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Dear Stockholder:

I am pleased to write my first letter to you as newly appointed Chief Executive Officer of Rafael Pharmaceuticals, Inc. Having first served as Chief Business Officer and more recently Chief Operating Officer, I would like to thank the Board, led by our Chairman Mr. Howard Jonas, for the trust they have placed in me. I would also like to thank you - our stockholders - for your commitment to Rafael. Having been in the industry for over thirty years in companies such as Novartis and Bristol Myers Squibb, I am truly excited about Rafael's future.

As an update on our recent activities, as you may notice from our logo we have renamed ourselves Rafael Pharmaceuticals, Inc. "Rafael" is the biblical angel of healing. In fact, the literal interpretation of Rafael is "God heals". At Rafael Pharmaceuticals, we take our name as our mission and are committed to develop breakthrough drugs, that we believe will change how oncologists practice medicine.

I would like to thank our team for achieving many milestones in moving the Company forward and welcome some new team members as well.

I want to welcome the following Board Members, whom we are extremely honored to have joined us, including:

Jean-Pierre Sommadossi, Ph.D.: Renowned entrepreneur and Principal Founder, Chairman and CEO of Atea Pharmaceuticals, Inc. Dr. Sommadossi is also the Principal Founder of Idenix Pharmaceuticals, Inc. and a Co-Founder of Pharmasset, Inc., both of which had successful multi-billion dollar exits. Dr. Sommadossi has agreed to serve as Vice Chairman of the Board.

Richard Axel, M.D.: University Professor in the Department of Neuroscience at Columbia University; Investigator at the Howard Hughes Medical Institute, and 2004 winner of the "Nobel Prize in Physiology or Medicine".

Richard Scheller, Ph.D.: Chief Science Officer of Google-backed 23andMe and 2013 winner of the Lasker Award. Dr. Scheller is also a former Head of Genentech Research and Early Development (2009-2014) and member of Genentech's original scientific team which synthesized Somatostatin; former member of Roche Corporate Executive Committee; previously a professor at Stanford University Medical Center (1982-2001) and an Investigator at the Howard Hughes Medical Institute.



Chi Van Dang, M.D., Ph.D.: Scientific Director of Ludwig Cancer Research and former Director of the Abramson Cancer Center of the University of Pennsylvania. Dr. Dang is considered by many to be the world's leading authority on cancer metabolism. Dr. Dang will also serve as Chair of Rafael's Scientific and Medical Advisory Boards.

Newly appointed counsel to the Board:

Jay P. Lefkowitz: Renowned lawyer within the pharmaceutical industry and a senior partner at Kirkland & Ellis and member of the Firm's Global Executive Management Committee; Adjunct Professor at Columbia Law School. Jay also had a distinguished career in government, serving as a White House advisor to two former Presidents and as United States Special Envoy for Human Rights in North Korea.

We have also made new appointments to our management team. Most notably we have added:

Tim Pardee MD, Ph.D. Chief Medical Officer: Dr. Tim Pardee is currently an Associate Professor and the Director of Leukemia Translational Research at the Comprehensive Cancer Center of Wake Forest Baptist Medical Center. Dr. Pardee received his Ph.D. and MD degrees with honors from The State University of New York at Buffalo. He went on to train in Internal Medicine at Massachusetts General Hospital, did his fellowship training at Stony Brook University Medical center and post-doctoral training in the laboratory of Scott Lowe at Cold Spring Harbor Laboratory.

Mike Hu, Ph.D. VP, Research and Development: Dr. Hu has 18 years of experience in clinical and pre-clinical research, pharmaceutical drug development, and academia. He has previously held leadership and management roles at Novartis, GlaxoSmithKline and Jazz Pharmaceuticals. Over his career, Dr. Hu has primarily focused on building up pipelines for big pharma and small biotech companies in oncology and hematology related therapeutic areas. He has contributed to the development, submission, approval and life cycle management of 18 drugs in various indications including multi-billion-dollar franchises. Dr. Hu earned his Ph.D. in Pharmaceutical Sciences from Shenyang Pharmaceutical University. His appointment in Rafael was intended to strengthen our foundation in science to build its R&D function even further.

Robert Chapman, Ph.D., Vice-President, Manufacturing: Dr. Chapman has extensive experience finding solutions to technical and regulatory challenges in CMC including process development, preformulation and analytical chemistry. Dr. Chapman has managed teams either directly or virtually, through CROs and CMOs, developing chemical and drug product processes and analytical methods, performing process and method validation and preformulation at Purdue Pharma and Cephalon. He led teams responsible for development and transfer to manufacturing of API processes at Roche and Mallinckrodt and performed Due Diligence at GSK, defining and mitigating risks associated with development of



contractual relationships with companies in areas ranging from research to clinical and pharmaceutical development. He earned his B.S. in chemistry from Southern Methodist University and his Ph.D in organic chemistry from Florida State University followed by post-doctoral training at the University of Texas, Austin.

Todd Spradau, Ph.D., Head of Intellectual Property: Dr. Spradau joined Rafael Pharmaceuticals as Head of Intellectual Property (IP) in March 2018. Dr. Spradau has more than 18 years of experience in intellectual property law, and has worked as in-house counsel for leading pharmaceutical companies for the past 15 years. At Rafael, he is responsible for strategic leadership of IP-related aspects of the business, including patent protection, licensing, regulatory exclusivity, and strategic planning. Prior to joining Rafael, Dr. Spradau served as Senior Director & Associate General Patent Counsel, BD for Teva Pharmaceuticals, where he conducted IP due diligence and agreement negotiation in support of Teva's specialty business development group. Todd earned his J.D. from NYU and his Ph.D. in organic chemistry from the University of Illinois at Urbana-Champaign.

We have many incredible additions to our Scientific and Medical Advisory Boards which can be found at our site www.rafaelpharma.com.

The foundation of our Company is our leading science in the field of cancer metabolism. On this facet, we have more recently characterized the major molecular targets that CPI-613 attacks (Zachar, et al., 2011, *J. Mol. Med.* **89**:1137; Stuart et al., 2014, *Cancer & Metabolism* **2**:4; Bingham, et al., 2014, *Exp.Rev.Clin.Pharma.* **7**: 837). We have continued to investigate the details of tumor cell responses to this novel agent class, with diverse implications both for immediate, near-term clinical development (6 months - 2 years) and for longer-term drug discovery and development (over the next 2-5 years). For example, we have discovered that the selective assault of CPI-613 on tumor cells activates a series of responses and regulatory circuits (apparently constituting an attempted survival or homeostatic response to the drug). Our novel insights into this response open several important new avenues to substantially improve clinical deployment of CPI-613. Two cases illustrate this new approach to improving clinical power. On one hand, the tumor cell response to CPI-613 accelerates uptake of proteins from the surrounding fluids (including tissue fluid in the tumors). Among these proteins is albumin and many traditional chemotherapeutic drugs are taken up by tumor cells as albumin complexes. Thus, we can predict which traditional chemotherapeutic drugs will synergize with CPI-613 in patients. On the other hand, the changes in tumor cell metabolism in response to CPI-613 exposure open extensive new avenues to exploit existing drugs targeting these processes to substantially enhance/expand CPI-613 efficacy.

FDA Interaction regarding End of Phase I studies:

One of our biggest milestones came in February 2017 with our first ever face-to-face meetings with the FDA. Two briefing packages, in both pancreatic cancer and Acute Myeloid Leukemia (AML), were reviewed. The review included evaluating broad aspects of



CPI-613 development including pre-clinical, clinical safety and efficacy experience in the Phase I trials. The agency guidance and discussion were very thoughtful and solid paths forward for both indications were discussed. For both the indications FDA clears way for pivotal trials.

Based on the agency's feedback, Rafael is planning to initiate Phase III registrational trials for both pancreatic cancer and acute myeloid leukemia by mid-2018.

In a Phase I trial for Metastatic Pancreatic Adenocarcinoma, 20 patients were dosed with CPI-613 in combination with modified FOLFIRINOX (a standard of care). The study identified a well-tolerated dose for CPI-613 with this chemotherapy regimen. Objective Response Rate (ORR) was achieved in 61% of patients, median Overall Survival (OS) and median Progression Free Survival (PFS) estimated as per the latest available data (March 2018) were 19.7 months and 9.9 months respectively. These values were substantially higher than the published historical Phase III cohort of FOLFIRINOX (ORR: 31.6%, median OS: 11.1 months and median PFS: 6.4 months). This study has demonstrated that CPI-613 can be given safely in combination with modified FOLFIRINOX with a very promising signal of increased efficacy. The result of this study was published in Lancet Oncology (May 2017).

Two trials were conducted to investigate the safety and efficacy of CPI-613 in combination with high dose cytarabine and mitoxantrone (CHAM) in patients with relapsed or refractory AML. Overall, the treatment was well tolerated. A total of 67 were patients dosed in this phase I study and 62 were evaluable for efficacy. In overall patient population, the Complete Remission (CR) was 42%. In elderly patients (60 years or older, N =32), the CR is 38% with median overall survival (OS) of 6.9 months. These values were substantially higher than historical cohort of HAMA (high dose cytarabine in combination with mitoxantrone and asparaginase) with 34% CR in overall patient population, 27% CR with 5.2 months median OS in elderly patients with relapsed or refractory AML.

Recently Rafael received Orphan Drug Designation (ODD) from FDA for Burkitt's Lymphoma (January 2018) and Peripheral T-Cell Lymphoma (March 2018). This makes us one of the only oncology company with five Orphan designations [Pancreatic Cancer, AML, Myelodysplastic Syndrome (MDS), Burkitt's Lymphoma and Peripheral T-Cell Lymphoma (PTCL)].

We have more recently developed several external collaborations with academic institutions such as Memorial Sloan Kettering Cancer Center (MSKCC) for Lymphoma, New York University (NYU) and Jefferson University for Pancreatic Cancer.

In collaboration with a large pharma, Rafael has started investigating CPI-613 in combination with immuno-oncology (IO) drugs in a pre-clinical setting. Based on the preclinical study result, this collaboration may extend further for the clinical development of CPI-613 in combination with IO drugs.



We have also published promising new clinical trial results of CPI-613 in both hematological malignancies and solid tumors.

Given these compelling results, we continue to believe in the long-term opportunity of CPI-613 to broadly treat cancer.

Intellectual Property

As a large part of the value of any pharmaceutical company, we continue to maintain our patent estate to CPI-613 and to build our patent estate to other lipoic acid derivatives . Our patent estate to CPI-613 includes three U.S. patents as well as patents in eleven foreign countries, including countries in Europe, Australia, Japan, China, Mexico, Israel, and other countries.

I look forward to steering Rafael toward the aims set out for it from the very beginning. The mantra of the Company was “conquering cancer”. We will do our best to make that mantra a reality.

Patients suffering from aggressive cancers with severe medical unmet needs are eagerly waiting for new drugs which can increase their survival and improve their quality of life. Keeping forefront the motto: “One Patient At A Time”, Rafael Pharmaceuticals is striving to help these patients and thereby bring a ray of hope.

Warm Regards,

Best Regards,

Sanjeev Luther
Chief Executive Officer
Rafael Pharmaceuticals, Inc.

“One Patient At A Time”

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