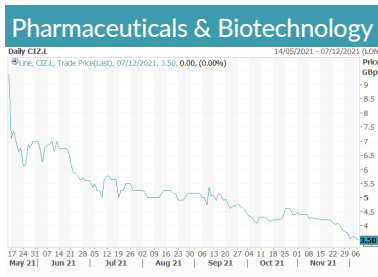




7 December 2021

**Market data**

EPIC/TKR	CIZ
Price (p)	3.6
12m high (p)	10.0
12m low (p)	3.5
Shares (m)	253.4
Mkt cap (£m)	9.1
EV (£m)	8.3
Free float	72%
Country of listing	UK
Market	LSE Main

Description

Cizzle is a medical device company developing diagnostic tests for the early detection of cancer and companion diagnostics for autoimmune disease. Its first test will be used alongside a positive chest scan to confirm presence of lung cancer and reduce the high rate of false positives.

Company information

Executive Chair	Allan Syms
NED/Founder	Dawn Coverley
CFO	Nigel Lee
NED	John Treacy

www.cizzlebiotechnology.com

Key shareholders

Directors	5.3%
Yorkshire Cancer Research	12.8%
Finance Yorkshire	9.6%
University of Leeds	4.4%
University of Sheffield	4.4%
University of York	3.2%

Diary

Apr'22	Final results
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Analyst

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CIZZLE BIOTECHNOLOGY

News flow driven by deals

Cizzle Biotechnology (Cizzle), focused on cancer diagnostics, was spun out of the University of York to exploit the biomarker, variant CIZ1b, for early detection of different forms of lung cancer. There is high medical need for a simple blood test that allows early detection of lung cancer and potentially improve patient outcomes. Since listing, Cizzle has been considering how to develop a broader screening test that could be used to test for other cancers and developing a companion diagnostic for autoimmune disease. Cizzle continues to make progress, and has expanded the number of potential income streams through strategic partnerships.

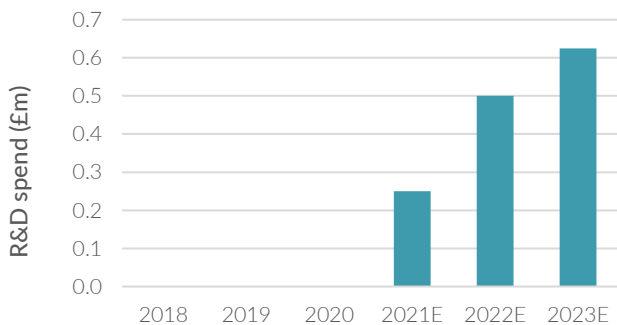
- **Strategy:** Cizzle is progressing a biomarker diagnostic assay for early detection of lung cancer, via a simple blood test, to improve the chances of survival, and to greatly reduce the need for unnecessary follow-up tests and tissue biopsies. Also, it is extending into related autoimmune disease with companion diagnostics.
- **China:** The company has recently signed a memorandum of understanding (MoU) with two local partners in China for the development, supply and commercialisation of its early lung cancer test. A full commercial deal covering all aspects of this arrangement, including supply and royalties, is currently being negotiated.
- **SGSC:** Cizzle has already converted an MoU with St. George Street Capital (SGSC), a UK-based medical charity, into two full deals. The first involves the development of a companion diagnostic for a late-stage clinical asset; the second involves a commercial and royalty deal, with potential to generate royalties of up to £5m.
- **FairJourney:** In July, Cizzle signed a collaboration deal with FairJourney Biologics (FJB) for the development and supply of proprietary monoclonal antibodies and reagents that will be the foundation for protein detection in its ELISA-based test. This was a key step highlighted in its admission document in May.
- **Investment summary:** Despite the deal news flow, which has expanded both the timing and interest in potential revenue streams, the shares have drifted since Cizzle was listed, leaving the company trading on an EV of just £8.3m. This suggests that there is considerable upside potential when investors become more aware of the company as further deals are announced and as development progress is reported.

Financial summary and valuation

Year-end Dec (£000)	2018	2019	2020	2021E	2022E	2023E
Sales	0	0	0	0	0	0
COGS	0	0	0	0	0	0
SG&A	-54	-22	-15	-300	-500	-550
R&D	0	0	0	-250	-500	-625
Other income	51	0	0	200	800	0
Underlying EBIT	-3	-22	-15	-370	-250	-1,425
Statutory EBIT	-3	-22	-15	-3,594	-250	-1,425
Underlying PBT	-3	-22	-15	-371	-251	-1,426
Underlying EPS (p)	-0.9	-6.9	-4.8	-0.2	-0.1	-0.5
Statutory EPS (p)	-0.9	-6.9	-4.8	-2.2	-0.1	-0.5
Net cash/(debt)	20	13	-3	855	535	-684
Equity issues	0	0	0	2,200	0	0

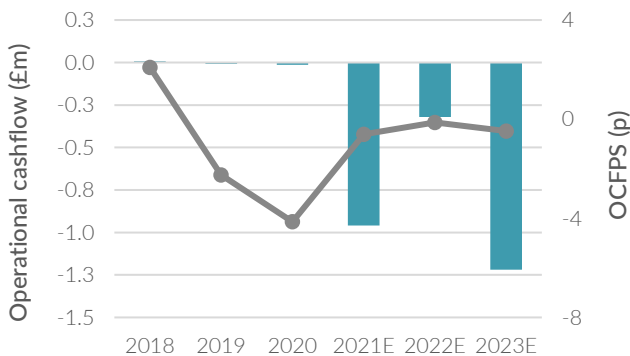
Source: Hardman & Co Life Sciences Research

R&D investment



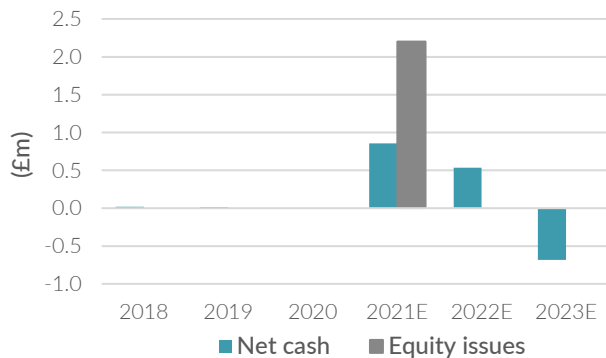
- ▶ Cizzle has successfully developed a prototype CIZ1b biomarker test on very limited resources.
- ▶ Much of the elucidation and understanding of CIZ1 was undertaken with grant funding.
- ▶ R&D investment will rise in order to develop the commercial CIZ1b biomarker test based on mAb direct-ELISA.
- ▶ Some of the rise in R&D investment will be reimbursed by partners.

Operational cashflow and OCFPS (RHS)



- ▶ Cizzle will have two costs: R&D investment and the general corporate overhead.
- ▶ Some R&D tax credits can be expected, but payment by HMRC is usually 6-12 months in arrears.
- ▶ Given that much of the work will be outsourced, Cizzle will have only modest working capital requirements.
- ▶ The underlying cash burn during 1H21 was a modest £119k.

Net cash and equity issues



- ▶ As part of its admission, Cizzle raised gross new capital of £2.2m (£1.97m net) through an institutional placing.
- ▶ At 30 June 2021, Cizzle had gross (and net) cash of £1.43m.
- ▶ Forecasts suggest that this will provide a cash runway of 18-24 months and that further funds will be required towards the end of 2022.

RHS=right-hand scale
 Source: Company data, Hardman & Co Life Sciences Research

Early lung cancer detection

The primary goal of Cizzle is to expand on the scientific work originally undertaken by Professor Coverley and her team at the University of York regarding the role and understanding of variants of Cdkn1A-interacting zinc finger protein 1 (CIZ1) in many common cancers, through the development of diagnostic tests – in particular, variant CIZ1b, for the early detection of different forms of lung cancer.

Lung cancer is generally first identified from a chest scan. Patients with suspicious scans then undergo further tests. However, these often result in false positives that require two-year follow-up. Eliminating 50% of these could help patients and generate substantial cost savings for healthcare providers.

Cizzle has a proven prototype test. However, to move this to a commercial product with CE marking, the company needs to address a number of points, including the development and supply of proprietary monoclonal antibodies and reagents that will be the foundation for protein detection in its ELISA-based test, optimisation of the reagents and buffer environment, and validation of the test with a retrospective trial.

Antibody development

A key step is the identification and development of an antibody for the detection of CIZ1b in its diagnostic test. In July, Cizzle announced that it had signed a collaboration with FJB for the development and supply of proprietary monoclonal antibodies and reagents that will be used for protein detection in its ELISA-based test. This agreement expanded on the original plan, in that a licensable antibody-complex could arise, which could be used by research scientists to further the global knowledge and understanding of the role of CIZ1 and its variants, and thereby provide Cizzle with the opportunity to generate additional income streams and to increase value.

FJB is a Portuguese-based biologics clinical research organisation, which acquired IONTAS, a Cambridge-based antibody company, in 2020. FJB has a >99% record of developing antibodies for a specific target in a timely manner, using phage display technology. This work is currently ongoing.

Commercialisation in China

At the end of November, Cizzle announced an MoU with the International Co-Innovation Centre for Advanced Medical Technology (iCCAMT) and Shenzhen Intelliphecy Life Technologies Co., Ltd. (Intelliphecy) for the development and commercialisation of its CIZ1b-based early lung cancer biomarker test in China. iCCAMT has good provenance with world-leading expertise, having been founded by German Medical Valley, Robert Bosch GmbH, Sinopharm Group and the government, with the aim of accelerating global med-tech innovation in China. Discussions are underway to convert this MoU into a full agreement.

The intention is that the parties will collaborate closely throughout the process, covering development, manufacture and commercialisation of the test. The MoU envisages that iCCAMT and Intelliphecy will fund all the activities in China, and that Cizzle will receive payment for monoclonal antibodies and reagents produced, as well as services provided, together with royalties on any sales of products and services in China.

It is anticipated that a similar commercial approach will be taken in China to that often adopted in the US for diagnostic tests – namely a laboratory developed test (LDT) – whereby a regulated service using a biomarker is being sold, as opposed to the sale of a regulated biomarker. This would result in a reduced timescale to reach commercialisation. Further details are likely to be released when the full agreement is concluded.

Relationship with SGSC

Since listing in May 2021, Cizzle has been investigating the best approach for developing a broader screening test that could be used for other cancers and to maximise its scientific opportunity. As part of this process, and given its limited resources, the company has concluded two deals with SGSC.

About SGSC

SGSC is a UK-based biomedical research charity that was formed to deliver much-needed treatments to patients in areas of high unmet medical need, in a timely manner. It is led by a group of highly decorated academics and ex-pharma executives. Clinical assets acquired by the charity are developed through SGSC's commercial arm, with the help of external investment.

Summary of key personnel at SGSC		
Name	Position	Experience
Clinical		
Prof. John Martin	Chair	Professor of Cardiovascular Medicine, University College Medicine.
Prof. Pete Coffey	Trustee	Professor of Ocular Biology and Therapeutics, UCL Institute of Ophthalmology.
Dr Raymond MacAllister	Trustee	Clinical Pharmacologist and Consultant Physician.
Dr Elin Haf Davies		Consultant at Great Ormond Street Hospital, Institute of Child Health (UCL), EMA, Aparito.
Operations		
Dave Tapolczay	CEO	Ex-CEO of MRC Technology. Has launched and held executive positions at several biotechnology companies.
Mike Johnson	Managing Director	Ex-MRC Technology and LifeArc.
Jamie Chorlton	Clinical Development	Multiple senior positions in biotech industry.

Source: <https://www.sgscapital.org/>

SGSC's strategy is to license existing clinical assets from pharmaceutical companies and to fast-track them through Phase II clinical trials, before out-licensing them for Phase III trials and commercialisation. SGSC has a number of programmes, but one of its more advanced involves an asset originally developed by AstraZeneca (AZN.L), known as AZD1656, in which Cizzle now has an economic interest.

AZD1656 is a potent and selective activator of glucokinase that was being developed by AZN for type II diabetes. SGSC recognised that the effects of AZD1656 on immune function might be useful to treat people with diabetes that had become infected with COVID-19. This was confirmed during 2021, with encouraging results in a Phase II clinical trial, known as ARCADIA, in 150 patients with either type I or type II diabetes, who were hospitalised with mild-to-moderate COVID-19. There was a strong trend towards reduced mortality in patients receiving AZD1656. Data from ARCADIA support the continued investigation of AZD1656 for the treatment of patients with COVID-19, with or without diabetes, and SGSC is now considering its options to progress AZD1656 through a Phase III trial.

Deals with Cizzle

The relationship between Cizzle and SGSC was initiated in June 2021, through an MoU between the two parties, which has now been formalised through two separate agreements with respect to the development and commercialisation of AZD1656.

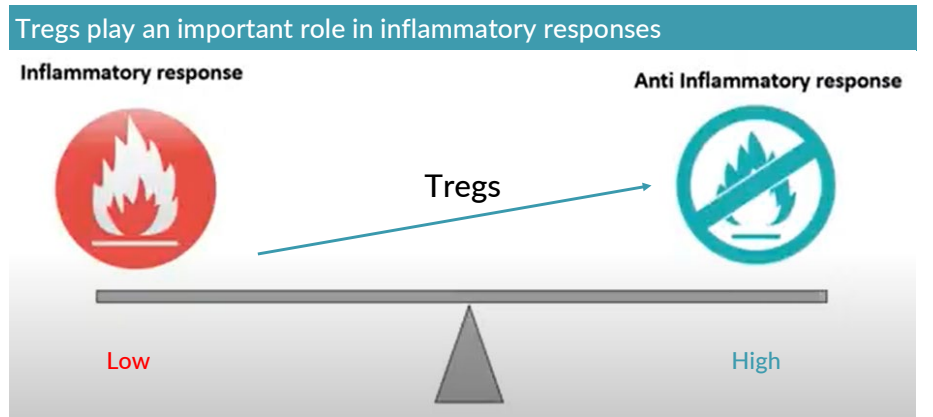
Royalty

In September 2021, Cizzle announced the conclusion of a royalty deal (see research report¹). In return for payments totalling £200k, Cizzle is entitled to receive royalties of up to £5m on net sales from the commercialisation of AZD1656.

Companion diagnostic

In October 2021, Cizzle and SGSC concluded an R&D agreement to develop a companion diagnostic platform for tests that can be used alongside SGSC’s therapeutic assets licensed from AZN, which seek to address unmet clinical needs in autoimmune disease. SGSC will pay Cizzle £0.2m on the commencement of the project and milestones totalling up to £1m. Our understanding is that the initial fee will be paid when SGSC has completed a pending funding round to finance the clinical trial programme.

The aim of this companion diagnostic is to provide valuable patient information to support the proposed mechanism of action of AZD1656, which is thought to be linked to the complex regulation of inflammation by activating the migration of regulatory T cells (Tregs) to sites of inflammation. Tregs are considered to have both stimulatory and inhibitory roles to maintain homeostasis of the immune response, since they are the principal immune suppressor cells, thereby maintaining the balance between the inflammatory and anti-inflammatory responses. In the absence of Tregs, the balance trips over to an inflammatory response, and *vice versa*. Tregs have been shown to inhibit T cell proliferation and cytokine production, thereby playing a critical role in preventing autoimmunity.



Source: Adapted from “Animated biology with Arpan”

Conclusion

Through these deals, and others highlighted on earlier pages, Cizzle is increasing its scientific knowledge, expanding its asset base and advancing the number of potential income streams, while not detracting from its core focus on cancer diagnostics.

Cash position

At the end of June, Cizzle had a net cash position of £1.43m. During 2H21, apart from the ongoing corporate overhead, a payment of £135k to SGSC has been incurred, which is expected to be countered by development income from SGSC, for the companion diagnostic development, estimated at £200k. Also, payments to FJB for the antibody development are expected to become due during 2H21. Consequently, we are forecasting a net cash position of c.£0.85m at the end of 2021.

¹ <https://www.hardmanandco.com/research/corporate-research/strategic-collaboration-with-sgsc/>

Financial summary

The income statement continues to be dominated by the investment in R&D and the corporate overhead during the forecast period. No income is expected, other than recoverable supply and development costs from its collaboration partners. Therefore, these costs will drop straight through to the cashflow statement, and determine the net cash position at the end of each financial year.

- ▶ **R&D:** The majority of the forecast R&D expense in 2021 is the payment to FJB for the antibody development work. In future years, the R&D will be a blend of the work for Cizzle's CIZ1b diagnostic and the companion diagnostic for SGSC, but most of the latter will be recoverable.
- ▶ **Administration:** Given that most activities are outsourced, the general corporate overhead is forecast to be kept at a relatively low level.
- ▶ **Exceptional items:** In 2021, the large exceptional reflects the reverse takeover and transaction costs associated with the creation of the new entity, known as Cizzle.
- ▶ **Net cash/(debt):** Tight control of its limited resources suggests that Cizzle will end the current year with c.£0.85m of cash, and no debts or lease liabilities.

Financial summary						
Year-end Dec (£000)	2018	2019	2020	2021E	2022E	2023E
Income statement						
Sales	0	0	0	0	0	0
COGS	0	0	0	0	0	0
SG&A	-54	-22	-15	-300	-500	-550
Share-based costs	0	0	0	-20	-50	-250
R&D	0	0	0	-250	-500	-625
Licensing/royalties	51	0	0	200	800	0
Underlying EBIT	-3	-22	-15	-370	-250	-1,425
Exceptional items	0	0	0	-3,224	0	0
Statutory EBIT	-3	-22	-15	-3,594	-250	-1,425
Net financials	0	0	0	-1	-1	-1
Underlying PBT	-3	-22	-15	-371	-251	-1,426
Statutory PBT	-3	-22	-15	-3,595	-251	-1,426
Tax liability/credit	0	0	0	50	100	125
Underlying net income	-3	-22	-15	-321	-151	-1,301
Underlying basic EPS (p)	-0.9	-6.9	-4.8	-0.2	-0.1	-0.5
Statutory basic EPS (p)	-0.9	-6.9	-4.8	-2.2	-0.1	-0.5
Balance sheet						
Share capital	3	3	3	25	25	25
Reserves	25	3	-12	1,846	1,695	395
Leases	0	0	0	0	0	0
Loans & borrowings	0	0	10	10	10	10
less: Cash & deposits	20	13	7	865	545	-674
Invested capital	8	-6	-5	1,017	1,186	1,105
Cashflow						
Underlying EBIT	-3	-22	-15	-370	-250	-1,425
Change in working capital	8	15	2	-199	-169	-144
Company op cashflow	7	-7	-13	-958	-369	-1,319
Capital expenditure	0	0	0	0	0	0
Equity issues	0	0	0	2,200	0	0
Change in net cash/(debt)	7	-7	-13	858	-320	-1,219
Opening net cash/(debt)	13	20	13	-3	855	535
Closing net cash/(debt)	20	13	-3	855	535	-684

Source: Hardman & Co Life Sciences Research

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