Collaboration with AstraZeneca and R&D Update

Wednesday, 25th March 2020

Opening Remarks

Iain Ross

Executive Chairman, Silence Therapeutics

Good afternoon everybody. We live in extraordinary times at the moment and I hope everybody is well and safe. For us at Silence it is an extraordinary day because we think we have done an extraordinary deal. To manage to get this concluded over the last couple of weeks has been quite a challenge.

What I would like to do is introduce our speakers this afternoon. What I am going to ask is for John Strafford, who is our Head of Business Development, to talk you through the collaboration that we have put together with AstraZeneca and for Rob Quinn, our Chief Financial Officer, to go through the numbers and give you some more detail. Then we will move through to Giles Campion who is going to give you an update on our R&D. Then we will move to an extensive interaction in terms of the Q&A session.

Suffice for me to say we are very, very excited about this deal. We think it is a further validation of our proprietary platform. We have already done deals, as you know, with Mallinckrodt and also Takeda. We feel this is a very exciting collaboration that we have put in place. What I would like to do now is to hand to John Strafford who led the negotiations and let John take you through and describe a little bit about the collaboration going forward.

Collaboration with AstraZeneca

John Strafford

Head of Business Development, Silence Therapeutics

I am John Strafford, Head of Business Development at Silence. AstraZeneca are building up a strong portfolio of oligonucleotide modalities and we are delighted that they have chosen Silence as their partner of choice to add siRNA to their drug discovery toolbox. The deal is a multi-target deal to develop treatments for cardiovascular, renal, metabolic and respiratory diseases. These represent two of AstraZeneca's three main therapeutic areas. CVRM includes indications such as cardiovascular disease, NASH, chronic kidney disease and heart failure. Respiratory includes diseases such as asthma, COPD and idiopathic pulmonary fibrosis.

In order to address these areas we will need to achieve delivery of our siRNA molecules to new tissue types such as the heart, kidney and lung. We will be collaborating with AstraZeneca to achieve this. We expect to start work on five targets within the first three years of the collaboration and AstraZeneca will have the option to extend the collaboration to a further five targets. AstraZeneca will be responsible for selecting the targets but we will work together with AstraZeneca on the validation of these prior to selection.

Our responsibilities in the collaboration will be mainly focused on the period prior to candidate nomination. We will lead the work to design, synthesise and optimise the siRNA molecules. This will be a very collaborative effort and AstraZeneca will be responsible for the work in disease models and prior to candidate nomination. At the point of candidate nomination

AstraZeneca will then take over non-clinical and clinical developments, including all the toxicology studies. We will retain responsibility for manufacturing for a period of time after candidate nomination and we will be responsible for supplying material for the toxicology studies as well as the Phase I. This is important as it will help us to build up our capabilities and strengths in manufacturing.

During the Phase I phase of development we will also have the option to negotiate to negotiate for co-development rights to two of the targets coming out of the collaboration. That will be two targets of our choice. We will be forming a JSC very shortly with AstraZeneca to manage the collaboration and we expect to select the first target very shortly after that as well.

Lastly before I hand over to Rob, this partnership really allows us to combine the scientific strengths of AstraZeneca with the capabilities we have built up over many years working in the field of siRNA. Together with AstraZeneca we feel we will be able to unlock the potential of our platform and develop treatments for many patients. Now I would like to pass over to Rob who will talk you through a bit more on the financials.

AstraZeneca Collaboration Financials

Rob Quinn

Chief Financial Officer, Silence Therapeutics

Our collaboration with AstraZeneca announced today significantly strengthens our balance sheet with $80 million in upfront payments, $60 million in cash and $20 million for equity. AstraZeneca will take a 5% equity stake in Silence and paid £4.07 per share, a small premium to yesterday's closing price. Alongside our current cash balance we now have over $110 million on a pro forma unaudited basis, leaving us in a strong position to move forward as fast as possible on our lead programmes, SLN360 for cardiovascular disease and SLN124 for iron overload disorders.

On current business plans we anticipate our cash runway extending beyond 2022. As well as the upfront payments, Silence will receive a $10 million option fee per target upon the point of candidate nomination. We expect the first $10 million option fee in 2022. Beyond that we are eligible for up to $140 million in development milestones and up to $250 million in commercial milestones per target. That is $400 million per target or $4 billion in total. We will also enjoy high single-digit to low double-digit royalties on net sales. With that I will now pass over to Giles Campion, our Head of R&D, to discuss today's R&D update.

R&D Update

Dr Giles Campion

Head R&D, Chief Medical Officer, Silence Therapeutics

The great news about this deal is not only that it is a great validation of our science but it also gives us the firepower to build the organisation and to pursue the development of our wholly-

owned assets due to enter the clinic this year. In that respect we have allocated highest priority to SLN360. Our confidence in the future of this asset is based on the preclinical profile which is shown on the graphs on the right. On top of an excellent safety profile the compound shows profound knockdown of the target in non-human primates such that three doses of 3mg/kg leads to greater than 90% knockdown of the entire 63-day duration of the experiment. It is data such as these that has attracted partners such as Mallinckrodt, Takeda and now AstraZeneca to our platform technology.

Given the extremely competitive preclinical profile and the global prevalence of LP(a)-related cardiovascular disorders we believe we have the potential to be best-in-class in an area of great unmet need. The first indications many individuals have that they have this genetic-based disorder is a sudden heart attack out of the blue that devastates their lives and gives concerns for their future health and that of their children. There is currently no approved medicine for this condition that affects up to 10% of the global population. As announced earlier, we had a very productive meeting with the FDA late last year and we are on track to file an IND in the second half of this year with preliminary data available in mid-2021.

Our development asset SLN124 is progressing and we are pleased to announce that we have very recently received rare paediatric disease designation by the FDA for ß Thalassemia. This comes with seven years of market exclusivity following FDA approval and full or partial waver of application fees and tax credits for the clinical testing expenses conducted after designation is received. It is also testament to the safety of the preclinical profile of this molecule.

We have previously announced that first dosing in patients would be achieved by Q1. However, given the emergence of the global COVID-19 pandemic emergency we have chosen to halt subjects in screening. Moreover, we are taking advantage to develop a new protocol with a broader population to be submitted shortly. As far as we can predict with the current situation we now guide to data in half-one 2021. We have taken robust steps during this time to ensure the health and safety of our employees and being able to take advantage of technologies that allow business continuity, including the remote operation of laboratory equipment. At the current time we are not reporting any significant impact on our discovering early development programmes, including the technology evaluation agreement with Takeda and the partnership with Mallinckrodt.

As we evolve to become a fully capable development organisation we have announced a new Scientific Advisory Board chaired by Professor Sir Gordon Duff. Sir Gordon is a previous Chair of the UK Committee on Safety of Medicines and of the UK Medicines & Healthcare Products Regulatory Agency, the MHRA. Sir Gordon is an expert on healthcare and UK science policy with a special interest in genetics of the inflammatory response. He was knighted in 2007 for his services to public health. He is joined by world-renowned clinicians and scientists, both in the area of oligonucleotide therapeutics as well as those having domain knowledge in our therapeutic areas of interest. Particularly Henry Ginsberg, who has been at the forefront of the LP(a) scientific world. We trust the expertise of these highly-respected scientists will guide us on our ambitious journey to develop important medicines with a major impact on patients' lives. I will now pass over to our Chairman.

Closing Remarks

Iain Ross

Executive Chairman, Silence Therapeutics

Other Recent Highlights from Q1

One of the things I was going to cover was the CEO recruitment. Obviously I have been asked a lot of questions about that and whilst I have to say I am quite enjoying the role of interim Chairman, especially when we get to negotiate and announce deals such as the ones we are announcing today, I am very well aware that we need to get a full-time leader to come in and take the company forward, working with what I can say is an excellent management team. Where I got to is that obviously COVID-19 has slightly halted the face-to-face interactions but I have continued to interview suitable candidates not only face-to-face in the early months of this year but also in video conferences.

I can tell you that we now have a number of candidates who are going to enter the data room this week to do some further due diligence on the company and I am hoping that they will then start to have discussions directly with our IP attorney to understand the IP position of the company and also to speak directly to Giles Campion to get a bit more information on the science. Inevitably the appointment of this person will be delayed a little bit because nobody is going to take a job until they have actually met the team that they are going to be working with. However, I am confident that we will be able to announce the appointment of somebody within the next couple of months with a view to that person starting as soon as possible when it is safe to do so. I have to say we are getting a very high calibre of candidates and it may well be that a couple of them are listening in to this announcement.

The other thing I would say is that the technology evaluation agreement we have with Takeda, as everybody knows we are not allowed to say what the target is but that is actually progressing very well and we hope within the next 12 months to be able to discuss that further. Other things that we have done during the quarter is we have opened our office in New York and Barbara Ruskin, our Senior VP for General Counsel and Chief Patent Officer, is actually working out of there. We are hoping to recruit a couple of other people there. We are also expanding our US Investor Relations. We have made it very clear at some point in the future we will look to move more towards the US but we will continue certainly over the remainder of this year attending presentations whether it be virtually or in person to raise our profile.

Platform Validation: Putting the Pieces in Place to Unlock Value

I think that Silence is actually at a pretty exciting place. We have now got Mallinckrodt, Takeda and AstraZeneca BD partnerships which have all been negotiated and led by John Strafford, and those underpin and validate our platform. We are very excited about SLN360 and hoping that that will move into the clinic later this year. Also SLN124 which we are extremely excited about but we could not proceed by putting patients into the clinic until the current situation is resolved. The segment at the bottom of our pie chart suggests that we really are beginning to focus more on the biotech investors and all I can say on this point is that we have a number of people doing due diligence on the company. We would hope to make further announcements as the year goes on.

Silence Therapeutics – Summary

In summary we think we have got an extraordinarily valuable platform and we have got a growing clinical pipeline. However, what we have to do is we have to have the ambition now. We have got a strong balance sheet and we need to start growing this organisation. Some people say, 'How on Earth could a company like Silence take SLN360 further forward?' Actually if we build the right infrastructure and get the right leadership in place we will do that. All large companies start small. I have a very strong and experienced team working with us and whoever the new CEO is they are going to be extremely pleased with the talent that they have in their team. We are very much focused on targeting indications and rare diseases and we are about developing products in the cardiovascular area and complement-mediated diseases as well. We have a strong financial position. We will strengthen that position as we go forward and we are very excited about the readouts that we will get certainly at the beginning of next year.

Q&A

Ishmael Dixon: Firstly you mentioned that the first deal or target you expect to be announced soon. Can you give us an idea of how over the three years you expect the other four to be phased in terms of them describing the target to you? Secondly, if you could remind me, given the number of deals that you have signed now and all the potential targets and tissues with Mallinckrodt, AZ and Takeda, are there now any indication areas that you are genuinely offside on or exclusive arrangements in place? Thirdly if you could build on the tissue targeting. The candidate nomination phase includes the identification of the delivery mechanism and/or vehicle. Many thanks.

John Strafford: In response to your first question on the phasing of targets, as we communicated we anticipate starting work on the first five targets within the first two years of the collaboration and we expect them to be interspersed throughout that period. We are not going into further details on the exact timing of that but clearly we structure that to manage our resource alongside our other pipeline programmes as well.

In terms of therapeutic area exclusivity all of the deals that we have closed, the Mallinckrodt, the Takeda and the AstraZeneca deal are all target-based deals. None of them include any exclusivity on particular therapeutic areas. Then the last question related to tissue targeting. This is an area that AstraZeneca have done a lot of work in over recent years. They have been building up their capabilities in the oligonucleotide space. They have chosen us to work with them on the siRNA field but we can draw from a lot of the knowledge that they have built up on delivery of oligonucleotides over recent years into the collaboration. It is also something that we are actively working on and we will collaborate to achieve delivery to these new tissue types.

Craig McDougall: Congratulations on that outstanding announcement. I wanted to follow on a little bit from an earlier question. If you could outline the nature of the work and the phasing of it and when it will begin in earnest. What proportion of our resource can be devoted to that whilst managing our own programmes? Iain, in that regard I think you touched upon it in your summary but how do we best take the SLN360 programme forward? What is our capability in how we look to develop that corporately?

John Strafford: Clearly once we select the initial targets and AstraZeneca will have the responsibility for the selection of targets, we expect the first target to be selected very soon. AstraZeneca have a few very exciting targets that they are ready to put into the collaboration and then there are other targets that they will be carrying out validation work on. We will be working on some of that with them as well throughout the research collaboration. As each target is selected we will work together with AstraZeneca through the joint steering committee to develop a research plan for that particular programme. Clearly for each target and each particular delivery approach they will be quite unique in terms of the research plan. We cannot go into great amounts of detail on the details of each research plan but broadly in terms of the activities, as I mentioned, Silence will be responsible for the [inaudible], the synthesis of those siRNA molecules and also optimising them. We will work together collaboratively to achieve the delivery extrahepatically to different tissue types potentially drawing technology from both parties. Then we will be working collaboratively to the point of candidate nomination at which point AstraZeneca take over most of the work. Hopefully that answers your question.

Iain Ross: Craig, the answer to your other question is it is about having ambition. We have actually already got a programme of recruitment ongoing which commenced at the beginning of the year. We are recruiting at the moment for 44 positions and those positions will be very much focused in the clinical area, in project management and also in manufacturing. Today's deal just consolidates our commitment to being able to fill those positions and moving forward obviously because of the healthcare environment at the moment some of those positions may be delayed. However, I do know that a number of interviews are going on over video conference. We are going to build an infrastructure that is suitable and actually growing the company. The big question is how far do we take SLN360? If Giles Camion was answering this question he would say, 'All the way.' My view is we take it as far as we can at the moment and depending on our financial resources that means getting that into the clinic and taking it through to the next stage. Now, if somebody comes along and wants to partner it then we have got to listen but we are determined to hang on to our assets not only SLN360 but some of the earlier stage pipeline assets that we have not even made people aware of, we do want to take forward. We are building, Craig, for success. We are building an organisation and it has already started. At some point somebody may come along and try and partner with us but at the moment we have no intention of doing so. However, as somebody said earlier on, one of the reasons we are getting a lot of interest in the company is because we have the SLN360 asset.

Craig McDougall: Thanks, that is very helpful but just a final point. Would we have more capacity for further collaborations and further partner activities in our current guise?

Iain Ross: I think what we have got to do, Craig, is we have got to be very careful. We have had quite a lot of conversations internally about this because we are in discussions with a number of companies at the moment. Certainly AstraZeneca was the furthest advanced but we even discussed exactly what the shape of that should be in order that we can actually produce and execute that collaboration. I would be surprised if we announced another deal of that sort of nature until we have actually got our infrastructure more up and running. As John says, we have not given exclusivity to people and we have got a number of other big pharma talking to us. However, what we need to do is we need to be able to deliver. I think

there would be a little hiatus in that type of transaction. Maybe directing more towards looking at how we strengthen our capability to deliver to different parts of the body. Perhaps some of our technology collaborations will come to the fore. Everybody is fighting to find the best way to deliver these molecules and we are no different from the others. We have a number of quite exciting discussions ongoing at the moment.

Craig McDougall: Okay, thanks so much for that. Congratulations again to you all. Thank you.

Iain Ross: Thanks very much. There are no more questions. If that is the situation, thank you very much indeed for everybody listening. We are very excited about this deal. We think it is going to be further validation of where we are going. Hopefully we will all get through the next two or three months and we will emerge even stronger for it. The last thing I would say is that Silence is working as far as normal as we can and we are continuing to develop the business. I wish you all well and a healthy few weeks. Thank you very much indeed.

[END OF TRANSCRIPT]