent hours and hours describing them, what my role is in different things and it's public information.

LAURIE WILSON: We will have to finish there, will you please thank and congratulate Ashok Saluja.

[Applause]

LAURIE WILSON: Now Professor Saluja, I'm sure we all wish you exceptionally well in this and we hope that it does come to fruition and that cautious optimism proves to be completely appropriate. You already have the medal but the Press Club would like to give you something as well, not quite in the same league perhaps. We recently published our 50th anniversary book; it has the highlights of probably the most important events. Not all speeches, but principally speeches, and the stories behind those speeches as well here. You mentioned Barry Marshall; you'll find Barry Marshall in here and other Australian Nobel laureates as well, particularly in this field. You mentioned Bill Gates, you'll find Bill Gates in here talking about the Gates Foundation, the medical research. And while there is a strong Australian flavour - as you would expect, there is an international flavour. In terms of Nobel laureates, you'll find - and you mentioned HIV/AIDS, you'll find Professor Barré-Sinoussi for instance as well who won the Nobel Peace Prize for her work, sorry, prize for her work in that area. So look, thank you again, congratulations and I hope you do find something in here that perhaps provides some further insights as well. Thank you.

ASHOK SALUJA: I will certainly read that. Thank you, thank you Mr [indistinct]…

[Applause]

* * **END** * *

TRANSCRIPT PRODUCED BY ISENTIA

www.isentia.com