**Raphael Pharmaceutical Issues Letter to Shareholders**

*Highlights Company's exclusive relationship with Rambam Health Care Campus, differentiated cannabinoid-based technology platform, promising lead product candidate for rheumatoid arthritis, recently commenced clinical study, broader pipeline opportunities, and overall mission and vision*

**New York, NY – July 9, 2024** – Raphael Pharmaceutical Inc. ("Raphael Pharmaceutical" or the "Company") (OTCQB: RAPH), a clinical-stage biotechnology company advancing a novel cannabinoid-based research platform, today issued the following letter to shareholders from its Chief Executive Officer and Chairman, Shlomo Pilo.

Dear Fellow Shareholders,

As we enter the second half of 2024, Raphael Pharmaceutical has reached an exciting and pivotal moment in its journey to create new, improved, cost-effective treatment options for a variety of inflammatory diseases based on the application of cannabinoids, which are naturally occurring compounds found in the cannabis plant.

In this inaugural letter to shareholders, I will touch on our research roots via an exclusive relationship with Rambam Health Care Campus ("Rambam"), our differentiated cannabinoid-based technology platform, our promising lead product candidate for rheumatoid arthritis, our recently commenced clinical study, our broader pipeline opportunities, and our corporate mission and vision.

Exclusive Relationship with Rambam

While Raphael Pharmaceutical has been a public company since May 2021, our research roots go back to 2019 when our Chief Technology Officer, Dr. Igal Louria-Hayon, established the Medical Cannabis Research and Innovation Center ("MCRIC") at Israel's esteemed Rambam Health Care Campus. One of the largest teaching hospitals in the country and a hub for groundbreaking medical innovation and research, Rambam provides cutting-edge medical facilities, labs, equipment, technologies, human donor cell banks, and databases that facilitate the cannabinoid research efforts of Dr. Louria-Hayon and his team of medical professionals at MCRIC.

In July 2019, we entered into a sponsored research agreement with Rambam, effectively providing Raphael Pharmaceutical with exclusive access to this world-class cannabinoid research and development program—a unique advantage, especially for a company of our size. Since 2019, we have been funding MCRIC's research in exchange for potential future royalties on product candidates under development. Dr. Louria-Hayon's expertise in cannabinoids and intercellular communications, along with over five years of cumulative research at MCRIC, has produced a differentiated research platform and promising product development opportunities for Raphael Pharmaceutical.

Differentiated Cannabinoid-Based Technology Platform

Our core research platform is distinguished by in-depth scientific understanding of the complex interplay among: (1) the human body's internal endocannabinoid system; (2) external cannabinoids derived from select strains of cannabis; (3) intercellular communications; and (4) inflammatory/immune cell response.

We are delving deeper than anecdotal evidence, deciphering the mechanisms by which cannabis works at the molecular and biochemical levels. Our proprietary real time-polymerase chain reaction method thus far has identified 12 different receptors to cannabinoids in both human and mouse models. We are mapping these receptors and decoding how cannabinoids impact the network of intercellular communications, particularly related to the function of immune cells during periods of inflammation.

Based on our knowledge of which cannabinoid receptors participate in the downregulation of inflammation in cells, we have created natural formulations containing highly purified cannabinoids from select non-psychoactive strains of cannabis with excellent anti-inflammatory potential. Our patentable formulations are designed to interact and communicate with the endocannabinoid system in the human body, activating cannabinoid receptors expressed by immune cells. We believe that our platform technology can be applied to a variety of chronic conditions linked to inflammation, such as rheumatoid arthritis.

Promising Lead Product Candidate for Rheumatoid Arthritis

The rheumatoid arthritis patient population is large and growing. According to a report published in *The Lancet Rheumatology* on September 25, 2023, the number of individuals globally with rheumatoid arthritis will grow by approximately 80% from 18 million in 2020 to an estimated 32 million in 2050. Despite the prevalence of this condition, we believe that there is an unmet clinical need to address the symptoms and suffering of these patients within the current treatment landscape. Meeting this need is our mission.

We are very encouraged by the progress to date of our lead product candidate ("HPC1") for the treatment of rheumatoid arthritis, which is a chronic autoimmune disease characterized by, among other symptoms, chronic joint pain and inflammation, fever, fatigue, and loss of appetite. Extensive preclinical research, including both in vitro and mouse model studies, by our partners at Rambam suggest that HPC1 reduces pro-inflammatory cytokines—such as TNF Alpha, Interleukin-1beta and Interleukin 6—thereby demonstrating potential to slow the progression of rheumatoid arthritis by acting as an anti-inflammatory agent.

We believe our HPC1 product candidate has the potential to become, if approved by the U.S. Food and Drug Administration ("FDA"), an attractive treatment option to existing rheumatoid arthritis therapies, some of which can produce pronounced side effects, be prohibitively expensive and/or deliver inadequate efficacy. We look forward to the opportunity to better serve rheumatoid arthritis patients with a novel therapy that improves quality of life and slows disease progression, in a cost-effective format.

Recently Commenced Clinical Study

In May of this year, we commenced an in-human proof of concept clinical study for HPC1 in the United States, under the coordination of the contract research organization Citruslabs. The study will evaluate the efficacy of HPC1 in patients with active rheumatoid arthritis. We enrolled the first of 12 total patients in May and anticipate completing the study as soon as the end of 2024. We will keep you updated as we progress toward this potential positive milestone, which could be a watershed moment for the Company. If the study proves successful, our go-forward pathways include potentially partnering with a larger organization or proceeding to Phase II trials on our own.

Broader Pipeline Opportunities

Among broader pipeline opportunities beyond rheumatoid arthritis, our pre-clinical research has demonstrated the potential of cannabinoid-based treatment for chronic lung inflammation. Using cells derived from human donors, as well as a mouse model for systemic inflammation and severe lung inflammation, we identified a specific high-cannabidiol, non-psychoactive strain of cannabis ("CBX") that appears effective in preventing cytokine storms while also inhibiting the migration of immune cells to the lungs. The findings of our research partner, Rambam, were published in *Frontiers in Immunology* in May 2022. We also are developing a novel molecule-based formula as a treatment for patients with autoimmune

disease and chronic lung inflammation. Our pre-clinical activities continue with the goal of commencing FDA Phase I clinical trials in 2025. We believe our cannabinoid-based technology platform can be applied to myriad other areas, ranging from oncology to personalized medicine, and we will keep you updated as we pioneer and advance new product candidates.

Mission and Vision

I will conclude this letter with some perspectives on our corporate mission and vision. First and foremost, we believe that medical solutions should be accessible to everyone ("*for the people*") and anticipate that our products will be affordable, lower-cost options – a small fraction of the price of existing drugs on the market. Our overriding goal is to deliver new products that enhance quality of life while improving outcomes for patients suffering from inflammatory diseases.

We envision an asset-light, low capex business model that contemplates royalty-based agreements and outsourcing arrangements with contract research organizations, growers, GMP-approved manufactures, and licensed-approved distributors. After pursuing clinical studies and approval for our products in the United States via the FDA, we intend to proceed to Europe via the European Medicines Agency ("EMA"), and then the rest of the world.

Our team believes our stock represents a modest investment for a company with potentially ground-breaking medical solutions that address vast and growing markets. Moving forward, we intend to interact with shareholders and members of the financial community on a more routine basis, maintaining a spirit of transparency and integrity in our communications.

I thank you for your continued support and look forward to updating you on our research progress during the second half of 2024 and beyond.

Sincerely,

Shlomo Pilo
Chairman and CEO

**About Raphael Pharmaceutical Inc.**

Raphael Pharmaceutical Inc. ("Raphael") (OTCQB: RAPH) is a clinical-stage biotechnology company focused on advancing a novel cannabinoid-based research platform for the treatment of various inflammatory diseases. Raphael's lead product candidate, HPC1, is a highly purified cannabinoid formulation developed for the treatment of rheumatoid arthritis.

For more information, please visit https://www.raphaelpharmaceutical.com/.

**Cautionary Note Regarding Forward-Looking Statements**

Certain statements contained in this press release constitute "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. These statements are predictive in nature and are identified by the use of the terms "will," "look forward to" and "aim," and similar words indicating possible future expectations, events or actions. Such forward-looking statements are based on current expectations, assumptions, estimates and projections about our business and our industry, and are not guarantees of our future performance. These statements are subject to a number of known and unknown risks, uncertainties and other factors, many of which are beyond our ability to control or predict, which may cause actual events to be materially different from those expressed or implied herein. The Company has provided additional information about the risks facing our business in its most recent annual report on

Form 10-K, and any subsequent periodic and current reports on Forms 10-Q and 8-K, filed by it with the Securities and Exchange Commission. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date the statement was made and are expressly qualified in their entirety by the cautionary statements set forth herein and in the filings with the Securities and Exchange Commission identified above, which you should read in their entirety before making an investment decision with respect to our securities. We undertake no obligation to update or revise any forward-looking statements contained in this release, whether as a result of new information, future events or otherwise, except as required by applicable law.

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