Zacks Small-Cap Research

Sponsored – Impartial – Comprehensive

October 6, 2021
John D. Vandermosten, CFA
312-265-9588 / jvandermosten@zacks.com

scr.zacks.com **10 S. Riverside Plaza, Suite 1600, Chicago, IL 60606**

Tiziana Life Sciences PLC (TLSA - NASDAQ)

1H:21 Financial Update

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 milciclib. The model includes contributions from the United States and global developed markets.

Current Price (10/5/2021)	$1.41
Valuation	**$7.50**

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.

Milciclib 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 milciclib in coming quarters. Tiziana employs 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.

SUMMARY DATA

52-Week High	**5.44**
52-Week Low	**1.37**
One-Year Return (%)	**-61.3**
Beta	**-0.02**
Average Daily Volume (sh)	**606,320**
Shares Outstanding (mil)	**97.3**
Market Capitalization ($mil)	**137**
Short Interest Ratio (days)	**0.18**
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**

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

ZACKS ESTIMATES

Revenue

(In millions of GBP)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2020	0.0 A	0.0 A	0.0 A	0.0 A	0.0 A
2021	0.0 A	0.0 A	0.0 E	0.0 E	0.0 E
2022					0.0 E
2023					0.0 E

Earnings per Share

	Q1	Q2	Q3	Q4	Year
2020	0.00 A	-0.03 A	0.00 A	-0.09 A	-0.12 A
2021	0.00 A	-0.08 A	0.00 E	-0.06 E	-0.12 E
2022					-0.10 E
2023					-0.11 E

WHAT'S NEW

First Half 2021 Results

Tiziana Life Sciences (NASDAQ: TLSA) updated on first half 2021 financial and operational results in a press release and SEC-filed Form 6-K. In the update, Tiziana reviewed recent clinical milestones for its candidates, new appointments, and financial results including plans to restructure as a Bermuda-incorporated company. We highlight major events year-to-date.

Highlights for the first half ended June 30th and to-date include:

- Completion of Brazil Phase I foralumab in COVID-19 - January 2021
- Appointment of Neil Graham MBBS, MD, MPH as CMO - January 2021
- Uplisting to LSE market, AIM delisting - January 2021
- Safety results from Phase I foralumab in COVID-19 - February 2021
- Thomas Adams, Ph.D. appointed Head of Drug Development - February 2021
- Phase II foralumab in COVID-19 planned - March 2021
- SPMS patient access granted - March 2021
- Strategic initiative with Takanawa Japan K.K. - May 2021
- Immunomodulation evidence in Phase I - May 2021
- UK-CTAP grant application - June 2021
- Kevin Schutz, Pharm.D. appointed VP of Regulatory Affairs - June 2021
- Phase II trial with foralumab in severe COVID-19 patients - June 2021
- Result of Annual General Meeting - June 2021
- Article publication on foralumab in COVID-19 patients - August 2021
- Files scheme for corporate reorganization - August 2021
- License Agreement to evaluate foralumab with CAR T & conference call - September 2021

Financial Results

Tiziana generated no revenue in first half 2021 and incurred operating expense of (£12.6) million which after adjusting for some minor non-operational items yielded comprehensive loss attributable to equity holders of (£12.6) million or (£0.074)[1] per share.

For the first half ending June 30, 2021 and versus the same period ending June 30, 2020:

- Research & development expense grew 473% to £4.4 million from £0.76 million, driven by expenses related to advancing TZLS-401 and TZLS-501;
- Operating expense grew 159% to £8.2 million from £3.2 million;
- Total comprehensive loss attributable to equity holders was (£12.6) million vs. (£3.9) million.

As of June 30, 2021, cash and equivalents totaled £38.6 million. This amount compares to a £48.2 million balance in cash and equivalents held at the end of 2020. Tiziana carries no debt on its balance sheet. Cash used in operations was (£9.4) million versus (£5.1) million for the six months ended 2021 and 2020, respectively.

[1] As calculated by the company. Our calculation using the reported 150.2 million basic and diluted average number of shares outstanding yielded a loss per share of (£0.084).

Anti-CD3 and CAR T: Joining with Precision

On September 2, 2021, Tiziana announced that it had entered into an exclusive licensing agreement with Precision BioSciences (NASDAQ: DTIL) to evaluate Tiziana's foralumab in conjunction with Precision's allogeneic CAR T portfolio. In this arrangement, foralumab, an anti-CD3 fully human monoclonal antibody, is being investigated as a lymphodepletion agent, an agent that purposely destroys the patient's immune system, including T cells, to make way for CAR T cells. Lymphodepletion is performed before receiving adoptive cell therapy (ACT). The aim is to determine whether or not foralumab can improve the outcome of ACT. Lymphodepletion typically comprises short-course chemotherapy to destroy T, B and NK cells. This can have the effect of debulking the tumor, altering the tumor phenotype, modifying the tumor microenvironment, and modulating the cytokine profile.[2] Common lymphodepletion agents include fludarabine and cyclophosphamide, typically used in combination. These agents have severe side effects and in the case of fludarabine, are associated with neurotoxicity. Foralumab has the potential to either replace or reduce the chemotherapy regimen, thereby improving the side effect profile for patients.

Foralumab may induce tolerance of allogeneic CAR T, or CAR T cells not from the patient's own body, but from a donor, which may attack the patient (host) in what is known as graft-versus-host-disease (GVHD). Allogeneic CAR T has advantages over autologous approaches in that generation of autologous CAR T cells can be challenging, especially in patients of advanced disease due to the length of time needed to generate the cells.[3]

The Cluster of Differentiation 3 (CD3) is a receptor on effector T cells. Precision's processing of T cells uses ARCUS gene editing to knock out the TRAC gene and depletes CD3, producing allogeneic CAR T cells that are greater than 99.9% CD3-negative. Lymphodepletion has been shown to augment T cell adoptive immunotherapy through enhanced intratumoral proliferation. Management has noted the potential of its anti-IL-6 receptor monoclonal antibody (TZLS-501) to be included in CAR T therapy to address cytokine storm syndrome, although this was not discussed as part of the deal with Precision.

Under the terms of the agreement, Precision gained exclusive license to use foralumab as a lymphodepletion agent to complement its CAR T portfolio in the treatment of cancers. Precision will be responsible for development, commercialization, and costs associated with its use of foralumab in exchange for upfront payment, certain milestone payments and royalties to Tiziana. Amounts for upfronts, milestones and royalties were not disclosed; however, some of the milestones are payable upon start of a Phase II and Phase III study and upfront payments will be received shortly after execution of the deal.

Tiziana Update Call with Analysts and Investors

On September 8, 2021 following the market close, Tiziana hosted a web conference addressing its recent exclusive license agreement with Precision BioSciences 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 not to express Cluster of Differentiation 3 (CD3), 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 the efficacy of Precision's T cells.

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 performed on anti-CD3 mAb, in particular the earlier generation OKT-3, a fully mouse anti-CD3 antibody developed by Johnson & Johnson and approved by the FDA. However, because it is a mouse antibody, it elicited a strong, negative immune reaction and formation of anti-drug antibodies and stimulated cytokine release syndrome. OKT-3 was withdrawn from the market as a result; however, it presented favorable clinical efficacy. 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

[2] Lymphodepletion optimization for CAR T-cell therapy (multiplemyelomahub.com)
[3] McCreedy BJ, Senyukov VV, Nguyen KT. Off the shelf T cell therapies for hematologic malignancies. Best Pract Res Clin Haematol. 2018 Jun;31(2):166-175. doi: 10.1016/j.beha.2018.03.001. Epub 2018 Mar 28. PMID: 29909917.

humanized anti-CD3 antibodies previously developed by PDL Biopharma. Efficacy for these iterations was satisfactory, but long-term treatment was limited by formation of anti-drug antibodies. To sidestep the immune response to the mouse elements, Tiziana's foralumab was designed as a fully human anti-CD3 mAb, and has not produced anti-drug antibodies in clinical work thus far and has not triggered the immune reactions observed in previous anti-CD3 candidates.

Precision's CAR T cells do not express CD3 and foralumab will not bind to them, providing 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 (sponsored by Provention Bio) 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 issues related to pharmacokinetic comparability.[4] Tiziana management has not seen anti-drug antibody response thus far in clinical evaluation nor has immunotoxicity been observed. Autoimmune disorders could be another area where a fully-humanized anti-CD3 antibody could become useful.

Other topics discussed during the call 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 systemic immunosuppression and toxicity.

Analyst questions then shifted direction towards Tiziana's clinical progress and expectations for upcoming milestones. Tiziana completed a Phase I study with 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 include 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 further efforts 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.

[4] 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

Corporate Reorganization

On August 20, Tiziana announced the official commencement of its strategic plan to change its corporate structure by establishing Tiziana Life Sciences as the Bermuda-incorporated, NASDAQ-traded parent of the Tiziana Group, subject to legal and shareholder approval. Existing shareholders, including American Depositary Share (ADS) holders, will have their shares exchanged, two-for-one, for the new parent company and the current company will then become a wholly-owned subsidiary. The new shares are expected to be listed while old shares are delisted from the London Stock Exchange and ADSs are delisted from the NASDAQ. The reorganization is intended to structure Tiziana in a manner more fitting to its US-centric operations, including enhanced trading and coverage characteristics, and reduce cost to shareholders. All outstanding options and warrants pursuant to the 2014 and 2016 Share Option Plans are intended to continue on the same basis but deliver the new shares. Likewise, holders of loan notes are intended to be converted as well.

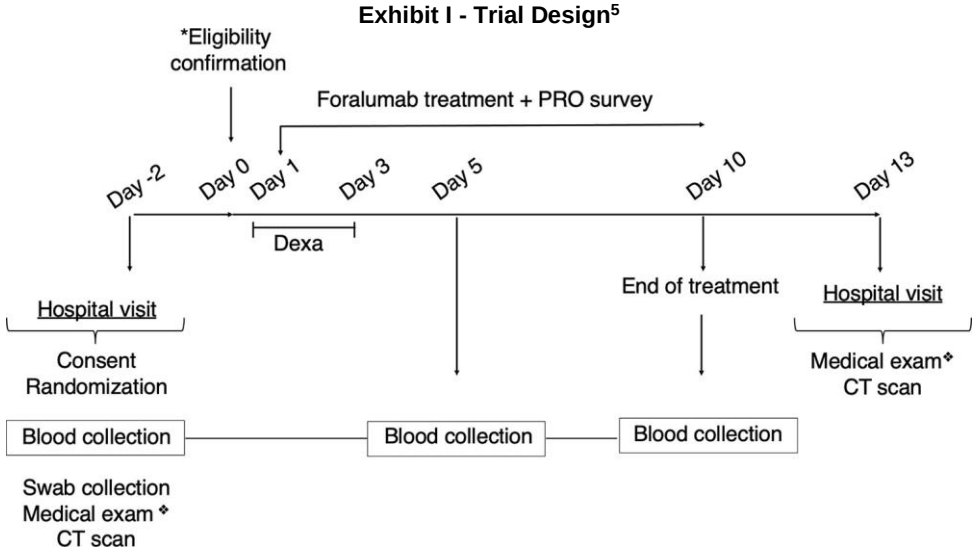
Intranasal Foralumab in Hospitalized, Severe COVID-19

On June 23, 2021, Tiziana announced that it had entered into a collaboration with FHI Clinical to conduct a Phase II trial for intranasal foralumab in hospitalized, severe COVID-19. The Phase II study will be conducted in Brazil, and is intended as a proof-of-concept effort, as well as to evaluate safety, tolerability and efficacy of the candidate in severe COVID-19 and pulmonary inflammation. In the trial, foralumab will be delivered intranasally through a metered atomizing device. The trial will be randomized, placebo-controlled and double-blind. It will expand on the findings of intranasal foralumab in mild to moderate, non-hospitalized COVID-19 patients announced in February and will examine attenuation of pulmonary pathology characteristic of severe COVID-19 patients. Up to seven sites in Brazil will participate in the study, targeting enrollment of 80 patients with CT-confirmed pulmonary involvement. The study will also evaluate foralumab's effect on resolution of symptoms via chest CT, inflammatory biomarkers, T cell subpopulations, safety and mucosal inflammatory response following 14 days of intranasal administration.

FHI Clinical is a subsidiary of FHI 360, specializing in clinical development of drugs for infectious diseases. FHI Clinical is involved with COVID-19 trials in all phases for vaccines and therapeutics, as well as observational studies to characterize SARS-CoV-2 infection. FHI Clinical has a network of clinical sites across 16 countries and 43 states in the US.

On August 17th, Tiziana informed investors via press release that a peer-reviewed article had been published featuring data from the foralumab trial in mild to moderate COVID-19 patients in Brazil, which was conducted in February. The article was published in *Frontiers in Immunology* titled "Nasal Administration of Anti-CD3 Monoclonal Antibody (foralumab) Reduces Lung Inflammation and Blood Inflammatory Biomarkers in Mild to Moderate COVID-19 Patients: A Pilot Study." The study was a collaboration with teams from Harvard Medical School and INTRIALS, a CRO based in São Paulo. The aim of the study was to assess safety of intranasal foralumab and its potential efficacy in treating immune hyperactivity and lung inflammation associated with mild/moderate COVID-19 patients. 39 patients were randomized into three cohorts: control, 100 µg foralumab + dexamethasone, and foralumab monotherapy.

Exhibit I - Trial Design[5]



[5] https://doi.org/10.3389/fimmu.2021.709861

Foralumab was well tolerated and all patients completed the study. No serious adverse events (SAEs) were observed. 11 patients experienced an adverse event including headache (n=4), burning in the nostril (n=1), retrosternal pain (n=2), pustular lesions and itching in cervical area (n=1), dysuria (n=1), tachycardia associated with anxiety (n=1), and insomnia (n=1). On the efficacy front, foralumab treatment resulted in significant reduction in lung inflammation, as observed with CT scans, which revealed improvement in clearance of lung infiltrates versus baseline. The CT data were correlated by reduction in levels of inflammatory markers such as IL-6 levels (69%; p=0.03) and CRP[6] (85%; p=0.03) at day 10. Management anticipates initiation of Phase II proof-of-concept study in Brazil to further evaluate

Summary

Tiziana Life updated on first half 2021 financial and operational results. We've highlighted major milestones year to date including a partnership with Precision BioSciences to evaluate foralumab as a lymphodepletion agent with allogeneic CAR T, Tiziana's intent to reorganize as a Bermuda-incorporated company and progress on the intranasal foralumab COVID-19 program. Additional highlights year-to-date included the appointment of multiple key positions in the firm, as well as preliminary work with Takanawa to survey for Japanese partners, as well as grant application submission to UK-CTAP proposing intranasal foralumab as a potential take-home therapy for COVID-19.

As Tiziana updates investors with its financial performance, our focus turns to the two Phase II trials in Crohn's Disease and Multiple Sclerosis. These programs drive the majority of the value in our assessment and address unmet needs in important indications. We maintain our target price of $7.50 per share.

[6] C-reactive protein

PROJECTED FINANCIALS

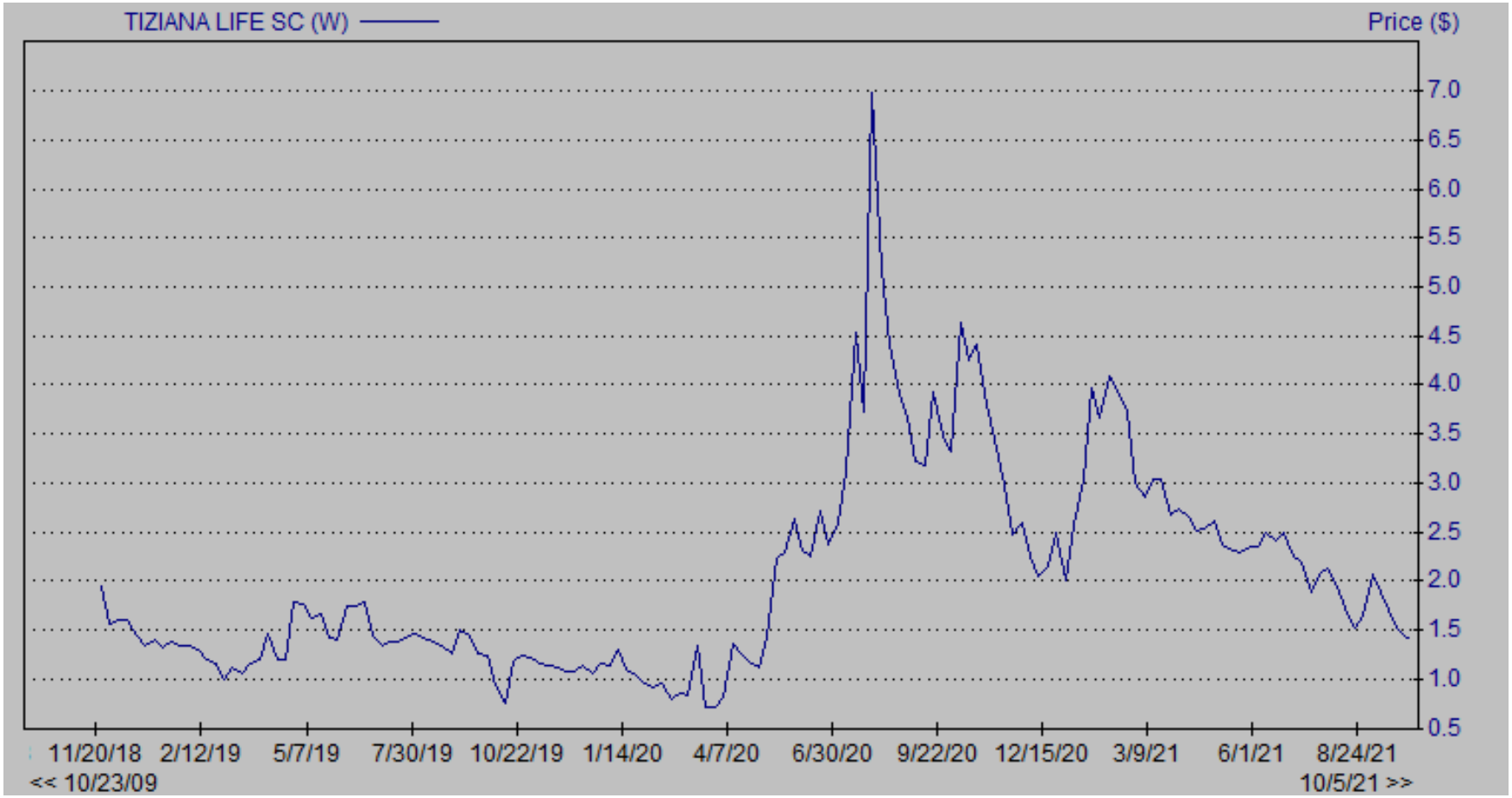
Tiziana Life Sciences PLC - Income Statement

Tiziana Life Sciences Plc	2020 A	1H A	2H E	2021 E	2022 E	2023 E
Total Revenues (£UK)	**£0**	**£0**	**£0**	**£0**	**£0**	**£0**
YOY Growth						
Research & Development	£4,667	£4,355	£11,350	£15,705	£20,801	£21,820
Operating Expenses	£8,724	£8,214	£2,809	£11,023	£5,968	£6,147
Income from operations	-£13,391	-£12,569	-£14,158	-£26,727	-£26,769	-£27,967
Operating Margin	*# DIV/0!*	*# DIV/0!*	*# DIV/0!*	*# DIV/0!*	*# DIV/0!*	*# DIV/0!*
Other Expense	£8,676	£24	£0	£24	£0	£0
	£0			£0	£0	
Pre-Tax Income	-£22,067	-£12,593	-£14,158	-£26,751	-£26,769	-£27,967
Provision for Income Tax	-£1,719	£0	£0	£0	£0	£0
Tax Rate	7.8%	0.0%	0.0%	0.0%	0.0%	0.0%
Net Income	**-£20,348**	**-£12,593**	**-£14,158**	**-£26,751**	**-£26,769**	**-£27,967**
Net Margin	*# DIV/0!*	*# DIV/0!*	*# DIV/0!*	*# DIV/0!*	*# DIV/0!*	*# DIV/0!*
Reported EPS	**-£0.12**	**-£0.084**	**-£0.06**	**-£0.12**	**-£0.10**	**-£0.11**
YOY Growth	124.8%	222.0%	-26.4%	1.0%	-15.3%	3.7%
Basic Shares Outstanding	169,065	150,224	220,000	220,000	260,000	261,970

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

HISTORICAL STOCK PRICE

Tiziana Life Sciences PLC – Share Price Chart[7]



[7] Source: Zacks Research System

DISCLOSURES

The following disclosures relate to relationships between Zacks Small-Cap Research ("Zacks SCR"), a division of Zacks Investment Research ("ZIR"), and the issuers covered by the Zacks SCR Analysts in the Small-Cap Universe.

ANALYST DISCLOSURES

I, John Vandermosten, hereby certify that the views expressed in this research report accurately reflect my personal views about the subject securities and issuers. I also certify that no part of my compensation was, is, or will be, directly or indirectly, related to the recommendations or views expressed in this research report. I believe the information used for the creation of this report has been obtained from sources I considered to be reliable, but I can neither guarantee nor represent the completeness or accuracy of the information herewith. Such information and the opinions expressed are subject to change without notice.

INVESTMENT BANKING AND FEES FOR SERVICES

Zacks SCR does not provide investment banking services nor has it received compensation for investment banking services from the issuers of the securities covered in this report or article.

Zacks SCR has received compensation from the issuer directly or from an investor relations consulting firm engaged by the issuer for providing non-investment banking services to this issuer and expects to receive additional compensation for such non-investment banking services provided to this issuer. The non-investment banking services provided to the issuer includes the preparation of this report, investor relations services, investment software, financial database analysis, organization of non-deal road shows, and attendance fees for conferences sponsored or co-sponsored by Zacks SCR. The fees for these services vary on a per-client basis and are subject to the number and types of services contracted. Fees typically range between ten thousand and fifty thousand dollars per annum. Details of fees paid by this issuer are available upon request.

POLICY DISCLOSURES

This report provides an objective valuation of the issuer today and expected valuations of the issuer at various future dates based on applying standard investment valuation methodologies to the revenue and EPS forecasts made by the SCR Analyst of the issuer's business.
SCR Analysts are restricted from holding or trading securities in the issuers that they cover. ZIR and Zacks SCR do not make a market in any security followed by SCR nor do they act as dealers in these securities. Each Zacks SCR Analyst has full discretion over the valuation of the issuer included in this report based on his or her own due diligence. SCR Analysts are paid based on the number of companies they cover. SCR Analyst compensation is not, was not, nor will be, directly or indirectly, related to the specific valuations or views expressed in any report or article.

ADDITIONAL INFORMATION

Additional information is available upon request. Zacks SCR reports and articles are based on data obtained from sources that it believes to be reliable, but are not guaranteed to be accurate nor do they purport to be complete. Because of individual financial or investment objectives and/or financial circumstances, this report or article should not be construed as advice designed to meet the particular investment needs of any investor. Investing involves risk. Any opinions expressed by Zacks SCR Analysts are subject to change without notice. Reports or articles or tweets are not to be construed as an offer or solicitation of an offer to buy or sell the securities herein mentioned.