

Tiziana Life Sciences PLC

(TLSA - NASDAQ)

Partnership with Precision

Based on our DCF model and a 15% discount rate, Tiziana is valued at approximately \$7.50 per ADR share. Our model applies a 15% probability of ultimate approval and commercialization for the portfolio of assets including foralumab and miliclib. The model includes contributions from the United States and global developed markets.

Current Price (9/14/2021) **\$1.66**
 Valuation **\$7.50**

SUMMARY DATA

52-Week High **5.44**
 52-Week Low **1.46**
 One-Year Return (%) **-49.1**
 Beta **-0.10**
 Average Daily Volume (sh) **674,260**

Shares Outstanding (mil) **97.3**
 Market Capitalization (\$mil) **162**
 Short Interest Ratio (days) **0.5**
 Institutional Ownership (%) **14.5**
 Insider Ownership (%) **39.5**

Annual Cash Dividend **\$0.00**
 Dividend Yield (%) **0.00**

5-Yr. Historical Growth Rates
 Sales (%) **N/A**
 Earnings Per Share (%) **N/A**
 Dividend (%) **N/A**

P/E using TTM EPS **N/A**
 P/E using 2020 Estimate **N/A**
 P/E using 2021 Estimate **N/A**

Zacks Rank **N/A**

OUTLOOK

Tiziana is a research and development company advancing a portfolio of candidates for autoimmune disease, cancer and COVID. The lead candidate, foralumab, is a fully human anti-CD3 antibody, being investigated in multiple sclerosis (MS), Crohn's disease (CD) and COVID, administered intranasally and orally via enteric coated capsules. Foralumab is also being used in allogeneic CAR T as a lymphodepletion agent in partnership with Precision BioSciences.

Miliclib is the second candidate and is being investigated as a combination product in multiple oncology indications. The third candidate, TZLS-501, is an anti-IL-6R receptor antibody expected to be the subject of an IND submitted in 2021. TZLS-501 is being investigated as a treatment for COVID and other pulmonary diseases such as ARDS.

Ph2 foralumab clinical trials for MS and CD are targeted for 2021 & Ph2 combination trials for miliclib in coming quarters. Tiziana differentiates itself in the use of intranasal, oral and inhaled formulations of mAbs that are able to avoid shortcomings of infused & subcutaneous administration.

Our valuation assumes a 2027 regulatory approval & 2028 commercialization of foralumab for both pMS and CD in conjunction with partners.

Risk Level **Above Average**
 Type of Stock **Small-Growth**
 Industry **Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue

(In millions of GBP)

	Q1	Q2	Q3	Q4	Year
	(Mar)	(Jun)	(Sep)	(Dec)	(Dec)
2019	0.0 A				
2020	0.0 A				
2021					0.0 E
2022					0.0 E

Earnings per Share

	Q1	Q2	Q3	Q4	Year
2019	0.00 A	-0.03 A	0.00 A	-0.03 A	-0.05 A
2020	0.00 A	-0.03 A	0.00 A	-0.09 A	-0.12 A
2021					-0.11 E
2022					-0.10 E

WHAT'S NEW

Tiziana Update Call with Analysts and Investors

Precision BioSciences

On September 8, 2021 following the market close, Tiziana Life Sciences (TLISA) hosted a web conference centered on its recent exclusive license agreement with Precision BioSciences (NASDAQ: DTIL) for foralumab lymphodepletion support of allogeneic chimeric antigen receptor T cell (CAR T) therapy in cancer. Precision specializes in allogeneic CAR T therapy which provides advantages over autologous CAR T. More broadly, Precision is a genome editing company offering its ARCUS genome editing program. Its primary clinical programs are in blood cancers including Non-Hodgkin lymphoma (NHL) and B cell acute lymphoblastic leukemia (B-ALL).

One of the key benefits of Precision's CAR T offering is that it can be administered off the shelf. Precision's CAR T cells are specially engineered to delete 99% Cluster of Differentiation 3 (CD3) expression, a receptor that is normally found on effector T cells. Foralumab is an anti-CD3 fully human monoclonal antibody (mAb) and is expected to bind to T cell CD3 receptors, thereby preventing them from clearing the allogeneic CAR T cells. The use of foralumab can replace other conditioning agents such as cyclophosphamide, which is associated with neurotoxicity. Thus, adding foralumab to the therapy is expected to spare Precision's T cells while suppressing the patient's T cells, improving the side effect profile and allowing Precision's T cells to have better efficacy.

Tiziana CEO, Dr. Kunwar Shailubhai, began the call with a review of foralumab. Foralumab is the only fully human anti-CD3 mAb. Much clinical development has been done on anti-CD3 mAb, namely OKT-3, a fully mouse anti-CD3 antibody developed by Johnson & Johnson and approved by the FDA. However, because of the mouse basis of the antibody, it elicited a strong, negative immune reaction and formation of anti-drug antibodies and stimulated cytokine release syndrome. OKT-3 was taken off the market as a result. But clinical efficacy was good. Thus, it was worth investigating the development of a fully human anti-CD3 antibody, especially for renal transplant or graft-versus-host-disease (GVHD). Visilizumab and teplizumab are follow-on humanized anti-CD3 antibodies previously developed by PDL Biopharma. Efficacy was good, but long-term treatment was limited by formation of anti-drug antibodies. To prevent the immune response to the mouse elements, Tiziana's foralumab is a fully human anti-CD3 mAb, and has not elicited anti-drug antibodies in clinical work thus far and has not triggered immune reactions observed in previous anti-CD3 candidates.

Precision's CAR T cells do not express CD3 and are not discernible to foralumab, making them an appropriate candidate for lymphodepletion. Proper lymphodepletion can extend the durability of the CAR T cell therapy and lower the risk of cancer recurrence. Cyclophosphamide and fludarabine chemotherapies are often used for lymphodepletion conditioning; however their use has been limited by neurotoxicity. Foralumab could replace other lymphodepleting agents, or even function by itself as a solution. Together, the allogeneic non-CD3-expressing CAR T with foralumab could provide better efficacy in currently unmanaged cancers.

Clinical Trials and Analyst Questions

Dr. Shailubhai updated on Tiziana's clinical progress. In the last year and a half, four trials were completed including Phase I trials for oral and nasal foralumab which laid the foundation for Phase II, as well as oral foralumab in Crohn's and nasal foralumab in multiple sclerosis. Tiziana also completed a preliminary trial in Brazil for COVID-19 and is currently targeting a Phase II for hospitalized COVID-19 patients.

During the Q&A session, topics began with teplizumab's (ProventionBio) recent BLA Complete Response Letter (CRL). Teplizumab is a humanized anti-CD3 antibody being developed for prevention of Type 1 diabetes that recently received a CRL from the FDA for its candidate teplizumab. Shailubhai cited deficiencies with CMC and there appear to have been issues that the FDA cited with pharmacokinetic comparability as well.¹ Tiziana management remains optimistic for foralumab, which is fully human and has not seen anti-drug antibody response thus far in clinical evaluation nor has immunotoxicity been observed. Shailubhai noted that autoimmune disorders could be another area where a fully-humanized anti-CD3 antibody could become useful.

¹ Provention Bio Receives Complete Response Letter (CRL) to Biologics License Application (BLA) for Teplizumab for the Delay of Clinical Type 1 Diabetes (T1D) in At-risk Individuals - Jul 6, 2021

Topics also reviewed the mechanism of lymphodepletion. When allogeneic (foreign) therapeutic CAR T cells are injected into the body, the patient's immune cells may attack the CAR T cells that are intended to treat the patient. Thus, cancer progression is an issue especially if CAR T therapy is terminated prematurely by the patient's own immune system. Lymphodepletion drugs are used to attenuate the patient's immune system, thereby enhancing clinical outcomes. However, neurotoxicity is an issue for lymphodepletion agents. Foralumab binds to CD3, depleting the cells expressing it (patient's non-CAR T cells), allowing the CAR T cells that were engineered and administered to work. Precision's CAR T cells lack CD3 and can be used for long periods of time avoiding whole-body immunosuppression and toxicity.

Analyst questions then shifted direction towards Tiziana's clinical progress and expectations for upcoming milestones. Tiziana completed Phase I nasal foralumab in COVID-19 with positive results. Foralumab was given once daily for ten consecutive days. Post-study analysis provided evidence that T regs were upregulated which is a favorable finding in light of a study conducted by Johns Hopkins where researchers found that T regs are depleted in COVID-19. By restoring T reg balance, foralumab may be able to provide clinical benefit for these patients.

Next steps for foralumab in Crohn's Disease is a Phase II multicenter trial in the US and Europe. Management anticipates the Crohn's study starting by end of this year or early next year. The nasal foralumab for secondary progressive multiple sclerosis (SPMS) program is underway and under the individual access program, one patient has completed three months of treatment. Management believes the data generated so far is favorable and nasal administration during the three months of therapy has shown no signs of toxicity. When complete, the data will be reviewed and will guide the next steps in conjunction with FDA guidance. Tiziana is also now considering a similar program in Europe.

Building on preliminary work in Brazil, Tiziana plans to target a total of 80 patients in multiple sites for its next trial of nasal foralumab in hospitalized COVID-19 patients. Tiziana must wait for the Agência Nacional de Vigilância Sanitária (ANVISA) or in English the Brazilian Health Regulatory Agency to grant approval to initiate the trial. Following approval, the trial should be able to begin a few weeks later.

Dr. Shailubhai concluded the call highlighting the recent additions to clinical leadership, Dr. Neil Graham, Dr. Kevin Schutz, as Tiziana continues its venture deeper into the clinic.

Summary

During an update call with investors Tiziana announced a deal with Precision BioSciences to use foralumab in allogeneic CAR T as a conditioning agent. This approach provides multiple benefits including the replacement of other immunosuppressive drugs that are associated with toxicity. We see this as a positive for the company, expanding the range of indications that can be pursued with this versatile anti-CD3 fully human mAb. The company is making progress in the rest of its portfolio as well, with a Phase II trial in Crohn's Disease to start soon, an active trial in SPMS and a COVID trial that is also expected to begin in the next weeks.

PROJECTED FINANCIALS

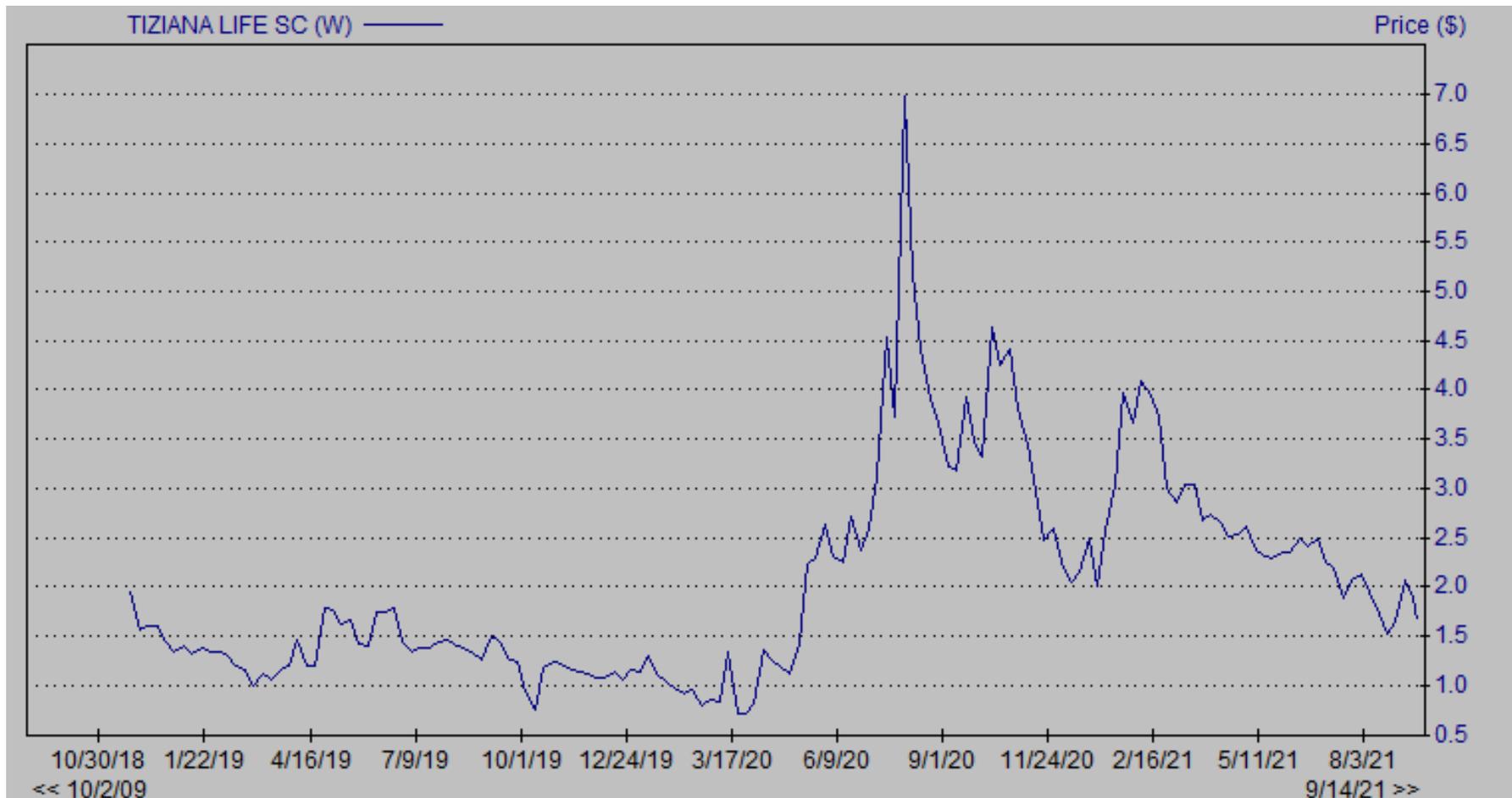
Tiziana Life Sciences PLC - Income Statement

Tiziana Life Sciences Plc	2019 A	1H A	2H A	2020 A	2021 E	2022 E
Total Revenues (£UK)	£0	£0	£0	£0	£0	£0
Research & Development	£2,910	£760	£3,907	£4,667	£19,312	£20,801
General & Administrative	£4,864	£3,169	£5,555	£8,724	£5,895	£5,968
Income from operations	-£7,774	-£3,929	-£9,462	-£13,391	-£25,207	-£26,769
Other Expense	£72	-£5	£8,681	£8,676	£0	£0
Pre-Tax Income	-£7,846	-£3,924	-£18,143	-£22,067	-£25,207	-£26,769
Provision for Income Tax	-£540	£0	-£1,719	-£1,719	£0	£0
Tax Rate	0.0%	0.0%	0.0%	7.8%	0.0%	0.0%
Net Income	-£7,306	-£3,924	-£16,424	-£20,348	-£25,207	-£26,769
Reported EPS	-£0.054	-£0.026	-£0.09	-£0.12	-£0.11	-£0.10
Basic Shares Outstanding	136,483	150,224	187,907	169,065	220,000	260,000

Source: Company Filing // Zacks Investment Research, Inc. Estimates

HISTORICAL STOCK PRICE

Tiziana Life Sciences PLC – Share Price Chart²



² Source: Zacks Research System

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