AN AUDIENCE WITH…

Menelas Pangalos


AstraZeneca

AstraZeneca, along with many of its big pharma peers, has struggled to deliver new drugs in recent years. In the hopes of turning the company around, its Chief Executive Officer Pascal Soriot recently shuffled the scientific management and promoted Menelas Pangalos to head up the discovery and early-stage development of small molecules. Pangalos has been with AstraZeneca since 2010 and has previously worked at Pfizer as head of neuroscience research and development (R&D), as well as at Wyeth and GlaxoSmithKline. Part of AstraZeneca's salvation may be in becoming less risk averse, he tells **Asher Mullard**.

What has changed with the recent transition?

The big difference is the focus Pascal Soriot has put on basic and translational science. As scientists, there's nothing better that you can hear. With [Executive Vice President of Global Medicines Development] Briggs Morrison, [Executive Vice President of MedImmune] Bahija Jallal and myself all running our respective parts of the organization and being involved in the strategic executive team, we can execute decisions more quickly and prioritize projects better.

We are also becoming less afraid to take risks. We became a little risk averse, always thinking "let's do one more experiment" rather than saying "I really believe in this mechanism and molecule. We should be moving this forward, we should be aggressive and we should be willing to take some smart risks". The stopper has been taken off us a bit.

I'm also excited about the power of having the small-molecule and large-molecule groups working together. In many organizations these groups compete with each other, and historically they maybe even competed with each other at AstraZeneca. We now all have one shared set of R&D goals and I'm seeing much more collaboration between our groups. There are lots of ways of combining our platforms and our molecules, and that's something we're thinking about pushing very hard.

How do you harmonize this focus on science with the fact that you are shrinking your R&D organization?

It's true, we are reducing the size of the R&D organization. But we've been doing that since 2010. We were just too large. We were four or five quite 'siloed' groups that weren't really talking to each other. We had self-standing R&D units, multiple high-throughput screening groups and multiple *in vitro* drug metabolism and pharmacokinetics (DMPK) groups. We've just consolidated them.

Last year I thought I had one of my most productive years, and that's on the background of working within a smaller group. We're more focused, more organized, have more scientific discipline and are working on fewer core areas. I feel that we're now getting to the right size, the right shape and the right focus. The reduction in size has made us better, not worse.

You mentioned that you are becoming less afraid to take risks. Can you provide some examples?

The Moderna deal is an example of us being less risk averse and more excited about stuff at the cutting edge. This is a very early technology in the mRNA space that has huge potential if it works. We're talking about being able to express any protein in the cell. There are still significant challenges in terms of delivery, formulation and safety, but the data the company has generated and the opportunities in the metabolic and cardiology space, we think, warrant the investment. If we can get delivery sorted out, this is potentially the next biologics platform. There's a relatively big "if", but if we can crack it I think it will be phenomenal and will open up some targets that you can't currently hit with either antibodies or with small molecules.

We've also done a deal with Isis, around an antisense STAT3 [signal transducer and activator of transcription 3] inhibitor for liquid tumours, which is moving very well through a Phase I programme. And we've done a deal with Regulus Therapeutics in the microRNA space, another innovative, risky therapeutic approach that has potential.

You have also re-jigged your therapeutic foci.

Yes, we are now going to focus on three core areas: respiratory, inflammation and immunity; cardiovascular and metabolic; and oncology. These are the three core areas in which we absolutely want to win from a business development perspective, from a collaboration perspective and from a pipeline perspective.

We've also got two areas that we're calling opportunistic: infection and vaccines; and neuroscience. We still have active groups in these opportunistic areas, but the relative investment in these is smaller. And these groups need to be a bit more creative about how they go about their business. The neuroscience group, for example, are raising funding for some of their projects from external sources. They've raised funding for one of their Parkinson's disease projects from the Michael J. Fox Foundation, and they've raised funding for one of their smoking cessation programmes from the US National Institute on Drug Abuse.

What is your favourite small-molecule programme at the moment?

I'm incredibly excited about olaparib, our PARP [poly(ADP-ribose) polymerase] inhibitor. The activity of that molecule is tremendous in the targeted *BRCA* patient population, and we may be able to broaden the patient population out as we learn more about the molecule. Hopefully we'll be moving into Phase III in the not too distant future.

If you'd asked me that 3 years ago it would have been more difficult to answer. But now I could reel off six or seven molecules in our pipeline that I'm excited by. It took us some time to get here. We inherited a lot of legacy programmes that we played out, because you don't save any money by closing them down. But the majority of the drugs we are developing are now from our new strategy, which is exciting to see.