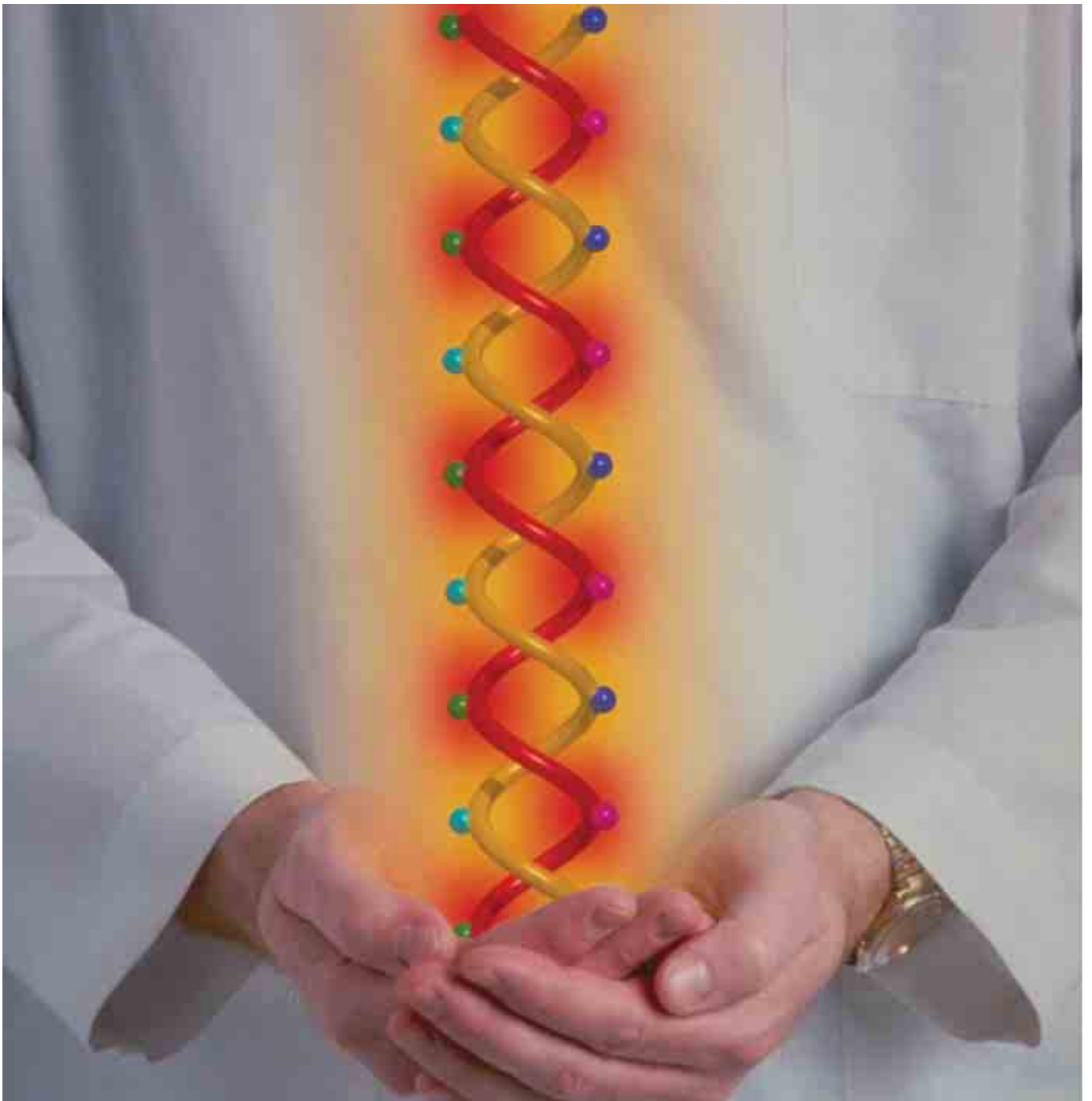


NEWSTATESMAN



BIOTECH BRITAIN

REALISING THE IMPOSSIBLE



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Biotechnology is the use of biological systems and living organisms, or their derivatives, to make or modify products or processes. While its use is commonly understood to refer to genetic engineering, the use of biotechnology currently has four main fields of application: medicine and healthcare, agriculture and food production, industrial (for example, enzymes as catalysts) and the environment.

This round-table discussion, sponsored jointly by the *New Statesman* and Pfizer, invited participants to examine the state of the biotechnology industry in this country.

Participants talk about their experiences of working as scientists and business managers. They attempt to identify the financial conditions and the sort of management that we need to build on the status that the industry has achieved in Europe, so that it can compete worldwide.

This and the other reports in the long-running series are available from the website: www.policyforum.co.uk. Your comments are welcome.

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Forum



Sue Nelson (chair)
Science and
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Using our experience of failure to drive forward miracles

Paul Rodgers examines the strengths and weaknesses of biotechnology in Britain

Curing the blind is the most dramatic of miracles, performed by Jesus on four occasions, says the Bible. Biotechnologists added their own version last month when an experimental gene therapy developed at University College London (UCL) restored the sight of Steven Howarth of Bolton. Biotechnology is rapidly becoming not just another tool in the hands of doctors but their primary means of doing the impossible.

But while the UCL case illustrates the huge potential of biotechnology to improve people's lives, it also points to the greatest threat facing the British biotech industry – that it will be seduced into moving to America. The same journal that carried the UCL team's results also had a paper from a US team doing similar work. Any company wanting to capitalise on the idea has a choice of where to settle.

"At every competitive level, the US performs even more strongly than the UK," warned Sir David Cooksey's Bioscience Innovation and Growth Team in "Bioscience 2015", its seminal 2003 report to the government. "The risk is that the bioscience sector will simply relocate

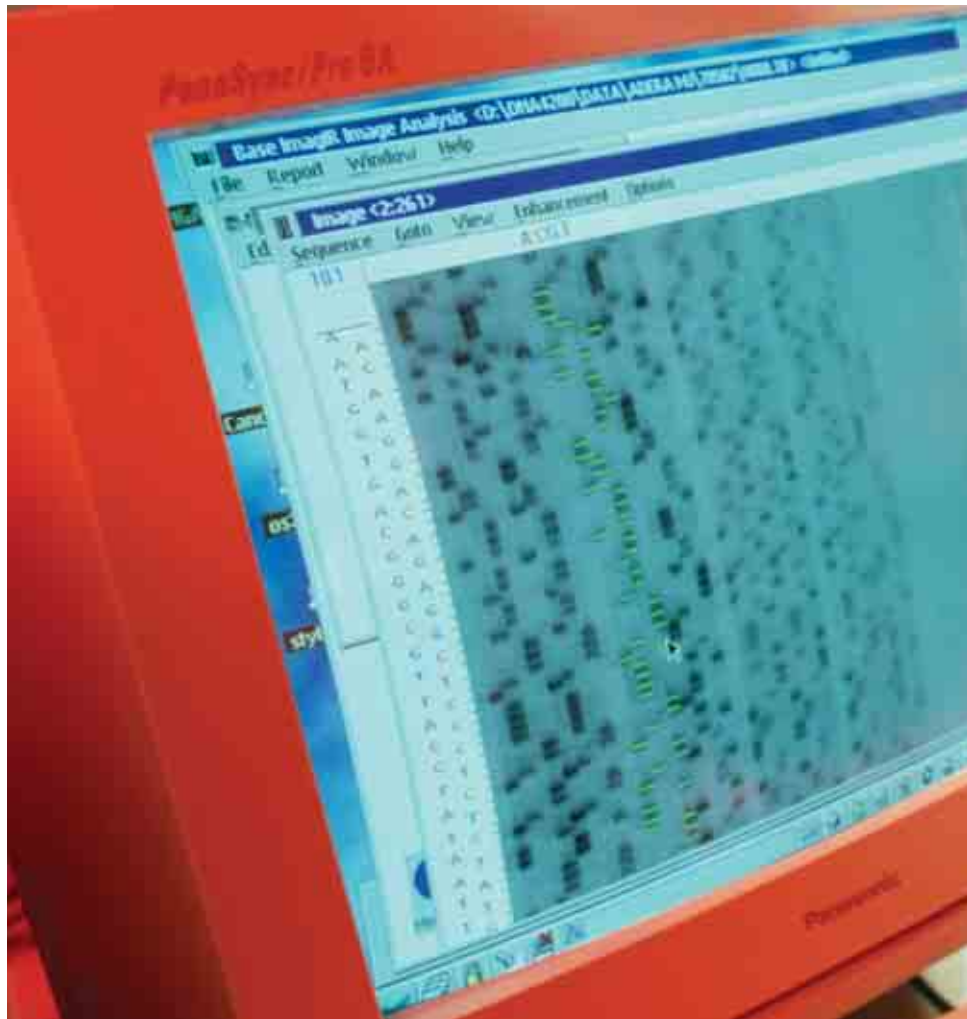
to the US, attracted to the world's largest end-market, the critical mass of established, profitable companies, the deep talent pool, and the generous funding from the \$27bn (£13.5bn) annual budget of the National Institutes of Health, through to the most developed public capital markets for technology in the world in Nasdaq."

NHS as a driver

One of the few advantages Britain has over America is the NHS, a large resource for clinical trials and a huge single customer. As a driver of biotechnology though, it has not lived up to its potential, said Sir David. Another is that the established pharmaceutical industry in Britain is strong. But big pharma has its own problems, with costs rising and makers of generics eating into sales. Companies must finely balance the costs of refilling their product pipelines with patentable modifications of their existing drugs (the relatively cheap option) or a potentially expensive punt on a new but unproven drug from a smaller biotech company.

The British biotechnology sector is Europe's biggest and is second in the world, after America's. In 2005, it boasted over 500 companies, employed 22,000 people, many of them highly skilled, and had earnings of £2.6bn, according to estimates from the BioIndustry Association. In addition, it is growing fast – by one-third annually, in terms of employment, and by almost one-half in terms of revenue. Yet, according to Ernst & Young, depending on how you measure it, America's industry is between five and 20 times bigger still.

These figures are admittedly arguable. "Biotechnology" is an amorphous phrase. By some definitions it began millennia ago with the fermentation of alcohol. A broad definition today would include companies dedicated to increasing crop yields through genetic modification and even some that produce biofuels. Take too narrow a view and you leave out second-tier companies, those which provide the expertise, the equipment and in some cases even the molecular building blocks that make the work of drug-development





companies possible. For example, Domantis, a Cambridge company acquired by GlaxoSmithKlein for £230m last year, has a library of 10 billion genetic sequences for domain antibodies, small molecules which when incorporated into other pharmaceuticals help them target particular cells.

A working definition of a biotech company might be one which is involved, either directly or in a supporting role, with the application of molecular knowledge of how cells work to human medicine, from cures for nail fungi to cancer. Its sub-sectors would include stem cells, which have not yet become specialised tissues; gene therapy, where new DNA is spliced into existing human genes; advanced diagnostic tests using molecular markers and the tailoring of treatments to fit an individual's particular genetic blueprint.

British roots

Britain's biotechnology industry has sound roots. In the 40 years to 2003, Britons won 23 Nobel prizes for biomedical research, including the 1962

laureates awarded to Francis Crick and James Watson of Cambridge University for exposing DNA's double-helix, the discovery of which made modern biotechnology possible. Most start-ups filling biotech incubators from London to Glasgow are still spin-offs from university research laboratories or teaching hospitals. However, while it is generally agreed that the science in Britain is top notch, the sector is plagued by two great weaknesses.

Development costs

The first is finance. The cost of developing new drugs has soared over the past three decades. According to the Tufts Center for the Study of Drug Development, research and development costs have risen 12-fold in inflation-adjusted terms, while the number of new "clinical entities" approved for use in the US merely doubled. Part of this is because the time it takes to get approval has risen; clinical trials in the early 1980s took an average of 30 weeks, now they take more than 70. However, most of the average cost of developing a new drug is spent on

the candidates that don't make it.

This is a problem for City investors, who don't tolerate failure as well as their counterparts on Wall Street. All it takes to send shivers down fund managers' spines is for a high-profile drug to disappoint in clinical tests, as happened last month with Digoxin Immune Fab, a treatment being tested by Protherics, a London-based biotechnology company. Though the treatment for pre-eclampsia, a leading cause of death in pregnancy, did help kidney function, it failed to make much difference to blood pressure.

Credit crunch

At least this drug made it to trial. As the credit crunch batters financial institutions, they are raising their demands of biotech companies. This has a knock-on effect. If venture capitalists can't see an exit, through flotation or a sale to a larger company, they become reluctant to invest. And many start-ups have trouble making their case. "Biotechnology 2015" warned that strong ideas were falling into an unfunded chasm between the initial grant-supported research in universities and the point at which venture capitalists could be persuaded to provide cash. Among its recommendations was a call for investment "in the 'bridge' between idea generation and commercial financing".

Weak management

Management is the other weakness. "Commercially skilled scientists will be vital for building a successful bioscience sector," notes Biotechnology 2015. "But most doctoral level scientists do not instinctively reach out for a business education." Researchers are happier in their labs than in the boardroom, wrestling with their "burn rate" – how quickly they spend. The failure of many start-ups is not because of bad ideas, but because they simply run out of money. Tolerance of failure is important at this level too. Managers who have seen one start-up company fail will be better placed to lead a successful venture on the second or third attempt, if they're given the chance.

Sir David announced in January that he will be reviewing how Britain's biotech sector is moving towards the goals he set five years ago. He's sure to find more companies, more employees, more drugs and more revenues. But it is this growth itself that will put pressure on managers and financiers, and make American shores look even more attractive.

Round table: A future for Biotech Britain?

Sue Nelson (chair) Thank you for coming. Clive, as chairman of the BioIndustry Association, how would you describe the state of our biotechnology industry?

Clive Dix The healthcare sector part of the biotechnology industry has gone through a stage where it is building without making a lot of noise. Many companies were formed in the past year. Although there is fantastic medical research in this country, nobody is moving that medical research to small companies – there is nobody funding that.

However, the situation is very healthy for companies that have already moved into that commercial arena. There is money available to grow those companies, but any biotech company in the public sector is struggling to find anyone to invest in it.

Andy Richards One of the leading venture capitalists (VCs) in this country told me this morning that more venture capital has gone into new biotechs this year than any year she could remember since 2000. These are big finances – £20m and £30m. The UK is the best place in Europe to do biotech because of the quality of the management that is recycling and the quality of science.

Public markets are awful so the business models those companies are investing in are looking at trade sell – no one ever hears about them.

On the angel side, there are many early-stage investment opportunities. However, there are gaps in finance at the early stage and too few people are angel investing, but there are moves to try to fill that gap.

The healthiest thing about this sector is the degree of recycling of funds. In Silicon Valley, when someone sets up a company, when they move on, sell out or get bought, they don't swan off with their millions. They recycle their expertise, effort and capital.

At the moment there is a high level of recycle, which is a very healthy sign. It is why some of those people say, "We would like a piece of the UK". If we can facilitate that, that's great. As our research and development (R&D) base in this country from big pharma shrinks, which it will in terms of people, it is going east.

We can recycle those great scientists and researchers back into more innovative companies. Those companies may not last very long or become big companies but, if they move up and do some great science, do some deals, get sold and recycle again, that is the sign of a healthy economy within a high grade sector.

Paul Cuddon The City has a very different view of biotech. Most public companies are fading at the moment. In the past week we have had two big clinical trial failures for Allozyne and Protherics. In the weeks before we have had GW and Renovo failing late-stage clinical trials.

I agree that the private market is healthy, but we do not want to be selling off all our best biotech companies before they reach an advanced stage of development. We need to finance these companies to phase-2 and 3 trials, where the UK retains more value from the companies. For that we need institutional investors and pension funds to supply the money.

Recently, the biotech companies have not rewarded institutional investors. Their share prices are massively down. Very few companies have been successful over the last five years, so the institutions are very depressed about biotech. Pension fund managers do not really want to invest in the sector any more.

The only way we are going to retain the value of the core science in biotech is by getting to the institutional markets, raising the £30m, £40m or £50m required to fund the stage trials. People need to know that others are making money so we can get more institutions involved in funding biotech and grow the sector. What happens now is that we sell off all our best assets to the likes of Pfizer or US companies, to Aventis or Novartis because we cannot afford to retain them in the UK.

Karl Keegan The public market has to pull private companies into the public arena. I agree with Paul that success is lacking. However, I disagree with Clive and Andy on the quality of management – it is appalling.

Paul Cuddon I agree with that.

Karl Keegan I was with an institutional healthcare analyst before this meeting and he is very concerned about "husband and wife" or "partner and partner" partnerships where both partners are taking money out. The perception among certain people is that biotechnology management is a lifestyle choice – you can get a very large salary, you are not delivering and you are failing on your business models. Drug development is full of failures. Companies have been around a long time and have not delivered on what management sets out to deliver. You can see these people being recycled into another nice job with another nice salary. The risk from management in public biotech is ruining its perception among fund managers.

Any biotech company in the public sector is struggling to find anyone to invest in it
Clive Dix

If only we could develop the ecosystem a little bit further, I think it would be a great thing for the UK
Ruth McKernan



Andy Richards It is not just failures that have pushed the share prices down. There is a particular set of dynamics in the public markets at the moment.

Karl Keegan Only two CEOs have made a difference in the past 18 months – Chris Blackwell of Vectura and Kieran Murphy of Innovata. Investors get the sense that those CEOs are interested in creating shareholders and are willing to work. I think the Department for Business, Enterprise and Regulatory Reform needs to address this, because without it you are not going to get this more general buy-in among the public markets.

Clive Dix That paints a very bleak picture of management. I can name twice as many good management teams as I can bad ones.

Sue Nelson Ruth, as a scientist who has held a number of management positions within the UK, do you think the UK's management is appallingly poor?

Ruth McKernan I have been to a lot of universities, and I have not been anywhere where I have not seen excellent science. However, I have not been anywhere where I have not thought, "That would be really good. If only we could harness that." This is even more apparent when I speak to small biotechs. If only we could develop the ecosystem a little bit further, I think it would be a great thing for the UK.

Karl Keegan You are building something that could be a long-term relationship and you are looking for an asset that you can take and develop. When a management team walks in, they have five minutes to sell their idea, and they get the basics wrong. They do not deliver on it. I disagree with Clive. Of the number of companies that have been around from 1997–2007, there are more management disasters than successes.

Paul Freemont I am an academic co-founder of a spin-out company from Imperial College so I can give you a perspective from how you start a company with two other colleagues – we are at the stage of looking

for series-A funding. In Imperial College, we have an enormous amount of translational activity going on. However, trying to develop relationships with big pharma in super drug discovery is exceedingly difficult. Not only do you have to get through to the right level, but there are internal politics within big pharma that are resistant to forming close, collaborative, links with small young companies.

Coming back to the question of management, we are looking now for a CEO. There is a bunch of people who get recycled around these start-up companies. They come in with failure no 1, failure no 2 and failure no 3, and the salaries they want are phenomenal.

Also, in drug discovery, there is a 10–15-year pipeline. Investors are not going to wait 15 years for a pay out. Managing that type of expectation and matching that for business is exceedingly difficult.

Ted Bianco At the Wellcome Trust, our mission is to foster research and improve human and animal health. In the biotech sector, you ask "What does the CEO add as value to a proposition?" For us, the journey has to have some value and significance.

There are a number of gaps at the early stage. There are neglected diseases, such as malaria; there are orphan diseases where there are no strong commercial drivers for product development. If you have a rare cancer, you might be in worse trouble than having malaria, because at least governments get upset about tropical diseases that affect millions of people.

An idea that is mainstream can also run into difficulty because the industry has large internal programmes of its own. So it needs real money to evidence it to a credible level.

The fourth gap is the transaction size. Investors and VC people, quite rightly, see the opportunity cost of entering small transactions. Often it is the small transactions that are needed at the C series and at the A series. We found ourselves having to create a translation award scheme specifically for small therapeutics. Generally they are costing £3m–£4m to take something any reasonable distance from lead optimisation to the clinic door, compared to hundreds of thousands of pounds to do something significant with a small engineering project. I do not see investment in European ventures in the space we are having to fill. As a charity, if we could leave it to market forces, we would.

Steve Yearley We all seem to think that we are talking about the same thing, but, within biotech, there are lots of different segments. The rational and appropriate strategy is different according to each.

Sue Nelson Let's do healthcare at the moment.

Steve Yearley Even within healthcare, biotech is a misleading label because there are many different kinds.

Andy Richards There is a continuum from biotechs with pharma.

Martyn Postle There are definitely flavours and trends

in investment in types of biotech but the definition of biotech that I would use are those companies that are competing for the same funds in early stage VC because those are the final amounts of funding.

A bottleneck is building up in terms of private that cannot go public. Last year in calendar 2007, we saw more acquisitions of UK biotech companies than in any other year, more than in 2006, which was more than in 2005. Last year, for the first time ever, there were more acquisitions of UK biotech companies than there were licensing deals involving UK biotech companies. That's a bit scary. A lot of these acquisitions are going overseas. So the return on this intellectual property (IP) is not going to flow into UK coffers. There is a risk that, unless we can see this private to public gateway opening up, we will start to see shrinking investment in early-stage biotech. The only exit that the privates are going to get is through acquisition to a larger biotech or pharma company, where the company will be overseas.

Clive Dix It is not that biotech companies are going for that trade exit, it is because the large pharmaceutical companies have had an innovation problem. They have all admitted that they do not have enough things to fill their pipeline so they have gone out with a lot of money and they have paid over the odds for companies. Until that innovation problem gets solved there you will never get a small biotech company to continue to grow.

Martyn Postle Big pharma needs to be able to access innovation that takes place in smaller companies. However, whereas traditionally you would have looked to access that innovation through a licensing deal, now pharma companies are finding that, as soon as they approach, particularly a private company, to try to negotiate a significant licensing deal, the VCs sniff this as their own potential exit and they are forced into acquiring the companies.

Sue Nelson Sarah, what about the innovation problem and the criticism of management?

Sarah Haywood I do think we all recognise that there

So you get bought out, is this not a perfectly legitimate exit? What are we gaining, what are we losing?
Shriti Vadera



is a significant problem with the pipelines of some of the big pharmaceutical companies and, quite rightly, they have sought to plug that in whichever ways they deem to be appropriate. The trade-sale route has been the predominant business model recently.

From my own observations, I see a shift within the pharmaceutical companies towards a more collaborative model again. I see pharmaceutical companies that want to encourage a vibrant and varied biotech industry, not just in the UK but internationally, because this provides us with a number of different opportunities for collaboration and effectively to start to look at biotechs operating as a more virtual part of the team.

While there is potential for loss of return on investment in IP through the income streams that will provide, we have to see the recycling of people as a positive thing. While you may have acquisitions that initially have biotechs forming virtual units, becoming units within a large pharmaceutical company, where they decide they do not want to maintain that model, at least we get the recycling back in.

Management is key in terms of "investability". I do not think it is something that we have managed to get right yet. It is not just an issue for government, it is an issue within the industry. We are looking actively at this issue of management capability.

[Baroness Shriti Vadera arrives]

Sue Nelson Baroness Shriti Vadera, do you think the biotech industry is going well for the UK?

Shriti Vadera Biotech is a critical part of the economy because of the innovation and R&D piece that is central. I know there is concern about the pipeline and access to finance and, when I came in, in January, I discussed with Sarah that we needed urgently to do a piece of work on access to finance. There are some access to finance problems across all sectors in the UK, which are really to do with size and the fact that the finance industry has floated upwards in size, it does not do the due diligence and has shorter pay-out requirements. Is there something specific in biotech that we are missing that we would need to do? That is why I specifically commissioned that piece of work.

Second, is the view that the industry feels that it cannot take itself from start-up to becoming a big, floated, company. My sense of this was, "does this matter?" So you get bought out, is this not a perfectly legitimate exit? What are we gaining, what are we losing? Is there a reason for us to be worried about it?

I think a trade sale is a perfectly legitimate form of exit but are there specific issues that we should be worried about? As ever, in every sector it is about skills, but I do not know which bit of the public sector was awful...

Andy Richards Biotechnology life science healthcare companies is the sector we were talking about.

Shriti Vadera We are coming across this issue in almost every sector that is very reliant on innovation – there are management capacity issues. What I have tried to figure

There is a gap before you can bring a piece of science to a stage where professional investors are in there
Ted Bianco



out is what we need to understand about the sector and what is it that we need to do as an intervention that is more generic? I understand that everybody can sit here and talk about that one sector but we have to look at it in the whole piece.

Third is whether there is any other impact on this sector that we should worry about as a result of the big pharmas having a pipeline problem? We understand that it is critically important and that it is about skills.

Sue Nelson Does the UK have the science base for these skills, particularly with the number of science graduates declining?

Andy Richards There is an issue in certain areas, chemistry, for example, but it is still pretty good.

Ruth McKernan Mostly, we do not have a problem recruiting really good scientists. We do need to worry about early-stage research and innovation going outside of the UK. If we want to fund something and build a partnership in the UK, and we have 356 collaborations in the UK right now, from a post-doc to a large multimillion collaboration, what I find is that, roughly, for what it will cost us to fund a post-doc in the UK, we can get two in the US and ten in China. So, while there are economic pressures on an industry that has a pipeline issue, either you buy the innovation at what it costs, or you take the option where you use the money you have as economically as possible.

Shriti Vadera I do not think people would have masses of complaints about us relative to Europe, although perhaps the uptake in the NHS could be better, but it is all about whether we compare with the US.

Andy Richards Exactly the same situation occurs in the US. Unless you have broken through that billion-dollar market cap area, you are dead in the US as a public company. Every company that was being invested in by VCs in the US is being invested in to go to trade sale. Some of us have been around in this sector through at least two other times when everyone has said, "The end of the world is nigh on

the public market." It will come back at some stage and change. The financing continuum changes very quickly. Two years ago you could not get money from Schroders and now you can. Two or three years ago, you could float on the alternative investment market (AIM) and now you cannot.

Ted Bianco On whether it is a science issue or a finance issue, there is a problem at the intersection between science and finance. You see this in the university sector, which is one-horse shows, where somebody has an idea but does not have the makings of a business with resilience and a natural pipeline. You might be able to assemble one, and that is what VCs did ten years ago. Concocting one might or might not be a good use of resources but the big companies engage by looking at individual propositions.

Ruth McKernan We are also in the business of looking at accelerators and incubators, going to the Imperial College incubator and understanding what somebody has already done a first cut of and they think it is worth investing in, and then maybe we would partner on. Rather than a super-tanker, we are seeing a fleet of boats where we can be a lot more convincing.

Ted Bianco In looking to license VCs, the large companies are now working in the same space. Differentiation is blurred because people are looking for things at similar points of clinical development.

What is wrong with that is that there is a gap before you can bring a piece of science to a stage where professional investors are in there. It requires a lot of due diligence, small transaction size, and the life science.

Martyn Postle We have just completed a study which looked at the correlation between the academic output of universities in each country with the number of life-science products in development originating from companies in those countries. It is almost a straight-line correlation. We did a piece of work last year when we only looked at one side of this equation and almost half of the products globally that are in development have originated from US companies. Surprisingly, number two is products that originated from UK commercial companies, number three was Japan and number four was Canada. I did not realise that the UK was going to be that far ahead of Japan and Canada. Behind them came Germany and France. We tried to look this year to see whether the UK is losing its position and the conclusion we reached is that we are not actually being caught, but the US is pulling even further ahead. In the UK, we rely more than other countries on biotech companies originating from clever academic spinouts. Switzerland has a healthy biotech industry, but the biotech companies are spin-offs from pharma.

Paul Freemont The UK punches miles above its weight in intellectual output and research publications and quality. That is well established. However, there is enormous shortfall in the short-term investment to

translate those ideas. There are academics that have been driven down the commercialisation path with just one idea which is not commercially viable. Universities are becoming more proactive in trying to ensure their innovations get commercialised.

The expectations within that early start-up phase are not being handled properly. They handle it better in the US, where they are au fait with one person pushing their idea out, trying to get investment in. It is part of that culture. We are beginning to develop it.

Sue Nelson In order to maintain its lead in the biotechnology industry, does the UK need a culture change in terms of its attitude towards investment?

Paul Freemont It is happening. I think there have been fabulous initiatives from the Biotechnology and Biological Sciences Research Council (BBSRC) and others. Government has played a role in pushing innovative thinking in the university sector. I do not know if the investors here would agree that the university sector is becoming more entrepreneurial in its outlook. The question is, how do we nurture it, and develop it into the American model?

Shriti Vadera Can I come back to whether people think there is an access to finance problem and at what stage.

Andy Richards There are gaps in that continuum. As soon as you plug those gaps there will be others. It will be constantly changing because the ecosystem is bigger than the US. Last night, a group of us, a loose group of angels, were looking at a company that has very good, very early-stage science. They have some patents and an idea, but they need £200,000 to do a proof of concept study *in vivo*, otherwise it is “uninvestable”. That money is very hard to find. It is not a natural grant from a research council, it is not an angel, you are never going to get it from a VC, and it is a gap.

Clive Dix The Scottish Enterprise Board does it. If you go to Scotland and they say, “This looks really interesting. We would need to see the data,” you can

go off, get the £100,000, and come back six months later having done it. That does not happen in England, the research councils start doing grade-A funding-type analysis before giving out the money. It cannot be done like that. If a partner says, “If this work is done we are interested,” you have to respond quickly.

Shriti Vadera So, you are saying that they are quite slow and bureaucratic and will not risk something.

Clive Dix Yes, and the poor guy doing the research cannot spend his time on the phone chasing grant applications for something. So it just dies.

Paul Cuddon In Belgium, the government, through the Flemish Institute, has a set fund for this early-stage research. They have €260m a year dedicated to nurturing IP so that, by the time it spins out into a company, it is ready to start the commercial process. They have tax incentives – once a royalty is gained on the IP, it is 80 per cent tax deductible. These incentives enable companies to become much more commercial at the later stage of development.

When the Belgian companies come out of government-funded research institutes, they are worth more than €100m. If you look at the UK, 50 of the 100 or so biotech companies are worth less than £20m. Many of them just have a single idea and, if that idea fails, there is no company. In Belgium they are nurtured. A group of *in silico* companies are put together by government, who would be picking off the IP from different universities and putting them together. By the time they get a chance to pass or fail, it is out of investors’ hands, and is at the next stage where angels, like Andy and the institutions, get involved.

Shriti Vadera It is creating diversity of the idea in the product pipeline before you have to go to commercial investment. Are you seriously suggesting that you feel comfortable with government doing this?

Paul Cuddon It has to. It has to take responsibility.

Clive Dix The sort of people who would manage that would not work in a government institute to do it. So it would not work. You would get second-rate activity.

Ted Bianco Most people who work in universities do so because of their intrinsic interest in the subject, and because they get to see the fruits of their science being applied. The universities are not clear whether they are running businesses; they are also charitable in their purpose. They are mandated to achieve some return on their IP, which is completely reasonable but, at an early stage, it is impossible to do that.

Sue Nelson Maggie, how does the public view biotechnology? It is often reported that they see it as one of the few sciences that makes scientists money.

Maggie Leggett We have, hopefully, moved away from that context where we had an anti-science

They handle it better in the US, where they are au fait with one person pushing their idea out, trying to get investment in
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Trade sales are good but, on the public side, we need to think carefully about what is going to restore faith to bring in investors for the longer term

Karl Keegan



public. However, we have plenty of evidence to show us that simplistic messages about the benefits of science, particularly when they are about money, do not go down well with the public. The other thing we need to learn from history is that, when we talk to the public about scientific advances, we need to talk to the academic community because industry will be viewed sceptically because of its financial motives.

Clive Dix The pharmaceutical industry still has a very bad press. What it does is save lives, but it does not find a way of translating that into what the public thinks. The public thinks it is just a load of greedy people who try to force toxic molecules on to humans.

Karl Keegan The financial industry is all about making money. If you do not like that, that is unfortunate. Trade sales are good but, on the public side, we need to think carefully about what is going to restore faith to bring in investors for the longer term. Whether it is a trade sale or a stand-alone ... is not the issue. It is what brands UK public biosciences as a success.

Shriti Vadera Does public opinion really matter in terms of this industry because it is the pharma at the other end of the scale who are going to face the issue?

Paul Cuddon Are you talking public investors?

Shriti Vadera No. Public investors are different. In the type of industry you are talking about, the group would really understand what they are investing in.

Martyn Postle As a research scientist, if I have a chance to be a research scientist for an arms company, a tobacco company or a biotech company, as a biotech person, I would like the image of the biotech industry to be above the other two so that I could attract the talent.

Steve Yearley If you compare medical biotech with every other kind, then medical gets all the thumbs up.

Nearly everything we have talked about, you could imagine being talked about in lots of other sectors. I

was expecting that we might be talking about some things that were distinctive. For example, there was all this hope about pharmacogenomics, how we were going to understand how medicines were dovetailed to particular consumers of them. As far as I can see, that has not paid off in the way we were hoping, yet that could have brought really big dividends.

Second, there are all the concerns about orphan diseases and the potential for organisations like the Genetic Interest Group, which mobilises patients who want drugs for their conditions. I was expecting us to talk about things such as technological capabilities for getting drugs to the people who can benefit from them most and how patient groups might want to see drugs accelerated, so they don't have to wait for all the testing. As far as I can see, we are having a kind of industry talk about where we get skills and knowledge. That is not as exciting as I was expecting it to be.

Ted Bianco There is something very healthy about a range of differently sized companies that produce products in this space. The idea that big companies dominate is unhealthy because they have certain expectations. It will be much healthier for the British system to have people who see a reasonable market being £100m through to £1bn and above, otherwise we will see India and China fill that space.

Shriti Vadera So, you feel the dominance of an exit through a trade sale is not entirely healthy?

Ted Bianco Exactly. Unless it is acquisitions of biotech within biotech – small fish eating slightly smaller fish. We need to diversify the size of the industry, with diversified views on market sizes, to maximise the innovation coming out of the universities. This is idiosyncratic because it is not directed. There is a real need to deal with the healthcare concerns of our populations. People are left hanging out to dry because they have a rare condition.

On skills, in the early stage of biotech, you need skills in due diligence, which is a question we have only just touched on. I do not think there is anywhere near enough availability of due diligence for early-stage investors to support them in risking their money.

You either get people to come forward and invest earlier because they do the due diligence and have a more informed position, or you open up the amount of free competitive space, so you agree: "At this stage in the science, it is so risky nobody in their right mind would invest for a financial return. We will all work together in a pre-competitive space." This is what Wellcome has done, for example, on things like working up features of the genomes. They have said, "Buy what you can in it but we will all club together to push it through a certain dangerous space in the science."

Andy Richards I agree with that. As long as people recognise that clarity of IP ownership is important. There has been a tendency to say, "Oh, consortium pre-competitive means do not worry about the IP." No, *do* worry about the IP. I sit on the board of the

commercial arm of Cancer Research UK and it has a very refined attitude to people giving donations to Cancer Research so that they can improve the lot of people who have cancer. However, that will not happen unless the great science being funded gets translated. We have identified a gap at concept level and we have put together a development lab. This takes great research from scientists who do not want to do the translation and gives it to a set of industrial people to take it forward so we can get it to the stage where we can license it. Critical to that is that we nail the IP early on.

Martyn Postle We have also been involved in advising consortia in pre-competitive situations but one party or another, recognising that pretty soon it will be competitive, is trying to build its position during the pre-competitive stage.

On trade sales, if you are looking to the economy, a trade sale is fine if the acquirer is also in the UK. If the acquirer is overseas, I cannot see where there is any benefit at all. This asset was discovered and developed in the UK. We want to get more tax income on these...

Shriti Vadera But that should be in the value that has been paid.

Paul Cuddon Then the money that comes in gets invested in another part of the company and it fails.

Andy Richards Yes, and that is the key. If I can just bring up the public market trade sale, there are some issues. The health of an ecosystem is due to the level of recycle. There is a problem in the public market where, when those big trade sales happen – the capital coming in does not recycle into other public companies, and that is partly due to the success of our public market. We have a very different public market to, say, Switzerland or Germany because it is so international. Switzerland does not have many new companies so, when an IPO occurs in Switzerland, they all back it.

Karl Keegan When you look at the UK sector in the *FT*, healthcare has become a diminishing proportion of the overall FTSE. If Glaxo and Astra are becoming less

important, then the smaller companies are even less important. That is a function of the cycle we are in.

Some valuations of trade sales are way above where the public market sees it. There is a big gap in perception.

Sue Nelson Perception is an important issue. You have the biotechnology industry appearing to promise drugs that will cure all, and the agricultural industry promising it will feed the world.

Paul Cuddon Science is good at communicating a potential cure for cancer, but that has little relevance to a final cure because it would be 15–20 years on. Many public companies are just making small advances, even with cancer drugs. We need companies to say, “This will, potentially, be more effective, safer and cheaper than the existing medicines on the market.” I think more companies will say, “This is the best cancer drug ever.” But that is not...

Clive Dix But when they have a product, their claim is very specific and very highly regulated.

Sue Nelson Maggie, why is there a difference between what the public sees biotech promise and what the industry says it promises?

Maggie Leggett We need to tease out two things. We are talking about what the media reports and what the public thinks. Generally, the public is fairly good at seeing through hyped-up headlines.

Sue Nelson I read in the broadsheets that golden rice would solve hunger across the world and feed most of south-east Asia. This is not tabloid journalism.

Martyn Postle About a month ago I was at a meeting in Cambridge called The Stem Cell Dream. The audience was the general public. Stem-cell scientists were trying to debunk the hype around stem cells, saying, “No, we do not have a cure for Parkinson’s around the corner through stem cells. This is where we are. This is how long it is going to take. These are the risks.” People came away with a much more balanced view than they would get otherwise.

Ruth McKernan I did the same thing in Canterbury last Saturday. I spent an hour-and-a-half explaining to a group of 250 non-specialist scientists and even some schoolkids all about stem cells. It was followed by an hour-long debate on ethics and an hour on legislation and regulation. The Archbishop of Canterbury was there. It was an excellent day. Many people said to me afterwards, “It is so great to really understand what scientists are doing, what is possible and what is not.”

Paul Freemont We underestimate the intelligence of the public.

Andy Richards I agree. If I hear a science story in the States, I know what has happened but the UK dumbs down its science stories more than anywhere else.

We have a very different public market to, say, Switzerland or Germany because it is so international
Andy Richards



In the last ten years, there has been an enormous growth in experimentation in forms of public engagement
Steve Yearley



Paul Freemont On the other hand, there is an enormous growth in laymen's science publications.

Sue Nelson Are you telling me the biotech industry is completely innocent of hyping its own product even though, surprise, surprise, its share prices could benefit from everybody perceiving...

Clive Dix That is a different matter. Small biotechs have to put forward a very strong story. A lot of the people who do that – this is where the management issue is – do not know how to do it properly. That is a big issue for them because they need money.

Ted Bianco Nobody's due diligence is so low that it is based on a *Sun* headline.

Clive Dix So those scientists or people who do that are not hyping?

Paul Freemont Steve was trying to say that we are on the cusp of some potential innovations and new biotechnology applications at the nano, hi-tech and synthetic biology levels. These are major potential opportunities – that is the application of the level of information we now have in molecular biosciences.

We have this massive amount of information about how biological systems work, which we are now beginning to re-engineer, apply in different ways and create new types of organisms, new types of devices. We should get the public engaged and say, "This is the potential. This is what we can do. We want your input."

Maggie Leggett The kind of public meeting you were talking about is incredibly valuable and repeated round the country, but the value of that compared with reading the newspaper or the online pages is...

Paul Freemont The MRC Mill Hill Institute and the Cancer Research UK London Institute are going to build one of the biggest biomedical centres in Europe.

It is the biggest biomedical research development in the UK for 30 years. The government is investing millions. It is going to be phenomenal. Yet the story on it I read in the *Evening Standard* was about the dangerous viruses that will be worked on in central London. What is that about?

Sue Nelson Which brings it back to why it is important for the public to be fully informed and to not have hype from either end.

Ted Bianco The industry motto, "fail quickly, fail cheaply", is sort of about "let us get straight about this, before we squander massive resources." In the academic sector there are not the same obvious drivers to make that happen. At Wellcome, we are often funding a blunt question/answer session about bottoming out that issue.

Steve Yearley In the past ten years, there has been an enormous growth in experimentation in forms of public engagement. Young post-docs are obliged to do it as a condition of their award. It is a growing enterprise and it involves hundreds of thousands of people every year in the UK.

I am also encouraged that the research councils are increasingly seeing a legitimate social science aspect to this. We were talking about synthetic biology. I work at the Genomics Pharm, which is an Economic and Social Research Council outfit but we have just got some money with you [Paul Freemont] to do work on synthetic biology and, from the start, people are thinking about the social and ethical implications.

It is progressive that both the science and the social science are seen as having to be resolved simultaneously, letting us think about what are the legitimate public anxieties and which things are totally out of proportion.

Paul Freemont The technologies coming through are going to underpin all of the biotechnology in the next 50 years, in my opinion. Drug discovery is one very important but small, in my opinion, part of the future of biotechnology. Other technologies are coming through that are going to be quite extraordinary in what they can achieve and will revolutionise how we buy pharmaceuticals, energy and materials.

Sue Nelson Could the success of the biotechnology industry dangerously skew the types of science that students want to study and go into? They might all want to get a job in the biotech industry.

Sarah Haywood I do not think that is what drives the decision-making, frankly.

Paul Freemont It is wonderful to see interdisciplinary sciences at the moment, and I think the UK is doing this really well – physicians, mathematicians and chemists with life scientists and biomedical scientists. We are beginning to train in interdisciplinary sciences.

Sue Nelson What about the scientists who want to make a specific area their life's work and are not thinking about the financial possibilities or the industrial possibilities?

Clive Dix They will have a stress-free life doing really nice stuff and enjoying it. Somebody else might spot what to do with it, and that is fine.

Ruth McKernan But when they start, they do not know that it is an area that will lead to anything.

There is a good-news story for the UK in stem-cell research and the work that has been done by the Human Fertilisation and Embryology Authority as well as the legislation, guidelines and regulations we have. When we decided to build a regenerative medicine unit, the science, the quality, and the environment in the UK was a very significant factor regarding where we would site it.

Ted Bianco The human genome project is something everyone is going to use as a tool. Anyone who over-hyped it is now feeling a bit awkward but, in time, it will fulfil its promise. The people currently working on it in are just interested in gene association, to look at multi-factorial disease. It will be many years before that turns into money and products, but thank goodness people do it.

Andy Richards Absolutely, if we are only going to fund applied research, that is a real problem.

Sarah Haywood There would be no new discoveries if you did not fund pure research.

Paul Cuddon The infrastructure needs to be in place so, when this blue sky research turns into a potential product, it needs to have the promise of potentially making money for people. I think that structure is not efficiently in place in the UK.

Sue Nelson I would like to go round the table and get a summing-up from each person in terms of what

I would like us to look at incentives for the academic and industrial sides to work more closely together
Sarah Haywood



you think the UK needs to do to get to the next stage, and if you think there is anything specific that could be done to improve the UK reputation and abilities in the biotech industry.

Andy Richards Science is important and there is some sort of link here with the healthcare system and access to medicines. People in the UK have lower access to new and hi-tech medicines than most people in Europe.

There are a lot of healthy things about the sector but there are significant gaps in the financing continuum and those will change. At the moment we have gaps around early stage and public markets. Once those are resolved there will be others. Ruth used the word "ecosystem". There are strong Darwinian pressures, you just have to have lots of change, evolution, and a heterogeneity of companies, approaches and people; then it will all work.

Ruth McKernan I would push the ecosystem a little further to symbiosis and say I believe there is a lot more scope for partnership, not just around money but around ideas. Pharma can contribute, and biotech – big biotech can help smaller biotech – and it would all be for the benefit of UK plc.

Ted Bianco I would like to build on that same theme. We have simply too many gaps. This includes transaction size but also includes expertise. So, the coming together of the industry and biotech would probably help. We need to run some experiments – people should try out a variety of interactions. I am aware that the companies are experimenting with how to work with the academics and so on, and more power to their elbow.

Paul Freemont Being able to access proof-of-concept funding quickly and easily; managing investors' expectations in areas like drug discovery; having long-term investors with long-term views – those are issues that other countries do manage.

On the academic side we need to develop much stronger relationships with industry. Getting industry's engagement in university activities, having a more transparent flow between these institutions, can only be good. There is an increased realisation that industry is relying more and more on academia for its potential future wealth.

Sarah Haywood I would like us to look at incentives for the academic and industrial sides to work more closely together. We need to have much more flexibility for people to move from one arena into another and back again.

Maggie Leggett Public opinion matters to the sector. It matters for the well-being of people in the sector and, most importantly, it matters for the acceptance of the technologies used. That is particularly important as we move into technologies like synthetic biology which raise some unique ethical

We need some end-to-end thinking that can take the high-quality academic output from universities and turn it into things that will benefit the UK economy
Martyn Postle



and social issues. I hope that will extend to scientists, moving into social science and out again so that we can get better nuance to public engagement.

Paul Cuddon We are unable to retain our most valuable IP within the UK at the moment. We cannot afford to fund the later stages of clinical trials and retain these drugs as products to the UK. We need to have a few more success stories coming through, by having better companies at an earlier stage. They need more financing at very early stages, development of the financing gap we talked about. I have been through a PhD recently and I think there is not enough accountability for people producing this research.

Commercial should not be a dirty word to academics. A better relationship between industry and academia can only help companies move forward and get products to the market.

Martyn Postle The UK definitely has a world-class asset in its biological and medical research. There is a lot of debate on the way in which this asset should be funded. We need some end-to-end thinking that can take the high-quality academic output from universities and turn it into things that will benefit the UK economy at the end.

Steve Yearley Something that is important for the overall health of the UK is thinking about the regional implications of innovation, as well as just UK plc.

Second, I think we need to be ready for both the business and financial opportunities but also the regulatory demands of biotechnology.

Clive Dix We should not worry about trade sales or what is happening in the public markets. Eventually there will not be any trade sales, people will get bored with that and the public markets will open back up again. What you can fix are quite simple things, such as proof of concept. Making it happen is a mindset.

Karl Keegan I like Paul's suggestion about pulling together. I think that part of it should include

commercial courses. There could be a little bit of government help to kick-start it. Some universities have it but I think that is something really simple the BioIndustry Association could get involved with.

Finally, one thing that the public is really bad at is understanding risk. Biotech is perceived as risky. Why can we not spend some money explaining the risk-reward profile in terms of the diseases that the industry is trying to address, and pilot the fruits of that? You need to capture the excitement of the generous fund manager to encourage more money to come back into the sector.

Sue Nelson What is the next step. How would you highlight the success of the UK? Do you want more coming from the top, from government, or from companies, or is it about being reported more positively in the press?

Karl Keegan Highlight some of those successful drugs that are on the market that may not necessarily be marketed by UK companies, look at the evolution of the IP, the idea, how it has transformed, and the angels like Andy. I remember Andy when he was in a small biotechnology company and the success and the trials and endeavours that they undertook. I remember Clive when he was in a biotech company. We should highlight their success stories.

Ted Bianco The public divides into the well and the patients. The US is much better at patient interest groups. Patients start informing themselves, particularly for diseases that are intractable. They notice the developments, they volunteer for trials.

We are all going to be patients, unless the truck hits us so hard that there is no intermediate care. We know that cancer charities collect money because people remember how their relatives were treated. We need to get somebody else to tell the story because it is always less convincing when you tell it yourself.

Karl Keegan FDA Advisory Committees always have patient representatives. You can have all the medics, all the industry guys saying something happens but, you get the person who is suffering, and their vote does matter sometimes.

Martyn Postle In the NHS, we train doctors and nurses on a "mother knows best" principle. So patient education does not take place at as high a level as it should in the UK.

Sue Nelson Journalism has taken a bit of a battering today. One of the reasons that a lot of science reporting will include a patient or somebody who has a particular disease that is related, say, to an innovation that is being described is because it is much better to show the public the application in a way that has relevance and affects lives.

Thank you everybody for coming here today, for the *New Statesman* and the Pfizer policy forum. It has been exactly what a good debate should be.



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