THIS ANNOUNCEMENT CONTAINS INSIDE INFORMATION FOR THE PURPOSES OF ARTICLE 7 OF EU REGULATION 596/2014 (WHICH FORMS PART OF DOMESTIC UK LAW PURSUANT TO THE EUROPEAN UNION (WITHDRAWAL) ACT 2018 ("EUWA")) ("UK MAR").

21 October 2024

Cizzle Biotechnology Holdings plc

("Cizzle", "Cizzle Biotechnology", or the "Company")

Execution of Strategic Licensing and Partnership Agreement for North America

Receipt of initial upfront US$300,000 Royalty Payment

Cizzle Biotechnology, the UK based diagnostics developer, is pleased to announce that it has today signed an exclusive licensing and partnership agreement for its proprietary CIZ1B biomarker test to help detect early-stage lung cancer, throughout the USA and Canada ("North America") (the "Agreement"). This is the critical first step in the Company's global licensing and partnership strategy to bring Cizzle's non-invasive, cost effective CIZ1B biomarker lung cancer blood test to market next year.

Execution of the Agreement follows the Company entering into a Memorandum of Understanding ("MOU") on 2 April 2024 with an independently funded USA based corporation, Cizzle Bio Inc ("BIO"). The Agreement meets an important planned milestone in the Company's licensing and partnership strategy to launch the CIZ1B biomarker test in North America, one of world's largest markets.

BIO brings a US based, highly experienced management team with extensive clinical expertise, who are incentivised through fixed milestone payments to accelerate the deployment of the test into the North American market. The Agreement aligns both parties' strategic goals through a royalty payment structure, including an initial payment to the Company of US$300,000 and equity participation where the Company can share in any future value of BIO.

Key Highlights

- **Exclusive North American License**: The agreement grants BIO exclusive rights to the CIZ1B biomarker technology for early lung cancer detection in North America.
- **Initial Payment**: Cizzle has received an upfront royalty payment of US$300,000 as part of a 10% royalty on gross sales after tax, with guaranteed minimum royalty payments totalling US$2 million over the next 30 months.
- **BIO's Funding**: BIO will cover all costs for clinical evaluations, accreditation, and marketing of CIZ1B diagnostic tests in North America.
- **Equity Stake**: Cizzle is entitled to receive capital stock in BIO pursuant to a simple agreement for future equity ("SAFE"), for no cash consideration, or a non-diluted cash bonus on a sale of BIO.
- **Global Benefits**: Cizzle retains rights to improvements and evidence of CIZ1B utility, to support sales in the rest of the world.

- **Revenue Streams for Growth:** Cizzle now has established revenue streams, positioning the Company to pursue its next strategic milestones. This includes expanding into new regions and advancing the development of a point-of-care ("POC") test.
- **Value-Creating Partnership:** The Agreement aligns the interests of both parties to create long-term value, ensuring Cizzle shares in BIO's success as they expand.
- **Collaboration with Moffitt Cancer Center**: BIO has already secured partnerships with leading US cancer centres, resulting in the Company announcing a collaboration with the Moffitt Cancer Center, the top cancer facility in Florida and the Southeast US.
- **Upcoming Laboratory Contract**: BIO expects to announce its first clinical lab contract soon.
- **Accreditation and Launch Timeline**: BIO aims to achieve CLIA accreditation for the CIZ1B biomarker test before the end of 2024, with a full market launch with approved reimbursement codes planned for April 2025.

The management team of BIO have already made significant progress in establishing relationships with clinicians, hospitals and US cancer centres of excellence which resulted in the Company announcing on 9 September 2024 a major clinical evaluation with the Moffitt Cancer Center, the number one cancer centre in the South East USA. This is a significant development because the project will be carried out in the real-world setting of a busy comprehensive cancer centre with a large lung cancer practice and a high volume, well-organised clinical thoracic research programme. While the blood sample tests for the Moffitt study will be conducted in Cizzle Biotechnology founder, Professor Dawn Coverley's, laboratory at the University of York, it is envisaged that future clinical evaluations in the USA will be conducted in BIO's planned network of CAP and CLIA accredited laboratories.

The Moffitt study highlights that of the low number of lung cancer patients surviving long term, most are early-stage patients who had surgical resection. Unfortunately, with current screening using low dose chest CT scans ("LDCT"), only 17%* are found with localised, potentially curable disease. Although LDCT is an effective tool in high-risk populations, only 3.9%* of eligible people obtain a scan. Moffitt believe that developing a high sensitivity and specificity blood-based biomarker would greatly facilitate the evaluation of the 1.6 million new lung nodules found yearly on CT scans in the USA, differentiating malignant from benign nodules. The study also recognises that a highly sensitive and specific biomarker could be employed for initial lung cancer screening with just a blood test at the primary care physicians' office. If positive, then this result would strongly argue for recommending a subsequent LDCT.

The Agreement with BIO addresses the funding and need for a US-based commercial and clinical team to deliver the CIZ1B test at scale, both in the laboratory and eventually as a point of care test in the US without requiring further Cizzle shareholder equity. With established revenue streams in place, Cizzle is now well-positioned to pursue its next strategic milestones, including expanding into new markets and advancing the development of a POC test in other regions.

BIO expects to shortly announce its first contract with a CAP (College of American Pathologists) accredited laboratory partner and to register the CIZ1B biomarker as a CLIA

(Clinical Laboratory Improvement Amendments) LDT (Laboratory Developed Test) with the FDA (US Food and Drug Administration). The aim is to achieve CLIA Certification in before the end of 2024 with the full product launch, with insurer reimbursement, planned in April 2025. BIO is also in discussions to further extend clinical evaluations at a number of other cancer centre's of excellence across the US.

Partnering with BIO and choosing the name Cizzle Bio strengthens the "Cizzle" brand and brings significant US funding to facilitate rapidly building the market in North America. In addition, this provides the Company an equity position in BIO, post the completion of its initial funding round for no cash consideration. BIO has already paid a non-refundable upfront fee of US$100,000 for its 120-day exclusivity period during the MOU, in addition to the US$300,000 upfront royalty payment now received.

*Source:
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9768892/#:~:text=As%20of%202020%2C%20LCS%2DLDCT,only%201.0%25%20%5B6%5D

Further Information

Cizzle's vision is to meet the challenges of early lung cancer detection, reduce premature cancer deaths, improve survival rates and increase quality of life for cancer patients by helping detect cancer as early as possible through a simple blood test.

It is widely considered that to beat cancer, early detection and diagnosis is arguably the single most important and impactful objective, with patients diagnosed early having the best chance of curative treatment and long-term survival, reducing patient stress and improving healthcare economic performance.

By focussing on the systematic development and commercialisation of novel and proprietary clinical diagnostic tests for the early detection of cancer, particularly where there is an unmet clinical need, the Company now has a platform technology based on the ability to detect a stable plasma biomarker, a variant of CIZ1 known as CIZ1B. 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.

The Company believes this pivotal phase to accelerate the development, regulatory approval and launch of its biomarker diagnostic tests in North America through the establishment of an independently financed and locally managed business is the appropriate route to take.

BIO, guided by Bill Behnke, a veteran healthcare executive, actively cultivates strategic partnerships across the healthcare spectrum—from cancer centers to insurance companies. These relationships enhance the reach and effectiveness of our diagnostic solutions, ensuring they benefit a wide and diverse patient population.

Commenting, Allan Syms, Executive Chairman of Cizzle Biotechnology, said:

"The Agreement with Cizzle Bio is the critical first step in the Company's global licensing and partnership strategy to bring our non-invasive, cost effective, CIZ1B biomarker lung cancer blood test to market in 2025. The structure of the Agreement aligns both parties to create

value for all the stakeholders and fulfils the Company's overarching vision to saving lives. We are delighted to have teamed up with a highly experienced team bringing clinical excellence and capability, as well as financial capacity to build a material business in North America. Working with the BIO team will secure significant guaranteed minimum and ongoing licensing revenue for the Company as well as free equity participation in BIO, allowing the Company to fund expansion in other regions using the same partnership model and focus on the development plans for a point of care test further enhancing the Company's value."

Bill Behnke, CEO of BIO, commented:

"Another very important milestone achieved in our tireless efforts to screen patients early and save lives. Cizzle Bio Inc is excited about commercializing all the wonderful research work that our UK partners have progressed over the years in lung cancer. Cizzle Bio, through our vast network in the USA is in discussions with multiple hospitals, cancer centers, advocacy associations, pulmonary critical care and primary care physician groups and screening programs. Our mission is clear, to screen as many patients as we can out of the 14.2 million recommended by the US Preventative Services Task Force that should be tested for lung cancer each year, resulting in saving millions of lives and increasing the 5.5% of people currently being test to a much more robust number."

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About Cizzle Biotechnology

Cizzle is developing a blood test to help in the early detection of lung cancer. Based on the pioneering work of Professor Coverley and colleagues, at the University of York, on a naturally occurring cell nuclear protein involved in DNA replication called CIZ1, they discovered that a variant called CIZ1B is highly associated with the presence of early-stage cancer. The company has now entered into commercial royalty bearing licensing agreements and collaborations with leading centres of excellence in cancer for the use of its proprietary technology as part of its strategy to bring its non-intrusive, cost-effective blood test to market. Cizzle was admitted to the Standard segment of the main market of the London Stock Exchange in May 2021.

For more information, please see https://cizzlebiotechnology.com

You can also follow the Company through its twitter account @CizzlePlc and on LinkedIn.

About Cizzle Bio Inc

Cizzle Bio Inc, a company registered in Texas USA, stands at the forefront of biotechnological innovation, dedicated to revolutionizing the detection of lung cancer through groundbreaking diagnostic tools. With exclusive rights to detect the CIZ1B Biomarker in the USA and Canada, we are driven by a commitment to improve early cancer detection and enhance patient outcomes.