Tiziana Life Sciences Provides Corporate Update

Tiziana Life Sciences is a dual-listed (NASDAQ:TLSA, AIM:TILS) clinical stage biotechnology company that specializes in the developing transformative therapies for autoimmune and inflammatory diseases, degenerative diseases and cancer related to the liver. Our clinical pipeline includes drug assets for Crohn's Disease, COVID-19 and Progressive Multiple Sclerosis and Hepatocellular Carcinoma. The Group combines field-leading medical scientists, providing deep knowledge and novel insights into disease mechanisms, together with a highly experienced clinical development team. Since its foundation in 2013, Tiziana Life Sciences has expanded its pipeline of assets to include clinical stage development therapeutic candidates in both oncology and immunology, as well as a pre-clinical drug discovery pipeline.

Key performance indicators

The Board monitors the Key Performance Indicators (KPIs) that it considers appropriate for the industry and stage of development of the Group. The Group is a research and development based biotechnology company concerned with a number of pre-clinical and clinical assets. These assets require sufficient investment to reach defined milestones by which the Group and its investors can judge the chances of ultimate success and thereby the value of the Group. At this stage of Group development significant sources of revenue generation are unlikely and the Group is cash consuming. The Group KPIs are therefore chosen to monitor the progress of the individual scientific programmes, the external market environment for the potential drugs being developed and the cash requirements of the Group.

Non-financial KPIs

Successful Progress in clinical trials

Completion of the Phase 2a Milciclib clinical trial.

- **In March 2019, the Independent Monitoring Committee, or IDMC, reviewed safety data from patients as of February 26, 2019 and concluded that the administration of Milciclib to patients with advanced HCC was not associated with unexpected signs or signals of toxicity.**
- **In June 2019, the Group completed the Phase 2a Milciclib clinical trial, with clinical safety and efficacy result reported in July 2019.**

Completion of Phase 1 Clinical Trials for Nasally and Orally Administered Foralumab.

- **27 healthy subjects were enrolled in and completed a Phase 1 clinical trial for progressive multiple sclerosis indication for nasally administered Foralumab.**
- **An enteric-coated capsule formulation using a proprietary and novel technology has been developed for oral administration of Foralumab.**
- **cGMP manufacturing of clinical trial materials for a Phase 1 study has been completed and an IND has been submitted in March 2019.**
- **On September 9, 2019, the FDA granted approval to initiate the Phase I clinical trials to evaluate the safety and pharmacokinetics of oral Foralumab at 1.25, 2.5 and 5.0 mg/day as a single ascending dose study. The study was completed in December 2019**

Financial KPIs

Cash consumption

The cash position of the business is measured on a continual basis with reference both to the general and administrative expenses required to run the Group, and more particularly to the cash required for ongoing research, development and acquisition of the Group's scientific assets. During 2019 the main use of the Group's funds was completion of Phase II for Milciclib on single agent trials, involving recruitment of patients across different countries (Italy, Greece and Israel) and completion of Phase I clinical trials with nasally and orally administered Foralumab in healthy volunteers. Management monitors its cash consumption on a monthly basis and a cash projection is presented at every quarterly board meeting.

The Group monitors current and projected cash consumption to ensure that there are sufficient funds available to develop the Group's scientific assets. The Group successfully raised additional cash during 2019 to fund research and development, to meet the Group's ongoing liabilities in respect of licence agreements, and for general working

capital purposes. The Group maintains a virtual operating model resulting in low cash consumption for general and administrative expenses during the period.

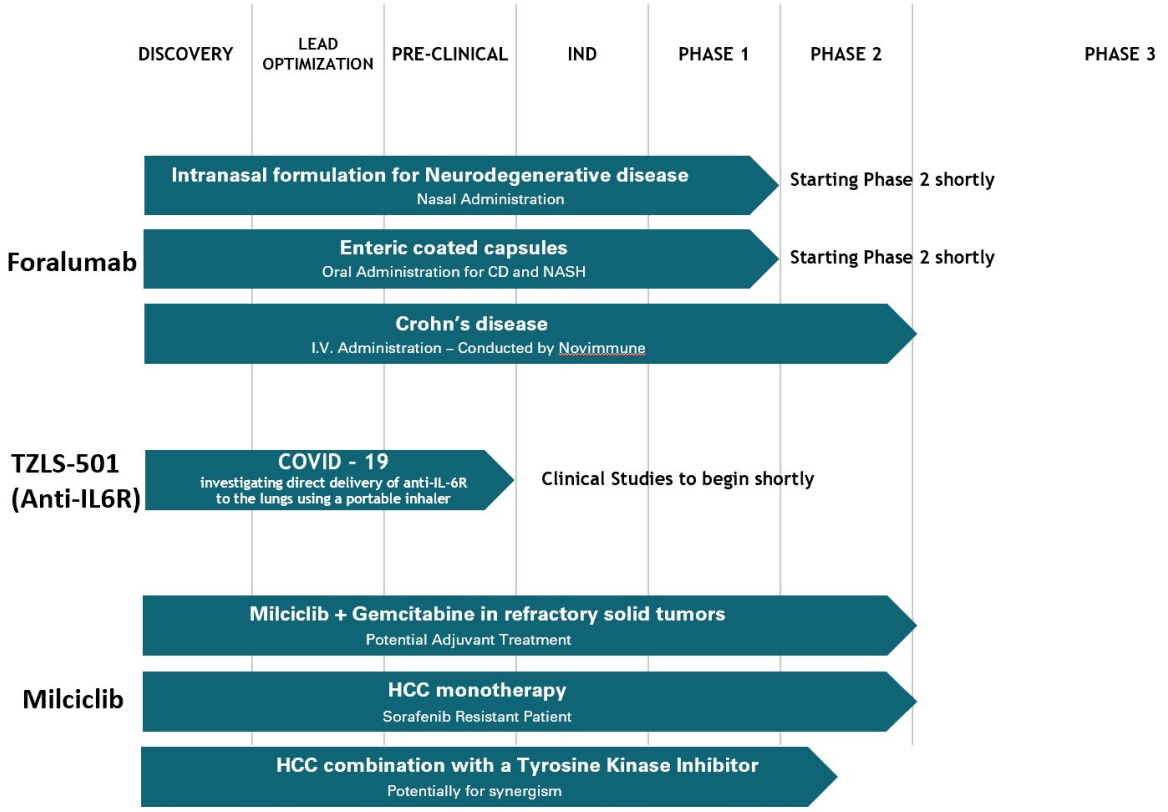
Share price
The Group monitors its share price to determine whether the market view of the Group's position and prospects is aligned with the view of management, and to consider the most appropriate time to raise further capital in the interest of the Group and current shareholders. The Group raised funds via an initial public offering of American Depository Shares on the Nasdaq Global market in November 2018 at a share price of $0.99 per share and ended the financial period at $0.75 per share.

Clinical Programmes

The Group is focused on the discovery and development of novel molecules and related diagnostics to treat high unmet medical needs in oncology and immunology.

Our lead product candidate in immunology are Foralumab (TZLS-401), which we believe is the only fully human anti-CD3 monoclonal antibody, or mAb, in clinical development. MAbs represent a single pure antibody produced by single clones and are an important class of human therapeutics for treating cancers and autoimmune diseases. In addition, we are accelerating development of another fully human monoclonal antibody anti-IL6R (TZLS-501) to treat acute inflammation resulting from infection with viral agents such as Coronaviruses. Antibodies produced in animals for use in humans, lead to strong, immune responses limiting their effectiveness and potentially leading to severe side effects. A process known as "humanization" removes most of the animal components of the antibody thereby lowering the immune response from the human immune system. The entire omission of other animal material, as in fully human antibodies, is the optimal goal to avoid incompatibility with the human immune system. Our lead product candidate in oncology is Milciclib (TZLS-201), which is an orally bioavailable, small molecule broad spectrum inhibitor of cyclin-dependent kinases, or CDKs, and Src family kinases. CDKs are a highly conserved family of enzymes that phosphorylate a specific group of proteins that are involved in regulating the cell cycle. The cell cycle is a series of events that takes place in cells leading to division and duplication of its DNA to produce two daughter cells. Src family kinases are non-receptor tyrosine kinase proteins encoded by the Src gene also involved in regulating cell growth and potential transformation of normal cells to cancer cells. We have a drug discovery pipeline of small molecule new chemical entities, or NCEs, and biologics. We employ a lean and virtual research and development, or R&D, model using highly experienced teams of experts for each business function to maximize value accretion by focusing resources on the drug discovery and development processes. Our mission is to design and deliver next generation therapeutics and diagnostics for oncology and immune diseases of high unmet medical need by combining deep understanding of disease biology with clinical development expertise.

DEVELOPMENT PIPELINE



Foralumab (TZLS-401 / NI-0401)

Foralumab is a fully human engineered anti-CD3 monoclonal antibody (mAB). It was in-licensed in December 2014 from Novimmune. In January 2016, Tiziana outlined its clinical development plan for Foralumab with initial plans to evaluate the drug in two clinical indications: non-alcoholic steatohepatitis (NASH) and inflammatory bowel disease (IBD).

As the only fully human engineered human anti-CD3 mAB in clinical development, Foralumab has significant potential advantages such as a shorter treatment duration and reduced immunogenicity. With completion of the intravenous dosing for our Phase 2a trial in Crohn's Disease, Foralumab's ability to modulate T-cell response enables potential extension into a wide range of other autoimmune and inflammatory diseases, such as GvHD, ulcerative colitis, multiple sclerosis, type-1 diabetes (T1D), inflammatory bowel disease (IBD), psoriasis and rheumatoid arthritis.

Foralumab is being developed as both an immunosuppressive and immunomodulatory agent, with therapeutic benefits of rendering T-cells unable to orchestrate an immune response and induction of immune tolerance via maintenance of regulatory T-cells. There is further potential for Foralumab to be combined with the Company's TZLS-501, a fully human anti-IL-6R mAB in development to target autoimmune and inflammatory diseases.

In November 2016, Tiziana announced new data for oral efficacy in humanized mouse models with Foralumab, a major milestone and a potential breakthrough for the treatment of NASH and autoimmune disease. This unique oral technology stimulates the natural gut immune system and potentially provides a therapeutic effect in inflammatory and autoimmune diseases with greatly reduced toxicity. Positive therapeutic effects with Foralumab were consistently demonstrated in animal studies conducted by Prof. Kevan Herold (Yale University) and Prof. Howard Weiner (Harvard University).

On 16 April, 2018, the Group entered into an exclusive license agreement with The Brigham and Women's Hospital, Inc. relating to a novel formulation of Foralumab dosed in a medical device for nasal administration. An investigational new drug application (IND) for the first-in-human evaluation of the nasal administration of Foralumab in healthy volunteers for progressive multiple sclerosis indication was filed in the second quarter of 2018. Subsequent to IND approval, a single-site, double-blind, placebo-controlled, dose-ranging Phase 1 trial with nasally administered Foralumab at 10, 50 and 250 µg per day, consecutively for 5 days to evaluate biomarkers of immunomodulation of clinical responses was initiated in November 2018. The trial conducted at the Brigham and Women's Hospital, Harvard Medical School, Boston, MA, in healthy volunteers. 18 subjects received Foralumab treatment and 9 patients received placebo. All nasal doses were well tolerated. The study was completed in September 2019. Phase 1 clinical data demonstrated that nasally administered Foralumab, was well-tolerated and no drug-related safety issues were reported at any of the doses. No drug-related changes were observed in vital signs among subjects at pre-dose, during treatment and at discharge. The mean blood pressure (BP) during the 5 days of treatment were; Cohort A (10 µg/d):124/73, Cohort B (50 µg/d): 119/67 and Cohort C (250 µg/d):113/65 compared to placebo:118/67). Heart rates, respiratory rates and oral temperatures were unchanged among the 3

cohorts compared to the placebo. Nasally administered Foralumab at the 50 µg dose suppressed cytotoxic CD8+ as well as perforin secreting CD8+ cells, which have been implicated in neurodegeneration in multiple sclerosis (MS). Treatment at 50 mg stimulated production of anti-inflammatory cytokine IL-10 and suppressed production of pro-inflammatory cytokine IFN-γ. Taken together, the treatment showed significant positive effects on the biomarkers for activation of mucosal immunity, which are capable of inducing site-targeted immunomodulation to elicit anti-inflammatory effects. Upon successful completion of the Phase 1 trial, we intend to initiate a Phase 2 study for nasally administered Foralumab in progressive multiple sclerosis patients in the second quarter of 2021.

An enteric-coated capsule formulation using a proprietary and novel technology has been developed for oral administration of Foralumab. cGMP manufacturing of clinical trial materials for a Phase 1 study has been completed and an IND has been submitted in March 2019.

On September 9, 2019, the FDA granted approval to initiate the Phase I clinical trials to evaluate the safety and pharmacokinetics of oral Foralumab at 1.25, 2.5 and 5.0 mg/day as a single ascending dose study. The study was completed in December 2019 at Brigham and Women's Hospital (Boston, MA USA). Formulated Foralumab powder encapsulated in enteric-coated capsule was well-tolerated at all doses tested and there were no drug-related safety issues observed even at the highest dose of 5 mg in this trial. Based on successful Phase 1 data, we intend to conduct a Phase 2 study using Crohn's Disease patients starting in the second half of 2020.

Milciclib (TZLS-201)

Milciclib, Tiziana's lead small molecule drug, was exclusively licenced in January 2015 from Nerviano Medical Sciences. Milciclib is an orally bioavailable, broad spectrum inhibitor of Cyclin Dependent Kinases (CDKs): 1, 2, 4, 5 and 7 and Src family kinases. Cyclin dependent kinases are a family of highly conserved enzymes that are involved in regulating the cell cycle. Src family kinases regulate cell growth and potential transformation of normal cells to cancer cells. A unique feature of Milciclib is its ability to reduce microRNAs, miR- 221 and miR-222, which silence gene expression. miR-221 and miR-222 promote the formation of blood vessels (angiogenesis) that are important for the spread of cancer cells (metastasis). Levels of these microRNAs are consistently increased in hepatocellular carcinoma ("HCC") patients and may contribute towards resistance to treatment with Sorafenib. As a result, the Group are investigating Milciclib both as a monotherapy and as a combination treatment with Sorafenib.

To date, Milciclib has been studied in a total of eight completed and ongoing Phase 1 and 2 clinical trials in 316 patients. In these trials, Milciclib was observed to be well-tolerated and showed initial signals of anti-tumour action. Prior to in-licensing, Milciclib was granted orphan designation by the European Commission and by the U.S. Food and Drug Administration ("FDA") for the treatment of malignant thymoma and an aggressive form of thymic carcinoma in patients previously treated with chemotherapy. In two Phase 2a trials, CDKO-125a-006 and CDKO125a-007, Milciclib showed signs of slowing disease progression and acceptable safety.

The Group initiated a Phase 2a trial (CDKO-125a-010) of Milciclib safety and tolerability as a single therapy in Sorafenib-resistant patients with HCC in the first half of 2017. Typically, this population of patients have an advanced form of the disease with poor prognosis and an average overall survival expectancy of 3-5 months In May 2018, the Independent Data Monitor committee (IDMC) completed an interim analysis of tolerability data from the first eleven treated patients and recommended expansion of the initial cohort to an additional 20 patients to complete the trial enrolment, which was completed in December 2018. .

In March 2019, the Independent Monitoring Committee, or IDMC, reviewed safety data from patients as of February 26, 2019 and concluded that the administration of Milciclib to patients with advanced HCC was not associated with unexpected signs or signals of toxicity. 28 out of 31 treated patients were evaluable, 14 completed the 6-month duration study. The most frequent adverse events such as diarrhea, ascites, nausea, fatigue, asthenia, fever, ataxia, headache, and rash were manageable. No drug-related deaths were recorded.

The clinical activity assessment in evaluable patients was based on the independent radiological review using the modified Response Evaluation Criteria in Solid Tumors (mRECIST).

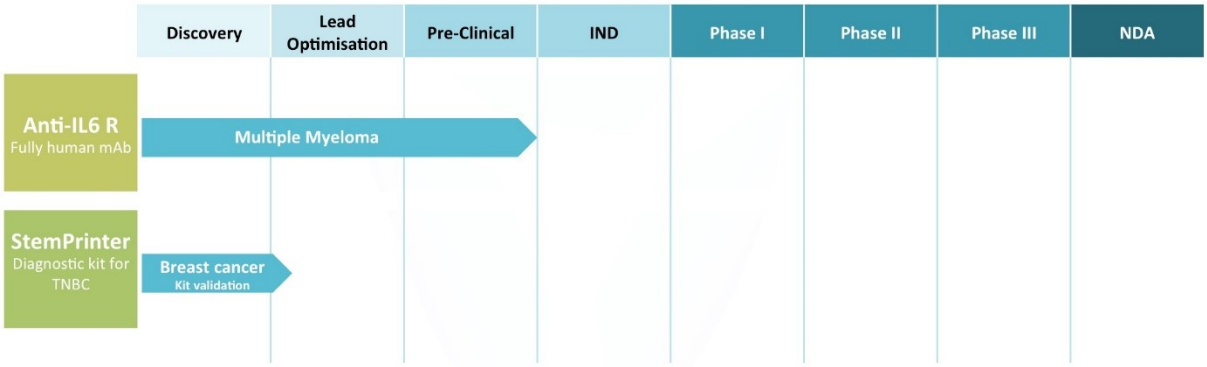
- 14 out of 28 (50%) evaluable patients completed 6-month duration of the trial.
- Both median TTP and PFS were 5.9 months (95% Confidence Interval ("CI") 1.5-6.7 months) out of the 6months duration of the trial.
- 16 of 28 (57.1%) evaluable patients showed 'Stable Disease'
- One patient (3.6%) showed unconfirmed 'Partial Response' (PR).
- 17 of 28 (60.7%) evaluable patients showed 'Clinical Benefit Rate' defined as CBR=CR+PR+SD (with CR representing Complete Remission).

The Phase 2a trial was completed in June 2019 with clinical safety and efficacy result reported in July 2019.

Since overexpression of CDKs and dysregulation in pRB pathway (regulates transcription factors critical for cell cycle progression) are prominently associated with tumor cell resistance to certain chemotherapeutic drugs, inhibition of multiple CDKs is an appealing approach to improve clinical responses in cancer patient's refractory to existing treatment options. A Phase 1 dose-escalation study of Milciclib in combination with gemcitabine in patients

with refractory solid tumors exhibited clinical activity in patients including those refractory to gemcitabine. We plan to explore a combination approach in patients with HCC.

Pre-Clinical Programmes



In pre-clinical development, the Group has two programmes:

Anti-IL6R (TZLS-501)

TZLS-501 is a fully human engineered mAb targeting the interleukin-6 receptor (IL-6R). Tiziana Life Sciences licensed the intellectual property from Novimmune in January 2017. This fully human mAb has a unique mechanism of action that binds to both the membrane-bound and soluble forms of the IL-6R resulting in lowering of circulating levels of IL-6 in the blood. Excessive production of IL-6 is regarded as a key driver of chronic inflammation, associated with autoimmune diseases such as multiple myeloma, oncology indications and rheumatoid arthritis, and the Group believes that TZLS-501 may have potential therapeutic value for these indications.

In preclinical studies, TZLS-501 demonstrated the potential to overcome limitations of other IL-6 blocking pathway drugs. Compared to Tocilizumab and Sarilumab, while binding to the membrane-bound IL-6R complex TZLS-501 has shown a higher affinity for the soluble IL-6 receptor as seen from the antibody binding studies conducted in cell culture. TZLS-501 also demonstrated the potential to block or reduce IL-6 signaling in mouse models of inflammation. The soluble form of IL-6 has been implicated to have a larger role in disease progression compared to the membrane-bound form. (Kallen, K.J. (2002). “The role of trans signaling via the agonistic soluble IL-6 receptor in human diseases”. Biochimica et Biophysica Acta. 1592 (3): 323–343.).

Recently, chronic inflammation is believed to be associated with severe lung damage observed with COVID-19 infections and acute respiratory illness. China’s National Health Commission has recommended the use of anti-IL6R mAbs for treatment of inflammation and elevated cytokine levels (“cytokine storm”) in COVID-19 patients.

StemPrintER

StemPrintER is a multi-gene signature assay intended for use in patients diagnosed with estrogen-receptor positive ER+/HER2 negative breast cancers. The Group believes this in-vitro prognostic test will be used in conjunction with clinical evaluation to identify those patients at increased risk for early and/or late metastasis. StemPrintER is designed to help physicians distinguish ER+/HER2 negative patients:

- with an elevated risk of early recurrence (<5 years) who could benefit from chemotherapy in addition to hormonal therapy
- with a high risk of late recurrence who could benefit from prolonged endocrine treatment up to 10 years
- with a low risk of early recurrence who might be spared chemotherapy or be eligible for less aggressive treatments

The diagnostic has a unique biological basis, being based on the detection of cancer stem cell markers, uses a reliable platform (qRT- PCR, FFPE), and has been evaluated in an initial retrospective validation study using a consecutive cohort of approximately 2,400 patients with breast cancer. The development team is preparing for a retrospective validation study using an independent cohort and has conducted a pre- submission meeting with the FDA.

Financial summary

Consolidated Statement of Comprehensive Income

The Group has made a loss for the year of £7,178k (2018 restated: £6,063k). The loss is detailed in the consolidated statement of comprehensive income on page 32.

Research and development costs were £2.9 million for the year ended December 31, 2019 as compared to £4.1 million for the year ended December 31, 2018, a decrease of £1.2 million. The decrease in cost is a result of the completion of the Miciclib Phase 2a of clinical trials during the first half of 2019.

Consolidated Statement of Financial Position

At the end of the year the Group cash balance amounted to £153k (2018: £4,165k) and the total assets of the Group amounted to £1,808k (2018: £5,436k). To bolster our cash reserves, the Group raised $10m via a public offering of American Depositary Shares ("ADSs") on the NASDAQ Global Market in March 2020

Fund raising

In the period, the Group successfully raised funds to further progress its on-going clinical trials and its pre-clinical pipeline.

On 1 November 2019, the Company announced that it had raised £1,434,000 cash by issue of convertible unsecured loan notes, with warrants attached. The Loan Notes are expected to be short term instruments and carry a coupon of 16% per annum and are convertible (together with all accrued interest) into ordinary shares of nominal value £0.03 each in the capital of the Company at a conversion price of 42p. The warrants issued in connection with the Loan Notes entitle the holders to subscribe for one additional share per conversion share at the same price of 42p. The warrants may be exercised for a period of up to 5 years from their issue.

COVID-19

We remain cognisant of the potential impact of coronavirus (COVID-19) on our operations and have taken the steps necessary to maintain the integrity of the Company's assets and the health and wellbeing of our employees. The Company is well financed, resilient and well positioned to weather any financial downturn occurring as a result of the outbreak. Indeed, the Company has raised additional funds through its ongoing "At the Market" or "ATM" Sales Agreement with Think Equity (a division of Fordham Financial Management, Inc.) to raise up to US$20m from the sale of ADSs.

We are also aware of the responsibility we have as a member of the global healthcare community we have developed investigational new technology to treat COVID-19 infections.

Outlook and strategy

We have continued to progress our pipeline of drugs to treat rare cancers and autoimmune and inflammatory diseases.

We have developed investigational new technology to treat COVID-19 infections, which consists of direct delivery of anti-IL-6 receptor (anti-IL-6R) monoclonal antibodies (mAbs) into the lungs using a handheld inhaler or nebulizer. Preclinical studies are ongoing and we hope to commence a trial investigating the direct delivery of an anti-IL-6 mAb to the lungs using a portable inhaler.

We have outlined our clinical development plan for Foralumab and anticipate to commence Phase 2 trials for oral administered Foralumab in Crohn's disease patients and nasally administered Foralumab in multiple sclerosis patients.

For Milciclib, we are planning to initiate a Phase 2b clinical trial in HCC patients with Milciclib in combination with a Tyrosine kinase inhibitors such as Regorafenib or Sorafenib.

We are continuing development of StemPrint ER diagnostic tester. Recently, StemPrintER results were announced, from a poster selected for discussion session at the American Society of Clinical Oncology (ASCO) Virtual Conference, demonstrating the superiority of StemPrintER stem cell based genomic prognostic tool versus the market leader, Oncotype DX, in predicting recurrence in ER+/HER2- postmenopausal breast cancer patients. Looking ahead, Tiziana is confident that it is well positioned to advance these programs to their next respective value inflection points.

We would like to thank the staff and Board members for all their contributions and shareholders for their continued support during a successful year.