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Initiating Coverage

Healthcare

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Tiziana Life Sciences Ltd (TLSA - $0.76 - Buy)

Innovative Routes of Immunotherapy| Initiate w/ Buy| PT $4

Key Points

Enabling Alternative Routes of Immunotherapy. Tiziana is one of the early movers in developing innovative approaches for alternative routes of immunotherapy. The target antibody market is large and offers significant opportunities for reformulation. Global market was valued at $150 billion in 2019 and is expected to grow to $300 billion by 2025. Tiziana is well-positioned with strong IP and differentiated assets that it is developing for human diseases. The management has the bench-to-market experience that is important for the success of the company.

Revolutionary Platform. The company is the first to switch from traditional routes of immunotherapy that are intravenous or subcutaneous. Oral administration is being developed for the treatment of Crohn's disease. This would be the first-ever oral immunotherapy for Crohn's disease patients. Nasal administration is more advanced. The company recently reported positive clinical results from the second patient with Secondary Progressive Multiple Sclerosis (SPMS) in the ongoing study at the Brigham and Women's Hospital in Boston. The treatment with Foralumab, a fully human anti-CD3 monoclonal antibody, was well-tolerated and improved clinical and PET imaging analyses. The third program, which is early-stage, is inhalation, delivery of antibody directly into the lungs for the treatment of lung disease.

Pipeline. Foralumab is being developed for nasal administration for multiple sclerosis. In oral administration, the company completed a Phase 1 trial in healthy volunteers. FDA was helpful in providing guidance to the company to move forward in Phase 1b in a healthy Crohn's disease patient. In addition, the company has subcutaneous administration for type 1 diabetes and inhalation administration for pulmonary fibrosis. These are early-stage programs. Milciclib is a small molecule compound. The company will be providing an update for the submission of a Phase 2 trial in the U.S. in KRAS-positive NSCLC.

Lead Asset. Foralumab is a monoclonal antibody against the CD3 antigen, which is expressed on T cells. It's a fully human anti-CD3 antibody. It has distinguishing features, such as it has so far not produced anti-drug antibodies. And because it is a non-FC binding asset or non-FC binding monoclonal antibody, it seems to have less toxicity.

Foralumab: Clinical Proof of Concept for Intranasal Delivery. Positive clinical data from two out of two SPMS patients validate the novel intranasal therapy with Foralumab, which appears to overcome the blood-brain barrier to allow therapeutic action of the drug.

Precision Biosciences Licensing Collaboration Validates Technology. The company also has a collaboration program with Precision Biosciences, where Foralumab will be developed in conjunction with Precision Bio CAR-T product for treatment of cancer.

Financials. We estimate the company's current cash position at $31 million. This cash position will fund operational needs through the end of 2022 and possibly the first quarter or second quarter of 2023 as well. The quarterly burn rate is estimated at $1.5 million to $2 million. There are sufficient resources on hand to move forward with the program.

Summary

The company's mission is to design and deliver next-generation therapeutics for oncology and immune diseases of high unmet medical need by combining a deep understanding of disease biology with clinical development expertise. The company has a drug discovery pipeline of small molecule new chemical entities and biologics. The company employs a lean and virtual R&D model using experienced teams of experts in the drug discovery and development processes.

Rating, Price and Target	
Symbol	TLSA
Rating	Buy
Price	$0.76
Price Target	$4.00

Market Data	
Market Cap (M)	$77.80
Shares Outstanding (M)	102.30
Average Daily Volume (000s)	300.00
Float (M)	58.30
Total Debt (M)	$0
Net Cash/Debt ($M)	$42.20
Dividend	NM

FYE Dec	2021A	2022E	2023E
EPS	(0.24)	(0.13)	(0.23)
Revenue (M)	-	-	-

Company Description

Tiziana Life Sciences is a clinical-stage biopharmaceutical company developing breakthrough therapies using transformational drug delivery technologies to enable alternative routes of immunotherapy. Tiziana's innovative nasal, oral and inhalation approaches in development have the potential to provide an improvement in efficacy as well as safety and tolerability compared to intravenous delivery. Tiziana's lead candidates, intranasal foralumab, the only fully human anti-CD3 mAb, and milciclib, a pan-CDK inhibitor, have both demonstrated a favorable safety profile and clinical response in patients in studies to date. The company was incorporated in 1998 and is headquartered in London, United Kingdom.

Innovative Routes of Immunotherapy

Overview

Tiziana is a biotechnology company that is focused on the discovery and development of novel molecules to treat high unmet medical needs in oncology and immunology.

Tiziana's mission is to design and deliver next-generation therapeutics for oncology and immune diseases of high unmet medical need by combining a deep understanding of disease biology with clinical development expertise. The company has a drug discovery pipeline of small molecule new chemical entities and biologics. The company employs a lean and virtual R&D model using experienced teams of experts focused on the drug discovery and development processes.

Tiziana is developing Foralumab, in-licensed IP from Novimmune in December 2014, as a potential treatment for neurodegenerative diseases such as progressive Multiple Sclerosis, Crohn's disease, and delayed onset of Type 1 Diabetes Mellitus (T1DM). Foralumab, a fully human anti-CD3 monoclonal antibody, has potential advantages such as shorter treatment duration and reduced immunogenicity. Oral or intranasal administration of Foralumab has the potential to reduce inflammation while minimizing toxicity and related side effects[1].

On June 8, 2022, the company reported positive clinical results from the second patient with Secondary Progressive Multiple Sclerosis (SPMS) in the ongoing study at the Brigham and Women's Hospital in Boston[2]. These results confirm the previously reported data from the first SPMS patient after three months of treatment. The treatment with Foralumab was well-tolerated and improved clinical and PET imaging analyses. Positive clinical data from two out of two SPMS patients validate the novel intranasal therapy with Foralumab, which appears to overcome the blood-brain barrier to allow therapeutic action of the drug.

The favorable safety, tolerability, and clinical responses from the first two SPMS patients were submitted to the U.S. FDA. The agency has now allowed Tiziana to treat an additional eight SPMS patients. As there are only a few options for non-active SPMS, Foralumab addresses a critical need for therapies to slow the progression of multiple sclerosis.

The company is also evaluating subcutaneous administration of Foralumab to delay the onset and progression of T1DM in at-risk individuals. cGMP manufacturing of Foralumab solution for subcutaneous injection drug product was initiated in April 2022, and IND submission is anticipated in the second-half of 2022.

In addition, the company is developing Milciclib, IP in-licensed from Nerviano in January 2015, as a potential treatment for pan KRAS mutations in NSCLC patients.

Prior to in-licensing, Milciclib was granted orphan designation by the European Commission and by the U.S. 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, Milciclib showed signs of slowing disease progression and acceptable safety.

The company also intends to evaluate Milciclib in combination with gemcitabine for the treatment of pan KRAS mutations in NSCLC patients. cGMP manufacturing of Milciclib capsules was completed in January 2022, and IND filing is anticipated in the second-half of 2022.

Takeaway

Enabling alternative routes of immunotherapy for the treatment of human diseases

Tiziana is one of the early movers in developing innovative approaches for alternative routes of immunotherapy.

The company's approaches to alternative routes of immunotherapy have a lot of potential for future development of immunotherapy, we believe. The company has about 300 patents or patent applications. This IP asset not only covers the completion of matter but also covers manufacturing, formulation technology, and disease indications.

The target antibody market is large and offers significant opportunities for reformulation. Global market was valued at $150 billion in 2019 and is expected to grow to $300 billion by 2025[3].

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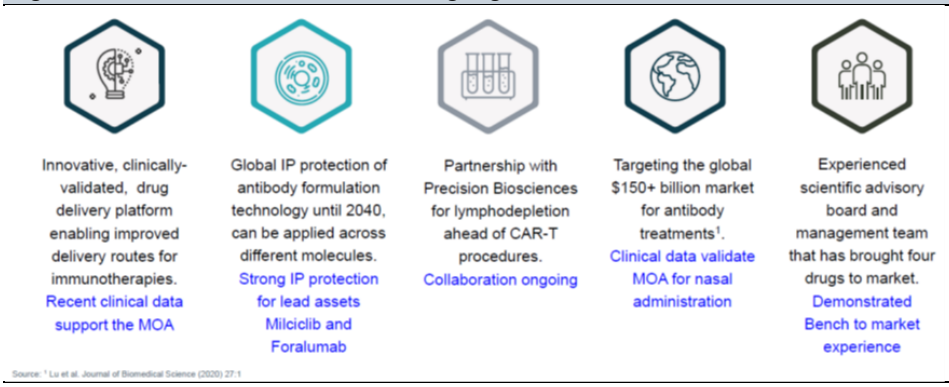
[1] Tiziana Life Sciences Ltd 20-F May 23, 2022
[2] https://bit.ly/TLSAPositiveClinicalResultsSecondSPMSPatientJune82022
[3] Lu et al. Journal of Biomedical Science 2020

Tiziana is well-positioned with strong IP and differentiated assets that it is developing for human diseases. The management has the bench-to-market experience that is important for the success of the company.

Figure 1. Tiziana Life Sciences Ltd - Highlights



Sources: Company Reports

Revolutionary Platform

The platform is revolutionary because the company is the first to switch from traditional routes of immunotherapy that are intravenous or subcutaneous. The problem with traditional routes is that although they are successful, patient compliance is poor.

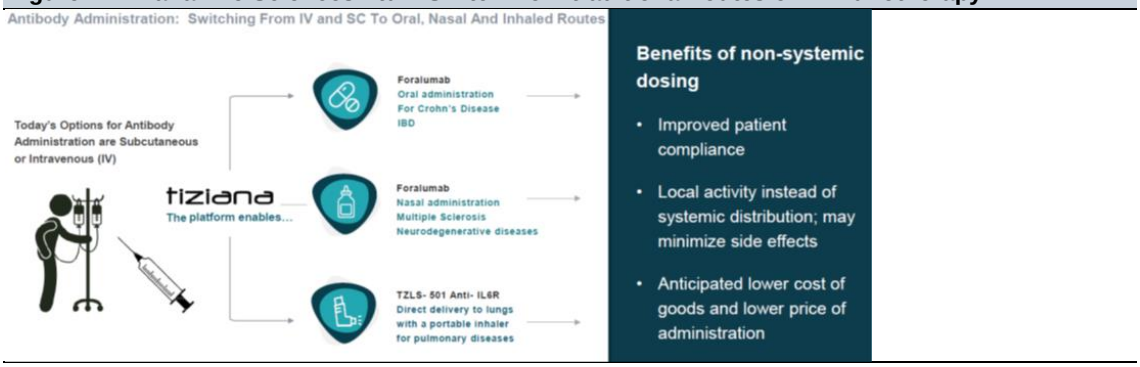
Importantly, when patients receive an injection or infusion of antibody, every two weeks or three weeks for two to three hours' duration, the drug level is high. And that seems to be producing most side effects. If you are able to give antibody or administer antibody in such a way that it can have local action, then you may be able to minimize toxicities and thereby increase efficacy.

Oral administration is being developed for the treatment of Crohn's disease. This would be the first-ever oral immunotherapy for Crohn's disease patients.

Nasal administration is more advanced. The company recently reported positive clinical results from the second patient with Secondary Progressive Multiple Sclerosis (SPMS) in the ongoing study at the Brigham and Women's Hospital in Boston. These results confirm the previously reported data from the first SPMS patient after three months of treatment of the first SPMS patient. The treatment with Foralumab, a fully human anti-CD3 monoclonal antibody, was well-tolerated and improved clinical and PET imaging analyses.

The third program, which is early stage, is inhalation, the delivery of antibody directly into the lungs for the treatment of lung disease.

Figure 2. Tiziana Life Sciences Ltd – Switch from traditional routes of Immunotherapy



Sources: Company Reports

Pipeline

The company's pipeline is focused. The board has been supportive of revising the pipeline so that it is prioritized as per the resources. The company is moving forward with this revised pipeline.

Foralumab is being developed for nasal administration for multiple sclerosis. The company also has animal data with Alzheimer's disease. The company is exploring that possibility in conversation with the FDA to move forward in that disease indication as well. Intranasal administration in multiple sclerosis patients is

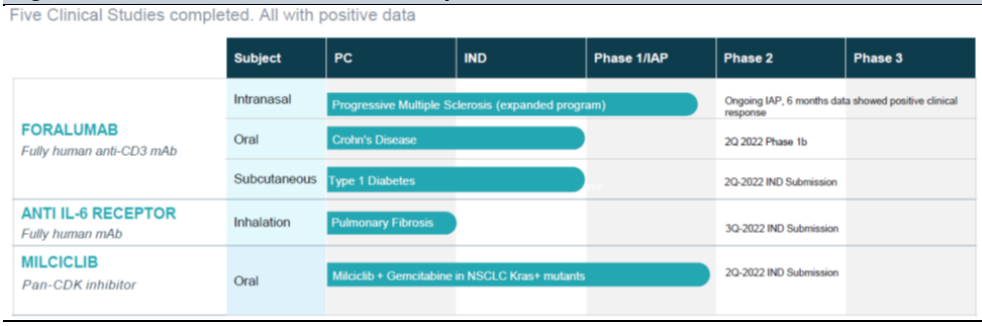
advanced, and the company reported six-month data. It recently reported on a second patient with three-month data.

In oral administration, the company completed a Phase 1 trial in healthy volunteers. FDA was helpful in providing guidance to the company to move forward in Phase 1b in a healthy Crohn's disease patient.

In addition, the company has subcutaneous administration for type 1 diabetes and inhalation administration for pulmonary fibrosis. These are early-stage programs.

Milciclib is a small molecule compound. The company will be providing an update for the submission of a Phase 2 trial in the U.S. in KRAS-positive NSCLC.

Figure 3. Tiziana Life Sciences Ltd - Pipeline

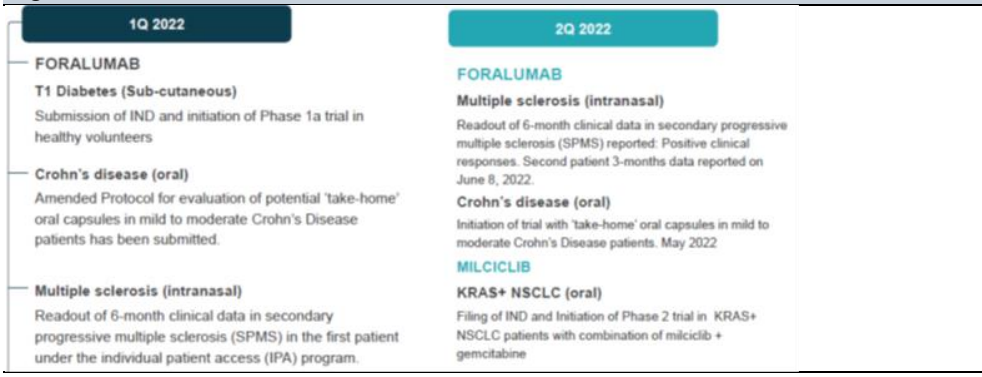


Source: Company Reports

Lead Asset

Foralumab is a monoclonal antibody against the CD3 antigen, which is expressed on T cells. It's a fully human anti-CD3 antibody. It has distinguishing features, such as it has so far not produced anti-drug antibodies. And because it is a non-FC binding asset or non-FC binding monoclonal antibody, it seems to have less toxicity.

Figure 4. Tiziana Life Sciences Ltd - Near-term Milestones



Sources: Company Reports

Historical development of anti-CD3 antibody

OKT3 is also an anti-CD3 antibody, but its origin is in the mouse. So, this antibody was developed by Johnson & Johnson (JNJ; not rated). It was approved by FDA with good clinical data. Unfortunately, being a mouse antibody produces immune reactions in the human body, and there were side effects.

For that reason, this antibody was taken off the market. But clinical data were compelling that companies like Eli Lilly (LLY; not rated) and GSK plc (GSK; not rated) tried to humanize it. All of them succeeded in humanizing antibody.

The further development of these humanized antibodies was that all of them developed anti-drug antibodies. Therefore, the repeated use of this antibody may not be possible. So, for that reason, these antibodies did not move forward. However, Teplizumab is a humanized, anti-CD3 antibody that is being developed by Precision BioSciences (DTIL; not rated) for Type 1 diabetes treatment.

Foralumab is a fully human anti-CD3 antibody. In the clinical studies the company has done to date, there was no indication of the development of anti-drug antibody.

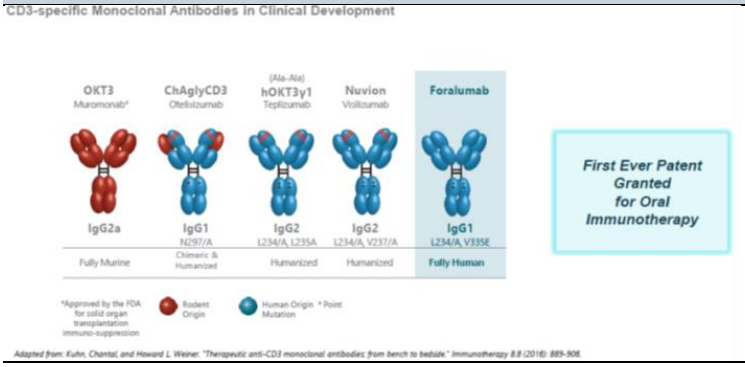
The company also has no problem with Chemical, Manufacturing, and Controls (CMC). In comparison, Teplizumab appears to have some CMC issues. So, the company may have distinct advantages with this asset, the anti-CD3 antibodies.

Foralumab has potential in several diseases. But the company is focused on three indications that are higher priority.

The company is developing oral administration for Crohn's disease, nasal administration for multiple sclerosis, and Type 1 diabetes. Type 1 diabetes is low-hanging fruit, and clinical data have already been validated with Teplizumab.

In addition to these three, the company also has a collaboration program with Precision Biosciences, where Foralumab will be developed in conjunction with its CAR-T product for the treatment of cancer.

Figure 5. Tiziana Life Sciences Ltd - Foralumab - Fully Human Anti-CD3 mAb in Clinical Trials



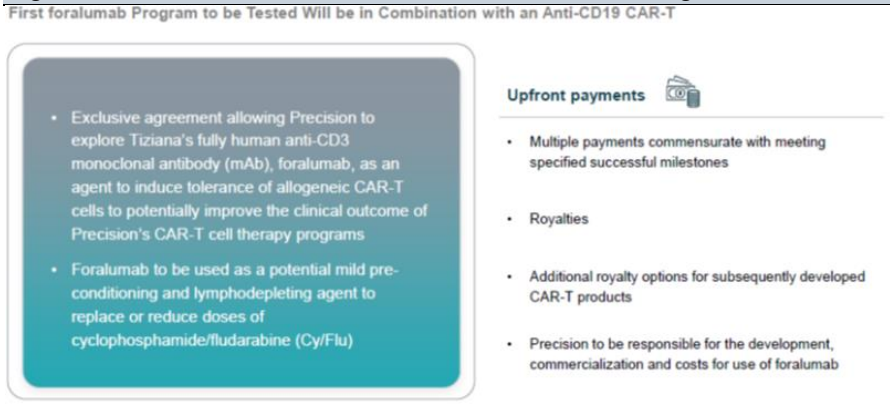
Sources: Company Reports

Collaboration with Precision Bio

Per the agreement, the company is to provide Precision Bio with the Foralumab drug substance, and all of the costs would be borne by Precision Bio.

Regarding the milestone payments, the company has already received the upfront payments from Precision Bio. This agreement also stipulates milestones for clinical development, as well as royalties for the commercialized product. This agreement is only for allogeneic CAR-T.

Figure 6. Tiziana Life Sciences Ltd - Precision Bio Licensing Collaboration Validates Technology



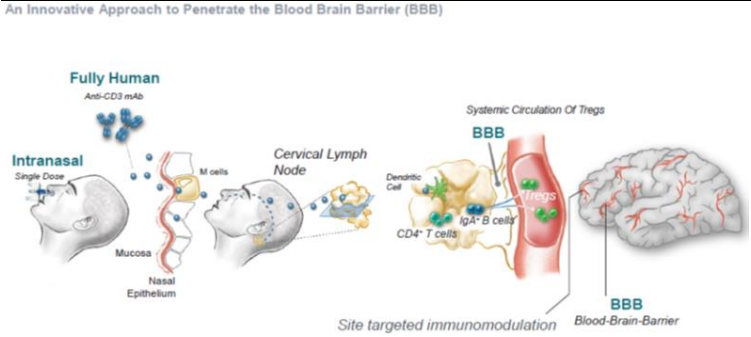
Sources: Company Reports

Intranasal administration of Foralumab produces clinical responses

When an antibody is delivered through the nostrils, it goes to the cervical lymph node, where it activates mucosal immunity. This leads to the production of T-regs (body defenders) which inhibit inflammation. T-regs can pass through the blood-brain barrier as they are physiological cells. This is an advantage and distinguishing aspect of the company's technology. Many other drugs fail because they cannot pass through the blood-brain barrier, especially in neurodegenerative diseases.

From P1 trial in healthy volunteers, based on biomarkers, the data indicates the penetration of T-regs through the blood-brain barrier providing the inhibitory effect on inflammation in the brain.

Figure 7. Intranasally-Administered Foralumab for Neurodegenerative Diseases



Sources: Company Reports

Six-month data on SPMS with nasal administration of Foralumab

The company has conducted Phase 1 trial in healthy volunteers. In addition to safety, there was no local irritation (this was a concern). Also, the biomarker analysis data indicated that Foralumab might act via normalization of the immune system.

Validate the mechanism – the company did a trial in Covid-19 patients. The data from these clinical trials are published as a full-length article[4].

Summary of data:

No local irritation, clean

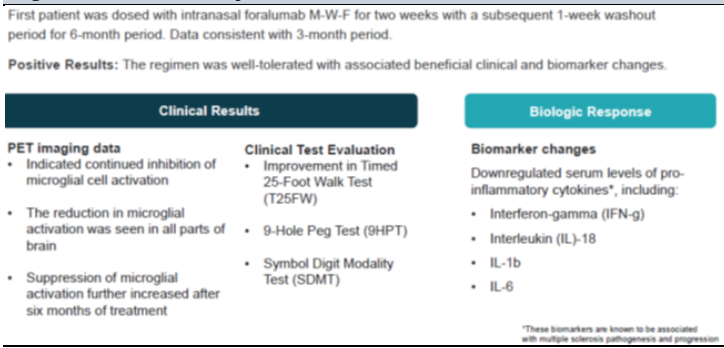
CT scans show clearly that the lung inflammation is disappearing

Blood samples. Biomarkers showed a significant reduction in IL-6, IL-18, IFN-g, and IL-1b

As Foralumab is fully human, it does not cross-react with CD3 antigen in primates and mice. FDA, therefore, allowed Tiziana to go straight into MS patients. Initially, the company had to show safety for three months. This data was promising. The company treated the patient for another three months. The company recently reported three-month data on treating a second patient. The FDA has granted the company permission to enroll up to eight additional patients.

The company also looked at whether the treatment has any effect on the inhibition of brain inflammation, which it did. This data was reported.

Figure 8. Intranasally Administered Foralumab in SPMS Patient: 6-Month Treatment Data



Sources: Company Reports

Microglial activation

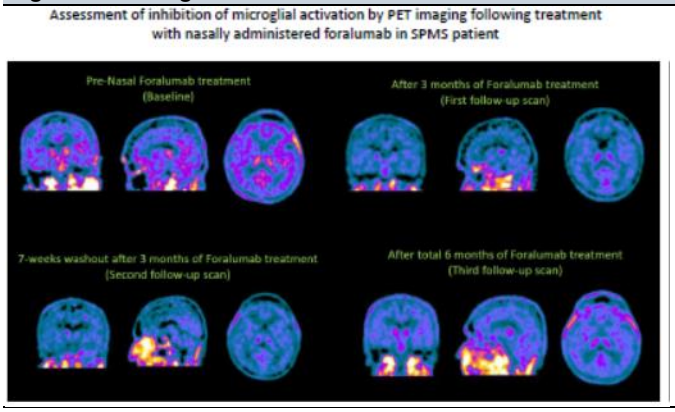
The company reviewed the microglial activation.

The red/yellow spots in the PET images indicate brain inflammation. After three months of treatment, the spots reduce.

The company presented this data to the FDA and did not treat the patients during this time (this is the seven-week washout). FDA allowed the company to resume treatment, where it saw sustained inhibition of microglial activation.

[4] https://pubmed.ncbi.nlm.nih.gov/34475873/

Figure 9. Microglial activation

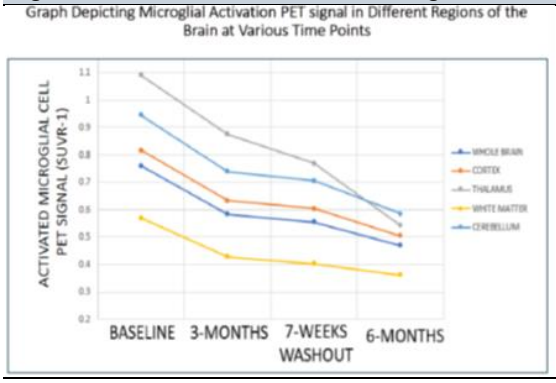


Sources: Company Reports

Numerical values of microglial activation

At the beginning baseline, the microglial activation was relatively high. And as the treatment proceeded, there was continual and sustained inhibition of microglial activation.

Figure 10. Numerical values of microglial activation



Sources: Company Reports

Thalamus

The thalamus is an important area of the brain, and that is where the brain inflammation is high. And microglial activation was reduced after a few months to 20%. But after six months, the reduction was up to 50%.

Figure 11. Intranasally Administered Foralumab in SPMS Patient: 6-Month Treatment Data

Percent Reduction* in Microglial PET Signal After Starting Intranasal Foralumab as Compared to Baseline, in Whole Brain and Selected Brain Regions

	WHOLE BRAIN	CEREBRAL CORTEX	THALAMUS	WHITE MATTER	CEREBELLUM
3 months	-23%	-23%	-20%	-25%	-22%
6 months	-38%	-38%	-50%	-36%	-38%

*Percent reduction is based on changes from baseline in SUVR-1, a surrogate index for PET binding potential. SUVR=Standardized Uptake Value Ratio, calculated with reference to a pseudo reference region in cerebral white matter that showed minimal change in PET SUV, across time points.

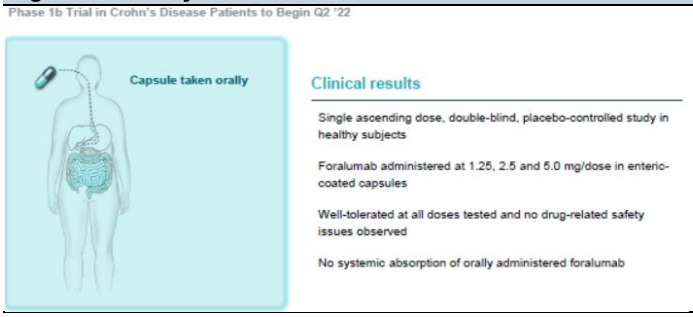
Published PET studies have shown an increase in activated microglial cells in patients with secondary progressive MS (SPMS), and an increase associated with higher scores on the Expanded Disability Status Scale (EDSS), a widely-used scale to measure disability.

Sources: Company Reports

Oral Foralumab for Crohn's disease

First-ever trial for immunotherapy for Crohn’s disease: no issue with safety in healthy volunteers. FDA has allowed the company to begin a P1b trial. The company expects to dose its first patient in June, and the trial will be completed by the end of the year.

Figure 12. Orally Administered Foralumab in Phase 1a Trial in Healthy Volunteers



Sources: Company Reports

Financials

We estimate the company's current cash position at $31 million. This cash position will fund operational needs through the end of 2022 and possibly the first quarter or second quarter of 2023 as well. The quarterly burn rate is estimated at $1.5 million to $2 million. There are sufficient resources on hand to move forward with the program.

Figure 13. Tiziana Life Sciences Inc - R&D Expenses by Program

	Year ended December 31,			
('000)	2021	2020	2019	2018
Foralumab	$ 3,372	$ 1,346	$ 1,750	$ 2,261
Milciclib	1,175	364	1,916	2,581
TZLS-0501	8,556	4,167	39	-
ACT-D	74	62	-	-
CAR-T	31	-	-	-
StemPrintER	-	54	9	166
Total direct research and development expense	13,208	5,993	3,714	5,008

Sources: Company Reports

Summary

The company's mission is to design and deliver next-generation therapeutics for oncology and immune diseases of high unmet medical need by combining a deep understanding of disease biology with clinical development expertise. The company has a drug discovery pipeline of small molecule new chemical entities and biologics. The company employs a lean and virtual R&D model using experienced teams of experts in the drug discovery and development processes.

Competitive Strengths

Tiziana R&D is focused on designing and delivering next-generation therapeutics and diagnostics for oncology and immune diseases of high unmet medical need by combining a deep understanding of disease biology with clinical development expertise.

Novel pipeline. The company has a pipeline of novel and proprietary drug candidates, including antibodies and small molecules, to address high unmet medical needs in the inflammation, autoimmune and oncology markets with significant commercial potential.

Technology. The company's technology enables the development of alternative routes of administration of antibodies, including oral delivery. Oral and nasal routes of delivery could alleviate the time and cost

Network of experts. The company has strong relationships with key opinion leaders who contribute to its clinical development efforts. Dr. Napoleone Ferrara, Dr. Arun Sanyal, Dr. Kevan Herold, and Dr. Howard Weiner are thought leaders on the scientific advisory committee.

Focus on oncology and inflammation. The management team, Dr. Kunwar Shailubhai, Jules Jacob, and Dr. Vaseem Palejwala, has experience in translating technologies from bench to market, and managing the global administration of clinical trials.

Intellectual Property. The company's intellectual property portfolio, in-licensed from Nerviano and Novimmune, provides it with a competitive advantage for the commercial development of small molecule NCEs and biologics. The company has retained the worldwide development and commercialization rights

of all of its product candidates. The company has submitted additional patent applications to further strengthen its IP.

R&D model. The company employs a lean and virtual R&D model using experienced teams of experts for each business function to maximize value accretion by focusing resources on the drug discovery and development processes.

Strategy

The company is focused on developing and delivering therapies and related diagnostics in both oncology and immunology.

Advance the clinical development of orally administered Foralumab for the treatment of Crohn's disease using a novel and proprietary oral formulation by initiating a Phase 1b trial in the Summer of 2022.

Development and cGMP manufacturing of product candidate Foralumab, a fully human mAb targeting the IL-6 receptor, for treating inflammatory and oncology indications.

Advance the clinical development and obtain regulatory approval for the lead oncology product candidate, Milciclib, as a combination therapy for the treatment of refractory solid tumors by filing an IND in the summer of 2022.

Continue development of platform drug delivery technologies that provide a competitive advantage over existing approved products - inhalation delivery, nasal delivery, and enteric delivery of mAbs.

Leverage relationships with KOLs to promote clinical trial success and future commercialization.

Valuation

Tiziana focuses its R&D efforts on treatments for cancer and autoimmune disease. The subset of people with these diseases who have the potential to benefit from treatment with the company's product candidates is based on estimates.

Further, the actual number of patients who receive the potential products could be less than the addressable market. Contributing factors include the lack of widespread availability and limited reimbursement for new therapies in underdeveloped markets.

The DCF analysis was used to determine the NPV of projected unlevered free cash flows utilizing an appropriate cost of capital for the discount rate. The rate reflects the relative risk associated with these cash flows, as well as the rates of return that security holders could expect to realize from alternative investment opportunities with similar risk profiles.

The market for drug candidates – Foralumab in Crohn's disease, multiple sclerosis, and type 1 diabetes; and Milciclib in NSCLC with KRAS mutations - is estimated by the company to be several billion US dollars per year in oncology and immunology.

We exclude any contribution from IL-6R and StemPrintER. In September 2020, the company transferred all the ownership rights and IP relating to StemPrintER along with $1.4 million in cash to its wholly-owned subsidiary, StemPrinter Sciences Ltd. We have excluded any contribution from such.

The 15% discount rate is consistent with the rate of return that shareholders could expect to realize from alternative investment opportunities with similar risk profiles.

Based on these assumptions, the discounted cash flow analysis indicated an estimated value per share of $3 for Foralumab and Milciclib. As of December 31, 2021, 102.3 million ordinary shares are outstanding.

Our price target of $4 is supported by DCF sum-of-the-parts valuation and $1 in estimated net cash/share (Figure 18). Our price target reflects the share dilution from potential financing.

Risks to valuation. The sizing of market opportunity has been summarized from scientific literature and patient foundations and may prove to be optimistic. If the company were to obtain significant market share for any product candidate, but the target populations are small, the company may never achieve profitability without obtaining marketing approval for additional indications. Other risk factors to our valuation include delays in clinical studies, adverse trial outcomes, and negative regulatory decisions.

Results of Operations

Revenues

To date, the company has not generated any revenue from product sales.

Operating Expenses

R&D Expenses

R&D expenses are primarily of costs incurred in connection with the R&D of product candidates and are expensed as incurred. The direct R&D expenses are tracked on a program-by-program basis for the product candidates and consist primarily of external costs - fees paid to outside consultants, CROs, and CMOs - in connection with preclinical development, manufacturing, and clinical development activities[5].

R&D activities are central to the business model. Product candidates in later stages of clinical development have higher development costs, primarily due to the increased size and duration of later-stage clinical trials and product manufacturing expenses. As a result, we expect R&D expenses to increase substantially over the next several years. The company will also incur additional expenses related to the milestone, royalty payments, and maintenance fees payable to third parties with whom the company has entered into license agreements related to the product candidates.

Figure 14. Tiziana Life Sciences Ltd – Results of Operations

	Year Ended December 31,	
	2021	2020
(in thousands, except per share data)		
Operating Expenses:		
Research and development	$ (13,208)	$ (5,993)
General and administrative	(13,311)	(11,203)
Realization bonus	(855)	(13,214)
Impairment of asset	-	(279)
Disposal of IP	-	2,663
Total Operating Expenses	(27,374)	(28,026)
Other Income/(Expense)	717	(312)
Tax credit	3,240	2,207
Net Loss	(23,417)	(26,131)
Foreign currency translation adjustment	(4,478)	3,474
Comprehensive Loss	(27,895)	(22,657)

Sources: Company Reports and ThinkEquity estimates

Results of Operations

R&D activities were $13.2 million for the year ended December 31, 2021, compared to $6.0 million for the year ended December 31, 2020. The increase is a result of the development of anti-IL-6R monoclonal antibodies compounds and the manufacturing of Foralumab.

Operating expenses were $13.3 million for the year ended December 31, 2021, as compared to $11.2 million for the year ended December 31, 2020. The increase includes the additional fair value charges of $3.5 million relating to the modification of existing options and the issuance of additional options.

There was a gain of $2.7 million arising on the disposal of the StemPrintER IP in the year ended December 31, 2020.

Figure 15. Tiziana Life Sciences Ltd – Balance Sheet Summary

	As of December 31,				
(U.S. dollars in thousands)	2021	2020	2019	2018	2017
Cash and cash equivalents	$ 42,186	$ 65,824	$ 200	$ 5,304	$ 64
Working capital	41,133	62,196	(5,846)	513	(2,302)
Total assets	48,826	70,656	2,378	6,920	2,471
Total shareholders' equity/(deficit)	41,280	62,386	(5,514)	519	(2,278)

Sources: Company Reports and ThinkEquity estimates

[5] Tiziana Life Sciences Ltd 20-F May 23, 2022

Liquidity

As of December 31, 2021, the company had cash and cash equivalents of $42.2 million.

Figure 16. Tiziana Life Sciences Ltd – Cash Flow

	Year ended December 31,		
(,000)	2021	2020	2019
Net cash used in operating activities	$ (21,762)	$ (11,335)	$ (6,796)
Net cash used in investing activities	(23)	(123)	(4)
Net cash provided by financing activities	130	75,346	1,680
Effect of exchange rate changes on cash and cash equivalents	(1,983)	1,736	16
Net (decrease)/increase in cash and cash equivalents	$ (21,655)	$ 63,888	(5,120)

Sources: Company Reports and ThinkEquity estimates

Cash Flows

Net Cash Used in Operating Activities

The use of cash in each of the years ended December 31, 2021, and 2020, resulted primarily from net losses, adjusted for non-cash charges and changes in components of working capital.

Net cash used in operating activities of $21.8 million during the year ended December 31, 2021, increased by $10.5 million compared to the year ended December 31, 2020.

Net Cash Used in Investing Activities

During the year ended December 31, 2021, the company used $0.02 million of cash in investing activities for the purchases of property and equipment offset by a finance lease receivable.

Net Cash Provided by Financing Activities

During the years ended December 31, 2021 and 2020, net cash provided by financing activities was $0.1 million and $75.3 million, respectively. This consisted of net cash proceeds from the sale and issuance of ordinary shares and ADS's, convertible loan notes, and the exercise of options and warrants.

Risks

The company faces risks, which include, but are not limited to the following:

The company may encounter substantial delays in clinical trials of its product candidates, may be unable to obtain required regulatory approvals, and may be unable to commercialize the product candidates on a timely basis.

The company may fail to demonstrate the safety and therapeutic utility of its product candidates to the satisfaction of applicable regulatory authorities, which would prevent or delay regulatory approval and commercialization.

Success in preclinical studies or clinical trials may not be indicative of results in future clinical trials.

The company depends on the enrollment of patients in clinical trials for its product. Delays in enrollment could prevent the company from proceeding with clinical trials of its product candidates and could adversely affect the results of operations.

The product candidates and the process for administering the product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval and limit their commercial potential.

The company has incurred net losses every year since its inception. The company may never achieve or maintain profitability. Net losses were $23.3 million, $26.1 million, and $9.3 million for the years ended December 31, 2021, 2020, and 2019, respectively. As of December 31, 2020, the company had an accumulated loss of $84.6 million. Substantially all of the efforts have been directed to the research and development of lead product candidates - Foralumab and Milciclib - as well as to building out the management team and infrastructure.

The company will need substantial additional funding to complete the development of its product candidates.

Limited operating history and no history of commercializing pharmaceutical products make it difficult to evaluate the success of the business to date and assess the prospects for future viability.

For additional risk considerations, please refer to the company's SEC filings.

Figure 17. Tiziana Life Sciences Ltd - Income Statement, FY14-FY23E

FY end December 31 *($'000, except per share numbers)*	2014	2015	2016	2017	2018	2019	2020	2021	2022E	2023E
Revenues	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -
Cost of sales	-	-	-	-	-	-	-	-	-	-
Gross profit	-	-	-	-	-	-	-	-	-	-
Operating expenses										
Research and development	1,309	9,609	4,007	6,015	5,510	3,714	5,993	13,208	8,000	17,000
Operating expenses	4,189	3,557	5,872	4,602	4,417	6,207	11,203	13,311	8,000	11,000
Realtization bonus	-	-	-	-	-	-	13,214	855	-	-
Impairment of non-current asset / Gain from disposal of IP	-	-	-	-	-	-	(2,384)	-	-	-
Total operating expenses	5,498	13,166	9,879	10,617	9,927	9,921	28,026	27,374	16,000	28,000
Loss from operations	(5,497)	(13,166)	(9,879)	(10,617)	(9,927)	(9,921)	(28,026)	(27,374)	(16,000)	(28,000)
Other income (expense), net	(86)	(28)	(12)	(12)	(12)	(91)	(312)	717	-	-
Income tax credit	99	-	121	1,912	1,945	689	2,207	3,240	1,000	-
Currency translation	-	-	-	-	-	(27)	3,474	(4,478)	-	-
Comprehensive loss	(5,484)	(13,193)	(9,770)	(8,716)	(7,994)	(9,323)	(22,657)	(27,895)	(15,000)	(28,000)
Net loss per diluted share	$ (0.24)	$ (0.15)	$ (0.11)	$ (0.09)	$ (0.06)	$ (0.07)	$ (0.16)	$ (0.24)	$ (0.13)	$ (0.23)

Sources: Company Reports and ThinkEquity Estimates

Figure 18. Tiziana Life Sciences Ltd – Valuation Comparable, Prices as of 6/11/22

(Amounts listed in USD. Numbers in millions, except per share data)

				Enterprise Value as a Multiple of:							Price as a Multiple of:		Projected
				Sales			EBITDA			EBIT	CY+1	CY+2	EPS
Company	**Stock Price [1]**	**Market Value of Equity**	**Enterprise Value[2]**	**LTM**	**CY+1**	**CY+2**	**LTM**	**CY+1**	**CY+2**	**LTM**	**EPS**	**EPS**	**Growth**
Precision BioSciences, Inc.	1.35	83.9	(23.6)	NM	NM	NM	NM	NM	NM	NM	NM	NM	0.0%
Nkarta, Inc.	13.29	643.3	495.6	NM	NM	NM	NM	NM	NM	NM	NM	NM	0.0%
Provention Bio, Inc.	3.98	254.6	170.2	NM	NM	NM	NM	NM	NM	NM	NM	NM	0.0%
TG Therapeutics, Inc.	4.59	610.4	456.4	57.69	29.04	4.82	NM	NM	NM	NM	NM	NM	0.0%
Immunovant, Inc.	3.39	395.0	(96.3)	NM	NM	NM	NM	NM	NM	NM	NM	NM	0.0%
AB Science S.A.	0.00	0.0	6.4	3.95	NM	NM	NM	NM	NM	NM	NM	NM	0.0%
MediciNova, Inc.	2.49	122.1	55.2	NM	NM	NM	NM	NM	NM	NM	NM	NM	0.0%
Altimmune, Inc.	8.55	366.9	188.4	52.27	83.95	65.94	NM	NM	NM	NM	NM	NM	0.0%
High				57.69x	83.95x	65.94x	0.0x	0.0x	0.0x	0.0x	0.0x	0.0x	0.0%
Average				37.97	56.49	35.38	NM	NM	NM	NM	NM	NM	0.0%
Median				52.27	56.49	35.38	NM	NM	NM	NM	NM	NM	0.0%
Low				3.95	29.04	4.82	0.0	0.0	0.0	0.0	0.0	0.0	0.0%
Tiziana Life Sciences Ltd	**0.76**	**77.8**	**35.7**	**NM**	**NM**	**NM**	**NM**	**NM**	**NM**	**NM**	**NM**	**NM**	**0.0%**

(1) Financial data provided by S&P CapIQ, Google Finance, Company Reports, and ThinkEquity estimates as of 06/11/2022

(2) Calculated as Market Value of Equity plus total debt, non-controlling interest and preferred stock, less cash & equivalents.

Sources: S&P CapIQ, Google Finance, Company Reports, and ThinkEquity estimates

Figure 19. Tiziana Life Sciences Ltd – 3 Years Rating and Price Target History

Date	Key Development
6/13/2022	Tiziana Life Sciences Ltd. Initiate with Buy. PT $4

Sources: S&P CapIQ, Google Finance, and ThinkEquity Estimates

Important Disclosures

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BUY (B) - Total return expected to exceed S&P 500 by at least 10%

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This Equity Ratings Distribution reflects the percentage distribution for rated equity securities for the twelve month period June 30, 2019 through June 30, 2020. Within the twelve month period ended June 30, 2020, ThinkEquity, LLC has provided investment banking services to 54% of companies with equity rated a Buy, 0% of companies with equity rated a Hold and 0% of companies with equity rated a Sell. As of June 30, 2020, ThinkEquity, LLC had twenty-three stocks under coverage: Buy 23 (100%), Hold 0 (0%), Sell 0 (0%).

ThinkEquity rating distribution by percentage (as of June 13, 2022):			
All companies under coverage:		All companies under coverage to which it has provided investment banking services in the previous 12 months:	
Buy (1)	100.00%	Buy (1)	60.34%
Hold (2)	0.00%	Hold (2)	0%
Sell (3)	0.00%	Sell (3)	0%