

Dr Patrick Vallance FRCP FMedSci

Senior Vice-President, Medicines Discovery and Development, GlaxoSmithKline

SPEECH at The Foundation for Science and Technology debate on 2nd February, 2011

1. Thank you very much for inviting me to present a perspective from the pharmaceutical industry – I recognise that our industry is very different from some others here, particularly as it relates to the fundamental uncertainties that remain in the science base on which we build. Our industry is going through a period of very major change. A change that will leave those that come through it looking very different from the pharmaceutical model of the past. So I want to start by placing some of those changes in context and to give a view on some of the ways in which I believe the industry will move. I will of course come back to the science settlement – which I welcome for the protection of biomedical investment - and how that can help.
2. The fundamental problem facing the industry is a failure to produce enough new medicines that people want to buy at the price at which they are offered. Our CEO, Andrew Witty, has described this in terms of a societal contract – we make new medicines that improve health, you pay significant sums for these, the money goes back to make more new medicines and society benefits for this and future generations. He has also pointed out that a failure to deliver enough new and important medicines for the perceived cost is why there has been an erosion of trust and confidence, there is a feeling that the contract has not been honoured.
3. The average cost to produce a new medicine is now \$1.6B and it takes on average 12 years. This cost and this timeline is too much, and across industry the number of new medicines making it through to market each year is no higher than it was 15 years ago
4. These observations are perhaps counter-intuitive when we consider in parallel the huge investment that governments and charities around the world have made in biomedical research and the accelerated pace of discovery in understanding biology and disease. There is a disconnect between discovery and invention – the practical application of the discovery to make a medicine.
5. So with that backdrop, what has been the response of the industry. I will not go into the realms of diversification of business models but stick to the question of science and pharmaceutical R&D.

6. First, companies are looking outward. It is clear that R&D cannot be undertaken solely by the scientists within the walls of any one company. Even with the 10,000 or so scientists we have in R&D at GSK, we form only a small fraction of the scientists in the world and there is no way we can know everything that we need to know. So there is an inexorable trend to do more R&D in partnership. This means with biotech companies and with academia and it means globally. There has been a trend to decrease internal spend and increase external spend and to spend that money wherever in the world the best opportunities lie.
7. Second, companies are looking to invest in drug discovery where they can see the best chance of making a medicine. This may seem obvious, but let me explain. On the day we select a target – the protein that we want to affect in order to change biology and alleviate disease – we know that well over 95% of the time we will not make it through to the end. However in some cases you can find that answer quickly, in others you may not find it until near the end and after spending hundreds of millions of pounds. The chances of picking the right target and being able to make robust decisions along the way are not equal across disease areas and change over time.
8. Let me give you two examples. In Psychiatry we know so little about how the brain works that to pick a target is very tough. The animal models are poorly predictive in this area, early clinical studies do not predict the outcome, patients are difficult to diagnose with certainty, the often unwanted effects of drugs that work on the brain are often very significant, the placebo response is high and even when you have a drug that works, it will fail 50% of the time in large scale registration studies. On the other hand, if you take a monogenic disease, you can be sure of the target, you can diagnose the disease with 100% accuracy, you know what you need to measure and the trials tend to be smaller and definitive. These types of consideration are why there is much more activity in some areas than others, why companies are shifting resources from some disease areas of drug discovery and development and why we will see more focus on medicines for smaller indications.
9. Third the nature of what is considered a medicine is changing. We no longer think of the classical small molecule white pill as the default option, antibody based treatments are here to stay, technologies based on antisense, gene therapy and even cell based therapies are beginning to populate pipelines. Even with conventional medicines, the link to diagnostics to

sub-define disease populations and interaction between medical devices and medicines is becoming increasingly important. These technological changes mean a move in some of the skill sets and approaches being taken across industry

10. These shifts across the industry have profound implications for a country like the UK that has had a very strong presence in big pharma R&D in the traditional model. There is another challenge. The UK punches above its weight in biomedical academia, has had a disproportionate representation of big pharma and is underweight on biotech. The new ecosystem requires that all three are present. This will need specific measures to encourage biotech start up, growth and sustainability.
11. I want to give you some examples of what we are doing at GSK and then come back to the question of the spending review and areas of importance for us. Our drug discovery activities are now about 50% internal and 50% external (a big change from even 4 years ago). We have deals with biotechs across the world and have done some deals in the UK, but not that many. We have significant partnerships with academia in the UK ranging from technology platform deals, to specific areas of biological expertise (for example with the Institute of Ophthalmology), to clinical trials, and increasingly to take advantage of where there are electronic health records to undertake effectiveness research (how do our medicines perform in the real world setting - , a question of key importance to payers). We are supporting the therapeutic clusters to enable access to clinical investigators and better characterised patient groups for specialist studies, and are proposing to undertake a new venture with the MRC to open up our Clinical Imaging Centre at the Hammersmith to a new model of PPP. We have also donated land at Stevenage to create a new model of a science park. Stevenage Bioscience Catalyst. We do see the UK science base as strong and believe that academia is increasingly willing to be true partners in some of these key areas. However so is the rest of the world. Remember Obama has committed to invest to “out educate and out innovate the rest of the world”. France and Germany are also investing as of course are China and emerging markets.
12. So let me get more specific, because I think this helps understand what we are really looking for. There are 4 key questions we have when making a new medicine: what target should we select, which molecule should we select as our medicine to tackle that target, how can we

demonstrate early in the clinic that the promise of the new medicine holds up and finally how can we demonstrate the value of our medicine to patients and the healthcare system. I would argue that in big pharma we are really good at parts of this and much less good at other parts. Academia and biotech has huge strengths in some of the parts we are not so good at. Playing more clearly to strengths in each sector is going to be key.

13. So what do we need? First we need a great workforce that is highly skilled and well linked into academia. The UK universities train well and that needs to continue at undergraduate and postgraduate level with domestic and overseas students, However I would like to see more flexibility of movement between academia and industry and back again.
14. Second, we need a great basic science activity – it is here that target identification and technology advances will emerge. This focus on basic science needs to be coupled with a willingness to translate into practical outcomes and needs a more vibrant approach to biotech creation. There are also schemes that we and others are putting in place to advance targets in true partnership with academia – this will require flexibility in approach to assessing research performance within academia and a better understanding of where value lies in terms at different stages of discovery (ie not to put too high a value too early – our tech transfer offices need to change).
15. Third, we need to be able to test our medicines early in the clinic and understand their potential. This area of experimental medicine has been a traditional strength in the UK, and was bolstered by Wellcome Trust, MRC and NHS R&D investment. I see this as a key area across the industry and one where the UK could make a big impact. De-risking in the clinic before the big clinical trial spend kicks in is a major priority. Being successful here would also lead to more likelihood of phase 3 investment.
16. Fourth I think that our clinical trials infrastructure has improved but it is unlikely that we will offer a particular advantage over other countries and in any case for global registration global studies are required. I do believe that there are two areas of advantage in the UK. One is that the NHS could choose to undertake a complete study of a new drug where the conventional market pull may be deemed weak and therefore the enthusiasm for big investment is low – for example some antibiotics, or new medicines for an area like premature labour. Another is that effectiveness trials based on electronic patient data is going to be important and the UK

should be at the forefront of this. It will require not just infrastructure but also expertise in data mining and signal detection. In all of these trial areas I welcome the recommendations in the AMS report on simpler regulation of research.

17. I want briefly to return to the area of when an area becomes “ripe” for drug discovery or invention with an example. Neuroscience is an area that has seen unprecedented investment in science yet in many areas is simply not ready for investment for drug discovery. It is an example where I believe with a key focus on those areas which would enable target validation and early clinical experimentation to improve prediction of clinical outcome, this will become an investment area for both biotech and Pharma. This I believe is the type of area where public investment with a clear aim can create an environment for industrial success.
18. So to summarise. I welcome the protection of the biomedical science budget and believe it is of key importance to our activities in the UK. I think the research councils are headed in the right direction and have moved positively in relation to interactions with our sector and the links between the NHS and research. I would like to see co-ordinated measures to stimulate the biotech environment in the UK and further use of REF to reward true collaboration with industry, risk taking with spin outs and staff mobility – this needs all sides to come together with some very clear and co-ordinated proposals quickly. Ensuring that we build on critical mass of excellence is key and I do believe in geographic clusters as being important to create the right environment for invention. In this respect the concentration of top class research universities, the formation of UKCMRI, the developments at Stevenage of the Catalyst science park and the skilled pharmaceutical workforce in the South East represent a clear opportunity.
19. I do think the science base is outstanding in the UK, I think others will find it hard to catch up with that and we do have an opportunity to play to our strengths. We must not damage that fundamental strength in science and I believe that that message is clearly understood by government and reflected in some of the ambitions in the spending review. Finally I am going to display my innate optimism – the advances in biomedical science will translate into huge opportunities for health and wealth improvement and that the opportunities for making new medicines have never been greater.