

CHIEF EXECUTIVE OFFICER'S Q&A

Interview with Terry Pizzie

In this section we have asked CEO Terry Pizzie some of the questions that are most frequently asked by investors and other stakeholders.

Q. Are you surprised by the continuing strong growth enjoyed by the RNAi market, especially given the rapid emergence of CRISPR?

A. No. RNAi modulation has seen a resurgence in interest following the launch of successful RNAi-based therapeutic drugs in the last few years. This has created a positive tailwind for the RNAi market and renewed interest in the gene silencing market from researchers in both the academic and pharma communities.

Q. How will the increase in capacity impact Cell Line Engineering?

A. We believe that we have an opportunity to significantly grow revenues and market share as a result of the increase in capacity that has been delivered through re-engineering our existing business processes in H1 and the introduction of automation in H2 of 2019. These changes have enabled us to launch more compelling solutions on both price and turnaround times. We expect the benefits of the increased capacity to come through more strongly in the first half of 2020.

Q. What is the significance of the collaboration with Mammoth Biosciences?

A. Having established our credentials in the very conservative bioproduction market, we believe that the opportunity now exists for us to become a technologically disruptive provider of next-generation CHO cell lines to an industry where greater flexibility, increased speed to market, cost reduction and a move towards next-generation biologics are key drivers.

Our strategic collaboration with Mammoth Biosciences is critical to this ambition because it will provide us with access to Cas enzymes that will offer similar benefits to CRISPR Cas9 in terms of speed and ease of gene editing but without the associated royalty burden.

Q. What are the advantages of base editing over gene-editing systems like CRISPR-Cas9?

A. CRISPR/Cas9, Zinc Finger Nucleases or TALENs all rely on generating double strand breaks (DSBs) to knockout the target gene. This is a highly efficient way of generating knockouts through the formation of small insertions or deletions of the DNA (indels) but also carries risk when applied to a therapeutic setting.

As base editing works by nicking the DNA instead of breaking it, the indel formation is substantially lower and the chance of errors being introduced is reduced. We believe base editors may therefore have the potential to provide more accurate gene editing with broad therapeutic applicability.

Q. What is the primary difference between the base editing platform offered by Beam Therapeutics and the one that you are commercialising with Rutgers?

A. Firstly, the two base editing systems are similar in that they both achieve base changes through a CRISPR/Cas mediated targeting of a chosen deaminase (the enzyme that actually edits the DNA bases) to the target site. However, the primary difference between the two systems result from how the deaminase is recruited into the Cas9-guide-RNA module (the "gps-like" system that directs the enzyme to the precise location at which the edits are to be made).

The Beam system is based on direct fusion between the deaminase and Cas9. The Rutgers system is more modular in design and there are no components that are directly fused to Cas9. What this means in practice, is that if you wish to change the deaminase which you want to use to effect a base change, it is relatively easy to do. However, with the Beam system, because the deaminase is directly fused to the large Cas9 module, swapping deaminases takes a bit more work. The two base editing platforms are protected by distinct patent portfolios.

Q. When will the platform be ready for customers to access?

A. We have spent a year evaluating the technology and it is already available for early access testing. We are now seeking 3–5 partners to assess and shape the development of its platform and expect a 12–18 month period of R&D before we have a fully commercialised product.

Q. What are your ambitions for the business in terms of growth?

A. We have been preparing the business for growth by doubling down on the parts of the business where we see high-growth opportunities. Our long-term ambition is to be able to accelerate our top-line growth to mid-teens growth rates, whilst also maintaining our margins above 65%. But we will not get there overnight. We have more work to do over the next 18 months to two years, particularly in terms of capitalising on our leadership in CRISPR screening and prosecuting the opportunities that we see in BioProduction and Base Editing.

Q. What are the financing needs of the business to achieve all you want to do?

A. We had £18.8m of cash at the year end and we aim to manage the business such that we conserve cash resources to provide us with options in the future. In April 2020 we raised gross proceeds of £6.9m through a share placing in order to provide additional financial flexibility and grow the business during the COVID-19 crisis.

Q. Is that what is behind the proposed secondary listing in the U.S.?

A. Partly. Our Board and advisers firmly believe that the U.S. capital markets would offer Horizon a larger pool of capital and a broader and deeper investor base. Any proceeds raised by the listing process would also allow us to accelerate our 'investing for growth' strategy.

Q. What sort of reception have you had so far in the U.S.?

A. It has been very encouraging. There has been a lot of interest in what we are doing and the feedback suggests that our equity story would have a strong resonance in the U.S. market once we are ready to launch.

Q. So where are you in the process and what are the next steps?

A. Actually the rules prevent me from commenting on any timeline. All I can say is that we have been working hard in preparing the business for this next stage of its development. Of course, the timing is not just down to our preparedness, it also depends upon market conditions over which we have absolutely no control. But rest assured we are working closely with our advisers and will move as soon as the timing is apposite.

TERRY PIZZIE, CHIEF EXECUTIVE OFFICER