Zacks Small-Cap Research
Sponsored – Impartial – Comprehensive
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Tiziana Life Sciences PLC (TLSA - NASDAQ)

Intranasal Foralumab in COVID-19

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 (6/23/2021)	$2.41
Valuation	**$7.50**

OUTLOOK

Tiziana is a research and development company developing three main candidates for a variety of indications in 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. 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 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 and 2028 commercialization of foralumab for both pMS and CD in conjunction with partners.

SUMMARY DATA

52-Week High	**12.17**
52-Week Low	**1.76**
One-Year Return (%)	**0.71**
Beta	**-0.10**
Average Daily Volume (sh)	**420,414**
Shares Outstanding (mil)	**97.3**
Market Capitalization ($mil)	**234**
Short Interest Ratio (days)	**0.4**
Institutional Ownership (%)	**5.2**
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)
2019	0.0 A	0.0 A	0.0 A	0.0 A	0.0 A
2020	0.0 A	0.0 A	0.0 E	0.0 E	0.0 E
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 E	-0.04 E	-0.06 E
2021					-0.11 E
2022					-0.10 E

WHAT'S NEW

Since our last update at the end of May, Tiziana Life Sciences PLC (NASDAQ: TLSA / LSE: TILS) has been busy with multiple activities. The company announced its virtual Annual General Meeting, to be held June 25, its application for a grant with the UK government to develop a "take home" treatment for COVID, appointment of Dr. Kevin Schutz as VP of Regulatory Affairs and entrance into a collaboration agreement with FHI Clinical to conduct its next COVID trial.

Intranasal Foralumab in Hospitalized, Severe COVID-19

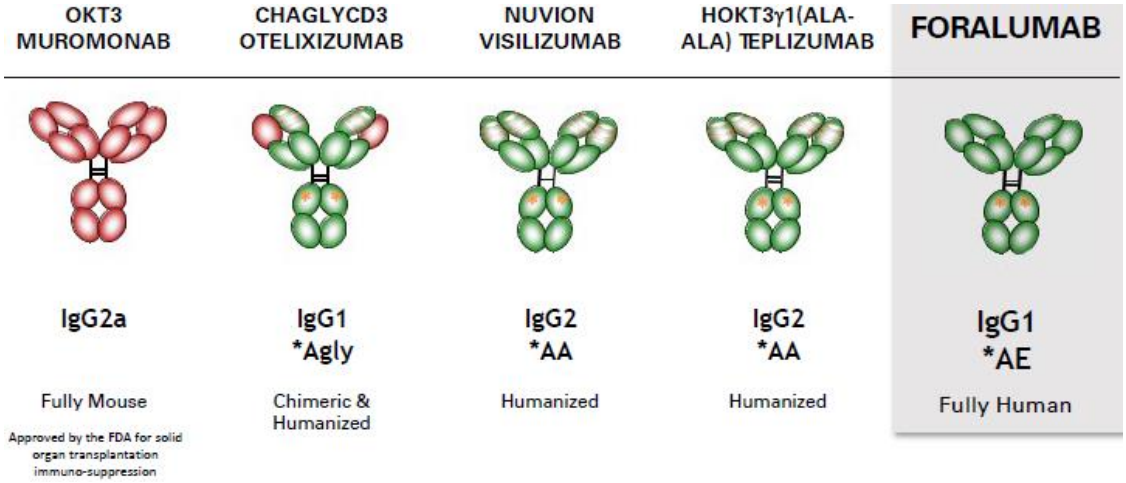
On June 23, 2021, Tiziana announced that it had entered into a collaboration with FHI Clinical to conduct a Phase II trial for intranasal foralumab in hospitalized, severe COVID-19. The Phase II study will be conducted in Brazil, and is intended as a proof-of-concept effort, as well as to evaluate safety, 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.

Foralumab

Foralumab is an anti-CD3 monoclonal antibody that reduces T cell activation and cytokine release by enhancing the production of IL-10, TGF-β and partial exhaustion of T cells. It specifically acts on the epsilon (ε) chain of the CD3-TCR complex. Foralumab immunogenicity is negligible as it is a fully human antibody, unlike its earlier counterparts with rodent elements. Due to its unique structure, it stimulates only minor cytokine release *in vivo* while maintaining CD3/TCR modulation and T-cell depletion, further contributing to its overall safety in intravenous use.[1]

Exhibit I – Evolution of Anti-CD3 mAbs[2]



[1] Dean Y, Dépis F, Kosco-Vilbois M. Combination therapies in the context of anti-CD3 antibodies for the treatment of autoimmune diseases. Swiss Med. Wkly 142, w13711 (2012).
[2] Source: Tiziana Life Sciences Corporate Presentation, January 2021.

Appointment of Dr. Kevin Schutz as VP of Regulatory Affairs

Tiziana announced the appointment of Kevin Schutz, Pharm.D. as its Vice-President of Regulatory Affairs on June 21, 2021. Dr. Schutz will lead interactions between Tiziana and regulatory entities as Tiziana progresses its clinical studies in the US, Europe and Asian countries. Dr. Schutz brings over 19 years of pharmaceutical industry experience including 14 years in Regulatory Affairs. Dr. Schutz' experience is in multiple fields including neurology, pulmonology, and other indications that Tiziana is currently considering. Tiziana's work in secondary progressive multiple sclerosis (SPMS) aligns well with Dr. Schutz' background. Over the course of his career, Dr. Schutz has worked with the FDA, EMA and PMDA (Japan).

UK Calls for 'Take-Home' Treatments for COVID-19, Tiziana Responds

In a June 17th press release, Tiziana informed that, in response to the United Kingdom COVID Therapeutics Advisory Panel's initiative to investigate therapies that can be delivered at home, Tiziana had submitted an application for a grant to support further development of nasally-administered foralumab in non-hospitalized COVID-19 patients. The grant application followed Tiziana results from a successfully-completed trial in Brazil that demonstrated take-home nasal-spray foralumab's immunomodulatory effects in COVID-19 patients, as evident from CT scans and inflammation markers including interleukin-6 and C-reactive protein.

Nasally-administered Foralumab Trial in SPMS Patient

On May 25, 2021, Tiziana announced that it had initiated a trial through the Individual Patient Expanded Access Program (EAP) of foralumab in a Secondary Progressive Multiple Sclerosis (SPMS) patient. This follows a previous release in late March that first introduced the effort that was cleared under the EAP. The first SPMS patient was dosed on May 24, 2021 with treatment to be administered over the following six months to examine long-term safety, tolerability and clinical response. Previous clinical work has been conducted in healthy volunteers and COVID-19 patients demonstrating the well-tolerated safety of nasally-administered foralumab, dosed up to 10 consecutive days, with no apparent severe adverse events. Treatment in these investigations also produced anti-inflammatory effects.

The SPMS patient will be treated at Brigham and Women's Hospital Harvard Medical School and will receive 50 mcg, or 25 mcg/nostril, in 3-week cycles. Dosing will be three times a week for the first two weeks followed by one week of rest in a repeating cycle that will continue for six months. The patient will be monitored during the period evaluating routine safety, tolerability and neurological behaviors. In addition, the study will also track microglial activation and will assess treatment response through immunological and neurodegenerative markers.

In the Space: Teplizumab FDA Advisory Committee Meeting

Foralumab rival teplizumab is scheduled for an FDA Endocrinologic and Metabolic Drugs Advisory Committee meeting, with related briefing documents posted on May 25. The advisory committee meeting is scheduled for 9 AM ET on May 27 to review Provention Bio's (NASDAQ: PRVB) candidate. The meeting was called to discuss potential merits of teplizumab, which, like foralumab, is an anti-CD3 monoclonal antibody (mAb). In contrast to foralumab, teplizumab is indicated in type 1 diabetes and contains some murine elements, while fully human foralumab is indicated in a multitude of conditions with a focus on multiple sclerosis, Crohn's Disease and COVID-19 symptoms. News of the advisory committee meeting for teplizumab signals the FDA's efforts and consideration toward the novel anti-CD3 mAb, which can set a precedent for the drug class.

Multiple Sclerosis and Its Subtypes

Multiple sclerosis (MS) is a neurological condition that affects the central nervous system (CNS), specifically white matter. The immune system mistakenly inflames and damages myelin, the insulating layer that wraps and protects axonal processes of nerves in the brain and spinal cord. Damage to the myelin sheaths of neurons prevents communication throughout the CNS and blocks effective transmission of electrical signals leading to various neurological findings. This autoimmune, inflammatory disease typically presents itself in the third or fourth decade of life. The causes of MS are unknown. Researchers have speculated that it may be related to virus and bacteria exposure, geographic location, genetics or immunological malfunctions. MS is clinically classified into four types: relapsing-remitting multiple sclerosis (RRMS), secondary-progressive multiple sclerosis (SPMS), primary-progressive multiple sclerosis (PPMS) and progressive-relapsing multiple sclerosis (PRMS). SPMS occurs when symptoms arise during a stage in remission and are not resolving with treatments, in contrast to PPMS which occurs when there are no periods of remission and the disease progresses.

Key reasons to own Tiziana shares:

- **Multiple Phase II-ready assets pursuing unmet needs**
  - **Fully human anti-CD3 - foralumab**
    - **Multiple Sclerosis**
    - **Crohn's Disease**
    - **COVID-19 / ARDS**
  - **Pan-CDK inhibitor - milciclib**
    - **Non-small cell lung carcinoma (NSCLC)**
    - **Hepatocellular carcinoma (HCC)**
  - **Fully human anti-IL-6 receptor – TZLS-501**
    - **ARDS, ILD, COVID-19 and other diseases**
    - **IND development underway**
- **Oral, nasal and inhaled administration of antibodies**
  - **Improved ease of use**
  - **No need for hospital-based infusion**
  - **Lower doses required for efficacy**
  - **Reduced systemic exposure and toxicity**
  - **Fewer side effects with reduced systemic exposure and toxicity**
  - **Focused distribution at the target organs in CD and severe lung disorders**
  - **Higher lung drug retention and efficacy while minimising toxicity to other organs**
- **Validation of intranasal foralumab technology in Phase I COVID-19 trial**
  - **Phase II trial announced**

Summary

Since our last update, Tiziana entered into a collaboration with FHI Clinical, extending work in COVID-19 to now assess the antibody in severe, hospitalized COVID-19 patients. The study will be conducted in Brazil and will evaluate parameters relating to pulmonary health and inflammation. Kevin Schutz, Pharm.D. was appointed Vice President of Regulatory Affairs where he will guide Tiziana as it interacts with regulatory agencies to progress its pipeline. Tiziana also submitted a grant to the UK-CTAP, featuring nasally-administered foralumab as a 'take-home' therapy for non-hospitalized COVID-19 patients. The company will also hold its Annual General Meeting tomorrow, June 25.

Through the Individual Patient Expanded Access Program, Tiziana initiated a trial for nasally-administered foralumab in secondary progressive multiple sclerosis (SPMS). The trial has enrolled its first patient and will evaluate the long-term safety and tolerability as well as monitor clinical efficacy through microglial activation and biomarkers relating to immunology and neurodegeneration. We are watching teplizumab, another anti-CD3 mAb indicated in Type 1 diabetes that has a target action date of July 2, 2021. An approval could establish a positive precedent for the drug class.

We were introduced to additional analysis of foralumab administered to healthy patients in a Phase I study. The assessment determined that nasally administered foralumab was well tolerated, systemic levels of the drug were minimal and that 50 mcg produced the most prominent effects. The 50 mcg dose produced favorable immunomodulation and diminished inflammatory responses over a two to three week period.

We recently initiated on Tiziana, a research and development company advancing three candidates for a variety of indications including 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-19, administered intranasally or orally via enteric coated capsules. 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. We maintain our target price of $7.50 per share.

PROJECTED FINANCIALS

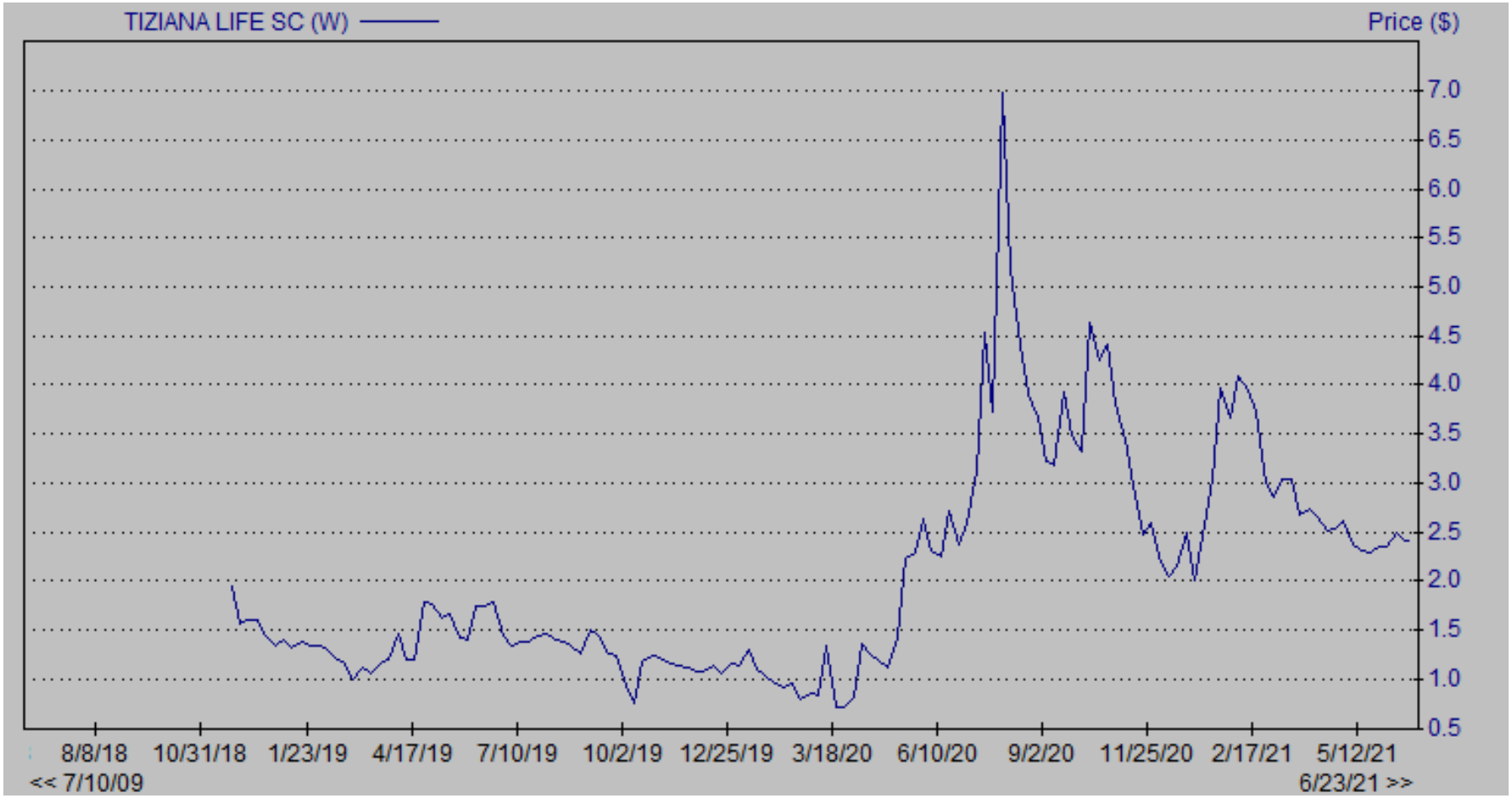
Tiziana Life Sciences PLC - Income Statement

Tiziana Life Sciences Plc	1H A	2H A	2019 A	1H A	2H A	2020 E	2021 E	2022 E
Total Revenues (£UK)	**£0**	**£0**	**£0**	**£0**	**£0**	**£0**	**£0**	**£0**
YOY Growth								
Research & Development	£1,507	£1,403	£2,910	£760	£3,875	£4,635	£19,312	£20,801
General & Administrative	£2,138	£2,726	£4,864	£3,169	£4,750	£7,919	£5,895	£5,968
Income from operations	-£3,645	-£4,129	-£7,774	-£3,929	-£8,625	-£12,554	-£25,207	-£26,769
Operating Margin						*# DIV/0!*	*# DIV/0!*	*# DIV/0!*
Other Expense	£5	£67	£72	-£5	£0	-£5	£0	£0
						£0	£0	£0
Pre-Tax Income	-£3,650	-£4,196	-£7,846	-£3,924	-£8,625	-£12,549	-£25,207	-£26,769
Provision for Income Tax	-£27	-£513	-£540	£0	-£1,500	-£1,500	£0	£0
Tax Rate	0.0%	0.0%	0.0%	0.0%	0.0%	12.0%	0.0%	0.0%
Net Income	**-£3,623**	**-£3,683**	**-£7,306**	**-£3,924**	**-£7,125**	**-£11,049**	**-£25,207**	**-£26,769**
Net Margin	*# DIV/0!*	*# DIV/0!*	*# DIV/0!*	*# DIV/0!*	*# DIV/0!*	*# DIV/0!*	*# DIV/0!*	*# DIV/0!*
Reported EPS	**-£0.027**	**-£0.027**	**-£0.054**	**-£0.026**	**-£0.04**	**-£0.06**	**-£0.11**	**-£0.10**
YOY Growth			1.0%	-1.6%	35.7%	6.1%	101.8%	-10.1%
Basic Shares Outstanding	136,464	136,501	136,483	150,224	194,600	194,600	220,000	260,000

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

HISTORICAL STOCK PRICE

Tiziana Life Sciences PLC – Share Price Chart[3]



[3] Source: Zacks Research System

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