Pharmaceuticals & Biotechnology

Source: Refinitiv

Market data

EPIC/TKR	**CIZ**
Price (p)	**4.9**
12m high (p)	10.0
12m low (p)	4.7
Shares (m)	261.1
Mkt cap (£m)	12.8
EV (£m)	11.5
Free float*	73%
Country of listing	UK
Market	LSE Main

**As defined by AIM Rule 26*

Description

Cizzle is a medical device company developing a companion diagnostic biomarker for the early detection of lung cancer. The blood 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.cizzlebiotecnology.com

Key shareholders

Directors	5.1%
Yorkshire Cancer Research	12.4%
Finance Yorkshire	9.4%
Rose Noble Ltd	5.8%
University of Sheffield	4.3%
University of Leeds	4.3%

Diary

Sep'21	Interim results

Analyst

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CIZZLE BIOTECHNOLOGY

Strategic collaboration with SGSC

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, to be used alongside a positive chest scan, that allows early detection of lung cancer. This should result in a significant reduction in the number of false positives, reduce the number of scans and improve patient outcomes. As part of its portfolio expansion and to increase the number of income streams, Cizzle has signed a commercial and royalty deal with respect to a clinical asset, known as AZD1656.

- **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.

- **SGSC:** Initially, Cizzle signed an MoU with St. George Street Capital (SGSC), a UK-based medical charity, to develop a companion diagnostic for one of its clinical assets, also with the potential to earn royalties. This has evolved into two deals, with the commercial and royalty deal signed, giving potential royalties of up to £5m.

- **AZD1656:** AZD1656 is a potent and selective activator of glucokinase that was developed initially by AZN for type II diabetes. Now licensed to SGSC, in a recent ARCADIA trial in 150 diabetic patients with COVID-19, AZD1656 was shown to have promise and be worthy of further late-stage development.

- **Risks:** Cizzle is a small company with a single asset and limited resources. Portfolio expansion through partnerships is expanding its income opportunities and reducing the risk, but success is dependent on further partnerships and out-licensing deals being signed, which can take time to be concluded.

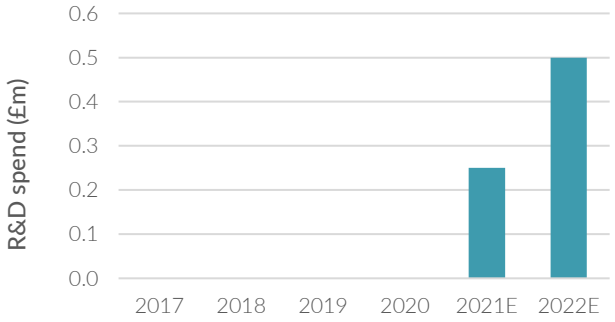
- **Investment summary:** Since Cizzle's listing, its shares have drifted while the market awaits news. Over the past few weeks, Cizzle has announced two new collaborations, which have the potential to expand the number and timing of income streams. Trading on an EV of just £11.5m, the market seems to be ignoring these deals, which suggests that Cizzle has considerable upside potential when investors become aware of these and as development progress is made.

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
Underlying EBIT	-3	-22	-15	-70	-550	-1,425
Reported EBIT	-3	-22	-15	-880	-550	-1,425
Underlying PBT	-3	-22	-15	-70	-550	-1,425
Statutory PBT	-3	-22	-15	-880	-550	-1,425
Underlying EPS (p)	-0.9	-6.9	-4.8	0.0	-0.2	-0.5
Statutory EPS (p)	-0.9	-6.9	-4.8	-0.5	-0.2	-0.5
Net (debt)/cash	20	13	0	1,590	1,225	222
Equity issues	0	0	0	2,200	0	0

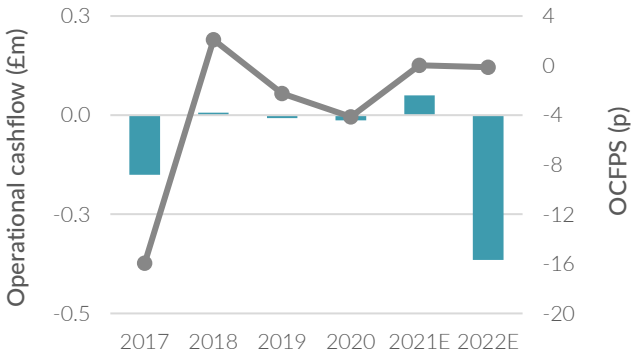
Source: Hardman & Co Life Sciences Research

R&D investment



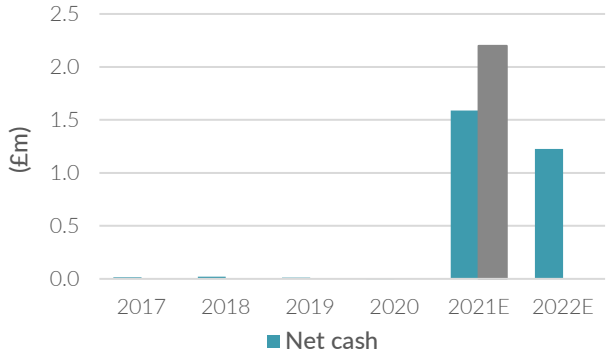
- Cizzle has successfully developed a prototype CIZ1b biomarker test on very limited resources.
- Much of the elucidation and understanding of CIZ1 was undertaken with grant funding.
- R&D investment will ramp up once funding is in place to develop the commercial CIZ1b biomarker test based on mAb direct-ELISA.

Operational cashflow and OCFPS



- 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 six to 12 months in arrears.
- Given that much of the work will be outsourced, Cizzle will have only modest working capital requirements.
- The 1H'21 cashburn is expected to equate to the underlying operating loss of ca.£200k.

Net cash and equity issues



- The prospectus states that the *proforma* net cash position was £1.89m, based on the balance sheets of both Cizzle and Bould at 30 June 2020.
- After allowing for expenses associated with the acquisition, fund raise and listing, we believe the net cash position was ca.£1.75m at the time of Admission.
- 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.

Source: Company data, Hardman & Co Life Sciences Research

Expanding income potential

Background

Cizzle is a spin-out from the University of York to exploit the biomarker, variant CIZ1b, for early detection of different forms of lung cancer. While its main focus remains a simple diagnostic blood test for the early detection of lung cancer, as part of this activity, the company has a diagnostic skillset and a close working relationship with other companies, e.g. FairJourney Biologics (FairJourney) for the development of antibodies. As such, Cizzle is potentially an attractive partner for other companies looking for these specialist services. From Cizzle's perspective, such relationships provide the opportunity to generate additional income streams and to increase value.

On 22 June 2021, Cizzle announced that it had signed an Memorandum of Understanding (MoU) with St George Street Capital (SGSC), a UK-based biomedical charity, whereby the two parties would collaborate to develop a companion diagnostic platform for certain therapeutic assets already licenced to SGSC by AstraZeneca (AZN). In addition, SGSC agreed to grant Cizzle potential royalties from the future commercialisation of these assets up to a maximum of £5m. Both were subject to Cizzle and SGSC entering into full agreements.

SGSC

SGSC was formed to deliver much-needed treatments to patients in areas of high unmet medical need, and is led by a group of highly decorated academics and ex-pharma executives. SGSC's strategy is to license existing clinical assets from pharmaceutical companies and to progress them through Phase II trials, before out-licensing them for Phase III trials and commercialisation.

Deal terms

There are to be two agreements between Cizzle and SGSC, the first (royalty deal) of which has been concluded, with the second (companion diagnostic) expected to follow shortly. Between them, they will cover the following:

- **Milestones:** For each diagnostic indication, SGSC will make a payment of up to £1m, from which Cizzle will fund the work to be undertaken to develop the companion diagnostic and any third parties contracted by Cizzle to assist.
- **Royalties:** Cizzle will be entitled to royalties of up to £5m from the commercialisation of the assets (AZD1656), plus further payments from the potential use of a companion diagnostic.
- **Consideration:** Cizzle has paid £200k to SGSC in consideration of the potential future royalty stream from the commercialisation of AZD1656 – £65k on signing the MoU and a further £135k on closing the full agreement.
- **Samples and regulation:** SGSC is responsible for providing Cizzle with clinical samples, reagents and patient and technical information. In addition, it will provide regulatory and technical advice on securing the required regulatory approvals for the companion diagnostic platform.

AZD1656

AZD1656 is a potent and selective activator of glucokinase that was being developed initially by AZN for type II diabetes. In Phase I trials, AZD1656 was shown to be safe and well-tolerated – both alone at doses up to 150mg BID (twice daily) for eight days in healthy human volunteers and in combination with other blood glucose control agents at a dose of 200mg daily for up to six months' duration in diabetic patients.

However, AZN appeared to take less interest in the project following a Phase II trial with diabetic patients in Japan, which showed that AZD1656 lowered HbA1c and fasting plasma blood (FPG) glucose levels initially, but the effect appeared transient, with HbA1c trending back towards pre-dose levels after four months. Consequently, AZN out-licensed AZD1656, along with other clinical assets, to SGSC under its "Open Access Programme".

ARCADIA trial

In August 2020, the UK Medicines and Healthcare products Agency (MHRA) permitted a randomised, double-blind, placebo-controlled Phase II trial, known as ARCADIA, to assess the safety and efficacy of AZD1656 in 150 patients with either type I or type II diabetes, who were hospitalised with mild-to-moderate COVID-19. The trial was funded by international investment through Excalibur Medicines Ltd and an HM Government grant through the UKRI/Innovate UK programme. Headline results were released on 9 September 2021.

Efficacy

ARCADIA reported a "strong trend" towards reduced mortality in patients receiving AZD1656; this was observed in both mortality on treatment and all-cause mortality, which were lower in the AZD1656 group compared with the placebo group. This trend was observed on top of patients receiving other medications, including dexamethasone, as part of standard-of-care. Certain clinically and biochemically defined subsets of patients appeared to benefit most from treatment with AZD1656.

Safety and tolerability

As seen in previous trials, AZD1656 was shown to be well-tolerated, with no serious adverse events in the ARCADIA trial. The degree of glycaemic control, as measured by the need to increase baseline medication requirements or the need to add additional diabetic medications, was no different between the AZD1656 group and the placebo group. The proportion of treatment-emergent adverse events was no different between the AZD1656-treated and placebo groups. Overall, no safety concerns were identified regarding the use of AZD1656 in this patient population.

Conclusion

Data from ARCADIA support the continued investigation of AZD1656 for the treatment of patients with COVID-19, with or without diabetes.

DCF valuation

We have constructed a simple DCF model, which takes account of the upfront payment by Cizzle. Based on the usual assumptions for a developmental drug regarding the time to reach the market, the likely royalty rate on net sales and the likely chances of regulatory approval, we calculate the risk-adjusted NPV of this project to be £0.9m.

Conclusion

Although Cizzle is best-known as a diagnostic company developing a lung cancer asset, it also has specialist knowledge and a skillset that are attractive to partner organisations, as seen by its recent deals with FairJourney and SGSC. Through these relationships, it is expanding its portfolio and potentially accelerating its income streams.

Value inflection points will arise in the event that i) the collaboration with FairJourney delivers on proprietary monoclonal antibodies and reagents that will be the foundation for protein detection in its ELISA-based test, which could be out-licensed as a research tool, and ii) AZD1656 is out-licensed by SGSC/Excalibur for late-stage development and commercialisation, improving the chances of receiving the royalty stream.

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