Check-Cap Issues Letter to Shareholders

ISFIYA, Israel, Jan. 5, 2022 /PRNewswire/ -- Check-Cap Ltd. (the "Company" or "Check-Cap") (NASDAQ: CHEK), (NASDAQ: CHEKZ), a clinical stage medical diagnostics company advancing the development of C-Scan®, the firs and only patient-friendly preparation-free screening test to detect polyps before they may transform into colorectal cancer (CRC), today issued the following letter from its chief executive officer, Alex Ovadia, to its shareholders and the investment community:

Dear Check-Cap Shareholders,

We have greatly appreciated your support throughout 2021, a year during which we have continued our progress as we prepare to initiate our U.S. pivotal study of C-Scan, including strengthening our manufacturing capacity, clinical affairs team and our balance sheet. As we begin 2022, I want to take the opportunity to share updates on our C-Scan program as well as provide a recap of our 2021 progress.

I will now walk you through our key updates in more detail:

U.S. Pivotal Study: In 2021, we received approval from the Food and Drug Administration (FDA) of our Investigational Device Exemption (IDE) application, permitting the Company to initiate the pivotal study in the U.S Recently, we submitted a supplement to the FDA to amend the study design to add a first part to the trial that is designed to enable further calibration of the system, specifically for the average risk U.S. population. We expect the agency to provide its feedback during Q1 2022 and subject to agency's approval for our amended study design, we anticipate beginning the initial part of the U.S. pivotal study in the March-April 2022 timeframe and th second part of the pivotal study in Q4 2022.

This expanded two-part pivotal study will initially focus on device calibration and enhancement of our algorithms, followed by a second portion which will compare performance of C-Scan to traditional colonoscopy, in accordance with the currently approved IDE. This second comparative portion of the study will be analyzed for statistical significance.

We plan to provide updates on the planned amended study design, as well as key milestones associated with the study progress, throughout 2022. In parallel, we continue to gather data at our Israeli sites to further calibrate th system.

Manufacturing: In 2021, Check-Cap significantly expanded C-Scan's manufacturing capacity and its on-site production line. Taken together, these supply chain and quality infrastructure improvements are designed to ensure optimized execution of the U.S. pivotal study. The Company plans to continue investing in infrastructure enhancements to further improve its capacity and quality.

Clinical Team: In the third quarter of 2021, we strengthened our clinical team, with the appointment of Dr. Hani Brenner-Lavie as Vice President of Clinical Affairs and additional clinical professionals. This expansion is critical to assure our preparedness for U.S. clinical operations as we roll out our pivotal study across multiple study sites. W also plan to enhance the team with additional U.S. clinical hires to allow pivotal study execution across the U.S. sites.

Breakthrough Device Designation: In early 2021, the FDA approved the Company's Breakthrough Device Designation. We believe that this strengthens C-Scan's recognition as an alternative method to address the significant unmet need for patient-friendly CRC screening.

CE Mark: In late 2021, the European Medical Device Regulation (MDR) issued a renewal of the Company's CE mark approval for an additional five years. This is a regulatory achievement for the Company, among the first medical device companies to comply with the strict requirements of this new advanced directive. The updated MDR CE approval does not only permit Check-Cap to commercialize C-Scan in Europe but provides further extern validation of the Company's quality systems. While currently we remain focused primarily on the U.S. market, the renewal enables us to continue to explore opportunities to launch C-Scan in other international markets.

Cash balance: In 2021, we raised net proceeds of $31.8 million from a registered direct offering in July, in addition to $19.2 million from a warrant exercise in the first quarter, which strengthened our financial position. As of September 30, 2021, our cash and cash equivalents, restricted cash and short-term bank deposits were $56.8 million. We continue to expect this cash to fund operations well into 2023.

Patents: In 2021, we were granted four new patents:

- "Position Estimation of Imaging Capsule in Gastrointestinal Tract" granted in the U.S, covering C-Scan's proprietary tracking technology, which enables real time tracking of the capsule and its activation when it moves throughout the colon. This functionality allows for optimal scanning along the gastrointestinal (GI) tract while maintaining low energy consumption during the procedure. The patent also covers the capsule positioning data recording utilized by the C-Scan analysis suite, which enables gastroenterologists to make a clinical decision and generate a report with their diagnosis and recommendations. Corresponding patents were issued in Japan and China and patents were approved for granting in Europe and Israel.
- "Image reconstruction with radioactive imaging" was granted in Israel, covering aspects of the technology developed by Check-Cap to perform image reconstruction of the data acquired by the C-Scan imaging capsule. This unique iterative algorithm is optimal for image reconstruction of X-ray fluorescence combined with Compton scattering for intra lumen colon imaging. Corresponding patents were also granted in the U.S, in Europe and China.
- "Nano particle detection with X-ray capsule" was granted in Europe, which covers aspects of a synergic technology for C-Scan, using gold nanoparticles attached to cancer avid antibodies that can allow selective detection of colon cancer tissue within the colon. This future technology developed by us has the potential t allow C-Scan to discriminately detect and localize cancer lesions in real time as well as potentially detect rar flat lesions that currently go mostly undetected with other screening technologies. A corresponding patent was also granted in the U.S.
- "Imaging capsule location detection" was granted in the U.S, which covers aspects of the technology developed by Check-Cap to positively identify entrance of the C-Scan capsule to the colon with high accurac A corresponding patent was also granted in Europe.

With these patents we have accumulated 54 granted patents and one allowed patent in main world markets, covering various aspects of our technology. In addition, we have 14 additional pending patents applications in the pipeline.

NASDAQ Listing Compliance: On December 23, 2021, we were notified by Nasdaq that we were not in compliance with the minimum bid price requirement for continued listing, which requires listed securities to maintain a minimum bid price of $1.00 per share. We have until June 21, 2022 to regain compliance with the minimum bid price requirement. In the event that we do not regain compliance after the initial 180-day period, w may then be eligible for an additional six-month extension if we meet certain listing requirements.

Looking Forward to 2022: We have had a productive year preparing our operations and clinical teams for our U.S. pivotal study and strengthening our balance sheet. Our near-term focus in the first quarter of 2022 is to obtain FDA approval of our amended pivotal study design and kick off our U.S. pivotal study following this approval.

Colorectal cancer screening rates remain low globally, especially due to the invasiveness of the colonoscopy procedure, with only about two in three adults[1] among the targeted screening population conducting a colonoscopy in the U.S. Adherence in other regions of the world, such as Europe and Asia, is even lower[2],[3]. Lo invasiveness tests, such as fecal occult blood tests (FOBT), exist and are included in multiple colorectal screening guidelines across countries. Other non-invasive tests such as liquid biopsy are in development. Yet, all these tests are primarily designed to detect cancer and demonstrate low sensitivity in detecting pre-cancerous polyps. As such, they do not necessarily provide patients with the time window to pre-empt the disease. We believe there is large unmet need for a patient-friendly colorectal cancer screening option, such as C-Scan, that can overcome barriers to colonoscopy screening while also enabling detection of polyps before they turn into cancer, versus detecting cancer once it has already appeared. We look forward to continuing to make clinical progress in 2022 and potentially making C-Scan available to the U.S. population as soon as possible.

We would like to thank our dedicated employees who work tirelessly to advance C-Scan, and you, our shareholders, for your continued partnership. We appreciate your support and aim to provide multiple progress updates throughout 2022.

Sincerely,
Alex Ovadia
Chief Executive Officer
Check-Cap

About Check-Cap

Check-Cap is a clinical stage medical diagnostics company aiming to redefine colorectal cancer (CRC) screening through the introduction of C-Scan®, the first and only patient-friendly preparation-free screening test to detect polyps before they may transform into colorectal cancer and enable early intervention and cancer prevention. Th Company's disruptive capsule-based screening technology aims to significantly increase screening adherence worldwide and help millions of people to stay healthy through preventive CRC screening. C-Scan uses an ultra-low dose X-ray capsule, an integrated positioning, control and recording system, as well as proprietary

software to generate a 3D map of the inner lining of the colon as it travels naturally along the gastrointestinal tract. C-Scan is non-invasive and requires no sedation. Unlike other capsule technologies, it requires no bowel preparation, allowing the patients to continue their daily routine with no interruption. C-Scan is not intended to replace colonoscopy. A positive C-Scan result should be followed by colonoscopy.

Legal Notice Regarding Forward-Looking Statements

This press release contains "forward-looking statements" about the Company's expectations, beliefs or intentions regarding, among other things, its product development efforts, business, financial condition, results of operations, strategies or prospects. Words such as "may," "should," "could," "would," "predicts," "potential," "continue," "expects," "anticipates," "future," "intends," "plans," "believes," "estimates," and similar expressions, as well as statements in future tense, often signify forward-looking statements. Forward-looking statements should not be read as a guarantee of future performance or results and may not be accurate indications of when such performance or results will be achieved. Forward-looking statements are based on information that the Company has when those statements are made or management's good faith belief as of that time with respect to future events, and are subject to risks and uncertainties that could cause actual performance or results to differ materially from those expressed in or suggested by the forward-looking statements. For a discussion of these and other risks that could cause such differences and that may affect the realization of forward-looking statements, please refer to the "Forward-looking Statements" and "Risk Factors" in the Company's Annual Report on Form 20-F for the year ended December 31, 2020 and other filings with the Securities and Exchange Commission (SEC). Investors and security holders are urged to read these documents free of charge on the SEC's web site at http://www.sec.gov. The Company assumes no obligation to publicly update or revise its forward-looking statements as a result of new information, future events or otherwise.

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[1] Colorectal Cancer Facts & Figures. American Cancer Society. 2017-2019.

[2] https://www.cancer-days.eu/res/file/presentations/2017/04-state-of-the-art-04b-seufferlein.pdf

[3] Schreuders EH, Ruco A, Rabeneck L*, et al.* Colorectal cancer screening: a global overview of existing programmes. *Gut* 2015;**64:**1637-1649.

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Additional assets available online: Photos (1)