Sirnaomics Ltd. 2021 Annual Results

Annual Results Presentation – Transcript

Dr. Patrick Lu, founder, chairman of the Board, Executive Director, President and CEO of Sirnaomics：

Welcome to the presentation of Sirnaomics 2021 annual results. We're pleased to announce our first annual results since our listing on the mainboard of the Hong Kong Stock Exchange on 30 December 2021. Today we will present to you the development of the company in the past year and our future plans.

Firstly, I would like to introduce the management team from Sirnaomics joining today's presentation. I am Patrick Lu, Founder, Chairman of the Board, Executive Director, President, and CEO of Sirnaomics. We also have Michael Molyneaux, our Executive Director, and Chief Medical Officer, David Evans, our Executive Director, and Chief Scientific Officer, and Nigel Yip, our China Chief Financial Officer.

Sirnaomics is an RNA therapeutic innovator on the global stage. Sirnaomics is the first clinical-stage RNA therapeutic company to have a strong presence in both the U.S. and China, powered by advanced RNAi & mRNA technologies. The company has proprietary delivery technology platforms that Polypeptide Nanoparticle-based, which we also call PNP Platform, GalNAc-based Technology Platform, and other global rights for our multiple delivery systems based on our technology. The company also has fast-growing clinical programs with two clinical assets that have covered the disease involving cancer, fibrosis, antiviral, and so on. In the area of oncology application using RNA-based therapeutics. Sirnaomics is taking the leading role on the global stage for novel therapeutic development. In addition, the company's early-stage R&D effort is fast-growing and generates a tremendous number of intellectual properties. And we have multiple programs at a later preclinical stage reached to IND-enabling stage. More importantly, the company already established a manufacturing facility which allowed us to have our fill and finish capacity, established in Guangzhou, to produce large-scale products with GMP compliance. Currently, we can have an annual capacity to produce around 50,000 vials of lyophilized human injectables with various product types.

In 2021, the company had achieved major accomplishments. We are well-capitalized. The successful IPO in December 2021 allowed us to have an additional $55 million which is going to be used to support our clinical program development and R&D effort. Over the last 18 months, the company has raised about US$280 million which provides a very strong cash position for the company's future efforts. We have a runway for more than two years to support our clinical development and our other business development and R&D development. The company actively executing our R&D strategy - we have multiple clinical programs based on two clinical assets, STP705 and STP707. In addition, the asset generated by our GalAhead™-based delivery system STP122G already demonstrated a long-lasting target knockdown and a therapeutic benefit, which was demonstrated in a non-human primate model. Our subsidiary, RNAimmune, is also developing an mRNA vaccine against COVID-19 called RIM730. In collaboration with Walvax, we have developed STP702 for the treatment of influenza. In addition, the company organization is also expanding. We currently have more than 170 full-time employees. Talent development and acquisition is another major effort we have undertaken during 2021. Right now, we already have a promotion of Chief Development Officer and the Chief Production Officer. We also have a new recruitment including the Vice President for CMC, Vice President for Regulatory Affairs, and Senior Director for clinical operation.

As the leading RNA therapeutics company, Sirnaomics has proprietary delivery technology covering multiple therapeutic areas. Polypeptide nanoparticle (PNP) platform represents the key strength of the company's delivery technology, which can address multiple diseases like oncology and fibrosis. In addition, the liver-targeted GalNAc technology also allows the company to develop novel therapeutics against infections and liver-related metabolic diseases. The GalNAc technology is well validated by Alnylam and other companies as a powerful delivery technology that already is sort of validated in the clinical setting and is even already proven for the market. Using these two technology platforms allow Sirnaomics to develop therapeutics and vaccines using both siRNA and mRNA as drug payloads. For siRNA therapeutics. Sirnaomics has already demonstrated the power of the PNP delivery system and RNA drug design, with a unique mechanism of action against cancer, fibrosis disease, anti-viral, and potentially liver metabolic diseases.

The company has broad and deep product pipelines covering oncology, fibrosis, medical cosmetic anti-viral, and liver-related metabolic diseases. In 2021, the company's clinical

program has grown tremendously from a single asset with two trials all the way to two assets with seven ongoing clinical trials. Our most advanced program is STP705 for the treatment of non-melanoma skin cancers, including isSCC and BCC, which has already reached phase IIb stage. We also have IV dosing indications with STP707. The long-term strategy for our clinical development involves two unique approaches. Firstly, we are going to develop our clinical programs in the US first, based on the successful efficacy and safety study results, we can further support our clinical development in China. Secondly, we can take advantage of orphan drug indicators indication regulatory benefit for both US and China.

Dr. Michael V. Molyneaux, Executive Director, CMO of Sirnaomics：

Thanks, Patrick. My name is Michael V. Molyneaux. I'm the Chief Medical Officer of Sirnaomics. I'm going to discuss some of the clinical data for the leading asset STP705. Our strategy is to study STP705 as a local delivery product. And our first indication is non-melanoma skin cancer. These are the results from the recently completed phase II study. In this study, we looked at five different dosing groups ranging from 10 micrograms up to 120 micrograms. We injected each patient once weekly, for up to six weeks. And then one week after the last treatment, the treated area was excised, and we examined it under the microscope by an independent dermatopathologist to see if there was any residual tumor left. The asset STP705 was injected directly into the skin tumor and then subjects need a biopsy confirmation of squamous cell carcinoma in phase II study entry. Overall, 76% of subjects across all groups (25 subjects) achieved Complete Histological Clearance. We had 90% complete histological which are very high clearance rates. This was combined with a very good response for the skin. So, we looked at the skin response in the cosmetic result, and in the majority of the dosing groups, as you can see, the post-treatment skin response was improved compared to pretreatments. So, what that means is the appearance of the skin was actually better at the end of treatment than prior to treatment. We feel that this is a very important differentiation from the product particularly if you're comparing us to, for example, surgery and facial laser. With surgery and facial laser, there's always some element of scarring. There were no serious adverse events and no adverse events related to the treatments overall an excellent safety profile. We also looked at tissue samples for gene target engagement and knockdown and we saw a significant reduction of both TGF-ß1 and COX-2 in the pretreatment versus the post-treatment tissues. And then we also saw the reduction of downstream oncogenic biomarkers such as Ki-67, NF-κB, and β-Catenin. So, overall, a very good biological response to the drug as well.

We've now initiated the phase IIb study for the treatment of isSCC. We started this in May 2021. And we plan to file IND in China in the second half of 2022 and then add China's sites to the study. We're going to look at a placebo group as well in this study, so it'll be a randomized, double-blind, placebo-controlled study, we're going to study up to 100 subjects and will do a 40-subject run in determining the best two doses to move into the larger subgroup. And we'll report this interim analysis sometime in the second half of 2022. And the endpoint is still complete response or histological clearance.

We're also looking at this drug STP705 for the treatment of BCC, which is the second type of non-melanoma skin cancer. We started this study in January 2021. And we recently released interim results. We're looking at five different dosing cohorts now a 30, 60, 90, 120 and 180 microgram dosing group. We're treating these subjects the same as in the isSCC study with a once-weekly injection for six weeks and then removal of the treated area one week after the last treatment. So far, we're seeing a dose-dependent response, we're seeing good levels of histological clearance. We've completed dosing for the 120-microgram dosing cohort and based on a very solid and strong safety profile, we're now adding a 180-microgram dosing cohort. We anticipate completing all of these subjects and a full report to be released in the second half of 2022. We see no significant cutaneous skin reactions and no treatment-related AE's or SAE's, Skin Response Scores showed no local reactions and there were no dose-limited toxicities noted to date. Overall, a continued excellent safety profile and we're seeing a nice response in terms of histological clearance.

To expand on the use of this asset we are looking at this as a potential modality for fat reduction or fat sculpting. The animal models that we did are the porcine model of mini pig and we compare this to a Kybella. Kybella is now an approved product for supplemental fat reduction of double chin. And we use the same animal model that Kybella used. In our model where we dose STP705 120 micrograms, and 200 micrograms one time. We compare that to Kybella dosing twice as per their label. And we use the Kybella dose that's currently being used in human subjects. Overall, we saw an improved response compared to Kybella and we saw a significant reduction in the fat compared to the control group. We plan on initiating a phase I study where we'll look at both safety and efficacy for fat reduction and this will start sometime in the first half of 2022. We anticipate having a full report on this in Q1 2023.

We're now actually looking at STP707 as well. This is the IV formulation asset which targets TGF-ß1 and COX-2. We've recently dosed the first subject in a solid tumor study. This is phase

I study dose escalation. We're also looking at this as an anti-fibrosis and PSC primary sclerosing cholangitis. We recently dosed the subject in that as well, in March. With the study of the solid tumor, we recently completed the first cohort, we've had a safety evaluation and the recommendation is that we proceed to the second dosing cohort. On the anti-fibrosis side, we will dose more cohorts in this study after a 60-day evaluation period. So based on the FDA's feedback, we will observe these subjects for 60 days, and then we'll start our next cohort of subjects. But overall, we've seen no significant safety concerns.

This is the GalNAc program where we specifically utilize GalAhead™. This is STP122G. This is animal data where the target is Factor XI. Factor XI reduction is used to aid in anticoagulation. So, this actual therapeutic target has a wide variety of indications that we can use. And the competitor would be the novel oral anticoagulants, many of which are coming off patent within the next five years. If you look at the data, we saw a very robust response with a significant reduction in Factor XI activity. And this also correlated with a very strong surgical response where we saw PTT was elevated. This is exactly what we want to see. And then the PT pathway of the prothrombin time pathway is preserved. That's why this target is potentially much safer than traditional anticoagulants and also potentially safer than the novel, like vitamins. And the robust response receiving the long duration of action suggests we could potentially dose this drug four times a year. We anticipate filling this IND late second half of 2022.

Dr. David Mark Evans, Executive Director and Chief Scientific Officer of Sirnaomics：

Hi, my name is David Evans. I'm the Chief Scientific Officer of the company. This slide shows STP908. STP908 comprises siRNA targeting highly conserved regions of two gene segments, SARS-CoV-2, and related viruses, including SARS, Omicron, and Delta. Formulated with our PNP, HKP(+H) into nanoparticles for delivery. We have demonstrated that IV administration of these nanoparticles delivers siRNA effectively to the lung. And so, we use this mode of administration to probe. A prophylactic model above where we administered one dose ahead of infection and the therapeutic model for all doses within a supposed infection with the virus below. As can be seen from this slide, both regimens produced a remarkable ability to rescue animals from a lethal dose of the virus. Mortality data suggests that 50% of the STP908 treated animals and both regimens survived at day 14.

Our non-wholly owned subsidiary company RNAimmune is developing mRNA vaccines using a proprietary delivery platform. They have developed an mRNA construct against COVID-19,

including Delta and other variants. The data suggest that these vaccines can generate a pronounced immune response in animals. And a neutralization of viral proteins by serum derived from treated animals, as well as the pronounced induction of antibodies that can block viral infection, resulting in mark inhibition of a number of different strains of SARS-CoV-2. They are planning to fill the product of the US FDA by the end of 2022.

Dr. Patrick Lu, founder, chairman of the Board, Executive Director, President and CEO of Sirnaomics：

I am very pleased to report to you that we have established Guangzhou fill and finish plan with GMP compliance. This particular facility is already up and running. It is at full capacity, which already produced multiple batches of drug products to support our preclinical development and clinical development. The successful establishment of this facility marks an important transition of Sirnaomics from a biotechnology company to a biopharmaceutical company with a large-scale product production capacity. Currently, this facility can produce up to 50,000 vials of lyophilized human injectables drug product.

Looking in the future, Sirnaomics' clinical pipeline, there will be multiple milestones. If we just look at this particular slide, there are multiple programs that have moved forward from last year to this year. And currently, we have 2 clinical assets with 7 clinical programs ongoing and by the end of this year, we will have 4 clinical assets with more than a dozen clinical trials ongoing. By the end of 2023, we will have 9 clinical assets, have more than 15 clinical trials moving forward. Based on the clinical development, Sirnaomics will continue being the leader in the RNA therapeutic development field and we will take the leadership position for oncology RNA therapeutic development. We believe Sirnaomics going to be the TOP 3 RNAi therapeutic company on the global stage and the leading company in Asia for RNA therapeutic development.

Nigel Yip, Vice President of Corporate Finance, China Chief Financial Officer of Sirnaomics：

Hi everyone, I am Nigel Yip, and I am the China CFO for Sirnaomics. Let me give you an overview of our P&L.

Our loss for the year increased to $216 million dollars as a result of an increase in (i) changes in fair value of financial liabilities; (ii) research and development expenses; (iii) administrative expenses; and (iv) listing expenses.

The loss of changes in fair value of financial liabilities, which is a non-cash item, increased to $146 million dollars, as a result of the increase in the valuation of the company. Admin expenses increased to $16 million dollars, contributed by expansion of business in terms of the number of employees and office space. Our research and development expenses increased to $41 million dollars, as a result of accelerated execution after the completion of our past fundraising activities. Such increase were in line with the Group's continuous R&D efforts to support the Group's advancing and expansion of pipeline. Listing expenses for professional parties concerning our IPO amounted to $12 million dollars. Cash spending in operating activities increases to $57 million dollars, representing our continual business expansion including both R&D and G&A. Net cash from financing activities increases to $171 million dollars, capturing proceeds successfully raised at our IPO and Series E round. We have a closing cash balance of $212 million dollars which is expected to at least support our runway for two years. This is the end of our presentation, Thank you.