Pharmaceuticals & Biotechnology

Source: Refinitiv

Market data	
EPIC/TKR	**CIZ**
Price (p)	**1.4**
12m high (p)	7.0
12m low (p)	1.3
Shares (m)	278.4
Mkt cap (£m)	3.9
EV (£m)	3.0
Free float	73%
Reporting currency	GBP
Country of listing	UK
Market	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	4.8%
Yorkshire Cancer Res.	11.6%
University of Sheffield	4.0%
University of Leeds	4.0%

Diary

Sep'22	Interim results

Analyst

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CIZZLE BIOTECHNOLOGY

Considerable progress in first year since listing

Cizzle Biotechnology (Cizzle), focused on cancer diagnostics, was spun out of the University of York to exploit the biomarker, variant CIZ1b, for the early detection of different forms of lung cancer. While implementing this strategy over the past year, Cizzle's interest has been broadened to include early detection of other cancers and companion diagnostic tests that can assist in the development and use of personalised medicines. In the 12 months since listing, Cizzle has secured key partners to generate monoclonal antibodies (mAb) and reagents for a commercial test, and signed licensing and royalty deals.

- **Strategy:** Cizzle is a diagnostic company that is progressing a biomarker diagnostic assay, which aims to deliver a simple blood test for lung cancer that can pick up the disease earlier to improve the chances of survival, and to greatly reduce the need for unnecessary follow-up tests and tissue biopsies.
- **Progress:** Since listing, Cizzle has generated mAb with key suppliers and developed reagents, optimised assay conditions needed for a commercial test, and signed development and commercial deals in the key markets of China and the US. It has also expanded potential long-term income streams through royalty deals.
- **Valuation:** Our DCF model has been updated to reflect timing of launch, market opportunity and commercial deals for the key markets of China and the US These revisions generated a risk-adjusted value of £15.9m for the test. Adding in the value of royalty agreements gives a sum-of-the-parts valuation of £23.0m.
- **Risks:** Cizzle is a small company with limited resources. Development of a commercial test kit for lung and other cancers is dependent on the optimisation of the mAbs and reagents and validation in a small trial. Development and commercial deals in key territories have greatly reduced R&D costs and risks.
- **Investment summary:** Since listing, Cizzle has delivered a stream of positive news, particularly the collaborations and strategic partnerships that accelerate the number and magnitude of potential income streams. Delivery of the detector mAbs and reagents for the commercial test was a significant milestone, and triggers the development in China and the US. Despite this news, the shares are underappreciated, leaving the company trading on an EV of just £3.0m.

Financial summary and valuation

Year-end Dec (£m)	2019	2020	2021	2022E	2023E	2024E
Sales	0	0	0	0	0	0
SG&A	-22	-15	-391	-500	-550	-605
R&D	0	0	-161	-350	-1,100	-650
Other income	0	0	0	400	600	0
Underlying EBIT	-22	-15	-851	-500	-1,300	-1,518
Statutory EBIT	-22	-15	-3,958	-500	-1,300	-1,518
Underlying PBT	-22	-15	-851	-500	-1,300	-1,518
Statutory PBT	-22	-15	-3,958	-500	-1,300	-1,518
Underlying EPS (p)	-6.9	-4.8	-0.5	-0.2	-0.4	-0.5
Statutory EPS (p)	-6.9	-4.8	-2.4	-0.2	-0.4	-0.5
Net cash/(debt)	13	-3	875	510	-420	-1,387
Equity issues	0	0	2,200	1,000	880	0

Source: Hardman & Co Life Sciences Research

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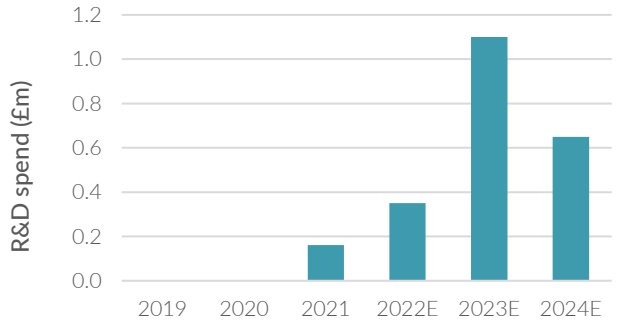
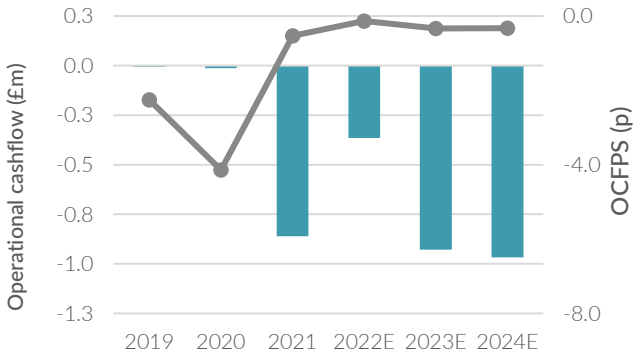
R&D investment



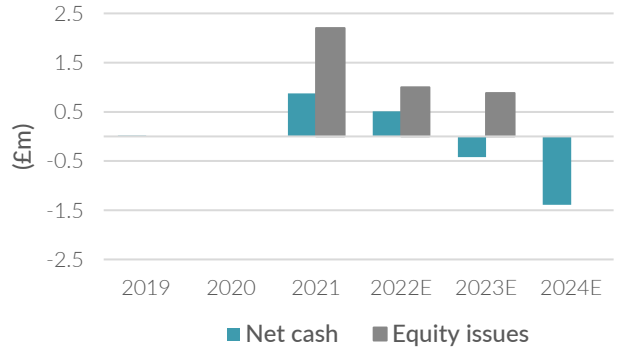
- Cizzle is developing a commercial test based on the CIZ1b biomarker, having successfully developed a prototype test on very limited resources.
- Much of the elucidation and understanding of CIZ1 in the early years was undertaken with grant funding.
- R&D investment will ramp up when appropriate funding is in place, although the requirements have changed with the signed licensing deals and the expanded contract with the University of York to include other cancers.

Operational cashflow and OCFPS



- Cizzle has two costs: R&D investment and the general corporate overhead.
- Tax credits on R&D can be expected, but payment by HMRC is usually six to 12 months in arrears.
- Given that much of the work will be outsourced, Cizzle will have only modest working capital requirements.
- The monthly cash burn during 2021 was a modest £123k. This burn rate in 2022 is expected to considerably lower at £30k, but dependent on the timing of R&D spend.

Net cash and equity issues



- On listing, Cizzle raised gross new capital of £2.2m (£1.97m net) through an institutional placing.
- At 31 December 2021, Cizzle had gross (and net) cash of £0.875m.
- Forecasts suggest that this will provide a cash runway of 12 months and that further funds will be required towards the end of 2022.
- Equity issues shown in 2022 and 2023 represent the shares issued to SGSC to acquire long-term royalty streams.

Source: Company data, Hardman & Co Life Sciences Research

Latest results – 2021 finals

Cizzle has reported its first set of full-year numbers following its reverse takeover by Bould Opportunities and re-listing of the shares in May 2021. The core ambition remains on the early detection of lung cancer from a simple blood sample through the commercialisation of its proprietary CIZ1b biomarker technology. Additionally, it will expand into early detection of other cancers and autoimmune diseases through its own research capability, strategic licensing deals and partnership programmes.

Operational highlights

- **Test development:** In June 2021, Cizzle signed a collaboration agreement with FairJourney Biologics (FJB) to develop a range of monoclonal antibodies (mAbs) and reagents for use in an immunoassay for the detection of CIZ1b biomarker. These mAbs may also be used in the future early detection of other cancers.
- **Research agreement:** In September 2021, Cizzle agreed a new research agreement with the University of York for the development of its blood test for the early detection of lung cancer, and potentially other forms of cancer. This was expanded further in April 2022, extending this work until March 2023.
- **Companion diagnostic:** In October 2021, Cizzle finalised an R&D agreement with St George's Street Capital (SGSC), a UK-based medical charity, for the development of a companion diagnostic test for autoimmune disease that can be used alongside certain SGSC assets licensed from AstraZeneca.

Post-period events

- **China:** Following an initial Memorandum of Understanding (MoU), in February 2022, Cizzle signed a full development and commercial agreement with a syndicate in China (see page 7) for its CIZ1b lung cancer test in China. Cizzle will receive a 10% royalty of future net sales and royalties.
- **United States:** In May 2022, Cizzle signed a Heads of Terms (HoT) with CorePath Labs, a full-service cancer reference laboratory, for the development and commercialisation of the CIZ1b diagnostic test for early-stage lung cancer test in the US. Cizzle will receive 15% royalty of future sales and services.

Financial highlights

- **Operating costs:** Given its limited resources, all costs are closely controlled. The main focus is on the delivery of the required antibodies, reagents and assay formats that will enable partners in China and the US to commence development.
- **Exceptional costs:** There were exceptional costs associated with the reverse takeover of Cizzle and the re-listing of shares of £3.1m, the vast majority of which was a non-cash, share-based expense.

Results summary – actual vs. expectations

Year-end Dec (£000)	2020 actual	2021 actual	Growth CER	2021 forecast	Delta Δ
SG&A	-15	-391	n/m	-400	+9
Share-based costs	0	-299	n/m	-20	-279
R&D	0	-161	n/m	-150	-11
Underlying EBIT	**-15**	**-851**	**-**	**-570**	**-281**
Equity issues	0	2,200	-	2,200	0
Gross cash	7	875	-	840	+37
Net cash/(debt)	**-3**	**875**	**-**	**840**	**+37**

Note: numbers may not add up exactly due to rounding
Source: Hardman & Co Life Sciences Research

Test development

At the time of the reverse takeover, Cizzle had developed and tested a prototype test for early detection of lung cancer based on the CIZ1b biomarker using Western Blotting (WB) and enzyme-linked immunosorbent assay (ELISA) assays, with high sensitivity and a clinically useful low false-positive rate. Published research indicated that the test was viable and could select a positive sample. The next stage has been to optimise this polyclonal point-of-care (POC) test with scalable mAbs and reagents for high-throughput applications in a hospital setting. The strategy was, and remains, to refine the prototype test with a more standardised ELISA test linked to a mAb that would be more suitable for commercial scale-up and kit manufacture.

Comparison of WB with ELISA

Characteristic	WB	ELISA
Detection method	Immuno	Immuno
Sensitivity	High	High
Specificity	High	High
False positives	Potentially high	Potentially high
Quantification of specific protein	Can be poor	Good
Determine size of protein	Good	Very poor
Technical expertise needed	High level	Low level
Use in screening	Cumbersome	High throughput

Source: BioRad, Hardman & Co Life Sciences Research

Antibody development

Critical for a commercial test has been the development and supply of proprietary mAbs 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.

Shortly after listing, in July 2021, Cizzle announced that it had signed a collaboration with FJB for the development and supply of proprietary mAbs and reagents that will be used for protein detection in its ELISA-based test.

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.

The agreement with FJB expanded on the original plan in two ways. First, the development of 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 the company with the opportunity to generate additional income streams and to increase value. Secondly, the aspirations of Cizzle were broadened to include diagnostic tests that could help in the development of personalised medicines, so called “companion diagnostics”, thereby expanding the potential customer base to include the pharmaceutical industry and providing the opportunity to secure long-term royalties.

Current status

During the course of its collaboration with FJB, Cizzle has increased greatly its knowledge on reagent performance and assay formats. On 5 July, the company reported that FJB has successfully generated and validated a reporter mAb for use in a sandwich ELISA test.

Additionally, Cizzle recognised the importance of having a range of mAbs to detect CIZ1b and has engaged with additional suppliers. This has resulted in the generation of a mouse mAb antibody that specifically detects CIZ1b and that assay conditions for its use are now being optimised. Further work is being undertaken to isolate rabbit mAbs arising from the initial proof-of-concept studies.

The importance of this additional work is to expand the potential of CIZ1b to include the detection of other cancers, thereby extending the market opportunity.

In summary:

- mAb to CIZ1b generated and now in assay optimisation phase
- mAb reporter protein developed and ready for test development
- Additional supplier agreements for the mAbs in place to expand potential uses
- Work initiated to extend test indications for other cancers

Out-licensing deals

During the first year since listing, Cizzle has completed two important out-licensing deals for its CIZ1b diagnostic test covering two of the most important territories in the world for lung cancer – China and the US.

China

Cizzle identified China as one of the key commercial opportunities in the world because of the high incidence of lung cancer and a market where there are serious challenges in being able to detect cancer early. Consequently, there is an enormous need for easy and effective screening and diagnosis of cancer among the Chinese population. Targeted testing would be expected to improve timely access to cancer care and save lives. On the basis that at-risk patients are screened every three years, iCCAMT estimates that 30m tests p.a. would be required.

At the end of November 2021, Cizzle announced an MoU with iCCAMT and Intelliphecy for the development and commercialisation of its CIZ1b-based early lung cancer biomarker test in China. This was converted into a full commercial agreement in February 2022.

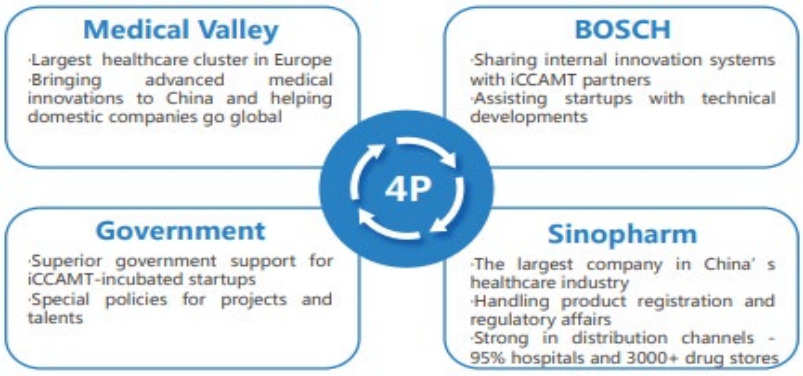
iCCAMT

iCCAMT has good provenance with world-leading expertise, having been founded by Medical Valley Germany, Robert Bosch GmbH, Sinopharm Group and local governments, with the aim of solving technical issues for innovative startups and accelerating global medtech innovation in China. As products evolve towards regulatory approval, iCCAMT assists with technology transfer and the establishment of local manufacturing.

iCCAMT partners

Source: iCCAMT website

iCCAMT four-partners ecosystem



Source: iCCAMT website

iCCAMT is based in Shanghai, providing an appropriate climate and infrastructure to promote innovation.

iCCAMT eco-chain for innovation

Source: iCCAMT website

Terms of the deal

The deal is good from Cizzle's perspective, because it promotes the development of its CIZ1b-based diagnostic test for lung cancer at little cost to the company, secures supply agreements for monoclonal antibodies and reagents used in the test, and will bring future royalties on sales.

- The partners are responsible for funding all activities in China, including the development, clinical trials, manufacturing of commercial test kits, and distribution of the product.
- Initial development will commence within 60 days of Cizzle supplying the immunoreagents to its partners in China.
- Cizzle will supply, and be paid for, all the monoclonal antibodies and reagents used in the test, for security and quality control.
- Cizzle is to receive a 10% royalty on net sales of all products and services using its proprietary CIZ1b technology.

Lung cancer in China

According to the World Health Organisation (WHO) and the National Cancer Research Centre[1], lung cancer is the leading cause of cancer-related mortality in China and has been increasing over the past decades. This has created a massive challenge for the government and health bodies, with significant effort and favourable policies for screening and prevention. Indeed, one of the aims of iCCAMT is to accelerate product development and clinical trials to achieve early adoption within major cancer centres throughout China. The other partner, Intelliphecy, is aiming to innovate technologies in the hope of winning the war against cancer, aspiring to out-smart cancer cells through artificial intelligence (AI).

- Lung cancer accounts for 20% of all cancer diagnoses in China each year.
- There are an estimated 785,000 new cases of lung cancer annually in China, and the WHO forecasts that this may rise to one million cases p.a. by 2025.
- In 2015, an estimated 630,500 patients in China died with lung cancer being cited as the primary cause, accounting for 27% of all cancer deaths.
- Compared with statistics in the rest of the world, lung cancer in China is found in a relatively younger age group, which is thought to be attributed to air pollution and smoking.
- iCCAMT estimates that 95.8m people in China have a high risk of developing lung cancer and, if screening were performed every three years, 30m tests p.a. would be required.

Test status

Everything is in place for iCCAMT to commence the test development as soon as the detection and reagent mAbs have been validated. iCCAMT has already secured strong interest from its national network of clinical centres and key opinion leaders, through which it is planning to undertake an initial pilot in 300 patients at China's premier cancer hospitals – the Cancer Hospital, Chinese Academy of Medical Sciences, National Cancer Centre, and Beijing Cancer Hospital, affiliated with Peking University – which will allow for a truly representative patient cohort to be included. If successful, this would be expected to accelerate adoption and product rollout in China.

[1] Dianqin Sun *et al*., Cancer burden in China: trends, risk factors and prevention. *Cancer Biol Med.* 2020 Nov 15; 17(4): 879–895. doi: 10.20892/j.issn.2095-3941.2020.0387

Unites States

Lung cancer is the second most common cancer among both men (after prostate) and women (after breast), in the US, excluding the ubiquitous skin cancer. The American Cancer Society (ACS) estimates that there will be about 236k new cases of lung cancer identified in 2022[2]. More people die from lung cancer in the US than from the next five most common cancer types, with the ACS predicting that 130k people will die from lung cancer in 2022. One of the reasons for this is that diagnosis tends to occur at too late a stage in the disease process, highlighting the need for an accurate early-stage test.

CorePath agreement

In May 2022, Cizzle announced that it had agreed HoT with CorePath to develop and offer the variant CIZ1b biomarker test via its cancer reference laboratory, which is accredited by both Clinical Laboratory Improvement Amendments ("CLIA") and College of American Pathologists ("CAP") and operates nationally throughout the US. Based in San Antonio, Texas, CorePath prides itself in speed, accuracy and technology associated with commercial labs while cultivating an environment of learning and understanding that, usually, can only be found in universities. It has a specialisation in haematopathology testing from blood and tissue samples, which fits in well with Cizzle's approach.

The proposal would see Cizzle receiving a 15% royalty and royalty sharing arrangement on the provision of all products and services associated with the CIZ1b test that have been provided by CorePath in the US.

Behnke agreement

As part of the process for identifying and facilitating the deal with CorePath, Cizzle worked with Behnke Group (Behnke), a Texas-based healthcare consulting firm with many years of experience collaborating with healthcare organisations both nationally across the US, and internationally. Subsequently, Cizzle expanded this relationship by entering into an agreement with Behnke to enhance its commercial aspirations for the US through Behnke's network of clinical and healthcare industry connections.

- Behnke will promote, identify and facilitate partnerships for Cizzle with healthcare providers and businesses in the US.
- Behnke will establish targeted lead generation campaigns to aid the direction of marketing and branding strategies and work with its network of US-based health systems, clinical diagnostic and pharmaceutical companies.
- Behnke will work with CorePath to enhance the development of Cizzle's CIZ1b test for the US market through CorePath's accredited laboratory.

[2] https://www.cancer.org/cancer/lung-cancer/about/key-statistics.html

Royalty deals

Since listing, Cizzle has additionally 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 and Conduit Pharmaceuticals (Conduit).

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/

About Conduit

Conduit is a UK-based private company, established in 2019, to fund the development of clinical assets licensed exclusively from large pharma companies. Conduit is led by a group of experienced executives and takes ownership of deprioritised assets from the major drug companies and funds them through Phase IIb. Following successful clinical trials, Conduit licenses out these assets, typically for development and sales milestones and retains a royalty income stream for the life of the patent. These income streams are then used to further develop its portfolio of programmes.

Summary of key personnel at Conduit

Name	Position	Experience
Dr David Tapolczay	CEO	Head of chemistry at Zeneca agrochemicals; VP at GlaxoSmithKline Pharmaceuticals; SVP at Millennium Pharmaceuticals.
Dr Freda Lewis-Hall	Proposed Chair	Chief Medical Officer and EVP at Pfizer; Medical Affairs at Vertex, Bristol-Myers Squibb, Pharmacia and Eli Lilly.

Source: https://www.conduitpharma.com/

The strategies of both SGSC and Conduit are similar and there is a close working relationship between the two organisations. They aim 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. They have 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 and Conduit 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.

Additionally, in February 2022, Cizzle entered into an agreement with Conduit Pharmaceuticals (Conduit) and SGSC to acquire a further economic interest in the commercialisation of AZD1656 for its use in the treatment of inflammatory pulmonary and cardiovascular diseases.

Royalties

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

The deal with Conduit/SGSC expanded the royalty opportunity for Cizzle to an additional 5%, which is uncapped. The total consideration for this 5% economic interest is £1.88m, which is being satisfied through the issue of new Ordinary shares. £1.0m was paid on signing, through the issue of 25.0m shares at 4.0p per share (57% premium to the previous day's closing price). The remaining consideration of £0.88m will be payable in new ordinary shares issued at 4.0 pence per share, on the earlier of receiving shareholder approval to issue the shares or the first anniversary of completion.

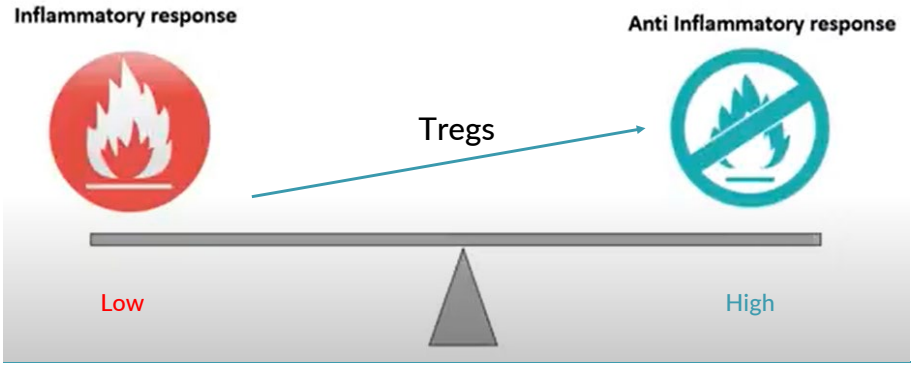
Companion diagnostic

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 the appropriate finance in place 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.

Tregs play an important role in inflammatory responses



Source: Adapted from "Animated biology with Arpan"

Summary

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.

Financial forecasts

Financial history

Historical information has been taken from the annual reports of Cizzle Biotech prior to its acquisition by Bould Opportunities to provide a track record of spending its limited resources wisely.

Income statement

- **Drivers:** The P&L account is dominated by two costs, the investment in R&D and the corporate overhead during the forecast period. No income other than reimbursement from partners for certain R&D expenditure is expected; therefore, these costs will drop straight through to the cashflow statement and determine the net cash position at the end of each financial year.
- **Administration costs:** Remuneration of the four directors represents ca.30% of SG&A and is relatively low by peer group standards, highlighting the careful use of limited resources.
- **R&D and tax credits:** Much of the R&D spend required to develop the CIZ1b test is being incurred by partners. R&D spending by Cizzle for test and future product development will attract R&D tax credits from HMRC.
- **Exceptional costs:** In 2021, there were exceptional costs with respect to the takeover of Cizzle and the Admission of shares on the LSE, the vast majority of which were non-cash. These have been treated as an exceptional item.

Income statement						
Year-end Dec (£000)	2019	2020	2021	2022E	2023E	2024E
Sales	0	0	0	0	0	0
COGS	0	0	0	0	0	0
SG&A	-22	-15	-391	-500	-550	-605
Share-based costs	0	0	-299	-50	-250	-263
R&D	0	0	-161	-350	-1,100	-650
EBITDA	-22	-15	-851	-500	-1,300	-1,518
Licensing/Royalties	0	0	0	400	600	0
Underlying EBIT	**-22**	**-15**	**-851**	**-500**	**-1,300**	**-1,518**
Exceptional items	0	0	-3,107	0	0	0
Statutory EBIT	-22	-15	-3,958	-500	-1,300	-1,518
Net financials	0	0	0	0	0	0
Underlying PBT	**-22**	**-15**	**-851**	**-500**	**-1,300**	**-1,518**
Reported pre-tax	-22	-15	-3,958	-500	-1,300	-1,518
Tax liability/credit	0	0	37	80	253	149
Tax rate	0	0	0	0	0	0
Underlying net income	**-22**	**-15**	**-814**	**-420**	**-1,047**	**-1,368**
Statutory net income	-22	-15	-3,921	-420	-1,047	-1,368
Ordinary 0.01p shares:						
Period-end (m)	0.31	0.31	253.45	278.45	300.45	300.45
Weighted average (m)	0.31	0.31	160.52	274.28	278.45	300.45
Fully-diluted (m)	0.31	0.31	196.30	310.06	314.23	336.23
Underlying basic EPS (p)	**-6.9**	**-4.8**	**-0.5**	**-0.2**	**-0.4**	**-0.5**
Statutory basic EPS (p)	-6.9	-4.8	-2.4	-0.2	-0.4	-0.5
Underlying fully-dil. EPS (p)	-6.9	-4.8	-0.4	-0.1	-0.3	-0.4
Statutory fully-dil. EPS (p)	-6.9	-4.8	-2.0	-0.1	-0.3	-0.4
DPS (p)	0.0	0.0	0.0	0.0	0.0	0.0

Source: Hardman & Co Life Sciences Research

Balance sheet

- **Net cash/(debt):** At 31 December 2021, Cizzle had gross cash of £875k and no debt or lease liabilities.
- **Intangible assets:** Investment into the royalty streams described earlier are recorded under intangible assets.

Balance sheet						
@31 Dec (£000)	2019	2020	2021	2022E	2023E	2024E
Shareholders' funds	7	-8	937	1,517	1,350	-18
Cumulated goodwill	0	0	0	0	0	0
Total equity	7	-8	937	1,517	1,350	-18
Share capital	3	3	25	28	30	30
Reserves	3	-12	912	1,490	1,320	-48
Provisions/liabilities	0	0	0	0	0	0
Long-term leases	0	0	0	0	0	0
Short-term leases	0	0	0	0	0	0
Long-term loans	0	0	0	0	0	0
Short-term debt	0	10	0	0	0	0
less: Cash	13	7	875	510	-420	-1,387
less: Deposits	0	0	0	0	0	0
Invested capital	**-6**	**-5**	**62**	**1,008**	**1,770**	**1,369**
Fixed assets	0	0	0	0	0	0
Intangible assets	0	0	200	1,200	2,080	2,080
Inventories	0	0	0	0	0	0
Trade debtors	*0*	*0*	*0*	*0*	*0*	*0*
Other debtors	*4*	*3*	*43*	*43*	*43*	*43*
Tax credit/liability	*0*	*0*	*37*	*80*	*253*	*149*
Trade creditors	*-1*	*0*	*-100*	*-110*	*-110*	*-110*
Other creditors	*-9*	*-8*	*-118*	*-206*	*-496*	*-793*
Debtors less creditors	-6	-5	-138	-192	-310	-711
Invested capital	**-6**	**-5**	**62**	**1,008**	**1,770**	**1,369**
Net cash/(debt)	13	-3	875	510	-420	-1,387

Source: Hardman & Co Life Sciences Research

Cashflow

- **Capital increase:** Funds raised at the time of the reverse takeover are being used to fund the R&D investment and general working capital requirement over the forecast period. Both the directors and the auditors highlight in the annual report that further funding will be required, at some point in time during the forecast period, to progress its planned product development activities.
- **Acquisitions:** The figures shown under both "acquisitions" and "equity issues" represent the issue of two tranches of shares to SGSC/Conduit to fund the aforementioned acquisition of the additional 5% royalty stream on AZD1656.
- **SGSC:** As part of the collaboration with SGSC to develop a companion diagnostic for certain of its assets, SGSC will be paying costs incurred by Cizzle. However, the precise timing of these potential receipts is difficult to predict.
- **Tax credits:** The usual tax credits on biotech R&D investment will become due and are usually received about 6-12 months after the period-end.

Cashflow						
Year-end Dec (£000)	2019	2020	2021	2022E	2023E	2024E
Underlying EBIT	-22	-15	-851	-500	-1,300	-1,518
Depreciation	0	0	0	0	0	0
Amortisation	0	0	0	0	0	0
Share-based costs						
Inventories	*0*	*0*	*0*	*0*	*0*	*0*
Receivables	*26*	*0*	*-19*	*0*	*0*	*0*
Payables	*-11*	*2*	*75*	*10*	*0*	*0*
Change in working capital	15	2	56	48	40	34
Other	0	0	0	0	0	0
Company op cashflow	**-7**	**-13**	**-860**	**-402**	**-1,010**	**-1,221**
Net interest	0	0	0	0	0	0
Tax paid/received	0	0	0	37	80	253
Operational cashflow	**-7**	**-13**	**-860**	**-365**	**-929**	**-968**
Capital expenditure	0	0	0	0	0	0
Free cashflow	**-7**	**-13**	**-860**	**-365**	**-929**	**-968**
Dividends	0	0	0	0	0	0
Acquisitions	0	0	-200	-1,000	-880	0
Disposals	0	0	0	0	0	0
Cashflow after invests.	**-7**	**-13**	**-1,163**	**-1,365**	**-1,809**	**-968**
Share repurchases	0	0	0	0	0	0
Equity issues	0	0	2,200	1,000	880	0
Cost of fundraise	0	0	-159	0	0	0
Change in net cash/(debt)	**-7**	**-13**	**878**	**-365**	**-929**	**-968**
OCFPS (p)	-2.3	-4.1	-0.5	-0.1	-0.3	-0.3
Opening net cash/(debt)	20	13	-3	875	510	-420
Closing net cash/(debt)	**13**	**-3**	**875**	**510**	**-420**	**-1,387**

Source: Hardman & Co Life Sciences Research

Valuation

As highlighted in our initiation report[3], we use a multi-disciplinary approach to provide readers with as much information as possible in order for potential investors to make an informed judgement about whether Cizzle represents a good investment opportunity. Here we highlight the changes in valuation that have occurred since Cizzle was re-listed in May 2021 and have introduced a sum-of-the-parts to reflect the additional income streams following the various licensing deals. One of the most important features over the past nine months has been the significant correction of valuation in the biotech sector, as evidenced by the declines in the NASDAQ Biotechnology Index (NBI) and the broader-based SPDR S&P Biotech ETF (XBI).

Biotech performance since 1 September 2021			
Date	NBI	XBI	CIZ
31 August 2021	5,402.5	135.1	5.15
6 July 2022	3,923.3	81.0	1.40
Change	**-27.4%**	**-40.0%**	**-72.8%**

Source: Refinitiv

DCF analysis

As stated in our initiation report, we believe that detailed discounted cashflow (DCF) analyses of key products and/or technologies through to patent expiry is the best approach to valuing biotech companies. For Cizzle, while this approach is still appropriate, we have some reservations because of the early development stage of the assets, the limited benchmark information available for liquid biopsies and predicting the impact of patent expiry.

[3] https://hardmanandco.com/research/corporate-research/early-detection-of-lung-cancer/

While many of our core assumptions regarding the CIZ1b test remain unchanged, we note the following observations necessitating some adjustments to the model:

- **Antibody development:** As part of the process to develop a proprietary antibody for the detection of variant-CIZ1b in the immunoassay, the project has evolved to create a range of mAbs and reagents for immunoassays, not only for early-stage lung cancer but potentially for other cancers. This has extended the previously predicted timescale for the delivery of these products by 6-9 months.
- **Competitor development:** Two UK-based competitors, Angle (AGL.L) and Oncimmune (ONC.L), are more advanced with their development of liquid biopsy tests. Oncimmune, via its US distribution partner Biodesix, has received Medicare coverage for its NodifyCDT lung nodule test. Angle received FDA approval of its Parsortix system for metastatic breast cancer in May 2022, which is expected to be advanced to include other cancers, including lung, in the near future. These could affect the market penetration of the Cizzle test.
- **Illumina/Grail:** Although it is not directly comparable, Illumina (ILMN.N), the major next gene sequencing company, has acquired Grail, a company developing an all-encompassing, multi-cancer early detection blood test – Galleri. Several $bn has been invested in this project and, with a cash-rich parent, this must be considered a major risk factor, even though the test is yet to be proven.
- **China development:** Our original model focused mostly on the opportunity available to Cizzle in the US and Europe. Earlier in 2022, Cizzle completed an agreement for the development and commercialisation of the CIZ1b test in China, a significant opportunity. This has been added to the model.
- **US development:** Our original model was based on a distribution and profit share arrangement for the US. The HoT signed with CorePath suggests a royalty and royalty sharing arrangement. Our model has been updated to reflect these updated terms.

Changes to DCF model

Our original DCF model, published in the initiation report dated 14 May 2021, used some broad assumptions with respect to timing of launch, market opportunity and commercial strategy. During the past year, content of announcements made regarding the market opportunities in China and the US have allowed the model to be tightened up. The key changes that influence the DCF model are shown in the following table.

Key changes to DCF assumptions

		May 2021	Current
Launch date	UK/Europe	2023	2025
	US	2025	2027
	China	-	2026
Initial test price	UK/Europe	£200	£150
	US	$400	$300
	China	-	CNY1,000
Margin/royalty	UK/Europe	65%	65%
	US	40%	15%
	China	-	10%

Source: Hardman & Co Life Sciences Research

Using these revised inputs, the risk-adjusted value of the Cizzle lung cancer test is £15.9m. We believe that our assumptions are quite conservative and are more likely to be adjusted in an upward direction when there is greater clarity regarding the launch and initial uptake of the test in the key markets. In addition, during the past year, Cizzle has expanded its interests to include early detection of other cancers. As this is still at a very early stage, no allowance has been made for additional value that might be created from these activities, potentially creating further upside potential.

Summary of DCF analysis			
WACC	NPV ($m)	NPV (£m)	Risk-adjusted NPV (£m)
8%	80.2	61.7	20.4
9%	70.8	54.5	18.0
10%	**62.7**	**48.2**	**15.9**
11%	55.5	42.7	14.1
12%	49.3	37.9	12.5

Source: Hardman & Co Life Sciences Research

DCF of SGSC/Conduit royalty stream

During the past year, through two deals with SGSC and Conduit, Cizzle has acquired an economic interest in the asset known as AZD1656. While the initial deal with SGSC caps the total royalty receipts at £5m, the second deal with Conduit is uncapped with an additional 5% being earned on of net sales of this drug. Both deals are accretive to valuation even on a risk-adjusted basis. For a total cost of £2.08m, the risk-adjusted DCF value of the royalty streams is £7.1m.

Sum-of-the parts DCF

Taken together, the sum-of the parts NPV for Cizzle generated by risk-adjusted DCF is £23.0m.

Comparative valuation

Our peer group analysis, putting the valuation of Cizzle into context against the stock market valuations afforded a group of similar UK-based companies. However, while this is a sound approach to take, in practice, it is much less straightforward, for a number of reasons:

- companies are all using slightly different technologies and approaches;
- even using the same approach, different targets/indications are being tackled;
- currently, UK biotechs, along with global biotechs, are being negatively influenced by market forces; and
- additionally, diagnostic companies associated with COVID-19 tests have seen significant devaluations as a result of changes in government policy towards testing.

The current global economic outlook, risk of inflation and worldwide uncertainties have made investors very cautious and risk-averse. Consequently, the market for biotech stocks, and diagnostic companies in particular, is extremely poor at the present time, which is being reflected in the extremely low valuations afforded by the market.

UK peer group valuations					
Company Ticker	Angle AGL	Cizzle CIZ	Genedrive GDR	Omega Diag. ODX	Oncimmune ONC
Share price	95.0	1.4	20.0	3.1	85.0
Shares in issue (m)	235.1	278.4	92.3	237.7	69.4
Market cap. (£m)	223.4	3.9	18.5	7.4	59.0
Cash (£m)	26.0	0.9	2.8	3.0	10.0
Debt (£m)	0.0	0.0	-0.2	-1.0	-10.5
EV (£m)	**197.4**	**3.0**	**15.9**	**5.4**	**59.5**
Relative EV (x)	65.3	-	5.2	1.8	19.7

Share prices taken at close of business on 7 July 2022
Source: Hardman & Co Life Sciences Research

UK peer comparison – share price change since listing				
Company	17 May'21 (p)	7 Jul'22 (p)	Change	Comment
Angle	134.0	95.0	-29%	Despite recent FDA approval
Cizzle	7.1	1.4	-80%	Good progress being ignored
Genedrive	67.0	20.0	-70%	Late delivery of COVID-19 tests
Omega Diag.	69.0	3.9	-96%	Failed to meet expectations
Oncimmune	215.0	99.5	-60%	Devaluation of global biotech

Source: Refinitiv, Hardman & Co Life Sciences Research

Summary

There has been a significant market correction in biotech stocks over the past nine months and few companies in the sector have been able to buck the trend, even those with major news. Those that have outperformed have tended to be in receipt of takeover offers from major players. It is well known that this sector is capital-intensive, which is unattractive to risk-averse investors. Hence, the valuation correction has been particularly excessive to companies in need of a capital injection. Despite all the positive news, Cizzle has not been able to avoid this biotech valuation correction. However, this has left the stock greatly underappreciated by the market and offering significant upside potential, in our view.

Company matters

Registration

Cizzle Biotechnology Holdings plc is incorporated in England and Wales with company registration number 06133765.

Registered office:

6th Floor

60 Gracechurch Street

London

EC3V 0HR

Website: www.cizzlebiotechnology.com/

Board of Directors

Completion of the acquisition and readmission of its shares on the London Stock Exchange Main Market has triggered changes to the board of directors.

Board of Directors on Admission			
Position	**Name**	**Remuneration**	**Audit**
Executive Chair	Allan Syms		
Finance Director	Nigel Lee		
Non-executive director and founder of Cizzle	Dawn Coverley		
Non-executive director	John Treacy	C	C

C = chair

Source: Company reports

Allan Syms – Executive Chair

Allan is an experienced public and private company director, with a background in Corporate Finance, IPOs and managing strategic change. Allan holds a PhD in cancer research and began his corporate career at GE Healthcare (formerly Amersham International PLC). He has spent the past 30 years creating and, through private and public fundraising, building emerging technology businesses. He was previously an adviser to the Department of International Trade.

Prof. Dawn Coverley – Non-Executive Director, Founder of Cizzle

Dawn Coverley is a cell biologist with 20 years' experience in basic cancer-related research. After a first degree in Genetics (University of Leicester) and a PhD in biochemistry (Cancer Research UK), she moved to Cambridge University in 1992. Her research exploits experimental systems that reconstitute fundamental processes associated with DNA metabolism, including DNA repair and DNA replication. In 2001, she was awarded a senior research fellowship by the Lister Institute of Preventive Medicine and established a new research laboratory at the University of York. She founded Cizzle Biotech in 2005, and raised seed corn funding in 2006. She is currently principal investigator of an academic DNA replication research laboratory at York and, following the acquisition of Cizzle, will be a scientific advisor and sit on the board as an NED.

Nigel Lee – Finance Director

Nigel has been a director of CFO Solutions since 2003 which, historically, provided financial advisory and company secretarial services to Cizzle. In May 2021, he became part-time CFO of the company. Nigel qualified as a Chartered Accountant in 1988 and gained 11 years of audit and business advisory experience at PWC.

Advisors

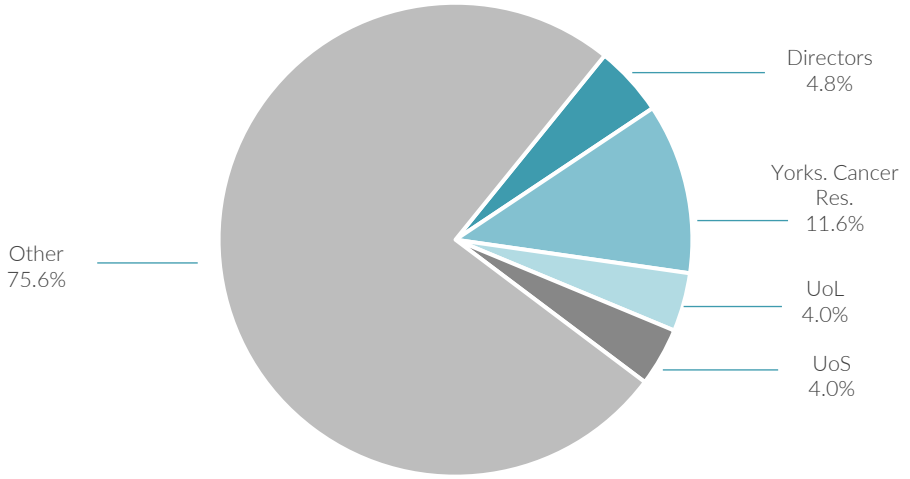
Professional advisors	
Role	**Advisor**
Financial Advisor	Allenby Capital Ltd
Corporate Broker	Novum Securities Ltd
Legal Advisers	Cooley (UK) LLP Shakespeare Martineau LLP
Auditors	PKF Littlejohn LLP
Financial Public Relations	IFC Advisory Ltd
Registrar	Neville Registrars

Source: Company reports, Hardman & Co Life Sciences Research

Share capital

On 7 July 2022, Cizzle had 278,447,788 Ordinary shares of 0.01p nominal value in issue. In addition, there are 12,350,000 warrants and 23,432,041 share options outstanding.

Shareholders



Source: Company reports, Hardman & Co Life Sciences Research

Risks

It goes without saying that investments in small, early-stage companies carry a significant risk, and investors must be aware of this fact.

In our opinion, the following risks are particularly relevant.

Stage of development

Development of an ELISA test for high-throughput laboratories and commercialisation is dependent on a mAb to detect the CIZ1b biomarker. This is the rate-limiting step in the whole process and licensing deals in the key territories of China and the US cannot progress without this mAb and associated reagents.

Patent robustness

As with all medtech and diagnostic products, there is risk that the IP is insufficiently covered by global patents.

Regulatory approval

Cizzle is operating in a field potentially subject to tight and changing regulation. Although its product could potentially be launched in the US as an LDT without formal regulatory approval, having FDA (via a PMA or 510(k)) and EU (via CE marking) regulatory approval confers considerable advantages and a certain level of market protection. Such regulatory processes are time-consuming and need to be supported, generally, by potentially expensive clinical trials. Additionally, alterations to the LDT regulations are under consideration.

Competition

Although the technical approach adopted by Cizzle is unique, with few researching CIZ1 globally, alternative technologies can be used to obtain similar outcomes, all with the aim of improving clinical decisions. There are a large number of companies developing and/or commercialising early-stage cancer diagnostic tests and this ignores the large specialist clinical laboratory groups that control much of the market.

Commercialisation and pricing

Although the commercialisation strategy is yet to be finalised, Cizzle will be helped by the fact that some competitor liquid biopsy biomarker products have been priced and are being reimbursed by payers in both Europe and the US at levels that will provide an adequate return. Strong pharmaco-economic data are required in order to obtain these pricing structures. However, as more products enter the market, it is conceivable that prices might come under some pressure.

Dilution risk

Our forecasts suggest that the current funding will be sufficient to reach particular milestones. However, in order to enact its long-term strategy, and to develop other tests, further funding will be required. Shareholders could suffer significant dilution if they do not participate in further funding rounds.

Share liquidity

An investment in the company might not be suitable for all recipients of this publication. Market liquidity is very poor at present, making it potentially difficult for investors to sell their shares.

Notes

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The full detail is on page 26 of the full directive, which can be accessed here: http://ec.europa.eu/finance/docs/level-2-measures/mifid-delegated-regulation-2016-2031.pdf

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