

THIS DOCUMENT IS IMPORTANT AND REQUIRES YOUR IMMEDIATE ATTENTION. If you are in any doubt about the contents of this Document you should consult a person authorised under the Financial Services and Markets Act 2000 who specialises in advising on the acquisition of shares and other securities.

This Document comprises a prospectus relating to Cizzle Biotechnology Holdings plc (the “**Company**”) dated 21 September 2022 (“**Prospectus**”). The Prospectus has been prepared in accordance with and has been approved by the Financial Conduct Authority (“**FCA**”) as the competent authority under Regulation (EU) 2017/1129, which is part of UK law by virtue of the European Union (Withdrawal) Act 2018 (“**Prospectus Regulation**”). The FCA only approves this Prospectus as meeting the standards of completeness, comprehensibility and consistency imposed by the Prospectus Regulation. Such approval should not be considered as an endorsement of the issuer or the quality of the securities that are the subject of this Prospectus. Investors should make their own assessment as to the suitability of investing in the securities. This Document has been drawn up as part of a simplified prospectus in accordance with Article 14 of the Prospectus Regulation.

This Document has further been prepared in compliance with the Prospectus Regulation Rules made under FSMA (“**Prospectus Regulation Rules**”), English law and the rules of the FCA and the information disclosed may not be the same as that which would be disclosed if this Document had been prepared in accordance with the laws of a jurisdiction outside England. This Document has been filed with the FCA and made available to the public in accordance with Rule 3.2 of the Prospectus Regulation Rules.

Application has been made to the FCA for all of the new ordinary shares of 0.01p each in the capital of the Company to be issued (the “**New Ordinary Shares**”) to be admitted to the standard segment of the Official List (by way of Standard Listing under Chapter 14 of the Listing Rules made by the FCA under Part VI of FSMA (“**Listing Rules**”)) and to the London Stock Exchange plc (the “**London Stock Exchange**”) for such New Ordinary Shares to be admitted to trading on the London Stock Exchange’s main market for listed securities (together, “**Admission**”). It is expected that Admission will become effective, and that unconditional dealings in the New Ordinary Shares will commence, at 8.00 a.m. on 26 September 2022. The Company’s Existing Ordinary Shares are traded on the London Stock Exchange’s main market for listed securities.

THE WHOLE OF THE TEXT OF THIS DOCUMENT SHOULD BE READ BY PROSPECTIVE INVESTORS. YOUR ATTENTION IS SPECIFICALLY DRAWN TO THE DISCUSSION OF CERTAIN RISKS AND OTHER FACTORS THAT SHOULD BE CONSIDERED IN CONNECTION WITH AN INVESTMENT IN THE NEW ORDINARY SHARES AS SET OUT IN THE SECTION ENTITLED “RISK FACTORS” BEGINNING ON PAGE 11 OF THIS DOCUMENT.

The Directors, whose names appear on page 20, and the Company, accept responsibility for the information contained in this Document. To the best of the knowledge of the Directors and the Company, the information contained in this Document is in accordance with the facts and this Document makes no omission likely to affect their import.

Cizzle Biotechnology Holdings plc

(Incorporated and registered in England and Wales under the Companies Act 2006 with registration number 06133765)

**Proposed Subscription of 35,666,665 New Ordinary Shares at 1.5p per share
Admission of the New Ordinary Shares to
the Official List (by way of Standard Listing under Chapter 14 of the Listing Rules) and to
trading on the London Stock Exchange’s main market for listed securities**

This Prospectus contains forward-looking statements, including, without limitation, statements containing the words “believes”, “expects”, “estimates”, “intends”, “may”, “plan”, “will” and similar expressions (including the negative of those expressions). Forward-looking statements involve unknown risks, uncertainties and other factors which may cause the actual results, financial condition, performance or achievements of the Company, or industry results, to be materially different from any future results, performance or achievements expressed or implied by those forward-looking statements. Factors that might cause such a difference include, but are not limited to, those discussed in the “Risk Factors” section of this Prospectus. Given these uncertainties, prospective investors are cautioned not to place any undue reliance on those forward-looking statements. The forward-looking statements contained in this Prospectus are made on the date of this Prospectus, and the Company and the Directors are not under any obligation to update those forward-looking statements in this Prospectus to reflect actual future events or developments.

The whole text of this Prospectus should be read. Investment in the Company is speculative and involves a high degree of risk. Your attention is also drawn to the section headed “Risk Factors” in this Prospectus which sets out certain risk factors relating to an investment in the New Ordinary Shares. All statements regarding the Company’s business, financial position and prospects should be viewed in light of the risk factors set out in the section headed “Risk Factors” in this Prospectus.

No legal, business, tax or other advice is provided in this Prospectus. Prospective investors should consult their professional advisers as needed on the potential consequences of subscribing for, purchasing, holding or selling New Ordinary Shares under the laws of their country and/or state of citizenship, domicile or residence. This Prospectus does not constitute an offer to sell, or the solicitation of an offer to buy or subscribe for, New Ordinary Shares in any jurisdiction

in which such offer or solicitation is unlawful and, in particular, this Prospectus is not for distribution in or into the United States of America, Canada, Australia, South Africa, the Republic of Ireland or Japan. The distribution of this Prospectus in other jurisdictions may be restricted by law. The New Ordinary Shares have not been and will not be registered under the applicable securities laws of the United States of America, Canada, Australia, South Africa, the Republic of Ireland or Japan and, subject to certain exceptions, may not be offered, sold, re-sold, renounced, taken up or delivered, directly or indirectly, in, into or from the United States of America, Canada, Australia, South Africa, the Republic of Ireland or Japan or to any national of the United States of America, Canada, Australia, the Republic of Ireland, South Africa or Japan or to any national of those countries. This Prospectus should not be distributed, published, reproduced or otherwise made available in whole or in part, or disclosed by recipients to any other person, in, and in particular, should not be distributed to persons with addresses in, the United States of America of America, Canada, Australia, South Africa, the Republic of Ireland or Japan. No action has been taken by the Company that would permit an offer of New Ordinary Shares or possession or distributions of this Prospectus where action for that purpose is required. Persons into whose possession this Prospectus comes should inform themselves about and observe any such restrictions. Any failure to comply with these restrictions may constitute a violation of the securities law or other laws of any such jurisdictions.

In making any investment decision in respect of Admission or the Subscription, no information or representation should be relied upon in relation to Admission or in relation to the New Ordinary Shares other than as contained in this Prospectus. No person has been authorised to give any information or make any representation other than that contained in this Prospectus and, if given or made, such information or representation must not be relied upon as having been authorised.

It should be remembered that the price of securities and the income from them can go down as well as up and this Prospectus contains references to past performance of the Company and its subsidiaries. Past performance is not a reliable indicator of future results.

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SUMMARY

1. Introduction, containing warnings

This summary should be read as an introduction to the prospectus issued by Cizzle Biotechnology Holdings plc (the “**Company**”) on 21 September 2022 (“**Prospectus**”) and any decision to invest in the securities should be based on a consideration of the Prospectus as a whole by the investor. The investor could lose all or part of the invested capital. Civil liability attaches only to those persons who have tabled the summary including any translation thereof, but only where the summary is misleading, inaccurate or inconsistent, when read together with the other parts of the Prospectus, or where it does not provide, when read together with the other parts of the Prospectus, key information in order to aid investors when considering whether to invest in such securities.

The securities to be admitted to trading on the regulated market of the London Stock Exchange plc (“**London Stock Exchange**”) for officially listed securities (“**Main Market**”) (“**Admission**”) are ordinary shares of 0.01p each in the capital of the Company (ISIN: GB00BNG2VN02). The Company may be contacted by writing to the company secretary, SGH Company Secretaries Limited, 6th Floor, 60 Gracechurch Street, London EC3V 0HR or by calling, within business hours, on 020 7264 4444. The Legal Entity Identity number (“**LEI**”) for the Company is 213800G3OS3SA2J1Y358.

The Prospectus was approved on 21 September 2022 by the Financial Conduct Authority of 12 Endeavour Square, London E20 1JN (“**FCA**”). Contact information relating to the FCA can be found at <https://www.fca.org.uk/contact>.

2. Key Information on the Issuer

2.1 Who is the issuer of securities?

The Company was incorporated with limited liability under the laws of England and Wales on 1 March 2007 with registered number 06133765 as a public company limited by shares under the Companies Act 2006 (the “**Act**”) and regulations made thereunder. It is domiciled in the United Kingdom and is subject to The City Code on Takeovers and Mergers (“**City Code**”). The Company’s LEI is 213800G3OS3SA2J1Y358.

2.1.1 Principal Activities

The Company was admitted to the Standard Listing segment of the Official List and to trading on the Main Market of the London Stock Exchange on 14 May 2021. Initially under the name of Bould Opportunities plc, the Company changed its name to Cizzle Biotechnology Holdings plc, following the acquisition of Cizzle Biotechnology Limited (“**Cizzle Biotechnology**”). Cizzle Biotechnology is a spin-out from the University of York, founded in 2006 around the work of Professor Dawn Coverley and colleagues. The Company and Cizzle Biotechnology (the “**Group**”) is focused on patent protected technology for the early detection of lung cancer through the development of a blood test for the CIZ1B biomarker.

2.1.2 Major Shareholders

The following persons, directly or indirectly, have an interest in the Company’s capital or voting rights which is notifiable under English Law:

| Name | At the date of this Prospectus | | On Admission of the New Ordinary Shares | |
|--|---------------------------------|-----------------------------|---|-----------------------------|
| | No. of Existing Ordinary Shares | % of Existing Share Capital | No. of New Ordinary Shares | % of Enlarged Share Capital |
| Hargreaves Lansdown (Nominees) Limited | 47,621,748 | 17.10% | - | 15.16% |
| JIM Nominees | 45,615,279 | 16.38% | - | 14.52% |
| Yorkshire Cancer Research | 32,382,330 | 11.63% | - | 10.31% |
| Interactive Investor Services Nominees Limited | 27,135,794 | 9.75% | - | 8.64% |
| HSDL Nominees Limited | 20,887,303 | 7.50% | - | 6.65% |
| Dawn Coverley | 13,359,041* | 4.80% | - | 4.25% |
| University of Leeds | 11,128,058 | 4.00% | - | 3.54% |
| University of Sheffield | 11,128,058 | 4.00% | - | 3.54% |
| Vidacos Nominees Limited | 10,739,219 | 3.86% | - | 3.42% |
| Barclays Direct Investing Nominees Limited | 9,071,059 | 3.26% | - | 2.89% |
| Alan Miller | 6,525,511** | 2.34% | 14,858,844** | 4.73 |

*this includes 7,055,548 shares held by Professor Dawn Coverley’s husband, Justin Ainscough, a founder scientist of Cizzle Biotechnology Limited

**held indirectly through a nominee

2.1.3 Key Managing Directors

The Company's board of directors ("**Board**") is comprised of Allan Syms (Executive Chairman), Dawn Coverley (Scientific Director and Non-Executive Director), Nigel Lee (Finance Director) and John Treacy (Non-Executive Director) ("**Directors**" and each a "**Director**").

2.1.4 The Company has engaged PKF Littlejohn LLP as its statutory auditors.

2.2 **What is the key financial information regarding the issuer?**

2.2.1 Selected historical financial information

Selected historical financial information for the Company and the Group

| | Group Audited Year ended 31 Dec 2021 £'000 | Company Audited Year ended 31 Dec 2021 £'000 |
|--|---|---|
| Revenue | - | - |
| Cost of sales and administrative expenses | (552) | (367) |
| Share option charge | (299) | (299) |
| Transaction costs | (303) | (479) |
| Reverse acquisition expenses | (2,804) | - |
| Loss from operations | (3,958) | (1,145) |
| Taxation | 37 | - |
| Loss of the period | (3,921) | (1,145) |
| | Group Audited As at 31 Dec 2021 £'000 | Company Audited As at 31 Dec 2021 £'000 |
| Total Assets | 1,155 | 23,092 |
| Total Liabilities | (218) | (133) |
| Net assets | 937 | 22,959 |
| Total Equity | 937 | 22,959 |
| | Group Audited Year ended 31 Dec 2021 £'000 | Company Audited Year ended 31 Dec 2021 £'000 |
| Net cash used in operations | (1,009) | (758) |
| Net cash used in investing activities | (154) | (519) |
| Net cash generated from financing activities | 2,031 | 2,041 |
| Net increase/(decrease) in cash and cash equivalent | 868 | 764 |
| Cash and cash equivalents at beginning of period | 7 | 84 |
| Cash and cash equivalents at end of period | 875 | 848 |

2.2.2 Pro forma financial information

Not applicable. There is no pro forma financial information in the Prospectus.

2.2.3 Qualifications to audit reports

The auditor's report within the financial statements for the Group for the year ended 31 December 2021 contains a statement on material uncertainty related to going concern, which indicates that the Group will need to raise additional funds in order to meet its committed liabilities during the going concern period.

2.3 **What are the key risks that are specific to the issuer?**

Pre-revenue business – The Group is still at an early stage of its development and there is no guarantee that the Group will generate significant or any revenues. For the foreseeable future, the Group will have significant reliance upon the success of the CIZ1B biomarker in the detection of lung cancer and there is no guarantee that the Group's intellectual property will result in a commercially viable test. It is also possible that technical and/or regulatory hurdles could lengthen the time required for the delivery of such a testing product. The Group's future growth and prospects will also depend on its ability to secure commercialisation partnerships, and on the success of those already made.

Competition and the pace of development in the healthcare industry - Certain competitors already have CE marking for lung cancer detection products. Existing or new competitors may have larger resources, greater market presence, economies of scale or a lower cost base than the Group. Rapid scientific and technological change within the biotechnology sector could lead to other market participants creating approaches, products and services equivalent or superior to the diagnostic testing products and services than those to be offered by the Group, which could adversely affect the Group's performance and success.

Attraction and retention of key management and employees - The successful operation of the Group will depend partly upon the performance and expertise of its current and future management and employees. The loss of the services of certain of these members of the Company's key management, or the inability to attract and retain a sufficient number of suitably qualified employees may have a material adverse effect on the Group.

Regulatory environment and the process for obtaining a CE marking or a 510(k) clearance – The Group's prospective future products will be subject to various laws, regulations and standards in each of the jurisdictions in which products are to be manufactured and distributed. There can be no guarantee that the Group's future products will ultimately obtain CE marking or FDA 510(k) clearance or that clearance can be obtained within the timescales or the budgets anticipated. The UK's exit from the EU may yet lead to a more complicated and uncertain process for obtaining regulatory clearance to market the Group's future products in the UK and the EU.

Complex research and development processes - Certain elements of the reagents and other components which are planned to be used in the Group's test for lung cancer are bespoke in their nature and may be difficult to reproduce in an optimised manner. Any unexpected delays or issues with this process may have an impact on the Group's anticipated development and commercialisation strategy and its timeline.

Ownership and protection of intellectual property rights - The Group's ability to compete will depend in part, upon the protection of its intellectual property ("IP"). Filing, prosecuting and defending patents in all countries throughout the world would be prohibitively expensive so it is possible that competitors will use the technologies in jurisdictions where the Group has not yet obtained patent protection in order to develop a competing product. In the event that litigation is necessary to defend the Group's IP, it could require the Group to commit significant resources. There is no guarantee that the result of such litigation would result in a favourable outcome to the Group. Any of these events may have a material adverse effect on the Group's business, financial condition, capital resources, results and/or future operations.

Future product liability risks - The Group's future business may expose it to potential product liability and indemnity risks. There can be no assurance that the necessary insurance cover will be available to the Group at a commercially acceptable cost or that, in the event of any claim, the level or extent of insurance carried by the Group now or in the future will be adequate, or that a product liability or other claim would not materially and adversely affect the business of the Group.

Lack of manufacturing process - The Group currently has no manufacturing process. Future manufacturing processes will be outsourced to a partner specialising in manufacture. These arrangements usually provide for an adequate volume of manufacturing capability. No assurance can be given that a future manufacturing partner (i) can be found to provide a product on commercially acceptable terms and (ii) will achieve and sustain the production yields required to meet the Group's future customers' demand for the Group's products, in either case this could have a material and adverse effect on the Group's business.

Future funding requirements – As a result of the Subscription and the Facility (as each defined below), the Group has sufficient financial resources to conduct its planned activities and cover its general operating costs and overheads for at least 18 months from the date of this Prospectus. Thereafter, the Company will need to raise additional funding should it wish to undertake development of additional future products beyond the core offering currently being contemplated and to further fund the corporate and operational overhead of the business, which is likely to remain pre-revenue at this point. If the Company is unable to raise additional capital when needed or on suitable terms, the Group could be forced to delay, reduce or eliminate future plans or aspirations should the current activity deliver potentially commercially viable results in the future. Any additional equity fundraising to finance opportunities arising may be dilutive for Shareholders. Any debt-based funding, should it be achievable, may bind the Group to restrictive covenants and curb its operating activities and ability to pay potential future dividends even when profitable. Finally, changes in interest rates could have an adverse impact on the Group's business by increasing the cost of capital and may negatively impact the Group's ability to secure financing on favourable terms. Any of these events could have a material adverse effect on the Group's business in the longer term.

3. Key information on the securities

3.1 What are the main features of the securities?

3.1.1 Description and class of securities

The securities subject to Admission are ordinary shares of 0.01p each which are denominated in UK Sterling and will be registered with ISIN number GB00BNG2VN02 and SEDOL number BNG2VN0. The issued share capital of the Company on Admission will consist of:

- 278,447,788 ordinary shares of 0.01p each in the capital of the Company ("**Ordinary Shares**") in issue ("**Existing Ordinary Shares**") held by the existing shareholders of the Company as at the date of this Prospectus;
- 33,333,333 new Ordinary Shares to be allotted and issued to subscribers pursuant to a proposed subscription, conditional on Admission, at a price of 1.5p per share ("**Issue Price**") pursuant to subscription letters ("**Subscription**") ("**Subscription Shares**");

- 666,666 new Ordinary Shares to be allotted and issued to Optiva Securities Limited as settlement of a commission fee of £10,000 payable in connection with the Subscription (“**Commission Shares**”); and
- 1,666,666 new Ordinary Shares to be allotted and issued to E3 Fund SP (“**Investor**”) as settlement of a commitment fee of £25,000 payable in connection with a funding facility of £500,000 entered into between the Company and the Investor on 20 September 2022 (“**Facility**”) (“**Facility Shares**”), (the Subscription Shares, the Commission Shares and the Facility Shares together being the “**New Ordinary Shares**”) (the New Ordinary Shares and the Existing Ordinary Shares together being the “**Enlarged Share Capital**”).

The Issue Price paid is in UK Sterling. The Company’s issued share capital as at the date of this Prospectus and following admission of the New Ordinary Shares pursuant to, inter alia, the Subscription is as follows:

| Share class | Number of shares in issue | |
|-----------------------------|-----------------------------------|--|
| | As at the date of this Prospectus | Following admission of the New Ordinary Shares |
| Ordinary Shares of 0.01p | 278,447,788 | 314,114,453 |
| A Deferred Shares of 0.01p* | 12,383,625,615 | 12,383,625,615 |
| A Deferred Shares of 0.99p* | 225,158,220 | 225,158,220 |

*these shares are not listed or admitted to trading on any stock market

3.1.2 Rights attaching to the securities

The New Ordinary Shares will, on Admission, rank *pari passu* in all respects with all other Ordinary Shares in issue and will therefore rank equally for all dividends or other distributions hereafter declared, made or paid on the ordinary share capital of the Company. Each ordinary share ranks *pari passu* for voting rights. Every shareholder present in person at a general meeting of the Company shall have one vote on a show of hands and, on a poll, every shareholder present in person or by proxy shall have one vote for every share of which he is the holder. The Directors can call a general meeting at any time. All members who are entitled to receive notice under the Articles must be given notice. On a winding-up, the liquidator may, with the sanction of a special resolution of the Company and subject to and in accordance with the Companies Act 2006 (“**Act**”) divide among the shareholders *in specie* or kind the whole or any part of the assets of the Company. Subject to the Act, the Company may, by ordinary resolution, declare dividends to be paid to members of the Company according to their rights and interests in the profits of the Company available for distribution, but no dividend shall be declared in excess of the amount recommend by the Board. All ordinary shares, including the New Ordinary Shares are freely transferable.

The rights attaching to the A Deferred Shares are minimal. Such shares do not carry any voting or dividend rights and are only be entitled to a payment on a return of capital (whether by winding up or otherwise) after an amount of £30 million has been paid in respect of each Ordinary Share (an extremely remote possibility). The A Deferred Shares are not listed or admitted to trading on any stock market and are not transferable without the prior written consent of the Company.

3.1.3 Dividend Policy

The present aim of the Directors is to retain any earnings for capital growth. Thus the Company does not expect to pay dividends in the foreseeable future but, subject to, *inter alia*, the availability of sufficient distributable profits, intend to commence the payment of dividends when it becomes commercially prudent to do so and intend to adopt a progressive dividend policy thereafter.

3.2 Where will the securities be traded?

Application will be made for the New Ordinary Shares to be admitted to the Official List of the FCA by means of a standard listing under Chapter 14 of the Listing Rules (“**Standard Listing**”) and to trading on the Main Market of the London Stock Exchange. It is expected that Admission will become effective and that unconditional dealings will commence on the London Stock Exchange at 8.00 a.m. on 26 September 2022.

3.3 What are the key risks that are specific to the securities?

General Investment - A number of factors outside the Company’s control could impact on its performance and the price of its New Ordinary Shares, including investor sentiment and local and international stock market conditions. Shareholders should recognise that the market price of shares may fall as well as rise and that the market price of the New Ordinary Shares may not reflect the underlying value of the Company.

Trading market for the New Ordinary Shares - The share price of publicly traded companies, including those listed on the London Stock Exchange, can be highly volatile and shareholdings illiquid. The price at which the New Ordinary Shares will be quoted and the price which investors may realise for their shares will be influenced by a large number of factors. Prospective investors should be aware that the value of an investment in the Company may go down as well as up. Investors may therefore realise less than, or lose all of, their investment.

Substantial sales of New Ordinary Shares - There can be no assurance that certain parties will not elect to sell their New or Existing Ordinary Shares. The market price of Ordinary Shares could decline as a result of any such sales of Ordinary Shares or as a result of the perception that these sales may occur.

The Company has not paid dividends in the past - There can be no assurance as to the level of future dividends (if any). The declaration, payment and amount of any future dividends of the Company are subject to the discretion of the Board, and will depend on, among other things, the Company's earnings, financial position, cash requirements and availability of profits. A dividend may never be paid.

4. Key information on the offer of securities to the public and/or the admission to trading on a regulated market

4.1 Under which conditions and timetable can I invest in the securities?

4.1.1 Terms and Conditions

The Company has issued 33,333,333 Subscription Shares at 1.5p per share conditional, *inter alia*, upon Admission occurring and becoming effective by 8.00 a.m. London time on or prior to 22 September 2022 (or such later date as the Company may specify). The subscribers' commitment is irrevocable. The rights attaching to the ordinary shares will be uniform in all respects and all of the ordinary shares will form a single class for all purposes. If any of the conditions are not satisfied, or, if applicable, waived, the Subscription will not proceed. The Subscription is not underwritten.

4.1.2 Expected Timetable

| Action | Timeframe |
|--|--------------------------------|
| Publication of this Prospectus | 21 September 2022 |
| Admission of New Ordinary Shares effective and commencement of dealing | 8.00 a.m. on 26 September 2022 |
| Expected date for CREST accounts to be credited | 26 September 2022 |
| Despatch of definitive certificates (where applicable) expected by no later than | 27 September 2022 |

4.1.3 Details of Admission

Application will be made for the New Ordinary Shares to be admitted to the Official List of the FCA by means of a Standard Listing and to trading on the Main Market of the London Stock Exchange. It is expected that Admission will become effective and that unconditional dealings will commence on the London Stock Exchange at 8.00 a.m. on 26 September 2022.

4.1.4 Distribution

The New Ordinary Shares will be available to be issued in either registered form (i.e. certified) or electronic form (i.e. via CREST). Where applicable, definitive share certificates in respect of the New Ordinary Shares to be issued are expected to be dispatched, by post at the risk of the recipients, to the relevant holders, not later than 27 September 2022. Prior to the dispatch of definitive share certificates in respect of any New Ordinary Shares which are held in certificated form, transfers of those New Ordinary Shares will be certified against the register of members of the Company. No temporary documents of title will be issued.

4.1.5 Dilution

The percentage dilution of the Existing Ordinary Shares as a result of the Subscription and the issue and allotment of the Commission Shares and the Facility Shares will be approximately 10.69%, 0.24% and 0.59%, respectively. Upon Admission, the New Ordinary Shares will represent approximately 11.35% of the Enlarged Share Capital of the Company.

In addition to the Subscription and the issue and allotment of the Commission Shares and the Facility Shares, if all outstanding options and warrants in the Company were to be exercised, the Existing Ordinary Shares would be diluted by 11.39%.

Warrants

On 14 May 2021, Shakespeare Martineau LLP was issued with warrants over 250,000 Ordinary Shares which have an exercise price of 10p per share ("**Shakespeare Martineau Warrants**"). The Shakespeare Martineau Warrants are exercisable until the third anniversary of issue) and will be automatically exercisable upon the price of the ordinary shares equalling 20p per share. If all of the Shakespeare Martineau Warrants are exercised then the Enlarged Share Capital of the Company will be diluted by approximately 0.08%.

The investors who took part in a placing of shares on 14 May 2021 received warrants over 11,000,000 Ordinary Shares in total, at a price of 15p per share, which are exercisable for three years from the date of issue on 14 May 2021 ("**2021 Placing Warrants**"). If all of the 2021 Placing Warrants are exercised then the Enlarged Share Capital of the Company will be diluted by approximately 3.38%.

On 14 May 2021, Pershing Nominees Limited were issued with warrants over 1,100,000 Ordinary Shares, exercisable at 10p per share ("**NSL Warrants**"). If all of the NSL Warrants are exercised then the Enlarged Share Capital of the Company will be diluted by approximately 0.35%.

Options

The Company has a historic Executive Share Option Scheme (“**Executive Scheme**”). As at the date of the Prospectus, the Company has granted the following options to subscribe for ordinary shares to CFO Solutions Limited (a company in which Nigel Lee is a director) which are outstanding as at the date of this Prospectus (“**CFO Options**”):

| Date of Grant | Options Issued* | Exercise Price (p) | Exercise Period | Expiry Date |
|----------------------|------------------------|-------------------------------|------------------------|--------------------|
| 26 August 2015 | 300 | 5.025 | 2017 - 2025 | 25 August 2025 |
| 27 October 2016 | 800 | 1.85 | 2017 - 2026 | 26 October 2026 |
| 9 November 2017 | 500 | 0.85 | 2018 - 2027 | 8 November 2027 |
| Total | 1,600 | | | |

**as recalculated in accordance with the share reorganisation undertaken by the Company on 13 May 2021*

Exercise of all of the CFO Options would result in the Enlarged Share Capital being diluted by approximately 0.001%. The CFO Options represent approximately 0.0004% of the Fully Diluted Enlarged Share Capital of the Company.

In addition to the CFO Options, Professor Coverley has been issued options over 3,689,096 Ordinary Shares at an exercise price of £0.015339313479508 per share, pursuant to an agreement dated 23 April 2021 (“**DC Bould Options**”). The DC Bould Options are exercisable within three years of 14 May 2021. Dawn Coverley intends to exercise the DC Bould Options in full following the publication of the Company’s interim results. Exercise of all of the DC Bould Options would result in the Enlarged Share Capital being diluted by approximately 1.16%. The DC Bould Options represent approximately 0.98% of the Fully Diluted Enlarged Share Capital of the Company.

On 22 February 2022, the Company entered into option agreements in relation to unapproved options granted over a total of 19,741,345 Ordinary Shares to the members of the Board as set out below as at 3 November 2021 (“**Management Incentive Options**”). The Management Incentive Options are exercisable at a price of 10p per share, subject to certain vesting criteria being met, based on key deliverables under the Company’s business plan. From vesting, the option holder has 10 years to exercise the option before expiry. Exercise of all of the Management Incentive Options would result in the Enlarged Share Capital being diluted by approximately 5.91%. The Management Incentive Options represent approximately 5.23% of the Fully Diluted Enlarged Share Capital of the Company.

| Director | Options Issued |
|-----------------|-----------------------|
| Allan Syms | 5,068,956 |
| Dawn Coverley | 12,672,389 |
| Nigel Lee | 2,000,000 |

4.1.6 Expenses

The estimated expenses incurred (or to be incurred) by the Company in connection with the Subscription and Admission are approximately £40,000 (exclusive of VAT). No expenses will be charged to investors.

4.2 **Why is this prospectus being produced?**

4.2.1 Reasons for the Subscription and Admission

The Company has conditionally raised gross proceeds of £500,000 by way of the in order to provide working capital for the Company’s strategy.

The Group is in the early stages of developing a blood test for the early detection of lung cancer. Its proof-of-concept prototype test is based on the ability to measure a stable blood plasma biomarker, a variant of CIZ1. CIZ1 is a naturally occurring cell nuclear protein involved in DNA replication, and the targeted CIZ1B variant is highly correlated with early-stage lung cancer. Published research led by Professor Coverley has demonstrated that CIZ1B can be measured with high sensitivity via an ELISA process, which should allow for testing in a high-throughput, hospital-friendly format. The Directors believe that this development overcomes an important barrier to clinical development and the application of this blood test for the early detection of lung cancer, which is essential to improve a patient’s chance of survival. The Board intends for Cizzle Biotechnology’s initial product to be a diagnostic immunoassay that can be readily performed by hospitals and reference laboratories, but a potential follow-on product could be a point of care test provided by a primary health care provider.

4.2.2 Use and estimated net amount of proceeds

The proceeds of the Subscription, which are expected to total approximately £500,000 (before expenses of £40,000 excluding VAT), will be put towards the development of a laboratory-developed test accredited service as a forerunner to taking the CIZ1B biomarker test through to CE marking and/or FDA 510(k) clearance.

In specific, it is anticipated that the net proceeds of the Subscription (£460,000) receivable by the Company will be applied as follows:

| | |
|--|---------|
| Monoclonal Antibody & Reagent Production | £30,000 |
| Clinical samples | £25,000 |

| | |
|--|----------|
| Kit Development, Manufacture & Clinical Trials | £230,000 |
| Health Economics | £10,000 |
| Patents | £10,000 |
| York Laboratory Support Costs | £50,000 |
| Development of LDT Certified Test | £25,000 |
| Marketing & Overheads | £20,000 |
| Salaries | £20,000 |
| Additional research | £40,000 |

According to the Company's forecasts, following a period of 18 months after the receipt of the net proceeds of the Subscription and assuming utilisation of the Facility in full during that period, the Company will need to raise additional funding should it wish to undertake development of additional future products beyond the core offering currently being contemplated and beyond that being funded by the cash deposits of the Company as a result of the Subscription, utilisation of the Facility and generated income and to further fund the corporate and operational overhead of the business, which is likely to remain pre-revenue at this point. It is likely following a period of 18 months after Admission, that the Company will need not less than £1 million (approximately £0.5 million to fund the corporate and operational overheads of the business and approximately £0.5 million for the future additional development of projects). Should the Company require further funding following the period of 18 months after Admission, the Company will seek further support from shareholders and other investors from the platform offered to it by virtue of its Standard Listing. In settlement of some of the Company's expenditure (approximately 10%) relating to, for example professional adviser fees, management would attempt to renegotiate those professional adviser and supplier payment terms (although this cannot be guaranteed), whilst the Company is seeking additional funding to support the development of further products. Like any substantially pre-revenue company which seeks to raise development capital, in the event future funding cannot be secured when needed following the period of 18 months after Admission, and capital and operational expenditure cannot be further reduced or delayed, then the Directors will consider all legal avenues open to them at the time. As part of a strategy to mitigate risk arising from insufficient working capital, the Company may attempt to secure new funding through a future placing of shares however it is recognised that the success and/or price of such placing, may be dependent on the Company achieving its key milestones for example in reagent generation, test manufacture and clinical validation to enable UKCA, CE marking, LDT and/or FDA clearance. The Directors will continually monitor the Company's cash position and together with its advisors determine whether it is necessary and of benefit to shareholders to consider any future placing of shares. However, according to the working capital projections of the Company, such funding will not be required within the 18 months from publication of the Prospectus. The Company will also seek licensing and joint venture fees and, if required, attempt to bring these commercial discussions forward which may also result in the sale of intellectual property rights and therefore potentially, the entire business. For the avoidance of doubt, the Company has not held any preliminary discussions regarding a possible sale of its IP. Further options could include seeking structured finance or debt financing through specialist loans. Delays or failure to secure additional capital or licence revenues will mean that cost reductions will be sought which would likely take the form of delaying discretionary capital. The impact of such cuts in expenditure are less material in the first few years as they are not aimed at the core product development programme. This is because the Company's product pipeline consists of "future products" for example a potential ELISA test kit, which are the core products to be developed during the period from the date of this Prospectus until 31 December 2023 and hence not subject to any need to reduce costs. Later products such as potentially point of care tests are defined as "additional future products" which would be developed during the period from the date of this Prospectus until 31 December 2023 are not essential to deliver the Company's strategic and commercial goals. Because the impact of expenditure cuts would be more likely in the later part of year two these cuts could only impact "additional future products" and therefore are less material to the development of the core products. The impact of cost reductions on future research in later years could mean the delay of such products as point of care tests which necessarily could reduce wider market adoption and impact potential future valuation of the Company. Like any pre-revenue company who needs to raise funds to develop a project, a failure to secure future funding is a possibility. Were the Company to be unable to fund itself, an administration would have to be considered.

4.2.3 Conflicts of Interest

There are no material conflicts of interest pertaining to the Subscription or Admission.

21 September 2022

RISK FACTORS

The attention of prospective investors is drawn to the fact that an investment in the New Ordinary Shares may not be suitable for all such investors and will involve a variety of risks which, if they occur, may have a materially adverse effect on the Company's business, financial condition, results or future operations. In such case, the market price of the New Ordinary Shares could go down as well as up, and an investor might lose all or part of his or her investment. No assurance can be given that investors will realise a profit or avoid a loss on their investment. Prospective investors should ensure they are capable of evaluating the merits and risks of an investment and that they have sufficient resources to be able to bear any losses (which may be equal to the whole amount invested) which may result from such an investment.

In addition to the information set out in this Document, the following risk factors should be considered carefully in evaluating whether to make an investment in the New Ordinary Shares.

Additionally, there may be further risks of which the Company and the Directors are not aware or believe to be immaterial which may, in the future, adversely affect the Company's business, financial condition or results of operations and the market price of the New Ordinary Shares.

Before making a final investment decision, prospective investors should carefully review and evaluate the risks and the other information contained in this Document and consider carefully whether an investment in the New Ordinary Shares is suitable for them in the light of their personal circumstances and the financial resources available to them. Any prospective investor who is in any doubt as to any action he should take, should consult with an independent financial adviser authorised under FSMA, if the investor is in the United Kingdom or, if not, another appropriately authorised independent financial adviser, who specialises in advising on the acquisition of shares and other securities.

There can be no guarantee that the Company's objectives will be achieved.

RISKS RELATING TO THE COMPANY AND ITS BUSINESS

Pre-revenue business

The Group is still at an early stage of its development, has not generated revenues from its operations to date and has a history of operating losses. The generation of revenues is difficult to predict and there is no guarantee that the Group will generate significant or any revenues in the foreseeable future.

There are a number of operational, strategic and financial risks associated with early-stage companies. The Group will face risks frequently encountered by pre-revenue companies looking to bring new medical devices to the market. For the foreseeable future, the Group will have significant reliance upon the success of the CIZ1B biomarker in the detection of lung cancer. There is no guarantee that the Group's intellectual property will ultimately result in a commercially viable test for the detection of lung cancer. It is also possible that technical and/or regulatory hurdles could lengthen the time required for the delivery of such a testing product.

The Group's prospects, *inter alia*, rest initially upon the rate of consumer penetration for its test for the early detection of lung cancer, once fully developed. The Group's future growth and prospects will also depend on its ability to secure commercialisation partnerships on appropriate terms, to manage growth and to expand and improve operational, financial and management information, quality control systems and its commercialisation function on a timely basis, whilst at the same time maintaining effective cost controls. Any failure to expand and improve operational, financial and management information and quality control systems in line with the Group's growth could have a material adverse effect on the Group's business, financial condition and results of operations.

Competition and the pace of development in the healthcare industry

The Directors are aware of a number of competitor companies which are seeking to develop, commercialise or market alternative types of tests for the detection of cancer, including lung cancer. Certain competitors already have UKCA, CE of FDA 510K marking for lung cancer detection products. Existing or new competitors may have larger resources, greater market presence, economies of scale

or a lower cost base than the Group. Diagnosis of lung cancer needs to be made at a much earlier stage through the availability of an accurate in vitro diagnostic test. This is being addressed by a number of different technologies to the Group for example autoantibody technology and tests on circulating DNA including those based on single nucleotide polymorphisms (SNPs) and gene panels. It is therefore possible that the market may evolve and other tests and companies may provide alternative solutions. Few tests are aimed at early detection (cancer stages 1 and 2) or on reducing significantly the number of false positives achieved via CXT and chest CT scans. While many blood tests to detect tumour markers are available or under development, many are hampered as markers may also be produced by normal cells. In contrast, the Group's test is based on tumour-specific technology.

The Group operates within the biotechnology sector, a complex area of the healthcare industry. Rapid scientific and technological change within the biotechnology sector could lead to other market participants creating approaches, products and services equivalent or superior to the diagnostic testing products and services than those to be offered by the Group, which could adversely affect the Group's performance and success. Better resourced competitors may be able to devote more time and capital towards the research and development process, which, in turn, could lead to scientific and/or technological breakthroughs that may materially alter the outlook or focus for markets in which the Group will operate.

If the Group is unable to keep pace with the changes in the biotechnology sector and in the wider healthcare industry, the demand for its prospective future testing platforms and associated products and services could fall, which may have a material adverse effect on the Group's business, financial condition, capital resources, results and/or future operations. In addition, certain of the Group's competitors may have significantly greater financial and human resource capacity and, as such, better manufacturing capability or sales and marketing expertise. New companies with alternative technologies and products may also emerge. Any of these events may have a material adverse effect on the Group's business, financial condition, capital resources, results and/or future operations.

Attraction and retention of key management and employees

The successful operation of the Group will depend partly upon the performance and expertise of its current and future management and employees. The loss of the services of certain of these members of the Company's key management, particularly Professor Dawn Coverley and Dr Allan Syms or the inability to identify, attract and retain a sufficient number of suitably skilled and qualified employees may have a material adverse effect on the Group.

Regulatory environment and the process for obtaining a UKCA, CE marking, LDT or a 510(k) clearance

The Group's prospective future products will be subject to various laws, regulations and standards in each of the jurisdictions in which products are to be manufactured and distributed.

While the Board intends to develop the CIZ1B biomarker test to a point at which UKCA, CE Marking, LDT or FDA 510(k) clearance will be sought, there can be no guarantee that the Group's future products will ultimately obtain UKCA, CE marking, LDT or FDA 510(k) clearance. There can also be no guarantee that future UKCA, CE marking, LDT or FDA 510(k) clearance can be obtained within the timescales or the budgets anticipated by the Directors. The Group intends to pursue UKCA, CE marking approval, LDT accreditation or FDA 510(k) clearance via the use of retrospective testing data. However, if retrospective testing data is not sufficient to obtain UKCA, CE marking approval, LDT accreditation and/or FDA 510(k) clearance, then the Group may need to complete a prospective study, which it is anticipated would be more expensive and would take longer.

Any other potential delays in obtaining the UKCA CE marking approval, LDT accreditation or potentially FDA 510(k) clearance would adversely affect the timing of the Group's future product sales into the EU (or the USA in the case of a LDT or FDA 510(k) clearance). There is no guarantee that there will not be an extended period of requests for information or supporting data that could add to the timing for receiving the UKCA/CE mark (or potentially a LDT or FDA 510(k) clearance).

There are significant uncertainties associated with the exit by the UK from its membership of the European Union. Since 1 January 2021, there have been a number of changes, introduced through secondary legislation, to how medical devices are placed on the market in Great Britain (England, Wales and Scotland). These are:

- CE marking will continue to be recognised in Great Britain until 30 June 2023
- certificates issued by EU-recognised Notified Bodies will continue to be valid for the Great Britain market until 30 June 2023
- the EU no longer recognises UK Notified Bodies
- UK Notified Bodies are not able to issue CE certificates (other than for the purposes of the “CE UKNI” marking, which is valid in Northern Ireland) - and have become UK Approved Bodies
- a new route to market and product marking is available for manufacturers wishing to place a device on the Great Britain market
- since 1 January 2021, all medical devices, including in vitro diagnostic medical devices (IVDs), placed on the Great Britain market need to be registered with the MHRA. There is a grace period for registering:
 - Class IIIs and Class IIb implantables, and all active implantable medical devices and IVD List A products must be registered from 1 May 2021
 - other Class IIb and all Class IIa devices and IVD List B products and Self-Test IVDs must be registered from 1 September 2021
 - Class I devices, custom-made devices and general IVDs (that do not currently need to be registered) must be registered from 1 January 2022
- manufacturers of Class I devices, custom-made devices and general IVDs that, prior to 1 January 2021, were required to register their devices with the MHRA (i.e. UK-based manufacturers or third country manufacturers with Northern Ireland-based Authorised Representatives) must continue to register their devices from 1 January 2021 on the same basis as they do now rather than in line with the above dates

The Group’s lung cancer blood test will likely be classed as an IVD List B product.

It is anticipated that the MHRA wishes to strengthen regulation to protect patients post-Brexit. Changes to regulation could lead to potential delays in obtaining the UKCA CE marking approval, LDT accreditation or potentially FDA 510(k) clearance and there can be no guarantee that the Group’s future products will ultimately obtain UKCA, CE marking, LDT or FDA 510(k) clearance or that future UKCA, CE marking, LDT or FDA 510(k) clearance can be obtained within the timescales or the budgets anticipated by the Directors. The Group will closely monitor changes to regulation brought about by the MHRA and work with the MHRA to try to ensure that the Group’s products meet any changes in the standards.

There are possible further uncertainties as to the current and future fiscal, monetary and regulatory landscape in the UK. There is also uncertainty as to how, when and to what extent the continuing impact of Brexit, the COVID-19 pandemic, the ongoing armed conflict in Ukraine and potential low levels of economic growth, will have an impact more generally on the economy of the UK and the growth of various industries, consumer confidence, levels of investor activity and confidence in market performance.

The UK’s exit from the EU may yet lead to a more complicated and uncertain process for obtaining regulatory clearance to market the Group’s future products in the UK and the EU. In the event of such complications or delays in obtaining regulatory clearance for marketing in the UK or the EU, the Group will consider giving higher priority to compliance with the LDT and FDA 510(k) clearance process.

Following Brexit, the Group will need to comply with the Medical Devices (Amendment etc.) (EU Exit) Regulations 2019 if it is to market its future products in the UK.

Failure to comply with additional requirements as a result of regulatory change and/or failure to receive regulatory clearance may adversely impact the Company’s ability to develop and market its products which in turn may have an adverse impact on the business of the Group.

Complex research and development processes

Certain elements of the reagents and other components which are planned to be used in the Group's test for lung cancer are complex and bespoke in their nature and may be difficult to reproduce in an optimised manner. Any unexpected delays or issues with this process may have an impact on the Group's anticipated development and commercialisation strategy and its timeline.

Infringement of third party patents and other intellectual property rights

The Group's products may infringe or may be alleged to infringe existing patents or patents that may be granted in the future that may result in costly litigation and could result in the Group having to pay substantial damages or adversely affect the Group's ability to commercialise its products. No freedom to operate ("FTO") review has been undertaken (being the review and assessment of whether a business has the ability to operate freely as intended, without it infringing pre-existing third party intellectual property rights). Therefore, even if no intellectual property infringement claims have been brought to date, no review has been undertaken as to whether any such claims may be likely in the future. Some patent applications in Europe and the US may be maintained in secrecy until the patents are published. Patent applications in Europe, the US and many foreign jurisdictions are typically not published until 18 months after filing, and publications in the scientific literature often lag behind actual discoveries, others may have filed patents that may cover its technologies, its products or the use of its products. Additionally, pending prior patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover the Group's technologies, its products or the use of its products. As a result, the Group may become party to, or threatened with, future adversarial proceedings or litigation regarding patents with respect to its products and technology.

If the Group is sued for patent infringement, the Group would need to demonstrate that its products or methods either do not infringe the patent claims of the relevant patent or that the third party patent claims are invalid, and the Group may not be able to do this. If the Group is found to have infringed a third party's patent, the Group could be required to obtain a licence from such third party to continue developing and marketing its products and technology or the Group may elect to enter into such a licence in order to settle litigation or in order to resolve disputes prior to or during litigation. However, the Group may not be able to obtain any required licence on commercially reasonable terms or at all, which could prevent it from continuing to develop and market its products and technology. Even if the Group is able to obtain a licence, it could be non-exclusive, thereby giving its competitors access to the same technologies licensed to the Group, and could require the Group to make substantial royalty payments. The Group could also be forced, including by court order, to cease commercialising the infringing technology or products. A finding of infringement could prevent the Group from commercialising its products or force the Group to cease some of its business operations, which could materially harm its business. Claims that the Group has misappropriated the confidential information or trade secrets of third parties could have a similarly negative impact on its business.

Any such claims are likely to be expensive to defend, and some of its competitors may be able to sustain the costs of complex patent litigation more effectively than the Group can, because they have substantially greater resources. Moreover, even if the Group is successful in defending any infringement proceedings, it may incur substantial costs and divert management's time and attention in doing so, which may have a material adverse effect on the Group's business, financial condition, capital resources, results and/or future operations. Further, disputes can often last for a number of years, and can be subject to lengthy appeals processes before any final resolution is achieved through the various different courts and/or tribunals.

Despite no FTO review being undertaken, the Group currently believes that it is not in breach of any third party patents or other intellectual property rights.

A FTO search refers to whether it's commercially 'safe' for a company to make or sell products in target countries without infringing existing third-party rights. This is different from patent searches which consider whether there could be potential prior art issues relating to third party intellectual property used to form potential products. At the time of initial patenting it was unclear to Cizzle Biotechnology what the commercial product format would be and because of the complexity and cost associated with a FTO it was considered this should only be considered at the time of product design for commercial launch. The Group will consider the merits of conducting a FTO after product design, manufacturer and components have been resolved.

The Group believes that a FTO review is not fool proof and it can never be guaranteed that another party will not attempt to sue the Group, or any company reliant on intellectual property regardless of the presence of a FTO. Nor does a FTO guarantee a successful litigation outcome in such an event. Patents and applications identified will depend on the quality of the search and the interpretation of the service provider. Some applications by others may be on file but unpublished at the time of the search and therefore not considered as part of the study.

That being the case, whilst the Group may undertake a FTO at a later date, the Directors believe that it is reasonable to rely on the legal due diligence it has carried out to date. Furthermore, the Group plans to contract out manufacture and would seek protection within the supply agreement that the manufacturer will warrant that its design and product will not infringe third party intellectual property.

The Group is not aware of any claims of infringement related to its intellectual property or potential product designs. Since the core patents have now been granted and published, and no oppositions or relevant prior art have prevented validity of the patents it provides comfort that third parties will not provide subsequent oppositions which are in any event time limited and now likely to have expired.

Ownership and protection of intellectual property rights

The Group's ability to compete will depend in part, upon the successful protection of its intellectual property, in particular its patents and know-how. The Group seeks to protect its intellectual property through the filing of patent applications, as well as robust confidentiality obligations on its employees. Filing, prosecuting and defending patents in all countries throughout the world would be prohibitively expensive. It is possible that competitors will use the technologies in jurisdictions where the Group has not yet obtained patent protection in order to develop its own products which will then directly compete against the Group's product.

Certain of Cizzle Biotechnology's patents were assigned to Cizzle Biotechnology by institutions which funded the research work that was undertaken in relation to the invention claimed in these patents. There is always a risk that some of these funding institutions may later seek to invalidate such assignments claiming that patents have not been validly assigned to Cizzle Biotechnology.

Any such claims are likely to be expensive to defend, and the other litigating parties may be able to sustain the costs of complex patent litigation more effectively than the Group can, because they have substantially greater resources. Moreover, even if the Group is successful in defending any infringement proceedings, it may incur substantial costs and divert management's time and attention in doing so, which may have a material adverse effect on the Group's business, financial condition, capital resources, results and/or future operations. Further, disputes can often last for a number of years, and can be subject to lengthy appeals processes before any final resolution is achieved through the various different courts and/or tribunals. Furthermore, it cannot be guaranteed that a court will not rule against Cizzle Biotechnology were such claims to be defended.

Despite these precautions that may be taken by the Group to protect its intellectual technology and products, unauthorised third parties may attempt to copy, or obtain and use its technology and products. A third party may infringe upon the Group's intellectual property, release information considered confidential about the Group's intellectual property and/or claim technology that is registered to the Group. In addition, the Group may fail to discover infringement of its intellectual property, and/or any steps taken or that will be taken by it may not be sufficient to protect its intellectual property rights or prevent others from seeking to invalidate its intellectual property (for example, in response to a claim for infringement or where an attempt is made to "clear a path" for a new competing product) or block sales of its products by alleging a breach of their intellectual property. Third parties can bring material and arguments which the patent office granting the patent may not have seen at the time of granting the patent. Therefore, whilst a patent may be granted to the Group it could in the future be found by a court of law or by a patent office to be invalid or unenforceable or in need of further restriction. As a result of a validity challenge, a patent may be amended so as to narrow its scope to an extent that it may be more difficult to restrict activities of competitors. Applications filed by the Group in respect of new patents and trademarks may also not be granted or, if granted, may still be subject to opposition. In addition, there can be no guarantee that the patents or trademarks will be granted on a timely basis. Subject to certain time limits, there may, in certain circumstances, also be claims to entitlement, and/or

compensation arising from contributions made, to granted patents by those who have assisted with the relevant research or project.

The Board intends to defend the Group's intellectual property vigorously, where necessary through litigation and other means. In the event that litigation is necessary in the future in order to enforce the Group's intellectual property rights, determine the scope and validity of proprietary rights of other companies, and/or defend claims of infringement or invalidity, it could require the Group to commit significant resource to pursue the protection of its intellectual property and there is no guarantee that the result of such litigation would result in a favourable outcome to the Group, or the damages or other remedies awarded, if any, may not be commercially meaningful or represent acceptable compensation in respect to the infringement. Any of these events may have a material adverse effect on the Group's business, financial condition, capital resources, results and/or future operations.

The Company is not currently aware of any such active or pending litigation risk.

Future product liability risks

The Group's future business may expose it to potential product liability and indemnity risks. There can be no assurance that the necessary insurance cover will be available to the Group at a commercially acceptable cost or that, in the event of any claim, the level or extent of insurance carried by the Group now or in the future will be adequate, or that a product liability or other claim would not materially and adversely affect the business of the Group.

Lack of manufacturing process

The Group currently has no manufacturing process. Future manufacturing process will be outsourced to a partner specialising in manufacture. These arrangements usually provide for an adequate volume of manufacturing capability. No assurance can be given that a future manufacturing partner (i) can be found to provide a product on commercially acceptable terms and (ii) will achieve and sustain the production yields required to meet the Group's future customers' demand for the Group's products, in either case this could have a material and adverse effect on the Group's business.

Future funding requirements

As a result of the Subscription and Facility, the Group will have sufficient financial resources to conduct its planned activities and cover its general operating costs and overheads for at least 18 months from the date of this Prospectus. Thereafter, the Company will need to raise additional funding should it wish to undertake development of additional future products beyond the core offering currently being contemplated and to further fund the corporate and operational overhead of the business, which is likely to remain pre-revenue at this point.

The Company has budgeted for all near and short-term activities and plans, however in the longer term the potential for further research, development and production plans and additional initiatives may arise, which are beyond the scope of the Group's current planned activity and which may require additional financing which may not be available to the Group when needed, on acceptable terms, or at all.

If the Company is unable to raise additional capital when needed or on suitable terms, the Group could be forced to delay, reduce or eliminate future plans or aspirations should the current activity deliver potentially commercially viable results in the future. Any additional equity fundraising to finance opportunities arising may be dilutive for Shareholders. Any debt-based funding, should it be achievable, may bind the Group to restrictive covenants and curb its operating activities and ability to pay potential future dividends even when profitable. Finally, changes in interest rates could have an adverse impact on the Group's business by increasing the cost of capital and may negatively impact the Group's ability to secure financing on favourable terms. Any of these events could have a material adverse effect on the Group's business in the longer term but not for at least 12 months from the date of this Prospectus.

Timely completion of project milestones to commercialise the Group's technology

The Company must meet project milestones in order to commercialise its technology in line with market expectations and to ensure that its first product reaches the market at the most appropriate time to maximise the market opportunity. The Directors continually review project milestones and action to be undertaken at monthly operational and board meetings but no guarantee can be given that such milestones shall be achieved on time or at all. Material delays to project delivery may, among other things, damage relationships with key suppliers and other business partners and may risk other market

entrants building market share which may have an adverse effect of the Group's business. Delays in meeting project milestones may also delay the Company from generating potential revenue from licensing and current royalty deals.

Economic uncertainty

There are significant uncertainties as to the current and future fiscal, monetary and regulatory landscape in the UK. Economic and global political uncertainty, including the continuing impact of Brexit, the COVID-19 pandemic, the ongoing armed conflict in Ukraine and potential low levels of economic growth, are likely to put cost pressures on services which the Group requires for both research, development and professional advisory. The Company will continue to negotiate fixed price contracts with its professional advisors, however such contracts will need to be renewed and renegotiated periodically. In addition new adviser contracts may need to be entered into from time to time, most likely on a project to project basis. In each case, fixed prices may be higher than those prices paid by the Company in the past.

RISKS RELATING TO THE NEW ORDINARY SHARES

General Investment

A number of factors outside the Company's control could impact on its performance and the price of its New Ordinary Shares, including investor sentiment and local and international stock market conditions. Shareholders should recognise that the market price of shares may fall as well as rise and that the market price of the New Ordinary Shares may not reflect the underlying value of the Company. Economic and global political uncertainty, including the continuing impact of Brexit, the COVID-19 pandemic, the ongoing armed conflict in Ukraine and potential low levels of economic growth, continue to present significant challenges and may adversely affect the performance of the Group. It is also possible that currently unknown and unanticipated events, either domestic or international, may occur and have a negative effect on economic activity and adversely affect the performance of the Group.

Trading market for the New Ordinary Shares

The share price of publicly traded companies, including those listed on the London Stock Exchange, can be highly volatile and shareholdings illiquid. The price at which the New Ordinary Shares will be quoted and the price which investors may realise for their shares will be influenced by a large number of factors, which could include, but not limited to, the performance of both the Group's and its competitors' businesses, variations in the operating results of the Group, divergence in financial and operational results from analysts' expectations, changes in earnings estimates by stock market analysts, large purchases or sales of New Ordinary Shares, legislative changes and general economic, political and regulatory conditions. Prospective investors should be aware that the value of an investment in the Company may go down as well as up. Investors may therefore realise less than, or lose all of, their investment. Application has been made for the New Ordinary Shares to be admitted to a Standard Listing on the Official List. A Standard Listing will afford investors in the Company a lower level of regulatory protection than that afforded to investors in a company with a Premium Listing, which is subject to additional obligations under the Listing Rules. A Standard Listing will not permit the Company to gain a FTSE indexation, which may have an adverse effect on the valuation of the New Ordinary Shares.

Substantial sales of New Ordinary Shares

There can be no assurance that certain Directors or other Shareholders will not elect to sell their New or Existing Ordinary Shares. The market price of Ordinary Shares could decline as a result of any such sales of Ordinary Shares or as a result of the perception that these sales may occur. In addition, if these or any other sales were to occur, the Company may in the future have difficulty in offering Ordinary Shares at a time or at a price it deems appropriate.

Taxation

The attention of potential investors is drawn to paragraph 13 of Part IV of this Document. The tax rules, and tax treaties, including stamp duty provisions, and their interpretation relating to an investment in the Company, may change during the life of the Company and may alter the tax benefit of an investment made by the Company.

The levels of, and reliefs from, taxation may change. The tax reliefs referred to in this Prospectus are those that are currently available and their value may depend on investors' individual circumstances.

Any change in the Company's tax status or the tax applicable to holding New Ordinary Shares or in taxation legislation or its interpretation, could affect the value of the investments held by the Company, its ability to provide returns to Shareholders and/or alter the post-tax returns to Shareholders. Statements in this Document concerning taxation of the Company and its investors are based on current tax law and practice which is subject to change, possibly with retrospective effect. Shareholders should note that the tax legislation of the country in which they are resident and of the Company's country of incorporation may have an impact on the income received from the New Ordinary Shares.

The Company has not paid dividends in the past

There can be no assurance as to the level of future dividends (if any). The declaration, payment and amount of any future dividends of the Company are subject to the discretion of the Board, and will depend on, among other things, the Company's earnings, financial position, cash requirements and availability of profits. A dividend may never be paid. The Company's proposed dividend policy is set out in paragraph 10 of Part I of this Document.

FORWARD-LOOKING STATEMENTS

Some of the statements in this Document include forward-looking statements, which reflect the Company's or, as appropriate, the Directors' current views with respect to financial performance, business strategy, plans and objectives of management for future operations (including development plans relating to the Company's business).

These statements are identified by their use of terms and phrases such as "believe", "could", "envisage", "estimate", "intend", "may", "plan", "will" or the negative of those, variations or comparable expressions, including references to assumptions.

The Directors believe that the expectations reflected in these forward looking statements are reasonable, but they are subject to, *inter alia*, the risk factors described in the section entitled "Risk Factors" in this Prospectus and are based on assumptions and estimates and involve risks, uncertainties and other factors that may cause the actual results, financial condition, performance or achievements of the Company or industry results to be materially different from any future results, performance or achievement expressed or implied by such forward-looking statements.

New factors may emerge from time to time that could cause the Company's business not to develop as it expects and it is not possible for the Company to predict all such factors. Given these uncertainties, prospective investors are cautioned not to place any undue reliance on such forward-looking statements.

These forward-looking statements speak only as at the date of this Document and do not in any way seek to qualify the working capital statement. The Company, its Directors will review and update publicly any forward-looking statement, as a result of new information, future developments or otherwise, as required by the Market Abuse Regulation, Prospectus Regulation Rules, Listing Rules or DTRs, as appropriate. All subsequent written and oral forward-looking statements attributable to the Company, or individuals acting on behalf of the Company, are expressly qualified in their entirety by this section of the Prospectus entitled "Forward-Looking Statements". Prospective investors should specifically consider the factors identified in this Document which could cause actual results to differ before making an investment decision.

DIRECTORS, SECRETARY AND ADVISERS

| | | |
|------------------|----------------------|---|
| Directors | Allan John Syms | <i>(Executive Chairman)</i> |
| | Dawn Alison Coverley | <i>(Scientific Director and Non-Executive Director)</i> |
| | Nigel Ronald Lee | <i>(Finance Director)</i> |
| | John Michael Treacy | <i>(Non-Executive Director)</i> |

all of the Company's current registered office at: 6th Floor
60 Gracechurch Street
London
EC3V 0HR

Principal Place of Business 6th Floor
60 Gracechurch Street
London
EC3V 0HR

Website address <https://cizzlebiotechnology.com/>

Company Secretary SGH Company Secretaries Limited
6th Floor
60 Gracechurch Street
London
EC3V 0HR

Financial Adviser Allenby Capital Limited
5 St. Helen's Place
London
EC3A 6AB

Broker to the Company Novum Securities Limited
57 Berkeley Square
London
W1J 6ER

Auditor PKF Littlejohn LLP
15 Westferry Circus
London
E14 4HD

Solicitors to the Company Shakespeare Martineau LLP
No 1 Colmore Square
Birmingham
B4 6AA

Financial Public Relations Advisers IFC Advisory Limited
Birchin Court
20 Birchin Lane
London
EC3V 9DU

Registrar Neville Registrars Limited
Neville House
Steelpark Road
Halesowen
West Midlands
B62 8HD

EXPECTED TIMETABLE OF PRINCIPAL EVENTS

| | |
|--|-----------------------------------|
| Announcement of the Proposals | 21 September 2022 |
| Publication of this Document | 21 September 2022 |
| Admission of New Ordinary Shares effective and commencement of dealing | 8.00 a.m. on 26 September 2022 |
| Expected date for CREST accounts to be credited | 26 September 2022 |
| Despatch of definitive certificates (where applicable) expected by no later than | 27 September 2022 |

Notes:

1. All of the above timings refer to London time.
2. The events, times and dates above assume the completion of the Subscription and Admission.
3. Some of the times and dates above are an indication only and if any of the details contained in the timetable above should change, the revised times and dates will be notified to Shareholders by means of an announcement through a Regulatory Information Service.

ADMISSION AND SUBSCRIPTION STATISTICS

| | |
|---|----------------------|
| Market price per Existing Ordinary Share ¹ | 1.55p |
| Number of Existing Ordinary Shares in issue at the date of this Document | 278,447,788 |
| Number of New Ordinary Shares at the Issue Price | 35,666,665* |
| Issue Price | 1.5p |
| Enlarged Share Capital on Admission | 314,114,453* |
| Market capitalisation of the Company on Admission at the Issue Price | £4.7 million |
| Percentage of the Enlarged Share Capital represented by the New Ordinary Shares | 11.35%* |
| Gross proceeds of the Subscription | £500,000 |
| Estimated Expenses | £40,000 |
| Estimated net proceeds of the Subscription | £460,000 |
| EPIC/TIDM symbol | CIZ |
| ISIN for the New Ordinary Shares | GB00BNG2VN02 |
| SEDOL for the New Ordinary Shares | BNG2VN0 |
| FISN for the New Ordinary Shares | BOUD OPPO |
| Legal Entity Identifier (LEI) | 213800G3OS3SA2J1Y358 |

Website address

<https://cizzlebiotechnology.com/>

**includes 33,333,333 Subscription Shares, 666,666 Commission Shares and 1,666,666 Facility Shares.*

Notes:

- (1) Based on the closing mid-market price of an Existing Ordinary Share on 20 September 2022, being the latest practicable date prior to the publication of this Document.

PART I

LETTER FROM THE CHAIRMAN

CIZZLE BIOTECHNOLOGY HOLDINGS PLC

(Incorporated in England and Wales under the Companies Act 2006 with registered number 06133765)

Directors:

Allan John Syms (*Executive Chairman*)
Dawn Alison Coverley (*Scientific Director and Non-Executive Director*)
Nigel Ronald Lee (*Finance Director*)
John Michael Treacy (*Non-Executive Director*)

Registered Office:
6th Floor
60 Gracechurch Street

London
EC3V 0HR

Dear Shareholders and, for information purposes only, Optionholders

**Proposed Subscription of 35,666,665 New Ordinary Shares at 1.5p per share
Admission of the Enlarged Share Capital to
the Official List (by way of Standard Listing under Chapter 14 of the Listing Rules) and to
trading on the London Stock Exchange's main market for listed securities**

1. Introduction

The Company will announce on 21 September 2022 that it has conditionally raised gross proceeds of £500,000 by way of the Subscription and secured a further £500,000 pursuant to the Facility in order to provide working capital for the Group's strategy.

This Document, which comprises a prospectus prepared in accordance with the Prospectus Regulation Rules of the FCA, sets out the details of, and reasons for, the Subscription and explains why the Board consider the Subscription to be in the best interests of the Company and its Shareholders as a whole.

The Group is developing a blood test for the early detection of lung cancer. Its proof-of-concept prototype test is based on the ability to measure a stable blood plasma biomarker, a variant of CIZ1. CIZ1 is a naturally occurring cell nuclear protein involved in DNA replication, and the targeted CIZ1B variant is highly correlated with early-stage lung cancer.

Published research led by Professor Coverley has demonstrated that CIZ1B can be measured with high sensitivity via an ELISA process, which should allow for testing in a high-throughput, hospital-friendly format. The Directors believe that this development overcomes an important barrier to further clinical development and the application of this blood test for the early detection of lung cancer, which is essential to improve a patient's chance of survival.

In addition to implementing a strategy to develop a regulatory approved commercial, diagnostic laboratory immunoassay for early-stage lung cancer, the Group has broadened its interests to include the detection of a range of other early-stage cancers. It has also expanded its potential customer base to include the pharmaceutical industry through a contract to develop a diagnostic test that can help in the development of personalised medicines, so called "companion diagnostics", and has secured royalty bearing rights to the sale of such medicines in the longer term.

The Board intends for the Group's initial product to be a diagnostic immunoassay that can be readily performed by hospitals and reference laboratories, but a potential follow-on product could be a point of care test provided by a primary health care provider.

The Board continues to apply the majority of its funds towards the development of a certified CIZ1B biomarker diagnostic test. Further details regarding the Group and its technology can be found in sections 2 and 3 of this Part I.

The purpose of this Document is to provide Shareholders with further information regarding the reasons for the Subscription and proposed use of net proceeds

2. Background and History

The Company was admitted to the Standard Listing segment of the Official List and to trading on the Main Market of the London Stock Exchange on 14 May 2021 when it completed a placing of 22,000,000 new ordinary shares at 10p per share to raise gross proceeds of £2.2 million (“**Initial Listing**”). Initially under the name of Bould Opportunities plc, the Company changed its name to Cizzle Biotechnology Holdings plc, following the acquisition of Cizzle Biotechnology Limited (“**Cizzle Biotechnology**”). Cizzle Biotechnology is a spin-out from the University of York and is a biotechnology business focused on the early detection of lung cancer via the development of an immunoassay test for the CIZ1B biomarker. Cizzle Biotechnology was initially funded by Yorkshire Cancer Research, White Rose Technology Seed Corn Fund, Finance Yorkshire Seedcorn LLP and Viking Members, who with management, invested in the project to support the development of a prototype blood test.

Cizzle Biotechnology was founded in 2006 by Professor Coverley, a cell biologist working out of the University of York. Professor Coverley has 20 years’ experience in basic cancer-related research and is currently principal investigator of an academic DNA replication research laboratory at York and Scientific Director and Non-Executive Director of the Company.

The Group’s research and development is undertaken in laboratories at the University of York and by leading third party biologics development companies. The Group therefore has minimal facilities costs. On 10 August 2021, the Company entered into a research agreement with the University of York for the development and validation of molecular tools with potential applications in cancer diagnosis and therapy. The agreement formalised the relationship and provides both seconded staff and access to the University’s state of the art research facilities to support reagent generation work. This agreement has been extended for a further period of 12 months.

All intellectual property rights arising from the work are owned by the Group and strengthens the Group’s position in creating new solutions for early cancer diagnostics and therapeutic tools for the early detection tests for lung cancer and potentially other forms of cancer.

Since its admission to the Standard Listing segment of the Official List and to trading on the Main Market of the London Stock Exchange, the Company continues to implement its strategy to develop a regulatory approved commercial, diagnostic laboratory immunoassay for early-stage lung cancer.

In addition, the Group has broadened its interests in the detection of a range of other early-stage cancers, has agreed terms to develop companion diagnostics that can help in the development of personalised medicines, and secured royalty bearing rights to the sale of such drugs in the longer term.

3. Technology

CIZ1 is a naturally occurring cell nuclear protein that is involved in DNA replication amongst other biological functions. CIZ1 expression has been found to be altered in the main forms of lung cancer, and the Board is developing the application of the Group’s technology in the early detection of this cancer and in the future its application for the detection of other common solid tumours.

The Group’s current technology is based on the ability to measure the CIZ1B variant of this protein, which is a stable blood plasma biomarker. The laboratory test developed by Professor Dawn Coverley at The University of York, has been used to validate the use of CIZ1B to detect lung cancer, and a proof of concept prototype test developed, which is compatible with potential use within a hospital laboratory setting.

Agreements have been entered into to commercialise the Group’s technologies that measure CIZ1B in the early detection of lung cancer in China and the USA.

On 22 July 2021, the Company entered into a collaboration agreement with FairJourney Biologics (“**FJB**”) to expand its range of monoclonal antibodies and reagents that are the foundation for ELISA assays, and in the future point of care tests, not only for early-stage lung cancer but potentially also for other cancers with unmet clinical need. An update on the Group’s progress to develop these antibodies for use in its proprietary early lung cancer tests was released on 5 July 2022 together with the announcement of a new project that may extend the range of early-stage cancers that its technology can detect, with a focus initially on breast cancer.

The Group has significantly increased its knowledge on reagent performance and assay formats over the past year and has generated monoclonal reporter antibodies from its collaboration with FJB. The Group also recognises that it is important to develop a range of different monoclonal antibodies to measure CIZ1B and additional suppliers have been engaged. The Group now has a mouse monoclonal antibody that specifically measures CIZ1B and assay conditions for its use are now being optimised. Further work is being done to isolate rabbit monoclonals arising from the Group’s initial proof of concept studies. In parallel, new projects have been initiated to evaluate the use of CIZ1B for the detection of other cancers, which has led to an initial focus on breast cancer, which could widen the utility of this important cancer biomarker.

On 10 August 2021, the Company entered into a research agreement with The University of York for developing the Group’s blood test for the early detection of lung cancer, and potentially other forms of cancer. A further new agreement was announced in April 2022 that extended this work into 2023.

A research and development agreement was entered into on 22 October 2021 with St George Street Capital Limited (“**SGSC**”), the UK based biomedical charity, to develop a companion diagnostic test for autoimmune disease. Its aim is to develop tests that will operate alongside SGSC’s programme for the development of therapeutic assets licensed to SGSC from one of the world’s largest pharmaceutical companies, Astra Zeneca. This seeks to address unmet clinical needs in a variety of autoimmune diseases and will significantly broaden the Group’s product pipeline, for which SGSC will pay the Group £200,000 upfront on commencement of the project, and further milestone payments totalling £1 million.

On 1 February 2022, an agreement was executed with the International Co-Innovation Centre for Advanced Medical Technology (“**iCCAMT**”) and Shenzhen Intelliphecy Life Technologies Co., Ltd. (“**Intelliphecy**”), to develop and market the Group’s proprietary early lung cancer diagnostic tests in China. iCCAMT backers include German Medical Valley, Robert Bosch GmbH and Sinopharm Group. iCCAMT and Intelliphecy are funding all activities in China, including development, clinical trials, manufacture and distribution. An initial pilot of 300 patients has been planned.

On 5 May 2022, the Company signed a heads of terms to partner with CorePath Laboratories (“**CorePath**”), a full service cancer reference laboratory, to develop and offer its proprietary early-stage lung cancer test throughout the USA. This envisages the parties entering into a full commercial agreement in due course, combining CorePath’s proven expertise and knowledge in providing premier pathology services and consultants for patients, oncologists, clinicians, academic affiliates and biopharma companies across the USA, with the Group’s proprietary biomarker for early-stage lung cancer detection.

Intellectual property

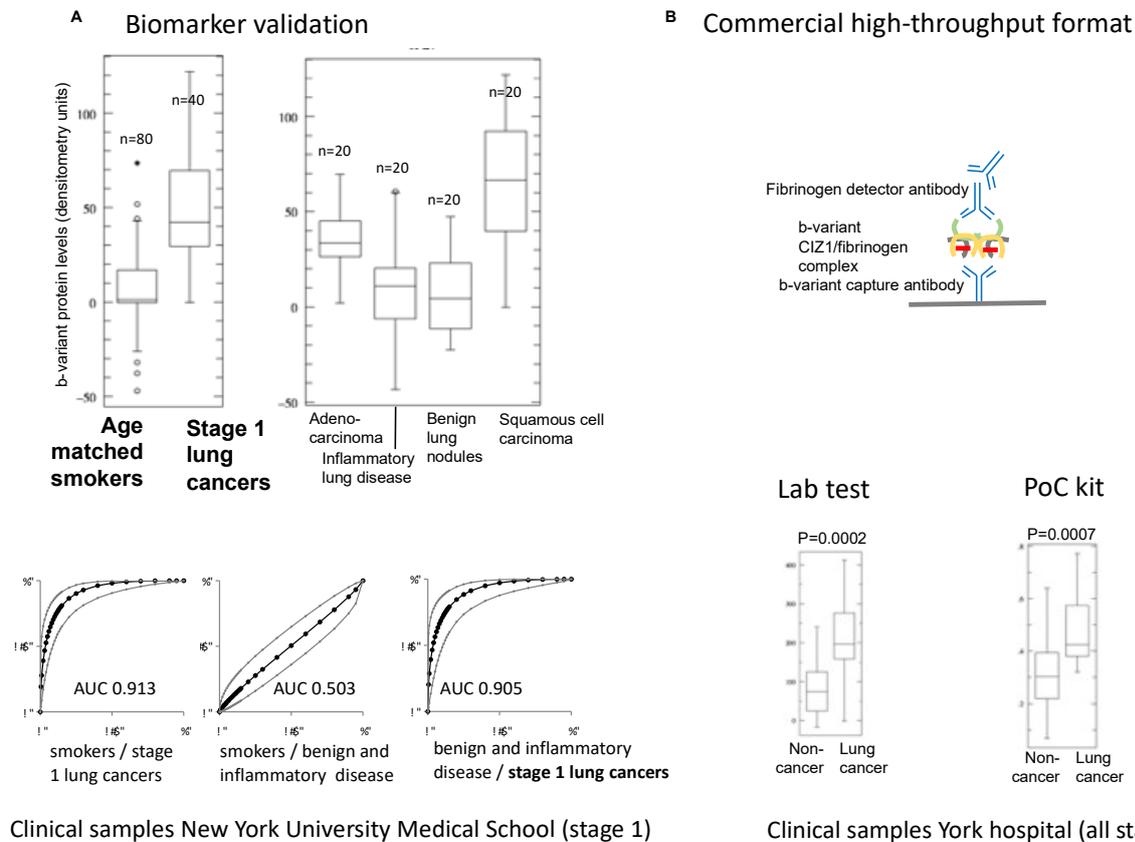
The Group has had patents granted to protect its core technology. Further details regarding the Group’s intellectual property can be found in section 5 of this Part I.

Prototype validation

The Group currently has a laboratory test, which has been used to validate the use of CIZ1B to detect lung cancer and a proof-of-concept prototype test which is compatible with potential use within a hospital laboratory setting.

To date, the Group’s clinical validation has been based on Western Blot analytical techniques. Proof-of-concept has been demonstrated via 486 plasma samples derived from four independent sample sets, including samples from patients with different types of lung cancer, asthma/COPD, and heavy smokers.

Figure 1: Test results from cohort 2, and comparison of formats



Source: A) 'Variant Ciz1 is a circulating biomarker for early-stage lung cancer'; Gillian Higgins, Katherine M. Roper, Irene J. Watson, Fiona H. Blackhall, William N. Rom, Harvey I. Pass, Justin F. X. Ainscough, and Dawn Coverley; *Proceedings of the National Academy of Sciences*, November 6, 109 (45) (2012). B) 'A quantitative immunoassay for lung cancer biomarker CIZ1b in patient plasma'. Coverley D, Higgins G, West D, Jackson OT, Dowle A, Haslam A, Ainscough E, Chalkley R, White J *Clin Biochem* 50, 336-343 (2016).

As illustrated in Figure 1A above, the Group's clinical validation work has demonstrated that patients with the most common forms of lung cancer have higher levels of CIZ1B in their blood than patients with non-malignant lung nodules, even at stage 1. Figure 1B shows that a proof-of-concept prototype immunoassay format, which is compatible with potential use in hospital laboratories, is similarly able to measure CIZ1B in patient blood samples.

Technology development

The Board's strategy is to develop the Group's prototype test into a commercial, UKCA, CE marked and/or FDA 510(k) cleared diagnostic immunoassay that can be readily performed as a sufficiently reliable test in a hospital setting.

Initially this will start as a laboratory developed test ("LDT") that is designed, manufactured and used within a single laboratory. In the USA this will be Corepath and in China via iCCAMT.

LDTs can be used to measure or detect a wide variety of analytes (substances such as proteins, chemical compounds like glucose or cholesterol, or DNA), in a sample taken from a human body. While the uses of an LDT are often the same as the uses of FDA-cleared or approved in vitro diagnostic tests, some labs may choose to offer their own test. For example, a hospital lab may run its own vitamin D assay, even though there is an FDA-cleared test for vitamin D currently on the market. The FDA does

not consider diagnostic devices to be LDTs if they are designed or manufactured completely, or partly, outside of the laboratory that offers and uses them.

LDTs are important to the continued development of personalised medicine, so it is important that in vitro diagnostics are accurate so that patients and health care providers do not seek unnecessary treatments, delay needed treatments, or become exposed to inappropriate therapies.

In order to pursue this, the Group is working with selected manufacturers to produce antibodies, reagents and kits that may be used to validate its test format in clinical trials as well as specialist oncology centres of excellence in China and a Clinical Laboratory Improvement Amendments (“CLIA”) and College of American Pathologists (“CAP”) accredited laboratory CLIA in the USA.

Although the Directors believe that the Group’s initial product will be an immunoassay performed by hospitals and reference laboratories, a future follow-on product, could be a point of care test provided by a primary health care provider.

The Directors believe that the Group’s prototype test, once commercialised, will present the following potential advantages.

Potential advantages to the patient:

- the test could allow for reduced exposure to radiation due to a reduced need for repeated CT scanning;
- the test is intended to be relatively non-invasive, involving a small blood sample;
- the test is intended to be convenient, in so far that it will not require attending specialist scanning units within hospitals; and
- the test could provide patients with reduced waiting times until diagnosis.

Potential advantages to the health care system:

- the test could reduce the burden on fixed resources, by freeing up CT scanners; and
- the test could allow for fewer patients needing costly, ultimately futile interventions.

Potential competitive and commercial advantages:

- because early detection saves lives, there should be significant demand for blood based diagnostic assays for the early detection of lung cancer;
- no other approach currently known to the Directors matches the potential sensitivity and specificity of CIZ1B for early-stage cohorts;
- CIZ1B was discovered by analysing genes that control normal cell proliferation, then studying forms that are evident in tumours and which change its function. The Directors believe that many competitor products are based on the detection of panels of analytes that correlate with disease in symptomatic patients, but which are not necessarily part of the disease process.

Companion Diagnostics

A research and development agreement was entered into on 22 October 2021 with SGSC, the UK based biomedical charity to develop a companion diagnostic test for autoimmune disease. Its aim is to develop tests that will operate alongside SGSC’s programme for the development of therapeutic assets licensed to SGSC from one of the world’s largest pharmaceutical companies, Astra Zeneca. This seeks to address unmet clinical needs in a variety of autoimmune diseases which will significantly broaden the Group’s product pipeline for which SGSC will pay the Group £200,000 upfront on commencement of the project and then further milestone payments totalling £1 million.

Royalty Investment in AZD1656

On 18 September 2021, the Company entered into a royalty sharing agreement with SGSC to grant the Group potential royalty payments from the commercialisation of SGSC’s therapeutic asset AZD1656 of

up to £5 million, plus potentially further payments from the use of a companion diagnostic. During the year the Group paid a total of £0.2 million pursuant to this agreement.

This supports the strategy of building a portfolio of interests, including early cancer detection tests, companion diagnostics for non-cancer indications, and royalty bearing stakes in significant drug assets. SGSC has reported positive results from its ARCADIA clinical trial for diabetes patients with COVID-19 and have indicated this may be through the regulation of the patients' immune system (via controlling Regulatory T Cells or "Tregs"). Tregs act to suppress immune response and combat damaging cells potentially reducing serious cardiovascular disease, and also lung diseases that can be linked with the development of lung cancer.

On 11 February 2022, the Company entered into a further royalty deal in inflammatory pulmonary and cardiovascular diseases with Conduit Pharmaceuticals Ltd ("**Conduit**") and SGSC to acquire an additional 5% economic interest in the commercialisation of the AZD 1656 asset or such other assets being developed by Conduit or SGSC to treat inflammatory pulmonary and cardiovascular disease ("**SGSC and Conduit Royalty Sharing Arrangement**"). Under this agreement, the Group will receive 5% of all sums received by SGSC pursuant to any AstraZeneca ("**AZ**") commercialisation or sub-licence commercialisation of the AZD 1656 asset in inflammatory pulmonary and cardiovascular diseases, after the deduction of certain sums. The consideration due to SGSC is £1.88 million with the initial consideration of £1 million being settled through the issue of 25,000,000 new ordinary shares on 17 February 2022 at a price of 4p per share which, as stated in the agreement, was a premium to the Company's closing mid-market price on 11 February 2022. The remaining consideration of £0.88 million will be payable in either (i) cash, or (ii) new ordinary shares at 4p per share, at the Company's discretion, on the earlier of receiving shareholder approval to issue such shares or the first anniversary of the date of the agreement (i.e. 11 February 2023).

4. Future strategy for the Group

Key regulatory pathways

The Board intends to apply the majority of the net proceeds of the Subscription towards the development of a LDT accredited service as a forerunner to taking the CIZ1B biomarker test through to UKCA, CE marking and/or FDA 510(k) clearance.

The European Medicines Agency and the FDA have similar but different regulatory pathways for the approval or clearance to market cancer diagnostic tests (classified as *in vitro* diagnostic medical devices). A "medical device" includes *in vitro* diagnostic medical devices and active implantable medical devices.

The Medicines and Healthcare products Regulatory Agency ("**MHRA**") is responsible for regulating the UK medical devices market and has different rules that apply in Great Britain, Northern Ireland and the EU. Under the Northern Ireland Protocol, different rules apply in Northern Ireland to those in Great Britain.

Since 1 January 2021, there have been a number of changes, introduced through secondary legislation, to how medical devices are placed on the market in Great Britain (England, Wales and Scotland). These are:

- A new route to market and product marking (the UKCA marking) is available for manufacturers wishing to place medical devices on the Great Britain market.
- All medical devices, including *in vitro* diagnostic medical devices ("**IVDs**"), custom-made devices and systems or procedure packs, need to be registered with the MHRA before they are placed on the Great Britain market.
- A medical device manufacturer based outside the UK wishing to place a device on the Great Britain market, needs to appoint a single UK Responsible Person for all devices, who will carry out specified tasks, such as registration.
- CE marking will continue to be recognised in Great Britain until 30 June 2023.

- Certificates issued by EU-recognised Notified Bodies will continue to be valid for the Great Britain market until 30 June 2023.
- The EU no longer recognises UK Notified Bodies.
- UK Notified Bodies are not able to issue CE certificates - and have become UK Approved Bodies.

The European Medicines Agency, MHRA and the FDA have a risk-based approach to regulatory clearance, depending on how the test may impact patient treatment regimes. For example, using gene sequencing for a panel of mutations could be classified as a 'level 2' risk therefore, requiring less clinical evidence, and supporting the potential to obtain market clearance under the FDA's 510(k) pathway.

The FDA may seek evidence to support equivalence testing requirements for a FDA 510(k) application. Other biomarker cancer tests that use immunoassays and met the FDA's 510(k) requirements include those aimed at ovarian, colonic, breast and pancreatic cancers.

Regulatory strategy

The Company, together with its partners in the USA, China and elsewhere will enter into agreements with selected manufacturers and contract research organisations (“**CROs**”) to conduct reagent generation, and test development, and will move to manufacture and the clinical validation required to achieve approval, in the first instance via LDT accreditation and subsequently through an appropriate UKCA, CE marking and/or FDA 510(k) clearance. The development of an approved or certified test is proposed in three initial steps:

Step 1

- Technical development of the test reagents, manufacture of test reagents, and validation of test configuration on patient samples.

Step 2

- Development of a LDT certified test in accredited partner laboratories such as CorePath.

Step 3

- The production of a UKCA, CE marked and/or FDA 510(k) cleared product, following successful validation on retrospective clinical sample sets and control cohorts.
- Market launch and preparation for a clinical trial to support NHS and other global healthcare providers, adoption as a confirmative test for patients attending lung clinics with indeterminate lung nodules.

Reagent generation is ongoing and manufacture of test reagents and validation on clinical samples will follow in 2023.

The key deliverables within Steps 1 to 3 are as follows:

Step 1

- A standardised and validated secure supply of test reagents.
- A fully formatted assay, with known performance parameters, stability and shelf life.
- Sufficient tests and patient samples to support a retrospective clinical study.

Step 2

- Establishment stage consisting of feasibility and design, development, and validation.
- Implementation stage consisting of preliminary evaluation, verification, test launch, maintenance, and retirement.

If verification is completed and experiments meet acceptance criteria, then a new test can be launched into the clinical laboratory. A clinical laboratory will still perform test maintenance during the lifetime of the test. Finally, a test may be retired due to implementation of a new version.

Step 3

- Production of materials for the next stage
- A retrospective clinical study to satisfy UKCA, CE marking or FDA 510(k) clearance.
- A UKCA, CE marked or FDA 510(k) cleared quality-controlled test.
- An economic assessment of the specified patient pathway (asymptomatic, indeterminate lung nodules), to support NHS or other healthcare provider adoption.
- Preparations for the assembly of a prospective clinical consortium and the production of a prospective clinical trial plan.

The first part of Step 1 is to generate reagents that will comprise the diagnostic kit.

The Group is pursuing a multi-pronged approach to reagent generation in order to service both immediate and future plans for test formats. In the short term, an ELISA format for hospital use will be the Group's first CIZ1B diagnostic kit product, however the Group intends to support this by first commercialising a LDT in certified laboratories. This is supported by assay development work in partnership with its key suppliers using the Group's CIZ1B monoclonal antibody. While it is expected that LDT and ELISA assays this will form the basis of its first commercial tests, the Group is also engaged in additional projects to develop further reagents to detect a wider range of cancers and support the development of Lateral Flow Test formats.

The molecular characteristics will determine the choice of kit manufacturer, who typically specialise in one type of reagent or other. The Company has agreements with several monoclonal antibody providers and other reagent developers, who have been selected on the basis of their particular expertise in antibody generation and selection, and also their ability to optimise assay formats for their use.

The Directors believe that the outcome of the retrospective clinical study in Steps 2 and 3 and its acceptance by regulatory authorities could have a significant bearing on the subsequent stages in the Group's regulatory strategy.

The costs allocated to steps 1, 2 and 3 are detailed in paragraph 8 of this Part I, but in summary:

- Step 1 involves sourcing and producing appropriate reagents, clinical samples and developing a formatted assay that can be used for clinical trials. This includes reagent development (£30,000), purchasing clinical samples (£25,000) and validating the reagents at the University of York (£20,663). An estimated total of £75,663.
- Step 2 is largely the responsibility of the Company's partners in the USA and China and the majority of costs to develop and sell accredited test will be covered by those partners. An estimated total cost of £25,000.
- Step 3 involves the manufacture of tests for the retrospective validation and the clinical validation work itself (£230,000) which includes further testing and support work from the University of York (£50,000) and a health economic study (£10,000). An estimated total of £290,000.

There are also administrative overheads which are included in the overall overhead costs as detailed below in this paragraph 4 of this Part I. These are the expected costs based on the Director's knowledge and experience of the market. Staff costs have been considered separately as have other costs such as additional batch manufacture, samples, detector antibodies and planning. The Directors have assumed a conservative budget for a small retrospective clinical trial, having also considered the more detailed breakdown of reagents, antibodies and manufacturing costs.

The COVID-19 pandemic posed significant challenges for the bioscience industry and placed pressure on all aspects of the supply and testing pipeline. The Directors have estimated a three-month delay in delivering the original plans for the Company. For that reason, the Directors expect the main work for step 1 to be conducted approximately in the second half of 2022 and the main clinical validation work to be carried out approximately during the first half of 2023.

Save for monthly overheads, the main development expenditure would be undertaken in two phases – phase 1: £0.23 million during October 2022 to March 2023 and phase 3: £0.59 million during April 2023 to March 2024.

Commercial strategy and industry overview

The Directors believe that the following will advance the commercial prospects of the Group's test:

- Establish clinical proof points within NHS hospitals and global healthcare providers in the USA, China and elsewhere globally for a confirmative test to address the false positive rates associated with CT scanning.
- Marketing through manufacturing, commercial and licensing partners for a hospital laboratory test. The Directors have identified and contracted potential commercial partners for this process.
- Progress the partnership with iCCAMT and Intelliphecy to enter the Chinese lung cancer diagnostics market.
- Progress the partnership with CorePath to enter the USA lung cancer diagnostics market.
- Marketing through global platform product development licensing.
- Further development of the test for general screening and the obtaining of the LDT, UKCA, CE mark and/or FDA 510(k) clearance.
- Marketing through primary health care provider's and corporate diagnostic and pharmaceutical partner licensing.
- Continuing to develop intellectual property and testing protocols for new indications.

China

China is one of the key target markets identified for the Group, where there are serious challenges in being able to detect cancer early, and a great need for screening and diagnosing cancer. Targeted testing can improve timely access to cancer care and save lives. The Company entered into a Memorandum of Understanding (“**MOU**”) with the iCCAMT and Intelliphecy to develop and market the Group's proprietary early lung cancer diagnostic tests based on the CIZ1B biomarker in China. On 1 February 2022, a full commercial agreement was executed to develop and market early lung cancer diagnostic tests in China. This agreement will generate future revenues for the Group via a 10% royalty on the sales of all products and services using its proprietary CIZ1B technology and from payment for monoclonal antibodies and reagents.

iCCAMT, founded with German Medical Valley, Robert Bosch GmbH, Sinopharm Group, aims to accelerate global healthcare innovation in China. iCCAMT is dedicated to support innovative healthcare small and medium sized companies (“**SMEs**”) to grow in China and promote technology transfer. With global health technology network and supports from industry giants, iCCAMT has developed comprehensive platforms to strengthen cross-border health technology collaborations, and help global health technology companies enter the China market.

Intelliphecy is aiming to innovate technologies in the hope to win the war against cancer, aspiring to out-smart cancer cells with an intelligent prophecy. At the core of Intelliphecy's technology portfolio lies artificial intelligence driven big data analytics, which is devoted to predictive modelling of cancer hallmarks using quantitative information. Its research and development is grounded in both identification of cancer at early stage and prediction of optimal treatment strategies for individual cancer patients. Intelliphecy has established research collaborations with major cancer centres throughout China.

USA

Another key market is the USA and on 5 May 2022, the Company signed a heads of terms to partner with CorePath, a full service cancer reference laboratory, to develop and offer its proprietary early-stage lung cancer test throughout the USA. The proposal is that the Group would receive a 15% royalty and royalty sharing arrangements overall offering of products and services using CIZ1B via CorePath in the USA.

CorePath is a specialist oncology reference laboratory bringing together leading clinicians, scientists, academic affiliates and state of the art facilities and will be responsible for all activities in the USA including development, clinical trials and test validation for clinical use.

Founded and headquartered in San Antonio, Texas, as one of the few international laboratories with the ability to offer immunohistochemistry, cancer cytogenetics, molecular genetics and multicolour flow cytometry services at one location, CorePath brings academic expertise, compassion and state of the art technology to help physicians help their patients and achieve the most accurate time-sensitive results for early treatment. Together, they are a highly specialised team with a shared passion: "Caring for Lives." CorePath provides an extensive range of haematopathology services to healthcare providers across the USA and internationally. They work closely with the biopharma industry through a seasoned project management team with relevant scientific and therapeutic expertise in cancer drug study needs. Their team of board-certified pathologists are subspecialised in different areas of oncology to precisely diagnose cancers using cutting edge technology. Customers include ICON, Alexion, Covance, Ventana (Roche) and Becton Dickenson.

Lung cancer is the leading cause of cancer death in the USA, making up almost 25% of all cancer deaths. The American Cancer Society's estimates for lung cancer in the USA for 2022 are about 236,740 new cases of lung cancer annually and about 130,180 deaths from lung cancer each year (source: <https://www.cancer.org/cancer/lung-cancer/about/keystatistics.html>). Currently, there are no simple specific blood tests to detect lung cancer early when targeted interventions can improve timely access to cancer care and save lives. Yet it is estimated that about 8 million Americans qualify as high risk of lung cancer and are recommended by The United States Preventive Services Task Force (USPSTF) to receive annual screening with low-dose CT scans. If half of these high risk individuals were screened, over 12,000 lung cancer deaths could be prevented (source: Cheung LC, Katki HA, Charurvedi AK, Jemal A, Berg CD. Preventing Lung Cancer Mortality by Computed Tomography Screening: The Effect of Risk-Based Versus U.S. Preventative Services Task Force Eligibility Criteria, 2005-2015. *Anal of Internal Medicine*. 2018; 168(3):229-32. Doi: 10.7326/M17-2067).

Understanding CIZ 1

CIZ1 transcripts are alternatively spliced to yield 25 or more variants. Most are not fully characterised but some, including CIZ1B, appear to be inaccurate splicing events expressed only in tumours, while other 'normal' variants are associated with disease when expressed in the wrong developmental context. Studies from Professor Coverley's research group on the functional analysis of CIZ1 has informed our understanding of the altered forms detected in lung cancer libraries, and led to the focus on CIZ1B, and then to identify CIZ1B protein fragments in blood plasma. While more is now understood about CIZ1's function inside the nucleus, it not yet known whether circulating CIZ1B has biological significance in the blood, other than as a very potent marker of malignant lung tumours. Inside cells, CIZ1B is under investigation to uncover how it acts and whether it might be targeted as the basis of new drugs for early-stage lung cancer.

The Company intends to further support the research in Professor Coverley's laboratory with the aim of identifying further commercial opportunities in widening the number of cancers that can be detected at an early stage and also to consider additional assay or therapeutic configurations to solidify the Group's position in this space.

5. Intellectual Property

The Group has engaged Cooley LLP and Dennemeyer S.A. a specialist annuity provider to manage and renew its patent portfolio. The Group owns the following patents and pending patents which are integral to its business:

| Case Reference number. | Country | Application Number | Patent/Registration Number | Applicants | Title | Case Status | Expiry Date |
|------------------------|--------------------------|--------------------|----------------------------|------------------------------|---|-------------|-------------|
| P043162AU | Australia | 2003290240 | 2003290240 | Cizzle Biotechnology Limited | CIZ1 Replication Protein | Granted | 05/12/2022 |
| P043162CA | Canada | 2,507,403 | 2,507,403 | Cizzle Biotechnology Limited | CIZ1 Replication Protein | Granted | 05/12/2022 |
| P043162CHA | Switzerland | 10075508.1 | 2316966 | Cizzle Biotechnology Limited | CIZ1 Replication Protein | Granted | 05/12/2023 |
| P043162DEA | Germany | 10075508.1 | 2316966 | Cizzle Biotechnology Limited | CIZ1 Replication Protein | Granted | 05/12/2023 |
| P043162ESA | Spain | 10075508.1 | 2316966 | Cizzle Biotechnology Limited | CIZ1 Replication Protein | Granted | 05/12/2023 |
| P043162FRA | France | 10075508.1 | 2316966 | Cizzle Biotechnology Limited | CIZ1 Replication Protein | Granted | 05/12/2023 |
| P043162GBL | United Kingdom | 10075508.1 | 2316966 | Cizzle Biotechnology Limited | CIZ1 Replication Protein | Granted | 04/12/2023 |
| P043162ITA | Italy | 10075508.1 | 2316966 | Cizzle Biotechnology Limited | CIZ1 Replication Protein | Granted | 05/12/2023 |
| P043162US | United States of America | 10/537,228 | 7,833,702 | Cizzle Biotechnology Limited | CIZ1 Replication Protein | Granted | 05/08/2027 |
| P043162USB | United States of America | 14/615,045 | 9,541,555 | Cizzle Biotechnology Limited | CIZ1 Replication Protein | Granted | 05/12/2023 |
| P043206CN | China | 201180048228.2 | ZL201180048228.2 | Cizzle Biotechnology Limited | Methods and Compounds for the Diagnosis and Treatment of Cancer | Granted | 04/08/2031 |
| P043206JP | Japan | 2013-522291 | 5952815 | Cizzle Biotechnology Limited | Methods and Compounds for the Diagnosis and Treatment of Cancer | Granted | 04/08/2031 |
| P105215AU | Australia | 2016342546 | | Cizzle Biotechnology Limited | Variant CIZ1 Exosomes | Pending | 14/10/2036 |
| P105215CA | Canada | 3,002,320 | | Cizzle Biotechnology Limited | Variant CIZ1 Exosomes | Pending | 14/10/2036 |
| P105215CN | China | 201680072824.7 | | Cizzle Biotechnology Limited | Variant CIZ1 Exosomes | Pending | |
| P105215EP | European Patent Office | 16784956.1 | | Cizzle Biotechnology Limited | Variant CIZ1 Exosomes | Granted | 14/10/2036 |
| P105215JP | Japan | 2018-538961 | | Cizzle Biotechnology Limited | Variant CIZ1 Exosomes | Pending | |
| P105215US | United States of America | 15/768,946 | | Cizzle Biotechnology Limited | Variant CIZ1 Exosomes | Pending | |

The Group is not reliant on any registered trademarks.

The Group is prosecuting three patent families all aimed at protecting the use of CIZ1B for use in cancer diagnosis, or production of molecular tools for the same purpose. Cizzle Biotechnology's first filings were broad and will expire in 2023. A more recent patent family (derived from PCT/GB2016/05320) is focussed on the diagnostic test format which Cizzle Biotechnology is now developing, and is expected to provide the necessary patent protection until at least 2036 in USA, Australia, Canada, China, Japan and Europe.

Patents generally have a 20-year life and extending protection through additional filings may provide a further potential extension.

Other than the intellectual property set out above, there are no patents or other intellectual property rights, licences, industrial, commercial or financial contracts or new manufacturing processes which are or may be of fundamental importance to the Group's business.

6. Directors and Employees

The Board consists of four Directors, brief biographical details of which are set out below:

Dr Allan Syms (Executive Chairman), aged 65

Allan is an experienced international life sciences and technology senior executive, with over 30 years of experience at Board level often as founder or chief executive officer in creating, funding and building emerging technology businesses through to trade sale and IPO. After gaining a PhD in cancer biology at the Tenovus Institute of Cancer Research and postdoctoral fellowships at Baylor College of Medicine in Houston and Oxford University, he began his corporate career at GE Healthcare Limited (formerly Amersham International PLC) to develop novel diagnostic detection systems. He then worked with a number of UK leading universities to spin out and develop technology businesses. Allan has extensive experience in mergers and acquisitions, licensing and managing strategic change becoming corporate marketing director at Integra Biosciences AG a leading Swiss laboratory and diagnostics supplies company. He was previously a specialist adviser on China to the Department of International Trade.

Allan was appointed Non-Executive Chair on 21 May 2019 and was appointed Executive Chair with effect from Admission on 14 May 2021.

John Treacy (Non-Executive Director), aged 40

John is a London-based experienced financier who specialises in working with growing companies. He qualified as a solicitor in the London office of a major international law firm where he specialised in capital markets and mergers & acquisitions. From there he moved to practice corporate finance in the advisory teams of several prominent UK brokerages where he acted as an adviser to a number of AIM companies and advised on numerous IPOs, acquisitions, debt restructurings and placings.

John is also the Chair of the Audit and Risk Committee and the Chair of the Remuneration Committee.

Professor Dawn Coverley (Scientific Director and Non-Executive Director), aged 56

Dawn is a cell biologist with over 20 years' experience in cancer-related research. After a first degree in Genetics (Leicester), and a PhD in biochemistry (Cancer Research UK), she completed postdoctoral training at the University of Cambridge, then moved to the University of York to establish an independent research group in 2002, supported by the Lister Institute of Preventive Medicine. Her research exploits experimental systems that reconstitute fundamental process associated with genome and epigenome stability, and their contribution to the earliest stages of human cancers. She founded Cizzle Biotechnology Limited and raised early-stage funding in 2006 to begin development of her research findings into clinically useful products, focused on CIZ1B and the early detection of lung cancer. She is currently principal investigator of an academic research laboratory at the University of York and scientific director and non-executive director of the Company.

Dawn is also a member of the Audit and Risk Committee and Remuneration Committee

Nigel Lee (Finance Director), aged 61

Nigel has been a director of CFO Solutions Limited since 2003 which has provided financial advisory services to the Group since 2010, as well as company secretarial services since 2012. CFO Solutions Limited ceased providing these services to the Group on 14 May 2021. He is also a part-time finance director of Kent Surrey Sussex AHSN Limited. He was financial director/controller in two IT services and software companies from 1999 to 2003 and prior to that had 11 years of audit and business advisory experience at PricewaterhouseCoopers, including six years as a senior manager. Nigel qualified as a Chartered Accountant in 1988.

7. Details of the Subscription and Admission

Pursuant to the Subscription, the Company has conditionally raised £500,000, before expenses, through the issue of the Subscription Shares with investors at the Issue Price conditional, *inter alia*, upon Admission of the Subscription Shares becoming effective by 22 September 2022 (or such later time and/or date as the Company may specify, not being later than 30 September 2022).

Accordingly, if the condition is not satisfied, or, if applicable, waived, the Subscription will not proceed.

The Subscription is not underwritten. Each investor in the Subscription has undertaken to pay the aggregate Issue Price for the Subscription Shares issued to them in the manner and by the time directed by the Company.

Each investor for Subscription Shares agrees to become a member of the Company and agrees to subscribe for its allocated Subscription Shares at the Issue Price. To the fullest extent permitted by law, each investor acknowledges and agrees that it will not be entitled to exercise any rights to rescind or terminate or otherwise withdraw from such commitment at any time. By agreeing to subscribe for Subscription Shares, each investor has warranted, acknowledged and agreed, amongst other things, that it has the necessary capacity and authority to subscribe for its Subscription Shares and that it has complied with all laws applicable to the Subscription. If the conditions to the Subscription are not satisfied and the Subscription does not proceed, any monies received from investors will be returned without interest to the account of the drawee bank from which they were originally debited as soon as practicable.

The Subscription will result in the issue of 33,333,333 Subscription Shares (representing, in aggregate, approximately 10.61% of the Enlarged Share Capital). The Subscription Shares, when issued and fully paid, will rank *pari passu* in all respects with the Existing Ordinary Shares and therefore rank equally for all dividends or other distributions declared, made or paid after the date of issue of the Subscription Shares. See paragraph 10 of this Part I for the Company's dividend policy.

The Company has agreed to issue 666,666 new Ordinary Shares to Optiva Securities Limited, conditional on Admission, at the Issue Price as settlement of a £10,000 commission fee in connection with the Subscription ("**Commission Shares**").

The issue and allotment of the Commission Shares will result in the Existing Share Capital being diluted by approximately 0.24%. The Commission Shares will represent approximately 0.21% of the Enlarged Share Capital.

Application will be made for the Subscription Shares to be admitted to the Official List of the FCA by means of a standard listing under Chapter 14 of the Listing Rules ("**Standard Listing**") and to trading on the Main Market of the London Stock Exchange. It is expected that Admission will become effective and that unconditional dealings will commence on the London Stock Exchange at 8.00 a.m. on 26 September 2022.

The Subscription Shares will be eligible for CREST settlement and settlement of transactions in the Subscription Shares may take place within the CREST system if a Shareholder so wishes. CREST is a voluntary system and Shareholders who wish to receive and retain share certificates are able to do so. CREST is a paperless settlement system enabling securities to be evidenced otherwise than by a certificate and transferred otherwise than by a written instrument in accordance with the CREST Regulations. For more information concerning CREST, Shareholders should contact their brokers or

Euroclear at 33 Canon Street, London EC4M 5SB, United Kingdom or by telephone on +44 (0)207 849 0000. The Subscription Shares will have the ISIN number GB00BNG2VN02. The Subscription Shares will not be dealt on any other recognised investment exchange and no application has been or is being made for the Subscription Shares to be admitted to any other such exchange.

8. Use of proceeds

The proceeds of the Subscription, which are expected to total approximately £500,000 (before expenses of £40,000 excluding VAT), will be used to pursue Steps 1 to 3 identified in paragraph 4 of this Part I above and to provide working capital for the Company.

In specific, it is anticipated that the net proceeds of the Subscription (£460,000) receivable by the Company will be applied as follows:

| | |
|--|----------|
| Monoclonal Antibody & Reagent Production | £30,000 |
| Clinical samples | £25,000 |
| Kit Development, Manufacture & Clinical Trials | £230,000 |
| Health Economics | £10,000 |
| Patents | £10,000 |
| York Laboratory Support Costs | £50,000 |
| Development of LDT Certified Test | £25,000 |
| Marketing & Overheads | £20,000 |
| Salaries | £20,000 |
| Additional research | £40,000 |

According to the Company's forecasts, following a period of 18 months after the receipt of the net proceeds of the Subscription and assuming utilisation of the Facility in full during that period, the Company will need to raise additional funding should it wish to undertake development of additional future products beyond the core offering currently being contemplated and beyond that being funded by the cash deposits of the Company as a result of the Subscription, utilisation of the Facility and generated income and to further fund the corporate and operational overhead of the business, which is likely to remain pre-revenue at this point.

It is likely following a period of 18 months after Admission, particularly if the Company wishes to undertake development of additional future products beyond that being funded by the cash deposits of the Company as a result of the Subscription, utilisation of the Facility and generated income, that it will need not less than £1 million. Out of the £1 million minimum additional funding that would be required, approximately £0.5 million would be used to fund the corporate and operational overheads of the business and approximately £0.5 million would be used for the future additional development of projects.

Should the Company require further funding following the period of 18 months after Admission, the Company will seek further support from shareholders and other investors from the platform offered to it by virtue of its Standard Listing. In settlement of some of the Company's expenditure (approximately 10%) relating to, for example professional adviser fees, management would attempt to renegotiate those professional adviser and supplier payment terms (although this cannot be guaranteed), whilst the Company is seeking additional funding to support the development of further products.

The Company believes that the platform offered to it by a Standard Listing and the size of the Company's targeted market gives the Directors confidence in securing further funding to support the Company's current and future projects.

Like any substantially pre-revenue company which seeks a Standard Listing to raise development capital, in the event future funding cannot be secured when needed following the period of 18 months after Admission, and capital and operational expenditure cannot be further reduced or delayed, then

the Directors will consider all legal avenues open to them at the time. As part of a strategy to mitigate risk arising from insufficient working capital, the Company may attempt to secure new funding through a future placing of shares however it is recognised that the success of such a placing, or the price of such placing, may be dependent on the Company achieving its key milestones for example in reagent generation, test manufacture and clinical validation to enable UKCA, CE marking, LDT and/or FDA clearance. The Directors will continually monitor the Company's cash position and together with its advisors determine whether it is necessary and of benefit to shareholders to consider any future placing of shares. However, according to the working capital projections of the Company, such funding will not be required within the 18 months from publication of the Prospectus. The Company will also seek licensing and joint venture fees and, if required, attempt to bring these commercial discussions forward which may also result in the sale of intellectual property rights and therefore potentially, the entire business. There are several approaches to securing revenue from intellectual property. First is to commercialise products based on the Company's intellectual property. Secondly, is to licence the rights to use the intellectual property entirely or in addition to the potential future products produced. Thirdly, is an outright sale, rather than licensing all or part of the intellectual property. This may allow segmenting different applications of the intellectual property and selling those elements not core to the immediate commercial goals of the Company. The sale of all the intellectual property may in effect be the same as selling the Company as it would have little or no rights to continue access to the intellectual property and as such the Company may consider being wound up so it can distribute available proceeds to shareholders. For the avoidance of doubt, the Company has not held any preliminary discussions regarding a possible sale of its IP and is therefore not currently able to attribute a value to this proposed refinancing option. Further options could include seeking structured finance or debt financing through specialist loans.

Delays or failure to secure additional capital or licence revenues will mean that cost reductions will be sought which would likely take the form of delaying discretionary capital and management would attempt to renegotiate professional adviser and supplier payment terms, although this cannot be guaranteed. The impact of such cuts in expenditure are less material in the first few years as they are not aimed at the core product development programme. This is because the Company's product pipeline consists of "future products" for example a potential ELISA test kit, which are the core products to be developed during the period from the date of this Document until 31 December 2023 and hence not subject to any need to reduce costs. Later products such as potentially point of care tests are defined as "additional future products" which would be developed during the period from the date of this Document until 31 December 2023 are not essential to deliver the Company's strategic and commercial goals. Because the impact of expenditure cuts would be more likely in the later part of year two these cuts could only impact "additional future products" and therefore are less material to the development of the core products. The impact of cost reductions on future research in later years could mean the delay of such products as point of care tests which necessarily could reduce wider market adoption and impact potential future valuation of the Company.

Like any pre-revenue company who needs to raise funds to develop a project, a failure to secure future funding is a possibility. Were the Company to be unable to fund itself, an administration would have to be considered.

9. The Facility

The Company entered into a facility agreement with E3 Fund SP ("the **Investor**") on 20 September 2022 ("**Facility Agreement**") pursuant to which the Investor will make available to the Company a facility of £500,000, conditional on Admission, for the purpose of working capital, for a term of 18 months ("**Facility**").

Under the terms of the Facility, a commitment fee of £25,000 will become payable by the Company to the Investor on execution of the Facility Agreement to be settled by way of the issue and allotment of 1,666,666 new Ordinary Shares at a price of 1.5p per share ("**Facility Shares**").

An initial drawdown of £50,000 will be available to the Company 180 days following the payment of the commitment fee (by way of issue of the Facility Shares) and further drawdowns up to the amount of the

Facility may be requested by the Company or the Investor by either party giving notice written notice of such request.

Repayment of the Facility will be by way of issue and allotment of new Ordinary Shares in the capital of the Company at a price of 1.8p per share ("**Investor Shares**"). The Investor Shares are required to be issued to the Investor at the time of the relevant drawdown, will be credited as fully paid and will rank *pari passu* in all respects with all other Ordinary Shares in issue. Upon allotment and issue of the relevant Investor Shares, the Company will immediately make an application for all such shares to be admitted to the Official List of the FCA by means of a Standard Listing and to trading on the Main Market of the London Stock Exchange.

The percentage dilution of the Existing Ordinary Shares as a result of the issue and allotment of the Facility Shares will be approximately 0.59%. Upon Admission, the Facility Shares will represent approximately 0.53% of the Enlarged Share Capital of the Company.

Draw down of the Facility in full would result in the Enlarged Share Capital being diluted by approximately 8.12% as a result of the issue and allotment of Investor Shares. The Investor Shares represent approximately 7.35% of the Fully Diluted Enlarged Share Capital of the Company.

10. Dividend policy

The Directors consider that it is in the best interests of Shareholders for the Company to focus on capital growth at the current time. The Board therefore intends during the Company's current phase of development to retain future distributable profits from the business to the extent that they are generated. The Directors do not intend to declare or pay a dividend in the immediately foreseeable future but, subject to, *inter alia*, the availability of sufficient distributable profits, intend to commence the payment of dividends when it becomes commercially prudent to do so and intend to adopt a progressive dividend policy thereafter.

11. Board Warrants

The Board is considering issuing warrants to the directors of the Company in lieu of increasing remuneration in line with market-rate. As at the date of this Prospectus, no decision has been made as to the number of warrants which may be issued nor the terms on which such warrants may be issued.

12. Share dealing code

The Board has adopted a Share Dealing Code for PDMRs and their Closely Associated Persons, which complies with the requirements of MAR. The Share Dealing Code provides that there are certain periods during which dealings in the Company's Ordinary Shares cannot be made including the periods leading up to the publication of the Company's financial results, including interim results. The Company will take all reasonable steps to ensure compliance by PDMRs and their Closely Associated Persons with the share dealing code.

It should be noted that the insider dealing legislation set out in the UK Criminal Justice Act 1993, as well as provisions relating to market abuse, will apply to the Company and dealings in Ordinary Shares.

13. Code and takeover provisions

The Takeover Code is issued and administered by the Panel. The Takeover Code applies to all takeovers and merger transactions, however effected, where the offeree company is, *inter alia*, a listed or unlisted public company resident in the UK, the Channel Islands or the Isle of Man. The Company is such a company and, therefore, Shareholders are entitled to the protection afforded by the Takeover Code.

Mandatory bid

Under Rule 9 of the Takeover Code, where any person acquires, whether by a series of transactions over a period of time or otherwise, an interest (as defined in the Takeover Code) in shares which, taken together with shares in which he is already interested or in which persons acting in concert with him are interested, carry 30% or more of the voting rights of a company which is subject to the Takeover Code, that person is normally required to make a general offer to all the remaining shareholders to acquire their shares.

Similarly, Rule 9 of the Takeover Code also provides that when any person, together with persons acting in concert with him, is interested in shares which, in aggregate, carry more than 30% of the voting rights of such company, but does not hold shares carrying 50% or more of such voting rights, a general offer will normally be required if any further interest in shares is acquired by any such person.

Under the Takeover Code, a concert party arises when persons, pursuant to an agreement or understanding (whether formal or informal), co-operate to obtain or consolidate control of a company or to frustrate the successful outcome of an offer for that company. Under the Takeover Code, "control" means an interest, or aggregate interest, in shares carrying 30% or more of the voting rights of a company, irrespective of whether the interest or interests give de facto control.

If a "takeover offer" (as defined in section 974 of the Act) is made and the offeror, by virtue of acceptances of such offer, acquires or contracts to acquire not less than nine tenths in value of the New Ordinary Shares to which the takeover offer relates, then the offeror has the right to acquire compulsorily the remaining New Ordinary Shares of the minority Shareholders for the offer price within a fixed period. It would do so by sending a notice to the outstanding minority Shareholders telling them that it will compulsorily acquire their shares. Such notice must be sent within three months of the last day on which the offer can be accepted. The notice must be made in the prescribed manner. The squeeze-out of the minority Shareholders can be completed at the end of six weeks from the date the notice has been given, following which the offeror can execute a transfer of the outstanding shares in its favour and pay the consideration to the Company, which would hold the consideration on trust for the outstanding minority Shareholders. The consideration offered to the outstanding minority Shareholders whose shares are compulsorily acquired under the Act must, in general, be the same as the consideration that was available under the takeover offer.

Sell-out

In certain circumstances, the Act gives minority Shareholders the right to require an offeror who has made a takeover offer for the Company to buy their New Ordinary Shares, provided that at any time before the end of the period within which the offer can be accepted, the offeror has acquired (or unconditionally contracted to acquire) not less than 90% in value of the shares to which the offer relates and not less than 90% of the voting rights in the Company. A minority Shareholder can exercise this right by a written communication to the offeror at any time until three months after the period within which the offer can be accepted or a later date specified in the notice given by the offeror. An offeror would be required to give the remaining Shareholders notice of their rights to be bought out within the one month from the end of the period in which the offer can be accepted. The offeror may impose a time limit on the rights of the minority Shareholders to be bought out, but that period cannot end less than three months after the end of the acceptance period. If a Shareholder exercises his/her rights, the offeror is bound to acquire those shares on the terms of the offer or on such other terms as may be agreed.

14. Taxation

The attention of investors is drawn to the information regarding taxation which is set out in the "Risk Factors" section and in paragraph 13 in Part IV of this Document. That information is, however, intended only as a general guide to the current tax position under UK taxation law for certain types of investor. Investors who are in any doubt as to their tax position or who are subject to tax in jurisdictions other than the UK are strongly advised to consult their professional advisers.

15. Shareholder notification and disclosure requirements

The Company is subject to certain provisions of the Disclosure Guidance and Transparency Rules and, consequently, Shareholders are required to disclose to the Company the level of their interests in the ordinary share capital of the Company in accordance with those rules.

16. Anti-Bribery and Corruption Policy

The Bribery Act 2010 which came into force in the UK on 1 July 2011 prescribes criminal offences for individuals and businesses relating to the payment of bribes and, in certain cases, a failure to prevent the payment of bribes. The Company has therefore established procedures and adopted an anti-bribery and corruption policy designed to ensure that no member of the Group engages in conduct for which a prosecution under the Bribery Act may result.

17. Additional information

Your attention is drawn to the information included in Parts II to IV of this Document. In particular you are advised to consider carefully the risk factors contained in the “Risk Factors” section of this Document.

Yours faithfully,

Dr Allan Syms
Non-Executive Chairman

PART II

REGULATORY ENVIRONMENT

Cizzle Biotechnology Holdings plc intends to operate in a highly regulated market as further explained below. Its proposed products have to be compliant with global medical device regulations as determined by relevant notifying bodies (“**NB**”) such as The Medicines and Healthcare products Regulatory Agency (“**MHRA**”) in the UK or the US Food and Drug Administration (“**FDA**”) in the USA. It is illegal in these jurisdictions to sell products that are not cleared for sale for clinical use.

1. Regulatory Environment

Before placing a medical device on the European or other markets, manufacturers need to produce technical documentation providing evidence of conformity with the relevant legislation. In Europe, this needs to comply with the Medical Device Regulation (MDR) European Union (EU) Regulation 2017/745 (“**MDR**”).

Post-Brexit, MHRA is responsible for regulating the UK medical devices market and has different rules that apply in Great Britain, Northern Ireland and the EU. Under the Northern Ireland Protocol, different rules apply in Northern Ireland to those in Great Britain.

Since 1 January 2021, there have been a number of changes, introduced through secondary legislation, to how medical devices are placed on the market in Great Britain (England, Wales and Scotland).

With the aim of globally standardizing medical device regulatory submissions, the Global Harmonization Task Force (“**GHTF**”) created the ‘Summary Technical Documentation’ (“**STeD**”), intended to be a consistent, summarized or abridged form of the technical documentation, with sufficient detail to allow manufacturers to fulfil their obligations.

In the EU, a notifying body is an organisation that has been designated by an EU member state (the designating authority) to assess whether manufacturers and their medical devices meet the requirements set out in legislation.

CE Marking

“In order to be able to CE mark any device, a manufacturer must demonstrate that the stated device complies with the relevant essential requirements of the European directives. To demonstrate such compliance, it will usually be necessary to provide clinical data, which can consist of:

- *a critical evaluation of the relevant scientific literature currently available relating to the safety, performance, design characteristics and intended purpose of the device, where there is demonstration of equivalence of the device to the device to which the data relates and the data adequately demonstrates compliance with the relevant essential requirements; or*
- *a critical evaluation of the results of all the clinical investigations made; or*
- *a critical evaluation of the combined data provided from the two bullet points above.”*

(MHRA: Guidance on Legislation, Clinical investigations of medical devices – guidance for manufacturers, January 2020)

The processes to achieve compliance with EU Directive MDR 2017/745 can be complex.

FDA Clearance

The USA regulatory controls are documented in accordance with the Federal Food, Drug, and Cosmetic Act and the regulations in Title 21- Code of Federal Regulations (21 CFR) Parts 1-58, 800-1299. This regulatory framework is used by medical device companies to attain the FDA market authorization. It is based on the Title 21-CFR Quality System Regulations, which are defined for each device category.

According to the FDA regulations, companies follow requisite regulatory steps assessing the overall risk profile for each device and ensuring reasonable safety and effectiveness assurance while adhering to the respective marketing pathways. The marketing pathways include Premarket Notification (510(k)), De Novo Classification Request, Exempt, Premarket Approval, Product Development Protocol, Humanitarian Use Exemption and Biologics License Application.

This regulatory environment is at the core of the Board's strategy as it intends to develop Cizzle Biotechnology's prototype test into a commercial, UKCA, CE marked, LDT and/or FDA 510(k) cleared diagnostic immunoassay that can be readily performed as a sufficiently reliable test in a hospital setting.

The Board intends to apply the majority of the net proceeds of the Subscription towards the continued development of the CIZ1B biomarker test through to UKCA, CE marking, LDT and/or FDA 510(k) clearance.

Laboratory-Developed Tests ("LDT")

In the United States, clinical laboratory tests are either FDA-approved or laboratory-developed (LDTs). Often, FDA-approved tests are marketed by a medical device company and purchased by a laboratory, hospital, or physician's office. Labs may also develop their own tests in-house, for example, when an FDA-approved test is not available, when an FDA-approved test is modified for a new sample type, or when a new test is more esoteric in nature. It has been recommended that a test life cycle model can be followed to organise the establishment and implementation of either test type.

Definition of an LDT

The FDA considers an LDT to be an in vitro diagnostic ("IVD") device that is intended for clinical use and designed, manufactured, and used within a single laboratory such as CorePath. The lab needs to establish acceptable performance through analytical and clinical validation, and then re-verify performance as part of implementation.

CLIA requirements and limitations

Under the Clinical Laboratory Improvement Amendments ("CLIA"), the Centers for Medicare & Medicaid Services ("CMS") has regulated laboratories that develop LDTs. CLIA oversees and enforces the accreditation, inspection, and certification of medical laboratories. CLIA requirements address the laboratory's ability to perform laboratory testing accurately and reliably. CLIA prohibits the release of any test results prior to the laboratory establishing certain performance characteristics relating to analytical validity for the use of that test in the laboratory's own environment. CorePath is a CLIA and CAP accredited laboratory.

Compliance with CLIA requirements ensures that clinical laboratory practices are of high quality and that the methodologies selected for clinical use have the capability of providing the quality of results required for patient care. However, there are no requirements regarding the design, manufacture, and validation of the diagnostic device itself.

LDT Test Development Cycle

There are established measurement evaluations to organise each step of establishment and implementation to develop and implement a high-quality robust test.

The Establishment stage consists of: feasibility and design, development, and validation.

Feasibility and design: a literature review is conducted on clinical usefulness and intended use. A feasibility assessment should be carried out to assess legal rights for use of the intended test together with a marketing overview.

Development phase: optimises all reagents and instrumentation which should include creation of standard operating procedures (SOPs).

Validation: involves experimental proof steps with appropriate acceptance criteria to evaluate precision, accuracy, detection capability, analytical specificity, stability, and clinical validation.

Implementation: this stage consists of preliminary evaluation, verification, test launch, maintenance and retirement.

Preliminary evaluation involves getting familiar with the new test to ensure the test meets performance criteria. This is followed by a verification exercise to check precision, accuracy, and detection capability before launch.

(Source: Establishing and implementing LDTs utilizing the Test Life Cycle Model, Paula Ladwig, 22 March 2018 | Medical Laboratory Observer (mlo-online.com))

The Group has entered into agreements with selected manufacturers and contract research organisations to conduct the reagent generation, test manufacture and the clinical validation required to achieve UKCA, CE marking, LDT and/or FDA 510(k) clearance. Reagent generation will continue within the latter half of 2022. Manufacture of test reagents and validation on clinical samples will follow in 2023.

Commercial Risk

While the Board intends to develop the CIZ1B biomarker test to a point at which UKCA, CE Marking, LDT or FDA 510(k) clearance will be sought, there can be no guarantee that the Group's future products will ultimately obtain UKCA, CE marking, LDT or FDA 510(k) clearance. There can also be no guarantee that future UKCA, CE marking, LDT or FDA 510(k) clearance can be obtained within the timescales or the budgets anticipated by the Directors. The Group intends to pursue UKCA, CE marking approval, LDT accreditation or FDA 510(k) clearance via the use of retrospective testing data. However, if retrospective testing data is not sufficient to obtain UKCA, CE marking approval, LDT accreditation and/or FDA 510(k) clearance, then the Group may need to complete a prospective study, which it is anticipated would be more expensive and would take longer.

Any other potential delays in obtaining the UKCA CE marking approval, LDT accreditation or potentially FDA 510(k) clearance would adversely affect the timing of the Group's future product sales into the EU (or the USA in the case of a LDT or FDA 510(k) clearance). There is no guarantee that there will not be an extended period of requests for information or supporting data that could add to the timing for receiving the UKCA or CE mark (or potentially a LDT or FDA 510(k) clearance).

2. Governmental, economic, fiscal, monetary or political policies

In the UK (and adopted in some other countries), the National Institute for Health and Clinical Excellence ("NICE") provides national guidance and advice to the NHS to improve health and social care. It is non-departmental public body, sponsored by the UK's Department of Health and Social Care. NICE carries out technology appraisals, providing recommendations on the use of new and existing medicines and treatments within the NHS, based upon a review of clinical and economic evidence.

NICE's Medical Technologies Evaluation Programme identifies medical technologies that have the potential to offer substantial benefit to patients and/or to the NHS and that are likely to be adopted more consistently and more rapidly if NICE develops guidance on them. NICE has published a document entitled "Medical technologies evaluation programme methods guide" ("**Methods Guide**") which sets out guidelines and criteria that will be taken into account in selecting the medical technologies for the development of NICE guidance. The Methods Guide also details how the appraisal committee develops guidance on selected technologies routed to it for evaluation.

The methods set out in the Methods Guide are designed to ensure that the most appropriate medical technologies are selected for evaluation, and, when the appraisal committee produces guidance, that it is robust, developed in an open, transparent and timely way, takes into account valid and relevant evidence, and allows appropriate input from consultees and other stakeholders.

There are significant uncertainties associated with the exit by the UK from its membership of the European Union.

Since 1 January 2021, there have been a number of changes, introduced through secondary legislation, to how medical devices are placed on the market in Great Britain (England, Wales and Scotland). These are:

- CE marking will continue to be recognised in Great Britain until 30 June 2023
- certificates issued by EU-recognised Notified Bodies will continue to be valid for the Great Britain market until 30 June 2023
- the EU no longer recognises UK Notified Bodies
- UK Notified Bodies are not able to issue CE certificates (other than for the purposes of the “CE UKNI” marking, which is valid in Northern Ireland) - and have become UK Approved Bodies
- a new route to market and product marking is available for manufacturers wishing to place a device on the Great Britain market
- since 1 January 2021, all medical devices, including in vitro diagnostic medical devices (IVDs), placed on the Great Britain market need to be registered with the MHRA. There is a grace period for registering:
 - Class IIIs and Class IIb implantables, and all active implantable medical devices and IVD List A products must be registered from 1 May 2021
 - other Class IIb and all Class IIa devices and IVD List B products and Self-Test IVDs must be registered from 1 September 2021
 - Class I devices, custom-made devices and general IVDs (that do not currently need to be registered) must be registered from 1 January 2022
- manufacturers of Class I devices, custom-made devices and general IVDs that, prior to 1 January 2021, were required to register their devices with the MHRA (i.e. UK-based manufacturers or third country manufacturers with Northern Ireland-based Authorised Representatives) must continue to register their devices from 1 January 2021 on the same basis as they do now rather than in line with the above dates

The Group’s lung cancer blood test will likely be classed as an IVD List B product.

There are possible further uncertainties as to the current and future fiscal, monetary and regulatory landscape in the UK. There is also uncertainty as to how, when and to what extent the continuing impact of Brexit, the COVID-19 pandemic, the ongoing armed conflict in Ukraine and potential low levels of economic growth, will have an impact more generally on the economy of the UK and the growth of various industries, consumer confidence, levels of investor activity and confidence in market performance.

The UK’s exit from the EU may yet lead to a more complicated and uncertain process for obtaining regulatory clearance to market the Group’s future products in the UK and the EU. In the event of such complications or delays in obtaining regulatory clearance for marketing in the UK or the EU, the Group will consider giving higher priority to compliance with the LDT and FDA 510(k) clearance process.

Following Brexit, the Group will need to comply with the Medical Devices (Amendment etc.) (EU Exit) Regulations 2019 if it is to market its future products in the UK.

Currently, devices are regulated under:

- Directive 90/385/EEC on active implantable medical devices (EU AIMDD)
- Directive 93/42/EEC on medical devices (EU MDD)

- Directive 98/79/EC on in vitro diagnostic medical devices (EU IVDD)

These directives are given effect in UK law through the Medical Devices Regulations 2002 (SI 2002 No 618, as amended) (UK MDR 2002). These Regulations (in the form in which they existed on 1 January 2021) continue to have effect in Great Britain after the transition period.

This means that since 1 January 2021, the Great Britain route to market and UKCA marking requirements is still based on the requirements derived from current EU legislation.

Any future changes in legislation or regulation, and in particular the regulations relating to the testing of human blood or serum as part of a diagnostic test for disease, may have an adverse effect on the Group's operations and the returns available on an investment in the Company. The Group's ability to conduct business will be predicated on being in compliance with all licence requirements as specified by each relevant jurisdiction.

The Group may not continue to hold all of the necessary consents, approvals and licences required to conduct its business, and where new permissions are required, these may be delayed or not forthcoming. For example, the Coronavirus (COVID-19) epidemic has already delayed planned changes to the full implementation of the MDR. If any new approvals or licences are required in order for the Group to carry on its future business, the Group could face delays or prohibitions on the development, manufacture, sale or distribution of its products, which may have a material adverse effect on the Group's business, financial condition, capital resources, results and/or future operations.

PART III

FINANCIAL INFORMATION

The Company has produced annual statutory accounts for the financial year ended 31 December 2021 (“**2021 Accounts**”). The 2021 Accounts were audited by PKF Littlejohn LLP of 15 Westferry Circus, London E14 4HD who are registered to carry on audit work by the Institute of Chartered Accounts in England and Wales.

The auditor’s report within in the 2021 Accounts contained the following statement on material uncertainty related to going concern:

“We draw attention to note 2.2 in the financial statements, which indicates that the group will need to raise additional funds in order to meet its committed liabilities during the going concern period. As stated in note 2.2, these events or conditions indicate that a material uncertainty exists that may cast significant doubt on the group’s and parent company’s ability to continue as a going concern. Our opinion is not modified in respect of this matter.

In auditing the financial statements, we have concluded that the director’s use of the going concern basis of accounting in the preparation of the financial statements is appropriate. Our evaluation of the directors’ assessment of the group and company’s ability to continue to adopt the going concern basis of accounting included a review of the directors’ statement in note 2.2 to the financial statements and review of the company’s budgets for the period of the twelve months from the date of approval of the financial statements, including checking the mathematical accuracy of the budgets and discussion of significant assumptions used by the management.”

The 2021 Accounts were prepared in accordance with UK-adopted international accounting standards and the requirements of the Companies Act. The 2021 Accounts contain a description of the Company’s financial condition and are being incorporated by reference (as detailed below). The 2021 Accounts can be accessed from the Company’s website: <https://cizzlebiotechnology.com/publications/> by clicking on ‘Annual Report for the year ended 31 December 2021’.

Where the 2021 Accounts make reference to other documents, such other documents are not incorporated into and do not form part of this Document. The two tables below comprise a cross-referenced list of information incorporated by reference. The parts of the 2021 Accounts which are not being incorporated by reference are either not relevant for an investor or are covered elsewhere in this Document.

The 2021 Accounts include the following information which is incorporated by reference:

| Description | 2021 Accounts |
|--|----------------------|
| Consolidated Balance Sheet (or equivalent) | Page 33 |
| Company Balance Sheet (or equivalent) | Page 34 |
| Consolidated Income Statement (or equivalent) | Page 32 |
| Statement showing all changes in equity (or equivalent note) – Group | Page 37 |
| Statement showing all changes in equity (or equivalent note) – Company | Page 38 |
| Consolidated Cash Flow Statement | Page 35 |
| Company Cash Flow Statement | Page 36 |
| Accounting Policies and Notes | Pages 39 to 55 |
| Auditor’s Report | Pages 27 to 31 |

This information has been prepared in a form consistent with that which will be adopted in the Company’s next published annual financial statements having regard to accounting standards and policies and legislation applicable to those financial statements.

The 2021 Accounts also includes operating/financial reviews as follows, which are incorporate by reference:

| Description | 2021 Accounts |
|--------------------------------|----------------|
| Chair's Statement | Pages 2 to 4 |
| Strategic Report | Pages 6 to 10 |
| Directors' Report | Pages 11 to 13 |
| Directors' Remuneration Report | Pages 21 to 26 |
| Corporate Governance Statement | Pages 15 - 20 |

Certain financial information of Company and the Group is also set out below:

| | Group Audited Year ended 31 Dec 2021 £'000 | Company Audited Year ended 31 Dec 2021 £'000 |
|---|---|---|
| Revenue | - | - |
| Cost of sales and administrative expenses | (552) | (367) |
| Share option charge | (299) | (299) |
| Transaction costs | (303) | (479) |
| Reverse acquisition expenses | (2,804) | - |
| Loss from operations | (3,958) | (1,145) |
| Taxation | 37 | - |
| Loss of the period | (3,921) | (1,145) |

| | Group Audited As at 31 Dec 2021 £'000 | Company Audited As at 31 Dec 2021 £'000 |
|---------------------|--|--|
| Total Assets | 1,155 | 23,092 |
| Total Liabilities | (218) | (133) |
| Net assets | 937 | 22,959 |
| Total Equity | 937 | 22,959 |

| | Group Audited Year ended 31 Dec 2021 £'000 | Company Audited Year ended 31 Dec 2021 £'000 |
|--|---|---|
| Net cash used in operations | (1,009) | (758) |
| Net cash used in investing activities | (154) | (519) |
| Net cash generated from financing activities | 2,031 | 2,041 |
| Net increase/(decrease) in cash and cash equivalent | 868 | 764 |
| Cash and cash equivalents at beginning of period | 7 | 84 |
| Cash and cash equivalents at end of period | 875 | 848 |

Working Capital

In the opinion of the Company, taking into account the net proceeds of the Subscription and assuming full utilisation the Facility, the working capital available to the Group is sufficient for its present requirements, that is, for at least the next 12 months from the date of this Document.

Capitalisation and Indebtedness

The following table shows the Company's capitalisation as at 30 June 2022 and has been extracted without material adjustment from unpublished and unaudited financial information.

| | Company 30 June 2022 (£'000) Unaudited |
|---|---|
| Total Current Debt | |
| Guaranteed | - |
| Secured | - |
| Unguaranteed/Unsecured | - |
| Total Non-Current Debt (excluding current portion of non-current debt) | |
| Guaranteed | - |
| Secured | - |
| Unguaranteed/Unsecured | - |
| Total indebtedness | - |
| | |
| Shareholder Equity | 30 June 2022 (£'000) Unaudited |
| Share Capital | 3,496 |
| Legal Reserves | 33,563 |
| Other Reserves | 10,486 |
| Total Capitalisation | 47,545 |

Note that Legal Reserves include Share Premium of £33,563,000.

As at 20 September 2022, being the latest practicable date prior to the publication of this Document, there has been no material change in the capitalisation of the Company since 30 June 2022.

The following table sets out the unaudited statement of indebtedness of the Company as at 30 June 2022 and has been extracted without material adjustment from unpublished and unaudited financial information.

| | | Company |
|----------|--|---------------------|
| | | 30 June 2022 |
| | | Unaudited |
| | | £'000 |
| A | Cash | 417 |
| B | Cash equivalents | - |
| C | Other current financial assets | 383 |
| D | Liquidity (A+B+C) | 800 |
| E | Current financial debt (including debt instruments, but excluding current portion of non-current debt) | 85 |
| F | Current portion of non-financial debt | - |
| G | Current financial indebtedness (E+F) | 85 |
| H | Net current financial indebtedness (G-D) | (715) |
| I | Non-current financial debt (excluding current portion and debt instruments) | - |
| J | Debt instruments | - |
| K | Non-current trade or other payables | 880 |
| L | Non-current financial indebtedness (I+J+K) | 880 |
| M | Total financial indebtedness (H+L) | 165 |

As at 30 June 2022, the Company had no indirect or contingent indebtedness, save for the remaining consideration of £0.88 million due to SGSC pursuant to the SGSC and Conduit Royalty Sharing Arrangement (further details of which can be found in paragraph 9.1.13 of Part IV).

As at 20 September 2022, being the latest practicable date prior to the publication of this Document, there has been no material change in the indebtedness of the Company since 30 June 2022.

Investments

Save as disclosed in this Prospectus in relation to the SGSC and Conduit Royalty Sharing Arrangement, the Group has not made any investments since 30 December 2021, nor are there any investments by the Group which are in progress or for which firm commitments have already been made.

Production, sales and inventory, costs and selling prices

The Company has not had any production, sales and inventory and costs and selling prices since 31 December 2021 to the date of this Prospectus.

Significant Change in Financial Position

There has been no significant change in the financial position and financial performance of the Group which has occurred since 31 December 2021, being the date to which the audited financial information referred to in this Part III has been published.

PART IV

ADDITIONAL INFORMATION

1. RESPONSIBILITY

- 1.1 The Company (whose registered office address appears on page 20 of this Document), the Directors, whose names, business address and functions appear on page 20 of this Document, accept responsibility for the information contained in this Document (including any expressions of opinion) and that, to the best of their knowledge, the information contained in this Document is in accordance with the facts and this Document makes no omission likely to affect their import.

2. Incorporation and status of the Company

- 2.1 The Company was incorporated in England and Wales on 1 March 2007 under the name of Enfis Group plc with registered number 06133765 as a public company with limited liability under the Companies Act 1985.
- 2.2 On 23 December 2010, the Company changed its name to PhotonStar LED Group plc and then Bould Opportunities plc on 11 April 2019. On 25 May 2021, the Company changed its name to Cizzle Biotechnology Holdings plc.
- 2.3 The liability of the members of the Company is limited.
- 2.4 The principal legislation under which the Company operates is the Companies Act 2006 (as amended, consolidated or re-enacted from time to time) and the regulations made thereunder.
- 2.5 The registered office of the Company is at 6th Floor 60 Gracechurch Street, London, EC3V 0HR, telephone number: 020 7264 4417 (c/o SGH Company Secretaries Limited). The Company's website is <https://cizzlebiotechnology.com/>.
- 2.6 The information on the website does not form part of the Prospectus, save for where expressly stated to be incorporated by reference.
- 2.7 The Company Secretary of the Company is SGH Company Secretaries Limited of 6th Floor, 60 Gracechurch Street, London EC3V 0HR (telephone number: 020 7264 4417).

3. The Subsidiaries

- 3.1 The Company acts as the holding company of the Group.
- 3.2 The Company has the following subsidiaries which are private limited companies:

| Name | County of Incorporation | Principal Activity | Percentage of issued share capital owned by the Company |
|-------------------------------------|----------------------------|---|---|
| Cizzle Biotechnology Limited | England and Wales | Research and experimental development on biotechnology | 100% |
| Cizzle Biotech Ltd | England and Wales | Dormant | 100% |
| PhotonStar Limited (in liquidation) | LED (in England and Wales) | Design and development of LED lighting fixtures/With liquidator November 2018 | 100% |

- 3.3 The following table shows the issued and fully paid share capital of the Company immediately prior to Admission:

| | Nominal Value | Number of shares issued and credited as fully paid | Amount paid up |
|-------------------|----------------------|---|-----------------------|
| Ordinary Shares | 0.01p | 278,447,788 | £27,844.78 |
| A Deferred shares | 0.99p | 225,158,220 | £2,229,066.38 |
| A Deferred shares | 0.01p | 12,383,625,615 | £1,238,362.56 |

- 3.4 Assuming completion of the Subscription and the issue and allotment of the Commission Shares and the Facility Shares, the issued and fully paid share capital of the Company immediately following Admission is expected to be as shown in the following table:

| | Nominal Value | Number of shares issued and credited as fully paid | Amount paid up |
|-------------------|----------------------|---|-----------------------|
| Ordinary Shares | 0.01p | 314,114,453 | £31,411.45 |
| A Deferred shares | 0.99p | 225,158,220 | £2,229,066.38 |
| A Deferred shares | 0.01p | 12,383, 625,615 | £1,238,362.56 |

- 3.5 Pursuant to a share option scheme adopted by Cizzle Biotechnology on 31 May 2012 (“**Cizzle Option Scheme**”), Professor Coverley was granted options over 10,988 ordinary shares of £0.01 each in the capital of Cizzle Biotechnology for an exercise price of £5.15 per share (“**DC Options**”). Pursuant to an agreement dated 23 April 2021, Professor Coverley surrendered all of her DC Options in consideration for the issue of options over 3,689,096 Ordinary Shares in the Company at an exercise price of £0.015339313479508 per share exercisable within three years of the Initial Listing (“**DC Bould Options**”). In addition, in consideration of the waiver of outstanding salary of approximately £166,432 (as accrued from September 2017 up to the date of the Initial Listing and which was deferred by agreement of the directors in order to conserve cash for patent maintenance), Professor Coverley is entitled to a cash bonus from the Company equal to the total exercise price of the DC Bould Options of £56,588.20 (together with any tax payable thereon), payable on the exercise of the DC Bould Options. This cash sum will be used to settle the exercise price of the DC Bould Options upon exercise. Dawn Coverley intends to exercise the DC Bould Options in full following the publication of the Company’s next interim results.

- 3.6 On 22 February 2022, the Company entered into option agreements in relation to unapproved options granted over a total of 19,741,345 Ordinary Shares to the members of the Board as set out below as at 3 November 2021 (“**Management Incentive Options**”). The Management Incentive Options are exercisable at a price of 10p per share, subject to certain vesting criteria being met, based on key deliverables under the Company’s business plan. From vesting, the option holder has 10 years to exercise the option before expiry. Exercise of all of the Management Incentive Options would result in the Enlarged Share Capital being diluted by approximately 5.91%. The Management Incentive Options represent approximately 5.23% of the Fully Diluted Enlarged Share Capital of the Company.

| Director | Options Issued |
|-----------------|-----------------------|
| Allan Syms | 5,068,956 |
| Dawn Coverley | 12,672,389 |
| Nigel Lee | 2,000,000 |

3.7. The following resolutions of the Company were passed at the annual general meeting held on 27 June 2022:

- a. That, the Directors were generally and unconditionally authorised in accordance with section 551 of the Act and in substitution for all existing authorities under that section, to exercise all the powers of the Company to allot shares in the Company or to grant rights to subscribe for, or to convert any security into, shares in the Company (“**Rights**”) up to an aggregate nominal amount of £9,281.60 during the period commencing on the date of the passing of the resolution and expiring at the conclusion of the next annual general meeting of the Company or on 30 June 2023, whichever is earlier, and provided further that the Company shall be entitled before such expiry to make an offer or agreement which would or might require shares to be allotted or Rights to be granted after such expiry and the Directors shall be entitled to allot shares and grant Rights under such offer or agreement as if this authority had not expired
- b. That, subject to and conditional upon the passing of the resolution at a. above, the Directors were authorised pursuant to Section 570 of the Act to allot equity securities (as defined in Section 560 of the Act) for cash pursuant to the authority conferred by resolution a. above as if Section 561(1) of the Act did not apply to any such allotment, provided that this power shall be limited to:
 - (i) up to an aggregate nominal amount of £2,200.00 in connection with remaining consideration due of £0.88m to Conduit Pharmaceuticals Limited (“**Conduit**”) for the acquisition of a 5% economic interest in the commercialisation of the AZD 1656 asset or such other assets being developed by Conduit or St George Street Capital (“**SGSC**”) to treat inflammatory pulmonary and cardiovascular disease;
 - (ii) the allotment of equity securities in connection with an issue in favour of shareholders where the equity securities respectively attributable to the interests of all such shareholders are proportionate (or as nearly as may be practicable) to the respective number of Ordinary Shares in the capital of the Company held by them on the record date for such allotment, but subject to such exclusions or other arrangements as the Directors may deem necessary or expedient in relation to fractional entitlements or legal or practical problems under the laws of, or the requirements of, any recognised regulatory body or any stock exchange, in any territory; and
 - (iii) the allotment (otherwise than pursuant to sub-paragraph (i) and (ii) above) of further equity securities up to an aggregate nominal amount of £7,081.60;

provided that this power shall, unless previously revoked or varied by special resolution of the Company in general meeting, expire at the conclusion of the annual general meeting of the Company to be held in 2023. The Company may, before such expiry, make offers or agreements which would or might require equity securities to be allotted after such expiry and the Directors are hereby empowered to allot equity securities in pursuance of such offers or agreements as if the power conferred by this resolution had not expired.

4. Memorandum and Articles of Association

The following is a description of the rights attaching to the Ordinary Shares and A Deferred Shares based on the Company’s articles of association (the “Articles”) and English law. This description does not purport to be complete and is qualified in its entirety by the full terms of the Articles.

4.1 Rights attaching to Ordinary Shares

4.1.1 Voting

Subject to disenfranchisement in the event of:

- non-payment of calls or other monies due and payable in respect of Ordinary Shares; or

- non-compliance with a statutory notice requiring disclosure as to beneficial ownership of Ordinary Shares;

and, without prejudice to any special rights previously conferred and subject to any special terms as to voting upon which any shares may be issued or may for the time being be held and to any other provisions of the Articles, on a show of hands every shareholder who is present in person at a general meeting of the Company shall have one vote, and on a poll every shareholder who is present in person or by proxy shall have one vote for every Ordinary Share held.

4.1.2 *Dividends*

Subject to the Act, the Company at a general meeting may declare dividends to be paid to shareholders according to their rights and interests in the profits available for distribution, but no dividend shall be declared in excess of the amount recommended by the Board. Except insofar as the rights attaching to, or the terms of issue of, any Ordinary Share otherwise provide, all dividends shall be declared according to the amounts paid-up or credited as paid-up on the shares and apportioned and paid pro rata according to the amounts paid-up or credited as paid-up on the shares during any portion or portions of the period in respect of which the dividend is paid. The Board may from time to time pay to the shareholders such interim dividends as appear to the Board to be justified by the position of the Company. Any dividend unclaimed after a period of 12 years from the date it became due for payment shall be forfeited and shall revert to the Company. There is no fixed date on which an entitlement to a dividend arises in respect of Ordinary Shares.

4.1.3 *Distribution of assets on liquidation*

On a winding-up, the liquidator may, with the sanction of a special resolution of the Company and subject to and in accordance with the Act, divide among the shareholders in specie or kind the whole or any part of the assets of the Company, subject to the rights of any shares which may be issued with special rights or privileges.

4.1.4 *Pre-emption rights*

The Articles do not contain any provisions which set out a procedure for the exercise of pre-emption rights for members in respect of the issue of new shares in addition to that provided for by the Act.

4.1.5 *Transferability of Ordinary Shares*

All transfers of Ordinary Shares which are in certificated form may be effected by transfer in writing in any usual or common form or in any other form acceptable to the Board. The instrument of transfer shall be executed by or on behalf of the transferor and (except in the case of fully-paid shares) by or on behalf of the transferee. All transfers of Ordinary Shares which are in uncertificated form may be effected by means of a relevant system (as defined in the Current Articles).

The Directors may, in the case of shares in certificated form, in their absolute discretion and without assigning any reason therefore refuse to register any transfer of shares (not being fully-paid shares) provided that any such refusal does not prevent dealings in partly-paid shares which are admitted to trading on the London Stock Exchange from taking place on an open and proper basis. In addition, the Directors may refuse to register a transfer of shares (whether fully-paid or not) in favour of more than four persons jointly.

The Directors may decline to recognise any instrument of transfer relating to shares in certificated form unless the instrument of transfer is duly stamped, is in respect of only one class of share and is lodged at the Transfer Office accompanied by the relevant share certificate(s) and such other evidence as the Directors may reasonably require to show the right of the transferor to make the transfer.

4.1.6 *Changes in Capital*

Subject to the provisions of the Act and to any special rights conferred on the holders of any shares or class of shares, the Company may issue redeemable shares. Subject to the provisions of the Act and to any special rights previously conferred on the holders of any existing shares, any share may be

issued with such special rights or such restrictions as the Company may determine by ordinary resolution.

Subject to the provisions of the Act, the Company may, with the authority of an ordinary resolution reduce share capital, any capital redemption reserve and any share premium account in any manner. The Company may also, subject to the requirements of the Act, purchase its own shares.

4.1.7 *Untraced shareholders*

Subject to the Act, the Company may sell any shares of a member or person entitled thereto who is untraceable, if during a period of 12 years, at least three dividends in respect of the shares in question have become payable and the cheques or warrants for all amounts payable to such member or person in respect of his shares have remained uncashed or mandated dividend payments have failed and the Company has received no indication of the existence of such member or person within three months following advertisement by the Company in both a national daily newspaper and a newspaper circulating in the area of the last known address of the person entitled. The net proceeds of sale shall belong to the Company but the member or person who had been entitled to the shares shall become a creditor of the Company in respect of those proceeds.

If on two consecutive occasions dividend payments have been sent through the post to any holder of shares to his registered or other specified address but returned undelivered or left uncashed, the Company may cease to send such dividend payments until the person entitled thereto otherwise requires.

4.1.8 *Procedure for General Meetings*

Subject to the Act, the provisions of the Articles relating to general meetings apply as nearly as possible mutatis mutandis to every such meeting. The necessary quorum is two members present in person, by electronic facility or facilities or by proxy and entitled to attend and vote on the business to be transacted. The Chairman or deputy chairman shall preside as Chairman of the meeting and, if neither is present, the Directors present shall choose one of their number to be Chairman of the meeting. If there be no director present and willing to act, the members present and entitled to vote shall choose one of their number to be chairman of the meeting. Such Chairman at a meeting where a quorum is present may with the consent of the meeting adjourn the meeting.

4.1.9 *Votes of members*

Subject to the Act and to any special rights or restrictions as to voting attached to any class of shares at any general meeting, on a show of hands, every member present in person (or by proxy) has one vote on a show of hands and in the case of a poll, every member present in person or by proxy shall have one vote for every share of which he is a holder.

No member shall, unless the Directors determine otherwise, be entitled to vote in respect of any share held by him either personally or by proxy at a general meeting if any call or other sum presently payable in respect of that share remains unpaid or if he or any other person appearing to be interested in such shares has been duly served with a notice under section 793 of the Companies Act 2006 and is in default for the prescribed period.

4.1.10 *Non-UK shareholders*

There are no limitations in the Company's Memorandum or Articles of Association on the rights of non-UK shareholders to hold, or exercise voting rights attaching to, Ordinary Shares. Where a member has a registered address outside of the UK but has notified the Company of an address for the purposes of communications by electronic means at which notices, documents or other information may be served, sent or supplied to them, the member shall be entitled to receive such notices, documents or other information.

4.1.11 *Sanctions on shareholders*

A holder of Ordinary Shares loses his rights to vote in respect of Ordinary Shares if and for so long as he or any other person appearing to be interested in those shares fails to comply with a request by the

Company under the Act requiring him to give particulars of any interest in those Ordinary Shares within 14 days. In the case of shareholdings representing 0.25% or more, in nominal amount, of the share capital of the Company then in issue, or any class thereof, the sanctions which may be applied by the Company include not only disenfranchisement but also the withholding of the right to receive payment or dividends and other monies payable on and restrictions on transfers of, the Ordinary Shares concerned.

4.2 Rights attaching to Non-voting Deferred A Shares

4.2.1 *Income*

Holders of non-voting Deferred A Shares are not entitled to receive any dividend or other distribution.

4.2.2 *Capital*

On a return of capital on a winding up, each holder of non-voting Deferred A Shares is entitled to receive a sum equal to the nominal capital paid up or credited as paid up thereon but only after the aggregate sum of £30,000,000 has been paid to the holders of Ordinary shares and in proportion to the number of shares held and the holders of the non-voting Deferred A Shares shall not be entitled to any further participation in the assets or profits of the Company.

4.2.3 *Voting and General Meetings*

The holders of the non-voting Deferred A Shares have no right to receive notice of any general meeting of the Company nor any right to attend, speak or vote at any such general meeting.

4.2.4 *Reduction of Capital*

Neither the passing by the Company of any special resolution for the cancellation of the non-voting Deferred A Shares for no consideration by means of a reduction of capital requiring the confirmation of the Court, nor the obtaining by the Company nor the making by the Court of any order confirming any such reduction of capital, nor the becoming effective of any such order shall constitute a variation, modification or abrogation of the rights attaching to the non-voting Deferred A Shares. Accordingly, the non-voting Deferred A Shares may at any time be cancelled for no consideration by means of a reduction of capital effected in accordance with the Act without sanction on the part of the holders of the non-voting Deferred A Shares.

4.2.5 *Certificates*

No share certificates will be issued in respect of the non-voting Deferred A Shares.

4.2.6 *Transfer*

The non-voting Deferred A Shares shall not be capable of transfer.

5. Interests of the Directors

5.1 The interests of the Directors and their immediate families and the persons connected with them (within the meaning of section 252 of the Act) in the issued share capital of the Company or the existence of which could, with reasonable diligence, be ascertained by any director as at the date of this Prospectus are shown in the table below. None of the directors will be issued with any New Ordinary Shares on Admission.

| Director | As at the date of this document and on Admission | | | |
|-------------|--|--|--|-----------------------------|
| | Number of Existing Ordinary Shares | Percentage of Existing Ordinary Shares | No. of Existing Ordinary Shares over which options are granted | % of Enlarged Share Capital |
| Allan Syms | - | -% | 5,068,956 | -% |
| John Treacy | - | -% | - | -% |

| | | | | |
|---------------|-------------|--------|-------------|-------|
| Dawn Coverley | 13,359,041* | 4.80%* | 16,361,485 | 4.25% |
| Nigel Lee*** | 18,571 | 0.007% | 2,001,600** | 0.01% |

**this includes 7,055,548 shares held by Professor Dawn Coverley's husband, Justin Ainscough, a founder scientist of Cizzle Biotechnology Limited*

****all shares and options held by CFO Solutions Limited of which Nigel Lee is a director and shareholder*

- 5.2 Save as disclosed above, none of the Directors (or persons connected with the Directors within the meaning of section 252 of the Act) has any interest, whether beneficial or non-beneficial, in any share or loan capital of the Company.
- 5.3 There are no outstanding loans granted or guarantees provided by any company in the Group to or for the benefit of any of the Directors.
- 5.4 Save as disclosed above, and save as otherwise disclosed in this Prospectus, none of the Directors have any interest, whether direct or indirect, in any transaction which is or was unusual in its nature or conditions or significant to the business of the Company taken as a whole and which was effected by the Company since its incorporation and which remains in any respect outstanding or under-performed.
- 5.5 None of the Directors or any person connected with them (within the meaning of section 252 of the Act) is interested in any related financial product referenced to the Ordinary Shares (being a financial product whose value is, in whole or in part, determined directly or indirectly by reference to the price of the Ordinary Shares including a contract for difference or a fixed odds bet).

6. Additional information on the Directors

- 6.1 The names of all companies and partnerships of which the Directors have been a director or partner at any time in the five years preceding the date of this Prospectus and indicating whether they are current or past are set out below:

Allan John Syms (aged 65)

Current Directorships/Partnerships

Cizzle Biotechnology Holdings plc

Cizzle Biotech Ltd

Cizzle Biotechnology Limited

Fidaux Limited

Past Directorships/Partnerships

Mertz plc (dissolved)

Mypinpad Asia Ltd (Hong Kong)

Mypinpad China Ltd (Hong Kong)
(dissolved)

Nano Lab Ltd (dissolved)

John Michael Treacy (aged 40)

Current Directorships/Partnerships

Ananda Developments plc

Cizzle Biotechnology Holdings plc

Oscillate plc

Past Directorships/Partnerships

AIK Energy International Ltd (formerly AIK Energy Ltd)

Supply@Me Capital plc (formerly Abal Group plc)

Central Rand Gold Limited (Guernsey)

| | |
|---|--|
| Honye Financial Services Ltd (Cayman Islands) | China Sports Development Ltd (BVI) |
| URA Holdings plc | Digitalbox plc (formerly Polemos plc) |
| YTC Consultancy Services Ltd | Eight Capital Partners plc (formerly Monreal plc) |
| 72 Richmond Hill Limited | Epsilon Capital Limited |
| | Evrima plc (formerly Sport Capital Group plc) |
| | Palermo Football Club S.p.A (Italy) |
| | Pineapple Power Corporation plc |
| | Prefcap Limited |
| | South African Property Opportunities plc (Isle of Man) |
| | Sport Capital Group Holdings Limited (dissolved) |
| | Sport Capital Group Investments Limited (dissolved) |
| | Unione Sportiva Città di Palermo S.p.A (Italy) |

Professor Dawn Alison Coverley (aged 56)

Current Directorships/Partnerships

Cizzle Biotechnology Holdings plc

Cizzle Biotechnology Limited

Past Directorships/Partnerships

-

Nigel Ronald Lee (aged 60)

Current Directorships/Partnerships

CFO Solutions Limited

Cizzle Biotech Ltd

Cizzle Biotechnology Holdings plc

Cizzle Biotechnology Limited

Kent Surrey Sussex AHSN Limited

Past Directorships/Partnerships

Newco Limited

Startco Limited

- 6.2 None of the Directors have:
- 6.2.1 any unspent convictions in relation to indictable offences;
 - 6.2.2 had any bankruptcy order made against him or entered into any voluntary arrangements;
 - 6.2.3 save as disclosed in this paragraph, there were no bankruptcies, receiverships or liquidations of any companies or partnerships where any of the Directors were acting as (i) a member of the administrative, management or supervisory body, (ii) a partner with unlimited liability, in the case of a limited partnership with a share capital, (iii) a founder where the company had been established for fewer than five years or (iv) a senior manager, during the previous five years:
 - 6.2.3.1 Mr Treacy was appointed as a director of Sport Capital Group Holdings Limited on incorporation on 20 December 2018. This company was placed into a solvent members' voluntary liquidation on 31 May 2019 and on 24 July 2020, the company was dissolved. Mr Treacy was a director of Unione Sportiva Città di Palermo S.p.A. for approximately five weeks between the dates of 31 December 2018 until 4 February 2019. Unione Sportiva Città di Palermo S.p.A. was declared bankrupt by the Court of Palermo on 18 October 2019. It is not expected that there will be sufficient funds to make a distribution to creditors;
 - 6.2.4 been a partner in any partnership which has been declared bankrupt, placed in compulsory liquidation, administration or been the subject of a partnership voluntary arrangement whilst he was a partner in that partnership or within the 12 months after he ceased to be a partner in that partnership;
 - 6.2.5 been the owner of any asset or been a partner in any partnership which owned, any asset which while he owned that asset, or while he was a partner or within the 12 months after he ceased to be a partner in the partnership which owned the asset entered into receivership;
 - 6.2.6 been the subject of any public incrimination or sanction by any statutory or regulatory authority (including recognised professional bodies), save for Mr Treacy who was issued with a nine month suspension from the management of Italian football clubs on 3 September 2020 by La Corte Federale d'Appello following the bankruptcy of Unione Sportiva Città di Palermo S.p.A. as described at paragraph 6.2.3.1 above. Mr Treacy subsequently appealed this ruling to the Collegio di Garanzia dello Sport. The Collegio di Garanzia dello Sport, being the senior court, upheld Mr Treacy's appeal, and reversed the decision of La Corte Federale d'Appello, resulting in the suspension also being overturned;
 - 6.2.7 been disqualified by a court from acting as a director of any company or from acting in the management or conduct of the affairs of any company; or
 - 6.2.8 had any previous name.
- 6.3 None of the Directors have any material conflicts of interest between any duties owed to the Company and their private interests and/or other duties.

7. Significant Shareholders

- 7.1 Save as disclosed in sub-paragraph 5.1 above the Company is only aware of the following persons who, at the date of this Prospectus and immediately following Admission, represent an interest (within the meaning of Chapter 5 of the Disclosure Guidance and Transparency Rules) directly or indirectly, jointly or severally in 3% or more of the Company's issued share capital or could exercise control over the Company:

| Name | At the date of this Document | | On Admission of the New Ordinary Shares | |
|--|---------------------------------|-----------------------------|---|-----------------------------|
| | No. of Existing Ordinary Shares | % of Existing Share Capital | No. of New Ordinary Shares | % of Enlarged Share Capital |
| Hargreaves Lansdown (Nominees) Limited | 47,621,748 | 17.10% | - | 15.16% |
| JIM Nominees | 45,615,279 | 16.38% | - | 14.52% |
| Yorkshire Cancer Research | 32,382,330 | 11.63% | - | 10.31% |
| Interactive Investor Services Nominees Limited | 27,135,794 | 9.75% | - | 8.64% |
| HSDL Nominees Limited | 20,887,303 | 7.50% | - | 6.65% |
| Dawn Coverley | 13,359,041* | 4.80% | - | 4.25% |
| University of Leeds | 11,128,058 | 4.00% | - | 3.54% |
| University of Sheffield | 11,128,058 | 4.00% | - | 3.54% |
| Vidacos Nominees Limited | 10,739,219 | 3.86% | - | 3.42% |
| Barclays Direct Investing Nominees Limited | 9,071,059 | 3.26% | - | 2.89% |
| Alan Miller | 6,525,511** | 2.34% | 14,858,844** | 4.73 |

*this includes 7,055,548 shares held by Professor Dawn Coverley's husband, Justin Ainscough, a founder scientist of Cizzle Biotechnology Limited

**held indirectly through a nominee

7.2 None of the Directors, members of the senior management team nor any persons named in sub-paragraph 5.1 above has voting rights which are different to any other Shareholder.

8. Share Incentive Schemes

8.1 The Company has a historic Executive Share Option Scheme (“**Executive Scheme**”).

8.2 As at the date of this Document, the Company has granted the following options to subscribe for ordinary shares to CFO Solutions Limited (a company in which Nigel Lee is a director) which are outstanding as at the date of this Document (“**CFO Options**”):

| Date of Grant | Options Issued* | Exercise Price (p) | Exercise Period | Expiry Date |
|-----------------|-----------------|--------------------|-----------------|-----------------|
| 26 August 2015 | 300 | 5.025 | 2017 - 2025 | 25 August 2025 |
| 27 October 2016 | 800 | 1.85 | 2017 - 2026 | 26 October 2026 |
| 9 November 2017 | 500 | 0.85 | 2018 - 2027 | 8 November 2027 |
| Total | 1,600 | | | |

*as recalculated in accordance with the share reorganisation undertaken by the Company on 13 May 2021

- 8.3 The Company determines the fair value of its share option contracts on the grant date, adjusts this to reflect its expectation of the options that will ultimately vest, and then expenses the calculated balance on a straight-line basis through its statement of comprehensive income over the expected vesting period with a corresponding credit to its share option reserve. Subsequent changes to the expectation of number of options that will ultimately vest are dealt with prospectively such that the cumulative amount charged to the statement of comprehensive income is consistent with latest expectations. Subsequent changes in market conditions do not impact the amount charged to the statement of comprehensive income.
- 8.4 The Company determines the fair value of its share option contracts using a model based on the BlackScholes-Merton methodology. In determining the fair value of its share option contracts, the Company made the following assumptions (ranges are provided where values differ across tranches). Expected volatility was determined by reference to historical experience.

| Grant date | Share price | Exercise price | Expected option life | Expected volatility | Expected dividend yield | Risk free interest rate | Fair value at grant date |
|------------|-------------|----------------|----------------------|---------------------|-------------------------|-------------------------|--------------------------|
| 2021 | 9.38p | 1.53p | 10 years | 68% | 0% | 0.83% | 1.60p |
| 2021 | 4.40p | 10.00p | 10 years | 32% | 0% | 0.83% | 3.00p |

- 8.5 The CFO Options as set out in the table at paragraph 8.2 above are subject to the following terms:

8.5.1 Options granted on 26 August 2015

The options vested over a two-year period in equal instalments on 25 May 2016, 25 February 2017 and 25 August 2017, respectively. All options were granted subject to the satisfaction of certain performance criteria relating to CFO Solutions Limited's role as company secretary at the time, including the filing of Companies House returns and tax returns to the satisfaction of the board of directors then in office, becoming exercisable when the performance criteria was met and expiring on the tenth anniversary of the date of grant.

8.5.2 Options granted on 27 October 2016

The options vested over a three-year period in equal instalments on the anniversary of the date of the grant. All options were granted subject to the satisfaction of certain performance criteria relating to CFO Solutions Limited's role as company secretary at the time, including the filing of Companies House returns and tax returns to the satisfaction of the board of directors then in office, becoming exercisable when the performance criteria was met and expiring on the tenth anniversary of the date of grant.

8.5.3 Option granted on 9 November 2017

The options vested over a three-year period in equal instalments on the anniversary of the date of the grant. All options were granted subject to the satisfaction of certain performance criteria relating to CFO Solutions Limited's role as company secretary at the time, including the filing of Companies House returns and tax returns to the satisfaction of the board of directors then in office, becoming exercisable when the performance criteria was met and expiring on the tenth anniversary of the date of grant.

- 8.6 Exercise of the CFO Options will result in the Enlarged Share Capital of the Company being diluted by approximately 0.01%. The CFO Options represent approximately 0.0004% of the Fully Diluted Enlarged Share Capital of the Company.

- 8.7 In addition to the CFO Options, Professor Coverley has been issued options over 3,689,096 Ordinary Shares at an exercise price of £0.015339313479508 per share, pursuant to an agreement dated 23 April 2021 (“**DC Bould Options**”). The DC Bould Options were issued on the Initial Listing in consideration of the surrender of all of Professor Coverley’s historic options in Cizzle Biotechnology (the “**DC Options**”). The DC Bould Options are exercisable within three years of the date of the Initial Listing. Dawn Coverley intends to exercise the DC Bould Options in full following the publication of the Company’s next interim results. Exercise of all of the DC Bould Options would result in the Enlarged Share Capital being diluted by approximately 1.16%. The DC Bould Options represent approximately 0.98% of the Fully Diluted Enlarged Share Capital of the Company.
- 8.8 On 22 February 2022, the Company entered into unapproved option agreements in relation to options granted over a total of 19,741,345 Ordinary Shares to the members of the Board as set out below as at 3 November 2021 (“**Management Incentive Options**”) pursuant to a management incentive plan established by the Company on 3 November 2021 (“**Management Incentive Plan**”). The Management Incentive Options are exercisable at a price of 10p per share, an approximate 127% premium to the closing mid-market price of the Company’s shares on 3 November 2021 and are subject to certain vesting criteria being met, based on key deliverables being achieved, derived from the Company’s near to medium term business plan, together with further milestones identified by the Company. When step one of the performance and/or service conditions are deemed to have been met, to the satisfaction of such members of the Company’s Board who are not interested in the Management Incentive Plan, the option holder becomes unconditionally entitled to 50% of the options set out against their name below. Once all further performance and/or service conditions are deemed to have been met, the option holder becomes unconditionally entitled to the remaining options as set out against their name below and they are capable of exercise. From vesting, the option holder has 10 years to exercise the option before expiry. Exercise of all of the Management Incentive Options would result in the Enlarged Share Capital being diluted by approximately 5.91%. The Management Incentive Options represent approximately 5.23% of the Fully Diluted Enlarged Share Capital of the Company.

| Director | Options Issued |
|-----------------|-----------------------|
| Allan Syms | 5,068,956 |
| Dawn Coverley | 12,672,389 |
| Nigel Lee | 2,000,000 |

9. Material contracts

The following are summaries of each material contract, other than contracts entered into in the ordinary course of business, to which the Group is a party, within the period from 20 September 2020 to (and including) 20 September 2022 (being the period of two years immediately preceding the latest practicable Business Day prior to the publication of this Prospectus), or those which contain any provision under which any member of the Group has any obligation or entitlement which is material to the Group as at the date of this Document:

9.1.1 Cizzle Biotechnology Acquisition Agreements

On 23 April 2021, the Company entered into the Acquisition Agreements, pursuant to which the Company purchased the entire issued share capital of Cizzle Biotechnology from the Vendors. The Acquisition became effective of 14 May 2021 on the Initial Listing.

The consideration for the Acquisition was £21 million, satisfied by the issue of 206,310,904 Ordinary Shares in the Company. The limitation period in respect of warranty and indemnity claims under the Warrantor Acquisition Agreement expired on 31 March 2021 in the case of the general warranties, however in the case of a claim under the tax warranties or tax covenant, the limitation period does not expire until six years following completion of the Acquisition. The overall cap of the Warrantor in respect

of claims under the Warrantor Acquisition Agreement will not exceed the value of the shares received by the Warrantor. The Warrantor shall be entitled to settle any claim against them by selling such Ordinary Shares held by them as shall satisfy the claim.

The Acquisition Agreements are governed by the laws of England and Wales and the parties have irrevocably submitted to the exclusive jurisdiction of the courts of England and Wales in relation to any action or proceeding arising out of the Acquisition Agreements.

9.1.2 Lock-in and Orderly Market Deeds

On 23 April 2021, the Company, Novum Securities and the Locked-in and Orderly Market Parties each entered into a lock-in and orderly market agreement pursuant to which the Locked-in and Orderly Market Parties agreed that they would not, without the prior written consent of the Company and Novum Securities dispose of their ordinary shares in the Company or grant a right or charge over the shares for a period of 179 days commencing on the date of the Initial Listing, save in certain circumstances (“**Lock-in Arrangements**”). For a further 18 months thereafter, the Locked-in and Orderly Market Parties agreed that they would only dispose of the legal or beneficial interest in their shares through Novum Securities in order to maintain an orderly market, save where Novum Securities are unable to make the disposal within seven business days, following which the Locked-in and Orderly Market Parties may make the disposal through a broker of their choosing (“**Orderly Market Arrangements**”). Each Locked-in and Orderly Market Party gave warranties as to title and capacity over their holding over shares.

Whilst the Lock-in Arrangements have now ceased, the Orderly Market Arrangements are still in place until 14 May 2023. Novum Securities’ rights under these arrangements may be assigned to any successor broker duly appointed by the Company. Each agreement is governed by the courts of England.

9.1.3 2021 Placing Agreement

On 23 April 2021, Novum Securities, Allenby Capital Limited (“**Allenby Capital**”), the Company, the directors of the Company at that time (“**2021 Directors**”) and Dawn Coverley and Nigel Lee (as proposed directors at that time) entered into a placing agreement (“**2021 Placing Agreement**”) pursuant to which Novum Securities procured placees for the new ordinary shares to be issued on the Initial Listing (“**2021 Placing Shares**”) subject to the usual market standard conditions. The Company and the 2021 Directors provided customary warranties. Warranty claims were unlimited in terms of time and value in respect of the Company, but were limited to two full group audit periods plus six months (save for tax) in respect of the 2021 Directors. The warranty claims were also be limited to two times salary in respect of executive directors and one times salary in respect of non-executive directors. The Company indemnified Novum Securities and/or Allenby Capital in respect of a breach of the warranties, which was uncapped as to duration and quantum, save in the case of Novum Securities’ or Allenby Capital’s negligence, deceit, wilful default or fraud or material breach of the 2021 Placing Agreement, Takeover Code and (in the case of Novum Securities) the terms of the letter set out at paragraph 9.1.5 below, respectively. Post-admission restrictions applied to material variations to the terms of engagement of the 2021 Directors, any substantial transactions and any further share issues or grant of options without Allenby Capital’s prior consent. The agreement is governed by the laws of England and Wales.

9.1.4 Financial Adviser Engagement Letter

Pursuant to an agreement between Allenby Capital and the Company dated 16 March 2020, Allenby Capital was engaged by the Company to act exclusively as the lead financial adviser to the Company in connection with the Initial Listing for a corporate finance fee of £100,000 payable on admission on 14 May 2021.

Allenby has also been appointed under a separate agreement dated 22 April 2021 as an ongoing financial adviser for a period of not less than 12 months from the date of the Initial Listing for a fee of £25,000 per annum (reviewable by both parties following the minimum 12 month term). Under this arrangement, Allenby Capital are engaged to provide guidance and advice in connection with the Company’s ongoing admission to the London Stock Exchange Main Market as well as general corporate finance advice. In consideration for such services, the Company agrees to supply information to Allenby Capital as reasonably required for the performance of its duties, notify Allenby in advance and consult

on any matter contemplated by the Company which is material to its business and have in place sufficient procedures and controls to enable the Company to comply with the FCA and LSE rules and the EU Market Abuse Regulation, The engagement may be terminated with three months' notice.

9.1.5 Novum Securities Engagement Letter

Pursuant to a broker engagement letter entered into between the Company and Novum Securities on 17 March 2021 ("**Novum Engagement**"), the Company appointed Novum Securities to act as its joint broker in relation the Initial Listing. The appointment continues for a minimum of 24 months from the date of Initial Listing. During this period, the Company will give Novum Securities the first right of refusal on any fundraising on competitive terms.

As part of the payment terms in connection with the Initial Listing, the Novum Engagement provided that, on the date of the Initial Listing, the Company would issue to Pershing Nominees Limited 1,100,000 warrants over new ordinary shares in the Company, exercisable at the Issue Price as equals 5% of the gross aggregate value of the funds raised from investors introduced by Novum Securities in the Placing 1,100,000 10p per share ("**NSL Warrants**"). The NSL Warrants shall be exercisable at any time in the three years following the date of the Initial Listing. The Company agreed to retain Novum Securities as joint broker following the date of the Initial Listing and pay an annual corporate broking retainer fee at the rate of £25,000. In the first year this could be paid in either cash or equity at the 10p per share in order to not affect the working capital requirements. The Company has agreed to indemnify Novum Securities against any losses, damages, charges, expenses, claims, actions, liabilities, demands or proceedings arising in connection with, *inter alia*, Novum Securities carrying out the services under the Novum Engagement, provided such sum has not arisen as a result of Novum Securities' fraud, negligence or wilful default. The Novum Engagement does not contain a liability cap in relation to this indemnity.

The Novum Engagement also provided that the placees on the Initial Listing would receive warrants over a total of 11,000,000 Ordinary Shares at a price of 15p which are exercisable for three years from the date of the Initial Listing ("**2021 Placing Warrants**").

If the 2021 Placing Warrants are exercised then the Enlarged Share Capital would be diluted by approximately 3.38%. If the NSL Warrants are exercised then the Enlarged Share Capital would be diluted by approximately 0.35%.

9.1.6 Shakespeare Martineau Warrants

Shakespeare Martineau LLP was issued with warrants over 250,000 New Ordinary Shares on the date of the Initial Listing, which have an exercise price of 10p per share ("**Shakespeare Martineau Warrants**"). The Shakespeare Martineau Warrants became exercisable on 14 May 2021 and may be exercised at any time from that date until the third anniversary of the Initial Listing and will be automatically exercisable upon the price of the ordinary shares equalling 20p per share. The Company undertakes to find buyers in the market for such Ordinary Shares at that time. These warrants can be exercised through application to the Company.

If the Shakespeare Martineau Warrants are exercised then the Enlarged Share Capital will be diluted by approximately 0.08%. The Shakespeare Martineau Warrants represent approximately 0.07% of the Fully Diluted Enlarged Share Capital of the Company.

9.1.7 Share Option Agreement – Professor Dawn Coverley

Pursuant to a share option scheme adopted by Cizzle Biotechnology on 31 May 2012 ("**Cizzle Option Scheme**"), Professor Coverley was granted options over 10,988 ordinary shares of £0.01 each in the capital of Cizzle Biotechnology for an exercise price of £5.15 per share ("**DC Options**"). Subsequently and pursuant to an agreement dated 23 April 2021, Professor Coverley surrendered all of her DC Options in consideration for the issue of options over 3,689,096 Ordinary Shares in the Company on the Initial Listing at an exercise price of £0.015339313479508 per share, exercisable within three years of the Initial Listing ("**DC Bould Options**"). In addition, in consideration of the waiver of outstanding salary of approximately £166,432 (as accrued since September 2017 up to the date of the Initial Listing and which was deferred by agreement of the directors in order to conserve cash for patent

maintenance), Professor Coverley is entitled to a cash bonus from the Company equal to the total exercise price of the DC Bould Options of £56,588.20 (together with any tax payable thereon), payable on the exercise of the DC Bould Options. This cash sum will be used by the Company to settle the exercise price of the DC Bould Options upon exercise. Dawn Coverley intends to exercise the DC Bould Options in full following the publication of the Company's next interim results.

9.1.8 University of York Research Agreements

On 10 August 2021, the Company entered into a research agreement with the University of York for the development the Group's blood test for the early detection of lung cancer, and potentially other forms of cancer. The agreement contains confidentiality provisions and provides that any intellectual property arising from the results of the research shall vest in the Company. The project commenced on 13 September and terminated on 12 March 2022. On 7 April 2022, the Company entered into a new research agreement with the University to extend the research project for a further 12 months at a cost of £35,794 plus VAT on the same confidentiality and intellectual property terms. The agreement may be terminated by either party giving 3 months' written notice if in the reasonable opinion of that party it is no longer possible to achieve the objectives of the research project or in the event of a breach of the agreement (which cannot be rectified within 90 days). The Company agrees to indemnify the University and its employees against any loss, cost or claim arising out of the use of the research results under the agreement except to the extent that the such liability is caused by the University's gross negligence, wilful mis-design, misstatement or mis-transmission of any report or information. The University's liability under the agreement is limited to the amount of the fees due to it under the agreement. The agreement is governed by the laws of England and Wales.

9.1.9 SGSC Research and Development Agreement

On 22 October 2021, the Company entered into a research and development agreement with St George Street Capital ("**SGSC**") to develop a companion diagnostic test to address unmet needs in autoimmune diseases and pursuant to which SGSC has engaged the Company to carry out the required research. The agreement shall continue for a period of 24 months at which point it will either end or be renewed for a further 12 month period, unless terminated by either party with 90 days' written notice (such notice not to be given until after the 24-month period). The agreement may also be terminated by either party for material breach by the other party or failure to meet payment obligations under the agreement. The Company indemnifies SGSC for any losses, damages, liability, costs and expenses incurred by SGSC in connection with any action, demand or claim that use of the Company's intellectual property relating to research materials infringes the intellectual property rights of any third party, subject to certain exemptions. SGSC indemnify the Company on the same basis in connection with SGSC's intellectual property, subject to certain exemptions. The liability of both parties under the agreement is capped at £1 million. SGSC will pay the Group £200,000 upfront on commencement of the project, and further milestone payments totalling £1 million. The agreement is governed by the law of England and Wales.

9.1.10 Management Incentive Option Agreements

On 22 February 2022, the Company entered into option agreements in relation to unapproved options granted over a total of 19,741,345 Ordinary Shares to the members of the Board as set out below as at 3 November 2021 ("**Management Incentive Options**") pursuant to the unapproved share option scheme rules adopted by the Company on 3 November 2021 ("**Management Incentive Plan**"). The Management Incentive Options are exercisable at a price of 10p per share, an approximate 127% premium to the closing mid-market price of the Company's shares on 3 November 2021 and are subject to certain vesting criteria being met, based on key deliverables being achieved, derived from the company's near to medium term business plan, together with further milestones identified by the company. When step one of the performance and/or service conditions are deemed to have been met, to the satisfaction of such members of the company's board who are not interested in the Management Incentive Plan, the option holder becomes unconditionally entitled to 50% of the options set out against their name below. Once all further performance and/or service conditions are deemed to have been met, the option holder becomes unconditionally entitled to the remaining options as set out against their name below and they are capable of exercise. From vesting, the option holder has 10 years to exercise the option before expiry. The aggregate number of shares which may be placed under option under the Management Incentive Plan shall not exceed 10% of the Company's issued ordinary share capital for the time being. The options may not be transferred or assigned, save in respect of an option holder's

personal representatives on death. Exercise of all of the Management Incentive Options would result in the Enlarged Share Capital being diluted by approximately 5.91%. The Management Incentive Options represent approximately 5.23% of the Fully Diluted Enlarged Share Capital of the Company.

| Director | Options Issued |
|---------------|----------------|
| Allan Syms | 5,068,956 |
| Dawn Coverley | 12,672,389 |
| Nigel Lee | 2,000,000 |

9.1.11 Liquidity Equity Provider Engagement

Pursuant to an engagement letter dated 23 December 2021, the Company has engaged Axis Capital Markets Limited as its equity liquidity provider pursuant to which Axis will, *inter alia*, use reasonable endeavours to match buyers and sellers of the Ordinary Shares, prepare and publish research reports and commentary on the Company, provide intelligence on the Company's marketplace and provide advice on corporate and financial matters. Axis has been appointed for an initial period of 12 months following which, either party may terminate the engagement on giving 3 months' written notice. The engagement may also be terminated in the event of material breach of the agreement by the Company, the securities of the Company cease to be admitted to trading, insolvency of the Company or if Axis ceases to be regulated by the FCA, amongst other things.

The Company will pay an annual fee of £20,000 to Axis, together with a sales commission of 6% of the aggregate value of the funds raised from investors introduced by Axis or the Company, plus an additional commission representing a placing agent fee of 1% of the gross aggregate funds raised from investors introduced by Axis or the Company. In addition, the Company will grant Axis warrants on Admission, valid for 3 years from the date of issue, over ordinary shares equal to the value of 5% of the gross aggregate value of funds raised by Axis, exercisable at a 50% premium to the Issue Price. Should the Company be unable to pay the fees set out in the engagement letter, Axis will be entitled to instead accept other securities issued by the Company in lieu of cash.

The Company has agreed to indemnify Axis against any claims or losses in connection with, *inter alia*, Axis carrying out the services under the engagement, provided such sum has not been determined by a court to have arisen as a result of Axis' fraud, negligence or wilful misconduct or breach of the engagement where the circumstances giving rise to the breach were within Axis' reasonable control. Liability under the indemnity is not capped.

9.1.12 iCCAMT Licence Agreement

On 1 February 2022, a licence agreement was executed with the International Co-Innovation Centre for Advanced Medical Technology ("**iCCAMT**") and Shenzhen Intelliphecy Life Technologies Co., Ltd. ("**Intelliphecy**") (iCCAMT and Intelliphecy together being the "**China Partners**"), to grant the China Partners an exclusive and royalty-bearing licence to develop and use intellectual property and biological materials related to the CIZ1B variant in order to develop and market the Group's proprietary early lung cancer diagnostic tests in China. The licence will become non-exclusive, with the consent of the China Partners if the Company grants an exclusive worldwide licence to another licensee, on the condition that the China Partners are equitably compensated for any lost sales. The China Partners may grant sub-licences under the agreement on terms no less onerous. If the China Partners have not been able to validate reagents that specifically measure CIZ1B variants suitable for the development of a commercially valid product within one year of the date of the agreement, the parties will meet to discuss progress and either agree a revised development plan or terminate the agreement. The agreement may also be terminated for a breach of the terms of the agreement by either party (unless such breach can be rectified within 60 days), for insolvency or bankruptcy of the China Partners or in the event that the China Partners have been found to have misused the intellectual property. The China Partners will pay a 10% royalty to the Company on the sales of all products and services using its proprietary CIZ1B technology and from payment for monoclonal antibodies and reagents. The China Partners will be solely responsible for funding all activities in China including development, clinical trials, manufacturing, and distribution. The China Partners agree to indemnify the Company for any breach of the agreement terms

and for any use by its sub-licensees. The China Partners shall require its sub-licensees to indemnify the company on the same terms. The Company agrees to indemnify the China Partners for any use by the Company of the licensed IP in a way which is prohibited by the agreement. The agreement also contains confidentiality provisions.

The licence agreement is accompanied by a material transfer agreement dated 13 April 2022, which reiterates the intended use of the materials, confirms that the materials remain the sole property of the Company and further sets out permitted use of confidential information between the parties in order to protect proprietary materials being transferred to the China Partners in accordance with the above licence agreement.

9.1.13 Royalty Agreement in Inflammatory Pulmonary and Cardiovascular Disease

On 11 February 2022, the Company entered into an agreement with SGSC and Conduit Pharmaceuticals Limited ("**Conduit**") pursuant to which the Company has acquired a 5% economic interest in the commercialisation of the AZD 1656 asset or such other assets being developed by Conduit or SGSC to treat inflammatory pulmonary and cardiovascular disease ("**SGSC and Conduit Royalty Sharing Arrangement**"). Under this agreement, the Group will receive 5% of the balance all sums received by SGSC pursuant to any AstraZeneca ("**AZ**") commercialisation or sub-licence commercialisation of the AZD 1656 asset in inflammatory pulmonary and cardiovascular diseases, after the deduction of certain sums. The consideration due to SGSC is £1.88 million with the initial consideration of £1 million being settled through the issue of 25,000,000 new ordinary shares on 17 February 2022 at a price of 4p per share which, as stated in the agreement, was a premium to the Company's closing mid-market price on 11 February 2022. The remaining consideration of £0.88 million will be payable in either (i) cash, or (ii) new ordinary shares at 4p per share, at the Company's discretion, on the earlier of receiving shareholder approval to issue such shares or the first anniversary of the agreement (i.e. 11 February 2023). No warranties have been given and the agreement is governed by the laws of England and Wales.

9.1.14 CorePath Partnership Agreement

On 5 May 2022, the Company signed a heads of terms ("**HoT**") to partner with CorePath Laboratories PA ("**CorePath**") with the intention of forming a commercial relationship for the purposes of clinical pilots and trials, developing clinical and commercial relationships, developing and distributing CIZ products, reagents and laboratory services in the USA. The HoT envisages that the Company will receive a proposed royalty of 15% of sales of laboratory services and products based on the CIZ1B biomarker and other royalty sharing arrangements over products and services using the CIZ1B biomarker via CorePath in the USA.

The proposed partnership is conditional on (i) the approval by the board of directors of both parties, (ii) there being no material adverse change in the business or position of either party, (iii) there being no material adverse change in the technology, and (iv) there being no legislation or regulation proposed or passed that would prohibit or restrict the implementation of the proposed partnership.

The heads of terms are not legally binding save for costs and governing law. The HoT are, and all negotiations and agreement prepared in connection with the partnership will be, governed by the laws of England and Wales.

9.1.15 Marketing Agreement with Behnke Group

On 15 June 2022, the Company entered into a marketing agreement with The Behnke Group in the USA, pursuant to which The Behnke Group is engaged as a consultant with a view to provide strategic marketing and public relations advice in the USA. The agreement commenced on 1 February 2022 for an initial term of 12 months unless terminated by either party on one month's notice. The fees for the work undertaken shall be paid in a fees and share warrants package to be agreed between the parties. To date, the parties have not agreed a fee level but any such fee will be performance-related and paid out of revenues generated for the Company as a result of the services provided by The Behnke Group. The agreement does not grant any additional benefits, pension payments or holiday allowance.

9.1.16 Subscription Letters

Between 15 September 2022 and 20 September 2022, the Subscribers each entered into a subscription letter with the Company ("**Subscription Letters**") pursuant to which each Subscriber has undertaken to pay the aggregate Issue Price for the relevant number of Subscription Shares to be issued to them in the manner and by the time directed by the Company.

Each investor for Subscription Shares has agreed to become a member of the Company and agrees to subscribe for its allocated Subscription Shares at the Issue Price. To the fullest extent permitted by law, each Subscriber acknowledges and agrees that it will not be entitled to exercise any rights to rescind or terminate or otherwise withdraw from such commitment at any time. By agreeing to subscribe for Subscription Shares, each investor has warranted, acknowledged and agreed, amongst other things, that it has the necessary capacity and authority to subscribe for its Subscription Shares and that it has complied with all laws applicable to the Subscription. If the conditions to the Subscription are not satisfied and the Subscription does not proceed, any monies received from investors will be returned without interest to the account of the drawee bank from which they were originally debited as soon as practicable.

Application will be made for the Subscription Shares to be admitted to the Official List of the FCA by means of a Standard Listing and to trading on the Main Market of the London Stock Exchange.

Pursuant to the Subscription, the Company has conditionally raised £500,000, before expenses, through the issue of the Subscription Shares with investors at the Issue Price conditional, *inter alia*, upon Admission of the Subscription Shares becoming effective by 22 September 2022 (or such later time and/or date as the Company may specify, not being later than 30 September 2022).

In connection with the Subscription, the Company has agreed to issue 666,666 new Ordinary Shares to Optiva Securities Limited, conditional on Admission, at the Issue Price as settlement of a £10,000 commission fee ("**Commission Shares**"). The issue and allotment of the Commission Shares will result in the Existing Share Capital being diluted by approximately 0.24%. The Commission Shares will represent approximately 0.21% of the Enlarged Share Capital.

9.1.17 Facility Agreement

The Company entered into a facility agreement with E3 Fund SP ("the **Investor**") on 20 September 2022 ("**Facility Agreement**") pursuant to which the Investor will make available to the Company a facility of £500,000, conditional on Admission, for the purpose of working capital, for a term of 18 months ("**Facility**").

Under the terms of the Facility, a commitment fee of £25,000 will become payable by the Company to the Investor on execution of the Facility Agreement to be settled by way of the issue and allotment of 1,666,666 new Ordinary Shares at a price of 1.5p per share ("**Facility Shares**").

An initial drawdown of £50,000 will be available to the Company 180 days following the payment of the commitment fee (by way of issue of the Facility Shares) and further drawdowns up to the amount of the Facility may be requested by the Company or the Investor by either party giving notice written notice of such request.

Repayment of the Facility will be by way of issue and allotment of new Ordinary Shares in the capital of the Company at a price of 1.8p per share ("**Investor Shares**"). The Investor Shares are required to be issued to the Investor at the time of the relevant drawdown, will be credited as fully paid and will rank *pari passu* in all respects with all other Ordinary Shares in issue. Upon allotment and issue of the relevant Investor Shares, the Company will immediately apply for all such shares to be admitted to trading.

The Facility Agreement is governed by the laws of England and Wales.

10. Summary of Share Capital Structure and Fully Diluted Enlarged Share Capital

The following table shows a summary of the Company's share capital structure and Fully Diluted Enlarged Share Capital:

| | | Number | Percentage of Fully Diluted Enlarged Share Capital (%) | |
|---|--|--------------------------------|--|------------|
| Ordinary Share Class of 0.01p* | | | | |
| Fully Diluted Enlarged Share Capital | Enlarged Share Capital | Existing Ordinary Shares | 278,447,788 | 73.73 |
| | | Subscription Shares | 33,333,333 | 8.83 |
| | | Commission Shares | 666,666 | 0.18 |
| | | Facility Shares | 1,666,666 | 0.44 |
| | Investor Shares, Options and Warrants | DC Bould Options | 3,689,096 | 0.98 |
| | | Investor Shares | 27,777,777 | 7.35 |
| | | Shakespeare Martineau Warrants | 250,000 | 0.07 |
| | | 2021 Placing Warrants | 11,000,000 | 2.91 |
| | | NSL Warrants | 1,100,000 | 0.29 |
| | | CFO Options | 1,600 | 0.0004 |
| | | Management Incentive Options | 19,741,345 | 5.23 |
| | TOTAL | | 377,674,271 | 100 |
| | Deferred 'A' Share Class* | | | |
| | Deferred 'A' Shares of 0.99p | 225,158,220 | - | |
| | Deferred 'A' Shares of 0.01p | 12,383,625,615 | - | |
| | TOTAL | 12,608,748,905 | - | |

**The Deferred 'A' Shares are non-voting shares and are therefore not included in the Enlarged Share Capital or Fully Diluted Enlarged Share Capital figures*

If the Facility were to be drawn down in full and all Investor Shares were to be issued, the Enlarged Share Capital would be diluted by 8.12%.

If the Facility were to be drawn down in full and all Investor Shares were to be issued and if all options and warrants were to be exercised, the Enlarged Share Capital would be diluted by 16.83%.

11. Related Party Transactions

There have been no related party transactions since 31 December 2021 (being the date of the latest audited financial statements of the Company).

12. Litigation

12.1 Save as set out below in paragraph 12.2, there are no governmental, legal or arbitration proceedings (including any such proceedings which are pending or threatened) of which the Company is aware, which may have or have had during the 12 months immediately preceding the date of this Prospectus a significant effect on the financial position or profitability of the Company or any member of the Group.

12.2 On 19 June 2019, the Company and Antos Glogowski entered into a share purchase agreement in relation to the sale by the Company of the entire issued share capital of PhotonStar Technology Limited (“PTL”). As part of that transaction, the Company and PTL entered into a deed of settlement on the same date in relation to the settling of certain outstanding loans owed to the Company by PTL in exchange for 50% of certain R&D tax credits in respect of the year ended 31 December 2018 to the extent realised. Approximately £107,000 has been realised by PTL in respect of these R&D tax credits, of which the Company is entitled to approximately £53,500. This amount became due from PTL in April 2020. AG (as the owner of PTL) acknowledged the debt in writing and further acknowledged his intent to pay in May 2020. On 31 March 2022, the Company served a statutory demand on PTL for a sum of £56,424.86 but to date, has not received a response. The Company is taking advice from its professional advisers in relation to next steps.

13. Taxation

Shareholders should note that the tax legislation of the country in which they are resident and of the Company’s country of incorporation may have an impact on the income received from the New Ordinary Shares. The following paragraphs are intended as a general guide only for Shareholders who are resident in the UK for tax purposes, holding Ordinary Shares as investments and not as securities to be realised in the course of a trade, and are based on current legislation and HMRC practice. Any person who is in any doubt about his tax position, or who is subject to taxation in a jurisdiction other than the UK, should consult his own professional adviser immediately.

13.1 Taxation of dividends

13.1.1 General

Under current UK legislation, no tax is withheld from dividend payments by the Company. The Company assumes no obligation to withhold UK tax at source from dividend payments.

13.1.2 Individual Shareholders

13.1.2.1 A UK resident individual Shareholder will not be subject to income tax on a dividend such individual Shareholder receives from the Company if the total amount of dividend income received by the individual in the tax year (including the dividend from the Company) does not exceed a dividend allowance of £2,000, which will be taxed at a nil rate (the “Dividend Allowance”).

13.1.2.2 In determining the income tax rate or rates applicable to a UK resident individual Shareholder’s taxable income, dividend income is treated as the highest part of such individual Shareholder’s income (not including capital

gains). Dividend income that falls within the Dividend Allowance will count towards the basic or higher rate limits (as applicable) which may affect the rate of tax due on any dividend income in excess of the Dividend Allowance.

13.1.2.3 To the extent that a UK resident individual Shareholder's dividend income for the tax year exceeds the Dividend Allowance and, when treated as the highest part of such individual Shareholder's income, falls above such individual Shareholder's personal allowance but below the basic rate limit, such an individual Shareholder will be subject to tax on that dividend income at the dividend basic rate of 8.75%.

13.1.2.4 To the extent that such dividend income falls above the basic rate limit but below the higher rate limit, such an individual Shareholder will be subject to tax on that dividend income at the dividend higher rate of 33.75%.

13.1.2.5 To the extent that such dividend income falls above the higher rate limit, such an individual Shareholder will be subject to tax on that dividend income at the dividend additional rate of 39.35%.

13.1.3 Corporate Shareholders

UK resident corporate Shareholders (including authorised unit trusts and open-ended investment companies) and pension funds will not normally be liable to UK taxation on any dividend received on the Ordinary Shares.

13.1.4 Non-resident Shareholders

A Shareholder resident or otherwise subject to tax outside the UK (whether an individual or a body corporate) may be subject to foreign taxation on dividend income under local law. Shareholders to whom this may apply should obtain their own tax advice concerning tax liabilities on dividends received from the Company.

13.2 *Taxation of chargeable gains*

13.2.1 General

Shareholders who are resident for tax purposes in the UK may be liable to UK taxation on chargeable gains on a disposal of Ordinary Shares, depending upon their individual circumstances and subject to any available exemption or relief.

13.2.2 Individual Shareholders

United Kingdom resident individual Shareholders, depending upon their individual circumstances and any available reliefs, may be subject to capital gains tax at the prevailing rate on any disposals of Ordinary Shares. For individuals who are taxed at the basic rate, UK capital gains tax will be payable at the flat rate of 10%. For such individuals who are higher or additional rate taxpayers, UK capital gains tax will be payable at the flat rate of 20%. No indexation allowance is available to such Shareholders, but they may be entitled to an annual exemption from capital gains tax (£12,300 for the tax year 2022/2023).

13.2.3 Corporate Shareholders

Where a Shareholder is within the charge to corporation tax, a disposal of Ordinary Shares may give rise to a chargeable gain (or allowable loss) for the purposes of UK corporation tax, depending on the circumstances and subject to any available exemption or relief. Corporation tax is charged on chargeable gains at the rate applicable to that company. Indexation allowance may reduce the amount of chargeable gain that is subject to corporation tax, but may not create or increase a loss. The rate of UK corporation tax is 19%, currently scheduled to rise to 25% from 1 April 2023.

13.2.4 Non-resident Shareholders

A Shareholder who is permanently non-resident for tax purposes in the UK will not be liable to UK taxation on chargeable gains on disposing of Ordinary Shares unless the Shareholder carries on a trade, profession or vocation in the UK through a branch or agency and the Ordinary Shares disposed of are, or have been, used, held or acquired for the purposes of such trade, profession or vocation or for the purposes of such branch or agency. Such Shareholders may also be subject to tax under any law to which they are subject outside the UK.

13.2.5 Stamp Duty and Stamp Duty Reserve Tax

13.2.5.1 The statements below are intended as a guide to the general UK stamp duty and stamp duty reserve tax ("SDRT") position and do not apply to persons such as market makers, brokers, dealers or intermediaries.

13.2.5.2 In relation to stamp duty and SDRT:

- (a) The allocation and issue of the New Ordinary Shares will not give rise to a liability to stamp duty or SDRT.
- (b) Following Admission, the Ordinary Shares will be eligible securities traded on a recognised growth market (and not on any other recognised stock exchange) and accordingly no stamp duty or SDRT will be charged on the conveyance, transfer or sale of Ordinary Shares (nor will any stamp duty or SDRT be chargeable on any transfer of Ordinary Shares effected on a paperless basis through CREST).

14. General

- 14.1 Where information contained in this Prospectus has been sourced from a third party (as listed below), the Company confirms that such information has been accurately reproduced and, as far as the Company and the Directors are aware and are able to ascertain from information published by that third party, no facts have been omitted which would render the reproduced information inaccurate or misleading:
- 14.1.1 Part I – Letter from the Chairman: diagrams at Figure 1 within paragraph 3 (Technology); and
 - 14.1.2 Part I – Letter from the Chairman: information sourced within paragraph 4 (Future Strategy for the Group) under the heading 'USA'.
- 14.2 Novum Securities Limited of 57 Berkeley Square, London, United Kingdom, W1J 6ER has given and not withdrawn its written consent to the inclusion in this Prospectus of reference to its name in the form and context in which it appears.
- 14.3 Axis Capital Markets Limited of St Clements House, 27 Clements Lane, London EC4N 7AE has given and not withdrawn its written consent to the inclusion in this Prospectus of reference to its name in the form and context in which it appears.
- 14.4 PKF Littlejohn LLP of 15 Westferry Circus, London E14 4HD has given and not withdrawn its written consent to the inclusion in this Prospectus of reference to its name in the form and context in which it appears. PKF Littlejohn LLP who are also the auditors of the Company, is authorised and regulated by the Institute of Chartered Accountants in England and Wales.
- 14.5 The percentage dilution of the Existing Share Capital as a result of the Subscription and the issue and allotment of the Commission Shares and the Facility Shares is approximately 10.69%, 0.24% and 0.59%, respectively.

- 14.6 The percentage dilution of the Enlarged Share Capital as a result of the full draw down of the Facility resulting in the issue and allotment of the Investor Shares is approximately 8.12%.
- 14.7 The percentage dilution of the Enlarged Share Capital as a result of the issue and exercise of the following options and warrants are set out below:

| Options/Warrants | Percentage Dilution of the Enlarged Share Capital (%) |
|--------------------------------|--|
| DC Bould Options | 1.16 |
| Shakespeare Martineau Warrants | 0.08 |
| 2021 Placing Warrants | 3.38 |
| NSL Warrants | 0.35 |
| CFO Options | 0.001 |
| Management Incentive Options | 5.91 |

- 14.8 The accounting reference date of the Company is 31 December.
- 14.9 Assuming that the Subscription completes, it is expected that definitive share certificates in respect of the New Ordinary Shares will be despatched to Shareholders by hand or first class post by 27 September 2022. In respect of uncertificated New Ordinary Shares, it is expected that Shareholders' CREST stock accounts will be credited on 26 September 2022.
- 14.10 CREST is a paperless settlement procedure enabling securities to be evidenced otherwise than by a certificate and transferred otherwise than by written instrument. The Articles permit the holding and transfer of shares under CREST. The Company has applied for the New Ordinary Shares to be admitted to CREST and it is expected that the New Ordinary Shares will be so admitted, and accordingly enabled for settlement in CREST. The Ordinary Shares will be available to be issued in either registered form (i.e. certified) or electronic form (i.e. via CREST). The register of members of the Company is held and maintained by the Company's registrars, Neville Registrars Limited of Neville House, Steelpark Road, Halesowen, West Midlands B62 8HD.
- 14.11 The Company is not directly or indirectly owned or controlled by any party.
- 14.12 There are no arrangements known to the Company, the operation of which may at a subsequent date result in a change in control of the Company.
- 14.13 No dividends have been paid to shareholders by the Company in respect of any of the financial years covered by the historical financial information.
- 14.14 The Company regularly publishes announcements through the Regulatory Information Service and its website. The following is a summary of the information disclosed by the Company under the Market Abuse Regulation over the last 12 months which is relevant as at the date of this Prospectus:

| Date | Announcement Description |
|----------------|---|
| 18 August 2022 | Arcadia Clinical Trial Results Published for Cizzle Biotechnology's Royalty Bearing Interest in AZD1656 |
| 5 July 2022 | Update on Development of Proprietary Antibodies |
| 27 June 2022 | Result of AGM |
| 16 June 2022 | Marketing Agreement to Enhance Expansion in the US |
| 1 June 2022 | Posting of Annual Report and Notice of AGM |
| 30 May 2022 | Results for year ended 31 December 2021 |
| 6 May 2022 | Strategic Alliance re lung cancer detection in USA |

| | |
|-------------------|--|
| 11 April 2022 | Further Research Agreement with University of York |
| 7 March 2022 | Positive outcomes from Arcadia Trial re AZD1656 |
| 14 February 2022 | Royalty Acquisition Agreement |
| 3 February 2022 | China Royalty Agreement for Lung Cancer Detection |
| 25 November 2021 | Lung Cancer Detection Strategic Alliance in China |
| 4 November 2021 | Grant of Options |
| 22 October 2021 | Companion Diagnostic Supply Agreement with SGSC |
| 30 September 2021 | Interim results |
| 20 September 2021 | Agreement with St George Street Capital |
| 17 September 2021 | New Research Agreement with the University of York |
| 9 September 2021 | Encouraging progress on collaboration with SGSC |

14.15 There are no material conflicts of interest pertaining to the Subscription or Admission.

15. Documents Available

Copies of this Prospectus and the following documents will be available free of charge from the registered office of the Company during normal office hours, Saturday and Sundays excepted, for 12 months following the date of this Document and will also be available to download from the Company's website <https://cizzlebiotechnology.com/>:

- 15.1 memorandum and articles of association of the Company;
- 15.2 annual statutory accounts for the financial year ended 31 December 2021; and
- 15.3 all reports, letters and other documents, valuations and statements prepared by any expert at the Company's request which is included or referred to in this Prospectus.

21 September 2022

DEFINITIONS

Except where the context otherwise requires, the following definitions shall apply throughout this Document:

| | |
|---|--|
| "2021 Accounts" | the annual statutory accounts for the financial year ended 31 December 2021; |
| "2021 Placing Warrants" | the 11,000,000 warrants to subscribe for Ordinary Shares granted to the placees on the Initial Listing as more particularly described in paragraph 9.1.5 of Part IV of this Document; |
| "A Deferred Shares" | the A deferred shares of 0.99p and the A deferred shares of 0.01p each in the capital of the Company; |
| "Act" or the "Companies Act" | the Companies Act 2006 of the United Kingdom, as amended; |
| "acting in concert" | shall bear the meaning ascribed thereto in the Takeover Code; |
| "Acquisition" | the acquisition by the Company of the entire issued share capital of Cizzle Biotechnology which became effective on 14 May 2021, pursuant to the terms of the Acquisition Agreements; |
| "Acquisition Agreements" | the Warrantor Acquisition Agreement and the Investor Acquisition Agreement; |
| "Admission" | the admission of the New Ordinary Shares to the standard listing segment of the Official List and to trading on the London Stock Exchange's Main Market for listed securities; |
| "AIM" | the market of that name operated by the London Stock Exchange; |
| "Articles of Association" or "Articles" | the articles of association of the Company, a summary of which is set out in paragraph 4 of Part IV of this Document; |
| "Associates" | <p>an associate of a Director, being:</p> <ul style="list-style-type: none">(i) the family of such a person;(ii) the trustees (acting as such) of any trust of which the individual or any of the individual's family is a beneficiary or discretionary object (other than a trust which is either an occupational pension scheme as defined in regulation 3 of the Financial Services and Markets Act 2000 (Regulated Activities) Order 2001, or an employees' share scheme which does not, in either case, have the effect of conferring benefits on persons all or most of whom are related parties);(iii) any company in whose equity shares such a person individually or taken together with his or her family (or if a director, individually or taken together with his family and any other director of that company) are directly or indirectly interested (or have a conditional or contingent entitlement to become interested) to the extent that they are or could be able:<ul style="list-style-type: none">- to exercise or control the exercise of 30% or more of the votes (excluding treasury shares) able to be cast |

| | |
|---|---|
| | <ul style="list-style-type: none"> at general meetings on all, or substantially all, matters; or - to appoint or remove directors holding a majority of voting rights at board meetings on all, or substantially all, matters; (iv) any other company which is its subsidiary undertaking, parent undertaking or subsidiary undertaking of its parent undertaking; (v) any company whose directors are accustomed to act in accordance with a Director's directions or instructions; and (vi) any company in the capital of which a Director, either alone or together with any other company within (iv) or (v) or both taken together, is (or would on the fulfilment of a condition or the occurrence of a contingency be) interested in the manner described in (iii); |
| "certificated" or "in certificated form" | a share or other security not recorded on the relevant register of the relevant company as being in uncertificated form in CREST; |
| "CFO Options" | a right to acquire Ordinary Shares in the Company granted in accordance with, and subject to, the Company's Executive Share Option Scheme as more particularly described in paragraph 8 of Part IV of this Document; |
| "Commission Shares" | 666,666 new Ordinary Shares to be issued by the Company to Optiva Securities Limited at the Issue Price as commission in connection with the Subscription; |
| "Company" | Cizzle Biotechnology Holdings plc; |
| "Cizzle Biotechnology" | Cizzle Biotechnology Limited, a company registered in England and Wales with registered number 05249093; |
| "CREST" | the computerised settlement system (as defined in the CREST Regulations) operated by Euroclear which facilitates the transfer of title to shares; |
| "CREST Regulations" | the Uncertificated Securities Regulations 2001 (SI 2001/3755) as amended from time to time, and any applicable rules made under those regulations; |
| "DC Bould Options" | a right to acquire New Ordinary Shares in the Company granted to Dawn Coverley as more particularly described in paragraph 8.7 of Part IV of this Document; |
| "Directors" or "Board" | the directors of the Company at the date of this Document whose names are set out on page 20 of this Document, including any duly authorised committee of the board of directors of the Company and " Director " is to be construed accordingly; |
| "Disclosure Guidance and Transparency Rules" or "DTR" | the Disclosure Guidance and Transparency Rules sourcebook made by the FCA under Part VI of FSMA; |

| | |
|--|--|
| "Document" or "Prospectus" | this prospectus; |
| "Enlarged Share Capital" | the issued ordinary share capital of the Company immediately following Admission, comprising the Existing Ordinary Shares and the New Ordinary Shares; |
| "Euroclear" | Euroclear UK & Ireland Limited, the operator of CREST; |
| "Existing Ordinary Shares" or "Existing Share Capital" | the 278,447,788 ordinary shares of 0.01p in issue at the date of this Document; |
| "Facility" | a facility of £500,000 to be made available to the Company by the Investor, conditional on Admission, for the purpose of working capital, for a term of 18 months pursuant to the terms of the Facility Agreement; |
| "Facility Agreement" | a facility agreement between the Company and the Investor dated 20 September 2022, pursuant to which the Investor will make the Facility available to the Company, conditional on Admission as more particularly described in paragraph 9.1.17 of Part IV of this Document; |
| "Facility Shares" | 1,666,666 new Ordinary Shares to be issued by the Company to the Investor at the Issue Price by way of settlement of a commitment fee of £25,000 payable by the Company to the Investor on execution of the Facility Agreement; |
| "FCA" | the United Kingdom Financial Conduct Authority, the statutory regulator under FSMA responsible for the regulation of the United Kingdom financial services industry; |
| "FSMA" | the UK Financial Services and Markets Act 2000, as amended, including any regulations made pursuant thereto; |
| "Fully Diluted Enlarged Share Capital" | the issued ordinary share capital of the Company immediately following Admission, comprising the New Ordinary Shares to be issued pursuant to the Subscription, the issue and allotment of the Commission Shares and the Facility Shares and assuming that the Facility has been drawn down in full resulting in the issue and allotment of the Investor Shares and that the DC Bould Options, the Shakespeare Martineau Warrants, the CFO Options, the Management Incentive Options, the 2021 Placing Warrants and the NSL Warrants have been issued and exercised in full; |
| "GBP" or "£" or "pence" or "p" | pounds sterling and pence, the lawful currency from time to time of the United Kingdom; |
| "Group" | the Company and/or its current subsidiaries; |
| "HMRC" | Her Majesty's Revenue and Customs; |
| "Initial Listing" | the initial admission of the Company's ordinary share capital to the standard listing segment of the Official List and to trading on the |

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| | London Stock Exchange's Main Market for listed securities on 14 May 2021; |
| "Investor" | E3 Fund SP c/o, IFINA UK Ltd., Ifina House, 6 The Court, Holywell Business Park, Northfield Road, Southam, Warwickshire, CV47 OFS; |
| "Investor Acquisition Agreement" | the agreement dated 23 April 2021 made between (i) the Vendors (other than the Warrantor) relating to the Acquisition, details of which are set out in paragraph 9.1.1 of Part IV of this Document; |
| "Investor Shares" | 27,777,777 new Ordinary Shares to be issued in connection with the drawdown of the Facility pursuant to the terms of the Facility Agreement; |
| "ISIN" | international security identification number; |
| "Issue Price" | 1.5p per Subscription Share, being the price at which the Subscription Shares are to be issued; |
| "Listing Rules" | the Listing Rules made by the FCA under Part VI of FSMA; |
| "Lock-in Deeds" | the 2021 agreements between the Company, Novum Securities and each of the Locked-in and Orderly Market Parties, further details of which are contained in paragraph 9.1.2 of Part IV of this Document; |
| "Locked-in and Orderly Market Parties" | the Vendors (excluding The Ridings Early Growth Investment Company Limited and Nikki Hodges) and their Associates; |
| "London Stock Exchange" | London Stock Exchange plc; |
| "Main Market" | the regulated market of the London Stock Exchange for officially listed securities; |
| "Market Abuse Regulation" or "MAR" | the UK version of the Market Abuse Regulation (EU) 596/2014, which is part of UK law by virtue of the European Union (Withdrawal) Act 2018; |
| "New Ordinary Shares" or "New Share Capital" | the Subscription Shares, the Commission Shares and the Facility Shares; |
| "Novum Securities" | Novum Securities Limited, which is incorporated in England and Wales with company number 05879560 and having its registered office address at 57 Berkeley Square, London, United Kingdom, W1J 6ER, which at the date of this Document is authorised and regulated by the FCA; |
| "NSL Warrants" | the 1,100,000 warrants to subscribe for Ordinary Shares granted to Pershing Nominees Limited as more particularly described in paragraph 9.1.5 of Part IV of this Document; |
| "Official List" | the Official List of the FCA; |
| "Ordinary Shares" | ordinary shares of 0.01p each in the capital of the Company; |
| "Panel" | the UK Panel on Takeovers and Mergers; |

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| "Proposals" | means the Subscription and Admission; |
| "Prospectus Regulation" | the UK version of Prospectus Regulation (EU) 2017/1129, which is part of UK law by virtue of the European Union (Withdrawal) Act 2018; |
| "Prospectus Regulation Rules" | the Prospectus Regulation Rules issued by the FCA and made under Part VI of FSMA and pursuant to the Prospectus Regulation; |
| "Registrar" | Neville Registrars Limited of Neville House, Steelpark Road, Halesowen, West Midlands B62 8HD; |
| "RIS" of "RNS" | Regulatory Information Service authorised by the Financial Conduct Authority to disseminate regulatory announcements; |
| "Shakespeare Martineau Warrants" | the 250,000 warrants to subscribe for Ordinary Shares granted to Shakespeare Martineau LLP as more particularly described in paragraph 9.1.6 of Part IV of this Document; |
| "Share Dealing Code" | the Company's share dealing code as referred to in Part I of this Document; |
| "Shareholders" or "Existing Shareholders" | holders of Existing Ordinary Shares from time to time, each individually being a " Shareholder "; |
| "Standard Listing" | admission to the Official List of the FCA by means of a standard listing under Chapter 14 of the Listing Rules; |
| "Subscribers" | proposed subscribers for Subscription Shares at the Issue Price in the Subscription; |
| "Subscription" | the proposed conditional Subscription of the Subscription Shares at the Issue Price with Subscribers pursuant to the Subscription Letters; |
| "Subscription Letters" | the conditional agreements dated between 15 September 2022 and 20 September 2022 between the Company and each Subscriber relating to the Subscription and Admission, further details of which are set out in paragraph 9.1.16 of Part IV of this Document; |
| "Subscription Shares" | the 33,333,333 new ordinary shares of 0.01p each in the capital of the Company to be issued by the Company and subscribed for by Subscribers pursuant to the Subscription, conditional on Admission (and each a Subscription Share); |
| "Takeover Code" | the City Code on Takeovers and Mergers (as published by the Panel); |
| "uncertificated" or "in uncertificated form" | a share or other security recorded on the relevant register of the relevant company concerned as being held in uncertificated form in CREST and title to which, by virtue of the CREST Regulations, may be transferred by means of CREST; |
| "United Kingdom" or "UK" | the United Kingdom of Great Britain and Northern Ireland; |
| "VAT" | value added tax; |

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| "Vendors" | the vendors of the issued share capital of Cizzle Biotechnology which was acquired by the Company pursuant to the Acquisition Agreements; |
| "Warrantor" | Dawn Coverley; and |
| "Warrantor Acquisition Agreement" | the conditional agreement dated 23 April 2021 made between: (i) the Company; and (ii) the Warrantor relating to the Acquisition, details of which are set out in paragraph 9.1.1 of Part IV of this Document. |

GLOSSARY OF TECHNICAL TERMS

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| 510(k) or 510(k) clearance | A premarket submission made to the FDA to demonstrate that a medical device to be marketed in the USA is at least as safe and effective, that is, substantially equivalent, to a currently legally marketed device; |
| biomarker | A biological molecule found in blood, other body fluids, or tissues that is a sign of a normal or abnormal process, or of a condition or disease; |
| CE or CE marking | Conformité Européenne marking, a mandatory European health and safety product label used on many products placed on the single market in the European Economic Area. The CE marking certifies that a product has met European Union consumer safety, health or environmental requirements; |
| CIZ1 | 'Cdkn1A-interacting zinc finger protein 1', a naturally occurring protein comprised of 898 amino acid residues, which is found in the cell nucleus, and has been shown to play a role in DNA replication and cell cycle regulation; |
| CIZ1B | A variant of CIZ1, which is missing eight amino acids relative to CIZ1 and is being investigated by Cizzle Biotechnology as a biomarker for the early detection of lung cancer; |
| COPD | Chronic obstructive pulmonary disease, which is a group of lung conditions that cause breathing difficulties, including emphysema and chronic bronchitis; |
| CRO | A contract research organisation, being a firm that provides outsourced clinical trial services or other research support services to the healthcare industry; |
| CT | Computerised tomography, being a form of radiography where a three-dimensional image of a body structure is constructed by computer from a series of plane cross-sectional X-ray images; |
| DNA | Deoxyribonucleic acid, the carrier of genetic information; |
| ELISA | Enzyme-linked immunosorbent assay. Development of the ELISA was based on the observation that antibodies or antigens can be adsorbed to a solid surface and still participate in high-affinity binding. The term ELISA now refers to a wide range of immunoassays some of which do not involve enzymatic reactions. However, the commonality among all ELISAs is the use of antibodies, which play a major role in determining the sensitivity and specificity of the assay; |
| FDA | The U.S. Food and Drug Administration, the government agency that has regulatory jurisdiction over medical devices in the USA; |
| immunoassay | A biochemical test that measures the presence or concentration of a specified form of molecule in a solution through the use of an antibody or an antigen; |
| LDT | Laboratory-developed test; |

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| lung nodules | Small growths on the lung, which may be noncancerous or cancerous; |
| monoclonal antibody | a homogenous population of antibodies that recognize one epitope only. They are secreted by and purified from hybridoma cell cultures; |
| NHS | The UK's National Health Service; |
| point of care test or point of care testing | Point of care testing (POCT) is defined as 'diagnostic testing that is performed near to or at the site of the patient care with the result leading to possible change in the care of the patient'. In simple terms, it is laboratory testing performed in a non-laboratory setting, usually by appropriately trained non-laboratory staff; |
| primary health care provider | Primary health care providers could be a general practitioner (GP), but could also be other primary and community care staff and health and care organisations, providing integrated services to their local populations; and |
| western blot | An analytical technique which is used to pinpoint a specific protein in a given sample. It exploits the ability of an enzyme or fluorescence-labelled primary antibody to bind to its specific antigen. Although it has high sensitivity and specificity it can still produce erroneous results when the antibody reacts with a non-target protein. It is technically demanding, making it unsuitable for large-scale screening. |