Tiziana Life Sciences PLC (TLSA)
Rating: Buy

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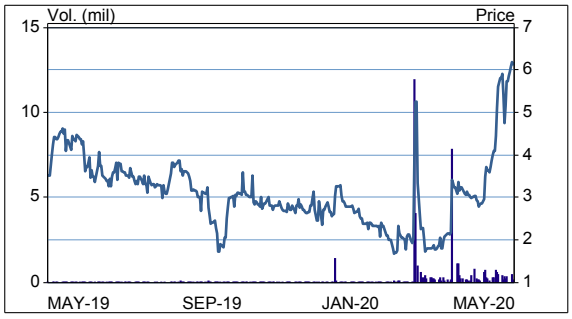
StemPrintER Value Driver; COVID-19 Context; Pipeline Updates; Reiterate Buy

Stock Data	05/28/2020
Price	$6.13
Exchange	NASDAQ
Price Target	$25.00
52-Week High	$7.70
52-Week Low	$1.54
Market Cap (M)	$197
Public Market Float (M)	8.8
Shares Outstanding (M)	29.4
3 Month Avg Volume	662,363
Short Interest (M)	0.07
Balance Sheet Metrics	
Cash (M)	£2.7
Total Debt (M)	£0.0
Total Cash/Share	£0.09
Book Value/Share	£(0.03)

General: Shares officially quoted in pence on London Exchange; American Depositary Shares trade on NASDAQ in dollars; HCW price target in dollars; estimates reflect pounds.

EPS Diluted			
Full Year - Dec	2019E	2020E	2021E
1st Half	£(0.03)A	£(0.04)	£(0.05)
2nd Half	£(0.02)	£(0.04)	£(0.06)
FY	£(0.05)	£(0.08)	£(0.11)



StemPrintER and SPARE validation data presentation today. In a poster slated to be presented this morning at the virtual American Society for Clinical Oncology (ASCO) 2020 Annual Meeting, scientists shall present the results of a comparative study benchmarking the StemPrintER and SPARE (together referred to as StemPrintER) genomics-based personalized medicine approaches against Oncotype DX, a well-known diagnostic test used to predict the likelihood of breast cancer recurrence. In our view, this constitutes a key potential value driver for current and future Tiziana shareholders, as the Board of Directors has already indicated that it plans to advance an initiative to spin out StemPrintER into a separate, standalone company.

Spinout should create added incentive to own Tiziana shares. We anticipate that the envisaged spinout shall permit Tiziana shareholders of record at the point of the spinout to receive shares of the new StemPrintER-focused entity in a *pari passu* manner. We note that evidence showing the superiority of StemPrintER to Oncotype DX should establish a reference for the future valuation of the StemPrintER entity, since Oncotype DX was the sole product of Genomic Health—a molecular diagnostics firm that was acquired by EXACT Sciences (EXAS; not rated) last year in a $2.8B cash-plus-stock transaction ($1.1B in cash and $1.7B in EXACT common stock). In conservatively ascribing a value of only 10% of the valuation of Genomic Health at the time of its acquisition by EXACT to StemPrintER, the future spinout entity dedicated to genomics-based personalized medicine could command a price tag of $280M. Since Tiziana currently trades at a market cap well below this level (roughly $200M), we see the future spinout of StemPrintER as a possible creator of additional shareholder value, a driver of a potential arbitrage opportunity and a derisking mechanism for current or near-term Tiziana shareholders. In effect, the prospect of receiving StemPrintER entity shares on a one-to-one basis could position Tiziana shareholders to obtain all future value creation stemming from Tiziana's entire portfolio of proprietary, innovative therapeutic candidates as upside. Our valuation and price target on Tiziana do not include any contribution from the StemPrintER platform. In anticipation of the StemPrintER spinout and near- and medium-term catalysts from Tizana's pipeline, we reiterate our Buy rating and 12-month price target of $25.00 per American Depositary Share (ADS) on TLSA. Investors should note that our price target on Tiziana's ADSs reflects the per-share price objective of £5.00 that we placed on the company's ordinary shares, which trade in London.

StemPrintER platform may disrupt breast cancer prediction. The genomics-based expression analysis underlying the original StemPrintER approach consists of a proprietary 20-gene stem cell signature derived from the transcriptional profile of normal mammary stem cells. This is capable of identifying breast cancers denoting poor prognoses via *in silico* analysis (i.e., using an algorithmic method). SPARE is an evolutionary iteration of this strategy, adding two well-established predictive clinicopathological parameters—lymph nodal status and tumor size—to the same 20-gene signature. A subset of five genes within this signature panel has been shown to retain similar predictive value, indicating that further optimization of the approach even beyond SPARE could be achieved.

Pharmacoeconomic and therapeutic value of distant recurrence predictive power appears high. The StemPrintER and SPARE tools were designed and optimized to predict distant recurrence in breast cancer patients. In particular, endocrine-responsive (ER+) breast cancer patients are either at high risk for late recurrence (roughly 40% event proportion after five to 10 years); at high risk for early recurrence (i.e., within less than five years); or at low risk of early recurrence. The SPARE and StemPrintER systems can distinguish between these groups, enabling appropriate deployment of adjuvant chemotherapy (i.e., proactive treatment for those at high risk of early recurrence, who are under-treated if mis-diagnosed, and elimination of non-beneficial treatment for those at low risk of early recurrence, who would not derive any survival benefit from chemo but are placed at greater risk of reduced quality of life and elevated healthcare system costs). While earlier-generation tests —e.g., Oncotype DX and MammaPrint—only predict early recurrence with moderate accuracy, later-generation tests (e.g., Prosigna, EndoPredict) can identify both early as well as late recurrence. The StemPrintER platform clearly outperforms the earlier-generation tests and could prove to be best-in-class among later-generation products. StemPrintER can also identify pre-menopausal women at high risk for late recurrence who would be eligible for extended hormonal therapy. We anticipate that the StemPrintER platform could be launched with CE Mark designation in multiple European countries within the next several months. Introduction into the U.S. market could occur next year as a laboratory-developed test (LDT) under CLIA certification, once validation on U.S. patient cohorts has been accomplished. Retrospective analysis should be considered appropriate in this context, since otherwise conducting prospective studies to determine predictive value based on early vs. late recurrence in breast cancer patients could take well over a decade to complete. For comparative purposes, we cite 2018 Oncotype DX sales for invasive breast cancer recurrence prediction, which reached almost $300M. While Oncotype DX was launched in 2004, we anticipate that StemPrintER uptake could be significantly faster than that of Oncotype DX once introduced, given its greater predictive power. ER+ breast cancer cases total roughly 1.3M worldwide, with approximately 300K in European Union countries alone.

COVID-19 therapeutic landscape hints at potential for TZLS-501. While the recent failure of Kevzara (sarilumab) in clinical trials with COVID-19-infected patients may have dealt a blow to the prospects of anti-IL-6 approaches, we note that recently Roche (RHHBY; not rated) teamed up Gilead Sciences (GILD; not rated) to test Roche's drug Actemra (tocilizumab), an anti-IL-6 antibody, in combination with remdesivir to treat cytokine storms in COVID-19-infected patients. This may bode well for Tiziana's TZLS-501, a fully human antibody targeting the IL-6 receptor (IL-6R)—binding to both membrane-bound and soluble forms, blocking the IL-6/IL-6R complex as well as depleting circulating levels of IL-6 in the blood. *In vitro* data has shown that TZLS-501 appears to be more potent at blocking IL-6 signaling than Actemra. We remind investors that the COVID-19 pandemic is perhaps the most serious public health threat globally today, having infected nearly 6M people and estimated to be responsible for approximately 360K deaths—with roughly 1.8M cases and over 100K deaths in the U.S. alone.

Multiple foralumab formulations target lucrative indications. Tiziana has established three different routes of administration for its anti-CD3 fully-human monoclonal antibody, foralumab—an oral capsule for treatment of Crohn's disease (CD); an intranasal formulation for treatment of secondary progressive multiple sclerosis (SP-MS); and an inhaled form to address lung inflammation and dysfunction in patients infected with the SARS-CoV-2 novel coronavirus, which is responsible for the global COVID-19 pandemic. We anticipate that proof-of-concept studies could start within six to 12 months for oral foralumab in CD and intranasal foralumab in SP-MS. The SP-MS indication is particularly intriguing, in our view—the principal competitor, from our vantage point, would be Ocrevus (ocrelizumab) from Roche (RHHBY; not rated). In 2019, Ocrevus generated $3.8B in sales—particularly noteworthy since the drug was only launched in 2H17.

Milciclib clinical data slated to be presented during ASCO 2020. In a press release earlier this month, Tiziana Life Sciences reported that updated data from clinical studies with milciclib, a small molecule pan-inhibitor of cyclin dependent kinases (CDKs), is slated to be presented this weekend during the ASCO 2020 virtual meeting. Phase 2a clinical data with orally-administered milciclib in sorafenib-resistant hepatocellular carcinoma (HCC) patients met the primary endpoint of the study, indicating that the drug was well-tolerated with manageable toxicities and no recorded drug-related deaths. Both median time to progression (TTP) and progression-free survival (PFS) were 5.9 months (95% confidence interval 1.5-6.7 months) out of the six-month duration of the trial. Approximately 57% of the 28 evaluable patients showed stable disease (SD); met at least once in an eight-week interval) and 3.6% achieved partial response (PR). The clinical benefit rate (defined as CBR=CR+PR+SD) was roughly 61% of patients. Five patients on compassionate use continued the treatment for a total of 9, 9, 11, 13 and 16 months, respectively. Two patients continuing the treatment have reached 16 months. Other milciclib data to be presented at ASCO 2020 comprises clinical results from an ongoing investigator-originated trial with a combination of oral milciclib and Stivarga (regorafenib) in liver transplant patients with recurrent HCC. Thus far, the study has shown mean alpha-fetoprotein (AFP) levels —a common tumor biomarker—were reduced by a mean of approximately 20% within one month of treatment. We note that regorafenib and sorafenib typically only generate survival benefit of a couple of months in second-line HCC and accordingly remain optimistic regarding the potential of milciclib in this arena.

Valuation methodology, risks and uncertainties. We use a discounted cash flow (DCF)-driven risk-adjusted net present value (rNPV) approach, which yields a ~$950M total firm value and price target of $25 per ADS, given 157M projected shares outstanding (roughly 31.4M ADSs based on five ordinary shares per ADS) as of mid-2021. Exchange rate: 1 US$ = £0.81. Investors should note that our valuation excludes all contribution from foralumab in areas beyond Crohn's disease; milciclib in cancers beyond HCC; TZLS-501 for any indication; and StemPrintER. Risks include: (1) delays in clinical studies with foralumab and milciclib; (2) adverse trial results with foralumab and milciclib; (3) negative regulatory decisions; (4) lower-than-anticipated market penetration rates; and (5) possible dilution risk.

Table 1: Tiziana Life Sciences PLC (TLSA)—Historical Income Statements, Financial Projections

FY end December 31
£ in thousands, except per share data

	2019E					2020E					
		1HA		2HE	2019E	1QE	2QE	3QE	4QE	2020E	2021E
Revenue											
Product revenue	-	-	-	-	-	-	-	-	-	-	-
Service revenue	-	-	-	-	-	-	-	-	-	-	-
Research and other	-	-	-	-	-	-	-	-	-	-	-
Total revenue	-	-	-	-	-	-	-	-	-	-	-
Expenses											
Cost of product and service revenue	-	-	-	-	-	-	-	-	-	-	-
Research & development	-	1,507	-	1,200	2,707	1,000	1,200	1,500	1,600	5,300	9,900
General and administrative	-	2,202	-	1,500	3,702	1,600	1,600	1,600	1,600	6,400	8,000
Total expenses	-	3,709	-	2,700	6,409	2,600	2,800	3,100	3,200	11,700	17,900
Gain (loss) from operations	-	(3,709)	-	(2,700)	(6,409)	(2,600)	(2,800)	(3,100)	(3,200)	(11,700)	(17,900)
Other income/expense											
Interest income/expense	-	(5)	-	(5)	(10)	-	-	-	-	-	-
Realized loss on marketable securities	-	-	-	-	-	-	-	-	-	-	-
Other income/expense	-	-	-	-	-	-	-	-	-	-	-
Total investment income and other	-	(5)	-	(5)	(10)	-	-	-	-	-	-
Loss before provision for income taxes	-	(3,714)	-	(2,705)	(6,419)	(2,600)	(2,800)	(3,100)	(3,200)	(11,700)	(17,900)
Provision for tax		27			27					-	-
Net loss/income	-	(3,687)	-	(2,705)	(6,392)	(2,600)	(2,800)	(3,100)	(3,200)	(11,700)	(17,900)
Net loss per share (basic)	-	(0.03)	-	(0.02)	(0.05)	(0.02)	(0.02)	(0.02)	(0.02)	(0.08)	(0.11)
Net loss per share (diluted)	-	(0.03)	-	(0.02)	(0.05)	(0.02)	(0.02)	(0.02)	(0.02)	(0.08)	(0.11)
Weighted average number of shares outstanding (basic)	-	126,049	-	126,049	126,049	142,716	144,741	151,791	156,841	149,022	156,966
Weighted average number of shares outstanding (diluted)	-	126,049	-	126,049	126,049	142,716	144,741	151,791	156,841	149,022	156,966

Source: Company reports and H.C. Wainwright & Co. estimates.

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RETURN ASSESSMENT

Market Outperform (Buy): The common stock of the company is expected to outperform a passive index comprised of all the common stock of companies within the same sector.

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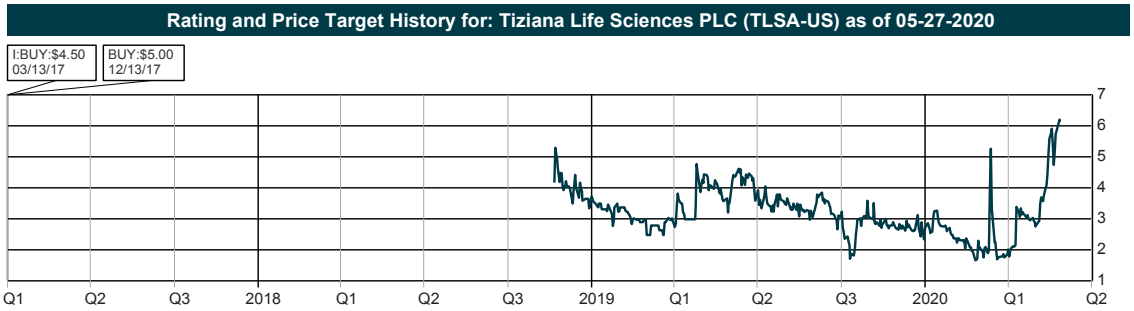

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Distribution of Ratings Table as of May 27, 2020				
			IB Service/Past 12 Months	
Ratings	Count	Percent	Count	Percent
Buy	382	90.52%	132	34.55%
Neutral	37	8.77%	7	18.92%
Sell	0	0.00%	0	0.00%
Under Review	3	0.71%	3	100.00%

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