UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

M.D.L. NO. 1430
CIVIL ACTION NO. 01-10861

IN RE LUPRON® MARKETING AND
SALES PRACTICES LITIGATION

MEMORANDUM ACKNOWLEDGING THE RECEIPT
AND REVIEW OF THE
A. DAVID MAZZONE PROGRAMMATIC REPORT #8

March 31, 2015

STEARNS, DJ.

On March 30, 2015, Dr. Philip Kantoff of the Dana-Farber/Harvard Cancer Center (DF/HCC), the principal investigator for the A. David Mazzone Research Awards Program (Program), and co-principal investigator, Dr. Jonathan Simon, President of the Prostate Cancer Foundation (PCF), submitted the eighth in a series of Program Reports. This Report covers the period from July 1, 2014, to December 31, 2014.

Prior to the reporting period, in 2014, the court authorized the distribution of the remaining $160,000 of Program funds. DF/HCC issued a special 2014 Request for Applications (RFA) to solicit grant proposals in the areas of Community Outreach and Disparities Research. With the additional money, the Program was able to fund two new Disparities Research grants of $90,000 and $50,000. The Program allocated the

remaining $20,000 to Student Training through the DF/HCC Cure Program. PCF also awarded its final $500,000 matching grant during the same period.

Dr. Kantoff and Dr. Simon report that the special RFA grants were awarded through the screening and evaluation process established in previous years for communicating, collecting, reviewing, and selecting projects. The DF/HCC RFAs were publicized in venues relevant to Community Outreach and Disparities Research. Proposals were vetted by peer reviewers with expertise in the field. A merit score for each proposal was determined based on the published review criteria after extensive discussion by the peer committee, which made the final recommendations to Dr. Kantoff.

The first grant ($50,000 for two years) was awarded to principal investigator Zoltan Szallasi, MD, Children's Hospital, Boston; co-principal investigator, Matthew Freedman, MD, DFCI; and collaborator Mark Pomerantz, MD, DFCI, for the research proposal: *Whole genome sequencing based identification of clinically relevant genomic aberrations specific to prostate cancer cases in African Americans*. In their application, the investigators noted that while the medical community has been long aware that prostate cancer disproportionately affects African

Americans (who are diagnosed at an earlier age, progress more quickly, and are three times more likely to die of the disease), no systematic study has ever compared the cancerous genome between African American and European American prostate cancer patients. The investigators will seek to identify somatic genomic aberrations that are predominantly present or absent in prostate cancers afflicting African Americans. To do so, they will analyze the cancer genome of twenty-seven African Americans and one hundred Caucasian patients to determine structural, copy number, and mutational variations that are predominantly present in one as opposed to the other group. Any genomic aberrations will be validated in an independent cohort and correlated with the clinical course of disease. The results will enable diagnosis and more aggressive treatments, and may also provide therapeutic targets.

The second grant ($90,000 for two years) was awarded to principal investigator Mark Preston MD, MPH, Brigham and Women's Hospital and collaborator Lorelei Mucci, ScD, Harvard School of Public Health for the proposal: *Do Baseline Prostate Specific Antigen (PSA) Levels Predict Advanced Prostate Cancer in African-American Men?* The investigators acknowledge that while prostate specific antigen (PSA) screening has been shown to reduce mortality from prostate cancer, the screening is

controversial because of the risk of over-diagnosis and over-treatment. The investigators note that no study to date has examined the predictive ability of PSA among African-American men, a group with a substantially higher prostate cancer incidence and mortality than white men. To enhance screening strategies, the investigators propose leveraging the Southern Community Cohort Study (SCCS), a well-established, prospective cohort that includes a high-proportion of African-American men, to determine the predictive ability of baseline PSA testing in African-American men during midlife.

As anticipated in the last report, the PCF issued an RFA for its final $500,000 Mazzone Special Challenge Award. It selected as grantees and principal investigators David Baltimore, Ph.D., President Emeritus, and Robert Andrews Millikan Professor of Biology at the California Institute of Technology (CIT); together with collaborators Owen N. Witte, M.D., University of California, Los Angeles (UCLA), professor of microbiology, immunology, and molecular genetics; Lili Yang, Ph.D., UCLA assistant professor of microbiology, immunology, and molecular genetics; and Michael T. Bethune, Ph.D., senior postdoctoral fellow in biology at CIT. Their study - *T Cell Receptor Gene Therapy for Treatment of Lethal Prostate Cancer* – will seek to devise a new strategy for discovering

antigenic targets of T cell immunity. By cloning T cell receptors (TCRs) that are enriched among prostate cancer-reactive T cells (that is, tumor-infiltrating T cells or T cells that expand when co-cultured with a prostate cancer cell line), the investigators hope to identify TCRs that recognize the most immunogenic prostate tumor antigens. They will then construct soluble reagents from these TCRs and use them to select cognate antigens from a library of HLA-A2-bound peptides displayed on the surface of yeast. This represents a fundamentally new approach to cancer antigen discovery that is expected to have broad applicability to other T cell-driven immune responses for which antigenic targets are unknown. The investigators will seek to promote the use of TCR gene therapy for prostate cancer, and to use a competition-based assay to select the prostate-reactive TCRs that are most highly expressed upon T cell transduction, thereby maximizing their potential for clinical application. They hope to provide proof-of-concept studies showing that the primary danger of TCR gene therapy – lethal graft-vs-host disease resulting from TCR mispairing – can be addressed by a novel and general strategy of swapping domains between the TCR α and β chains. This should streamline the development of new TCR gene therapies by establishing measures to improve the safety and efficacy of TCR candidates. By comparing TCR gene therapies in their efficacy, the

investigators will seek to categorize newly discovered antigens as therapeutic targets for SCPC and castration-resistant adenocarcinoma, or both. Finally, they will investigate the extent to which vaccination with these novel antigenic targets potentiates TCR gene therapy in vivo. All tumor models, antigenic vaccines, and TCRs tested will be of human origin.

The court firmly believes these three innovative studies will make an invaluable contribution to the goals of the Mazzone Program as it nears its conclusion. The court looks forward to receipt of the September 30, 2015 Annual Progress Report.

/s/ Richard G. Steams
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United States District Judge