Q: What are some of the key priorities for the year ahead for you personally, and for Autolus?

NK: Autolus is a clinical stage company, so the primary focus for the year ahead is delivering on our existing clinical trials: we have a broad clinical stage pipeline, with four product candidates in five haematological indications, and one solid tumour program.

At the same time, we’re also preparing for larger scale manufacturing to support future studies and, assuming future approval of our products, commercial launch. Finally, we are planning delivery of next-generation products for both haematological malignancies and solid tumours, with three next-gen versions of our lead programs.
What are some of the particular issues relating to manufacturing scalability of technology platforms in the T cell immunotherapy space, and how have you sought to address them?

NK: Designing and fixing a commercially viable process as early as possible is very important. It’s key because we want to minimize comparability risk when we introduce future process changes. And we want to be ready in time for commercial launch, because with this type of product, compelling efficacy can be apparent from early clinical studies which offers the opportunity of accelerated approvals, meaning very short development timelines.

So what we’re trying to do – what we have implemented to date - is essentially a process that is commercially ready from the beginning of our clinical trials. We’ve designed our processes to be fully closed and semi-automated, operated in a low-grade cleanroom, and we’ve also ensured we have frozen apheresis in and frozen finished product out. This means we can manage the challenges of scheduling and optimising the throughput of products through our manufacturing facility to efficiently get the product to the patient.

When it comes to scaling out of autologous T cell therapies there have been some interesting developments from the commercial trailblazers as they look to establish production in different regions of the world. How is Autolus looking ahead to a potentially global commercial scenario in this regard?

NK: We’ve designed and built our process based on what we feel is the right model for us, which is for semi-centralized manufacture – modular manufacturing established on a regional basis, with a small number of medium-sized facilities in key geographies.
Having an automated process that is easily transferable allows us to build the number of facilities over time, based upon demand. What we will do initially is to establish a launch facility for about a thousand patients/products per year in the UK, and our first commercial facility for about 5,000 therapies per year in the US.

I also think that given the number of products that need to be made for the indications we’re going for, it actually makes sense economically to go with this regional, central production model: not only do you have more consistency in terms of your testing, your operator experience and the overall quality systems, but using the facilities at full capacity and releasing products rapidly – we are talking about probably releasing a product every 45 minutes to an hour– means that the cost of the investment, the equipment and the labour is reduced due to economies of scale.

Q Looking further ahead, where do you see the long-term future of commercial autologous T cell therapy production in terms of the full spectrum of centralized-de centralized strategic manufacturing models?

NK: I do personally feel that pursuing a semi-centralized manufacturing model is more favourable really, because this model will provide a more consistent approach to quality and economic benefits as well. This is especially true right now, when we (as a field) have neither sufficiently advanced processes nor adequate product understanding, but even looking to a future where those issues have been resolved, I think I would still favour control of manufacturing in a small number of locations rather than at the patient’s bedside. But we shall see what the future brings!

Q In technological terms, where are the greatest current shortfalls, or missing pieces, in fully enabling optimal scale-out of these products, in your view?

Everyone acknowledges that our industry is still quite immature and many people have said it’s a similar scenario to the monoclonal antibodies space a few decades ago. Although we have seen amazing efficacy in the clinic, and marketed products are now doing great things for patients, the
Everyone acknowledges that our industry is still quite immature and many people have said it’s a similar scenario to the monoclonal antibodies space a few decades ago.

processes we have today have essentially come out of academic labs, and the supply chain that comes with them is not that developed, either. So the consumables and equipment suppliers are lagging behind: there’s lots of single-use material, lots of bespoke, high-priced options that have been designed for research and not for routine, large-scale manufacture. I think as demand increases, the suppliers are going to help solve these problems.

The other shortfall is not having deep enough product understanding. What we and everyone else has been doing to counter this is to look to fully characterise our products in order to generate that deeper understanding, and to improve control strategies, so that we have the appropriate release analytics. In tandem - and due to the fact that we are working with one patient-one batch - high throughput analytics are also very important.

Away from the manufacturing system and the process technologies themselves, the system to deliver the cells to and from the manufacturing facility, and the capacity of the clinical centres to deal with the number of products that potentially need to be stored in liquid nitrogen, are also areas that are being addressed and so will mature over time.

Q

Autolus was the first company to come on board with manufacturing at the new Cell & Gene Therapy Catapult facility in Stevenage, UK. How important is it to develop and maintain such public–private partnerships for GMP manufacturing?

NK: We feel we have benefited very greatly from collaborating with the Cell and Gene Therapy Catapult. It helped us as a company to build up future clinical trial capacity without having to invest a lot of capital upfront. Instead, we’ve been able to focus on getting our processes and technologies in place to generate clinical data as quickly as possible. And, at the same time, it’s also giving us the opportunity to test our systems and design in a suitable environment before we finalise our own facilities’ design.

Having a good quality agreement in place from the beginning, which very clearly states the responsibilities and accountabilities of both parties, is absolutely key for the success of collaborations like this one.