Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operation

The following discussion should be read in conjunction with the attached financial statements and notes thereto. This Quarterly Report on Form 10-Q, including the following sections, contains forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995. These statements are subject to risks and uncertainties that could cause actual results and events to differ materially from those expressed or implied by such forward-looking statements. For a detailed discussion of these risks and uncertainties, see "Risk Factors" in our Annual Report on Form 10-K. We caution the reader not to place undue reliance on these forward-looking statements, which reflect management's analysis only as of the date of this Quarterly Report on Form 10-Q. We undertake no obligation to update forward-looking statements to reflect events or circumstances occurring after the date of this Quarterly Report on Form 10-Q. Throughout this discussion, unless the context specifies or implies otherwise, the terms "ESSA," "the Company," "we," "us," and "our" refer to ESSA Pharma Inc. and its subsidiaries. For a discussion regarding our financial condition and results of operations for fiscal 2020 as compared to fiscal 2019 see Item 7 of our Annual Report on Form 10-K for the fiscal year ended September 30, 2020, filed with the SEC on December 15, 2020.

Overview

ESSA is a clinical stage pharmaceutical company, focused on developing novel and proprietary therapies for the treatment of prostate cancer with an initial focus on patients whose disease is progressing despite treatment with current standard of care therapies, including second-generation anti-androgen drugs such as abiraterone, enzalutamide, apalutamide, and darolutamide. The Company believes its latest series of investigational compounds, including its product candidate EPI-7386, have the potential to significantly expand the interval of time in which patients with castration-resistant prostate cancer ("CRPC") can benefit from anti-hormone-based therapies. Specifically, the compounds are designed to disrupt the androgen receptor ("AR") signaling pathway, the primary pathway that drives prostate cancer growth and prevent AR activation through selective binding to the N-terminal domain ("NTD") of the AR. In this respect, the Company's compounds are designed to differ from classical non-steroid anti-androgens. These anti-androgens interfere either with androgen synthesis (i.e. abiraterone), or with the binding of androgens to the ligand-binding domain ("LBD"), located at the opposite end of the receptor from the NTD (i.e. "lutamides"). A functional NTD is essential for activation of the AR; blocking the NTD inhibits AR-driven transcription and therefore androgen-driven biology.

The Company believes that the transcription inhibition mechanism of its preclinical compounds is unique and has the potential advantage of bypassing identified mechanisms of resistance to the anti-androgens currently used in the treatment of CRPC. The Company has been granted by the United States Adopted Names ("USAN") Council a unique USAN stem "-aniten" to recognize this new first-in-class mechanistic class. The Company refers to this series of proprietary investigational compounds as the "Aniten" series. In preclinical studies, blocking the NTD has demonstrated the capability to prevent AR-driven gene expression. A previously completed Phase I clinical trial of ESSA's first-generation agent, ralaniten acetate ("EPI-506") administered to patients with metastatic CRPC ("mCRPC") refractory to current standard of care therapies demonstrated prostate-specific antigen ("PSA") declines, a sign of inhibition of AR-driven biology. This inhibition, however, was neither deep nor sustained enough to confer clinical benefit and the Company made the decision to develop a more potent next generation drug which would also have a longer half-life. The Company has done so and is now in clinical trial with this next generation Aniten, EPI-7386.

According to the American Cancer Society, in the United States, prostate cancer is the second most frequently diagnosed cancer among men, behind skin cancer. Approximately one-third of all prostate cancer patients who have been treated for local disease will subsequently have rising serum levels of PSA, which is an indication of recurrent or advanced disease. Patients with advanced disease often undergo initial androgen ablation therapy using analogues of luteinizing hormone releasing hormone or surgical castration; this approach is termed "androgen deprivation therapy" ("ADT"). Most advanced prostate cancer patients initially respond to this androgen ablation therapy; however, many experience a recurrence in tumor growth despite the reduction of testosterone to castrate levels, and at that point are considered to have CRPC. Following diagnosis of CRPC, patients have been generally treated with anti-androgens that block the binding of androgens (darolutamide, enzalutamide, apalutamide or bicalutamide) to the AR, or inhibit synthesis of androgens (abiraterone). More recently, significant improvements in progression-free survival have been achieved by utilizing this latest generation of anti-androgens in combination with ADT earlier in the disease natural history, in newly diagnosed metastatic prostate cancer.

Since the mid-20th century it has been recognized that the growth of prostate tumors is in large part mediated by an activated AR. Generally, there are three means of activating the AR. First, androgens such as dihydrotestosterone can activate AR by binding to its LBD. Second, CRPC can be driven by variants of AR that lack an LBD, are constitutively activated, and consequently do not require androgen for activation. A third mechanism, of less certain clinical significance, may involve certain signaling pathways that activate AR independent of androgen activity. Generally, current drugs for the treatment of prostate cancer are directed against the first mechanism by either (i) interfering with the production of androgen, or (ii) preventing androgen from binding to the LBD. Over time, these approaches eventually fail due to mechanisms of resistance which all involve the LBD end of the receptor, whether at the DNA (AR amplification or LBD mutations) or RNA level (emergence of AR splice variants).

The Company believes that through their potential to block androgen-driven gene transcription through a unique mechanism involving the NTD and thereby bypassing these known mechanisms of resistance to current anti-androgens, the Company believes the Aniten series of compounds hold the potential to be effective in cases where current therapies have failed. The results from both extensive preclinical studies and the initial clinical experience support the Company's belief. In preclinical studies, the Aniten series of compounds has been observed to shrink prostate cancer xenografts, including tumors both sensitive and resistant to the second-generation anti-androgens such as enzalutamide. PSA declines were observed in the initial Phase I study as described below. Importantly with respect to the potential clinical application of NTD inhibition, recent studies by the Company and its collaborators have also suggested the potential advantage for combinations of the Company's Aniten compounds with current anti-androgens to inhibit AR-driven biology more completely than inhibition of the receptor from either end of the receptor alone.

The Phase I clinical trial of the first generation Aniten EPI-506 provided evidence regarding the safety and tolerability for the potential mechanism of transcription inhibition of AR-driven biology. Patients generally tolerated doses of EPI-506 at overall exposures consistent with those associated with therapeutic activity in animal models. Possible proof of concept was observed with short duration PSA declines of up to 37% being observed in some patients whose disease was highly refractory to second-generation anti-androgen treatment. However, this first-generation drug demonstrated poor pharmaceutical properties. The drug was rapidly metabolized in humans, leading to a very short half-life of circulating drug and suboptimal drug exposures. Consequently, very high doses were required to achieve modest drug exposures, with the relatively short half-life limiting the therapeutic exposure of the drug within a 24-hour period. This limitation, together with other demonstrated unfavorable pharmaceutical properties, led to the Company's decision to discontinue EPI-506 development in favor of focusing on the development of a next generation of Anitens. This next generation includes significantly more potent drugs designed also to exhibit increased resistance to metabolism and therefore a longer predicted circulating half-life. The Company's lead product candidate EPI-7386 has demonstrated these and other favorable characteristics in extensive preclinical characterization studies which the Company has presented in a series of poster presentations at scientific meetings over the last year.

While the potential importance of the NTD as a drug target has been appreciated for more than two decades, for technical reasons this has been a difficult target for therapeutic agent development. The NTD of the AR is flexible with a high degree of intrinsic disorder making it difficult for use in classic crystal structure-based drug design. The Company is not currently aware of any success by other drug development companies in developing drugs that bind specifically to this drug target. The nature of the highly specific binding of the Aniten compounds to the NTD, and the biological consequences of that binding, have been defined in recent scientific studies. The selectivity of the binding, based on *in vivo* imaging as well as *in vitro* studies, has been consistent with the favorable toxicological results observed in preclinical studies of the first-generation EPI-506 and the subsequent safety results observed in the Phase I trial of EPI-506. The Company is currently conducting, together with external academic and industry collaborators, extensive biophysical and biological studies to reveal more precisely the nature of EPI-7386 binding, and the specific consequent effects on prostate cancer biology.

The incidence of both metastatic and non-metastatic CRPC continues to rise, and using a dynamic progression model, Scher et al[1] projected a 2020 incidence of 546,955 and prevalence of 3,072,480. The Company believes that the Aniten series of compounds could ultimately hold potential benefit for many of those patients. In its early clinical development, the Company intends to initially focus on patients who have failed second-generation anti-androgen therapies (i.e. abiraterone and/or lutamides) for the following reasons:

- CRPC treatment remains a prostate cancer market segment with an apparent and significant unmet therapeutic need and is therefore a potentially large market;
- the Company believes that the unique mechanism of action of its Aniten compounds is well suited to treat those patients who have failed AR LBD focused therapies, and whose biological characterization reveals that their tumors are still largely driven by AR biology; and
- the Company expects that the large number of patients with an apparent unmet therapeutic need in this area will facilitate timely enrollment in its clinical trials.

Furthermore, the Company believes that a successful Phase I clinical trial will facilitate the early study of the combination of EPI-7386 with second-generation anti-androgens. The Company and its collaborators have developed preclinical *in vitro* and *in vivo* evidence supporting further evaluation of the combination of NTD inhibitors together with the LBD inhibiting anti-androgens. The Company believes that the application of two independent, complementary mechanisms of AR transcription inhibition may result in greater suppression of androgen activity and the delay or prevention of drug resistance. Recent progress in the clinical treatment of prostate cancer has resulted from the earlier utilization of anti-androgens in combination with classic ADT, consistent with the premise that more effective androgen suppression may yield clinical benefit. The Company believes that the introduction of NTD inhibitors such as EPI-7386 therefore has potential to improve androgen suppression, delay the emergence of resistance, and result in improved clinical benefit. The first collaboration, with Janssen Research & Development, LLC ("Janssen"), to study in clinical trials the safety and potential benefit of combination of EPI-7386 with abiraterone as well as the combination of EPI-7386 with apalutamide was recently announced.

The Company is party to a license agreement with the British Columbia Cancer Agency and the University of British Columbia dated December 22, 2010, as amended on February 10, 2011 and on May 27, 2014 (the "License Agreement"), which provides the Company with exclusive world-wide rights to the issued patents and patent applications related to the EPI-002 compound, the active compound of the previous clinical candidate EPI-506.

The Company believes that it has developed a strong and defensive intellectual property position for multiple EPI and Aniten structural classes, with 16 pending and maintained patent families which cover multiple EPI- and Aniten structural classes of compounds with different structural motifs/analogues. Patent applications are pending in the United States and in contracting states to the Patent Cooperation Treaty for the Aniten next-generation NTD inhibitors, with expiry between 2036-2040.

[1] Scher HI, Solo K, Valant J, Todd MB, Mehra M (2015) Prevalence of Prostate Cancer Clinical States and Mortality in the United States: Estimates Using a Dynamic Progression Model. PLoS ONE 10(10): e0139440. doi:10.1371/journal.pone.013944

Completed Phase I Clinical Study of EPI-506

The Company conducted an initial proof-of-concept Phase I clinical study utilizing the first-generation Aniten compound, EPI-506. The objective of the EPI-506 Phase I clinical trial was to explore the safety, tolerability, maximum tolerated dose and pharmacokinetics of EPI-506, in addition to anti-tumor activity in asymptomatic or minimally symptomatic patients with mCRPC who were no longer responding to either abiraterone or enzalutamide treatments, or both. Efficacy endpoints, such as PSA reduction, and other disease progression criteria were evaluated. Details relating to the design of the Phase I/II clinical trial of EPI-506 are available on the U.S. National Institutes of Health clinical trials website (see https://clinicaltrials.gov).

The Investigational New Drug (" IND") application to the FDA for EPI-506, to begin a Phase I clinical trial, was allowed in September 2015, with the first clinical patient enrolled in November 2015. The Company's Clinical Trial Application ("CTA") submission to Health Canada was subsequently also cleared. Based on allometric scaling, an initial dose level of EPI-506 of 80 mg was determined. However, following the enrollment of the initial cohorts, it became apparent that EPI-506 exposure was much lower in humans than projected. EPI-506 dosing was escalated aggressively to allow patients in the clinical study greater exposure to the drug. The highest dose patients ultimately received was 3600 mg of EPI-506, administered in a single dose or split into two doses daily. The initial data from the Phase I clinical trial was presented at the European Society of Medical Oncology meeting in September 2017.

Conducted at five sites in the United States and Canada, the open-label, single-arm, dose-escalation study evaluated the safety, pharmacokinetics, maximum-tolerated dose and anti-tumor activity of EPI-506 in men with end-stage mCRPC who had progressed after prior enzalutamide and/or abiraterone treatment and who may have received one prior line of chemotherapy. Twenty-eight patients were available for analysis, with each patient having received four or more prior therapies for prostate cancer at the time of study entry. Patients self-administered oral doses of EPI-506 ranging from 80 mg to 3600 mg, with a mean drug exposure of 85 days (range of eight to 535 days). Four patients underwent prolonged treatment (with a median of 318 days; and a range of 219 to 535 days at data cut-off), following intra-patient dose escalation. PSA declines, a measure of potential efficacy, ranging from 4% to 37% were observed in five patients, which occurred predominantly in the higher dose cohorts (≥1280 mg).

EPI-506 was generally well-tolerated with favorable safety results observed across all doses up to 2400 mg. At a dose of 3600 mg, gastrointestinal adverse events (nausea, vomiting and abdominal pain) were observed in two patients: one patient in the once-daily ("QD") dosing cohort and one patient in the 1800 mg twice-daily dosing cohort, leading to study discontinuation and a dose-limiting toxicity ("DLT") due to more than 25% of doses being missed in the 28-day safety reporting period. A separate patient in the 3600 mg QD cohort experienced a transient Grade 3 increase in liver enzymes (AST/ALT), which also constituted a DLT, and enrollment was consequently concluded in this cohort.

Although the Company believes that the safety results and possible signs of anti-tumor activity observed at higher dose levels support the concept that inhibiting the AR-NTD may provide a clinical benefit to mCRPC patients, the pharmacokinetic and metabolic studies revealed the limitations of the first generation agent EPI-506. Through its discovery research the Company had concluded that it should be feasible to develop a next generation of NTD inhibitor which would demonstrate greater potency, reduced metabolism and other improved pharmaceutical properties. As a result, the Company announced on September 11, 2017 its decision to discontinue the further clinical development of EPI-506 and to implement a corporate restructuring plan to focus research and development resources on its next-generation Anitens targeting the AR-NTD. The restructuring included a decrease in headcount and a reduction of operational expenditures related to the clinical program.

The Company's family of next-generation investigational Aniten compounds incorporate multiple chemical scaffold changes to the first-generation drugs which in preclinical studies retain NTD inhibition of the AR. In addition, they have shown improvement in a range of attributes when compared to the first-generation compound, EPI-506, in preclinical studies. In *in vitro* assays measuring inhibition of AR transcriptional activity, these product candidates demonstrated 20 times higher potency than EPI-506 or its active metabolite, EPI-002. In addition, the compounds have demonstrated increased metabolic stability in preclinical studies, suggesting the potential for longer half-lives in humans. Lastly, the compounds have demonstrated more favorable pharmaceutical properties relative to EPI-506. The Company believes that these product candidates, if successfully developed and approved, may offer advancements in ease and cost of large-scale manufacture, drug product stability, and suitability for commercialization globally. From this series of next-generation compounds, EPI-7386 was selected as the lead candidate for clinical development and an IND was submitted to the FDA on March 30, 2020 and was allowed by the FDA on April 30, 2020. A CTA was filed with Health Canada in April 2020 and clearance was subsequently received. The Phase I clinical trial of EPI-7386 "Oral EPI-7386 in Patients With Metastatic Castration-Resistant Prostate Cancer (EPI-7386)" was started in June 2020 with the first patient dosed in July 2020 and is currently actively enrolling patients (www.clinicaltrials.gov).

Our Strategy

The Company's initial therapeutic goal is to develop a safe and effective therapy for prostate cancer patients whose tumors have progressed on current anti-androgen therapy. However, preclinical and clinical studies that have evaluated the NTD inhibition of the Company's Aniten compounds suggest the potential to increase therapeutic activity by combining these agents with anti-androgens at an earlier stage of treatment. Therefore, while the Company's first priority is to continue Phase I clinical development of EPI-7386 as a single agent, in parallel the Company has also been conducting preclinical studies and planning clinical studies to evaluate EPI-7386 in combination with other agents. These preclinical studies are being conducted in collaboration with academic institutions. In addition, the Company has engaged in discussions with the relevant pharmaceutical companies in the prostate cancer space regarding potential collaborative clinical trials of combination therapy in earlier line patients. The first of these collaborations, with Janssen, was recently announced. In future preclinical studies, the Company intends to further explore other potential applications for AR-NTD inhibitors, including breast cancer and other AR-associated cancers.

The identification and characteristics of the IND candidate EPI-7386

The purpose of the next-generation program has been to identify drug candidates with increased potency, reduced metabolic susceptibility and superior pharmaceutical properties compared to ESSA's first-generation compounds. Structure-activity relation studies conducted on the chemical scaffold of ESSA's first-generation compounds have resulted in the generation of a new series of compounds that have demonstrated higher potency and predicted longer half-lives. Multiple changes in the chemical scaffold have also been incorporated with the goal of improving ADME (absorption, distribution, metabolism, and excretion) and pharmaceutical properties of the chemical class.

Several next-generation aniten molecules met prespecified preclinical target product profile goals regarding potency, stability, selectivity and pharmaceutical properties. On March 26, 2019, the Company announced the nomination of EPI-7386 as its lead clinical candidate for the treatment of mCRPC through inhibition of the NTD of the androgen receptor. In preclinical studies, EPI-7386 has displayed activity *in vitro* in numerous prostate cancer models including models where second-generation anti-androgens are inactive. In addition, EPI-7386 is significantly more potent, metabolically stable and more effective in preclinical studies compared to ESSA's first-generation compound, EPI-506. Lastly, EPI-7386 has demonstrated a favorable tolerability profile in all animal studies of the compound conducted to date.

Following IND-enabling studies, ESSA filed an IND for EPI-7386 in mCRPC at the end of the first calendar quarter of 2020, and following the receipt of clearance by the FDA and allowance by Health Canada, commenced clinical testing of EPI-7386 in July 2020, allowing for accommodations to the planned timeline as a result of the impact of the COVID-19 situation at individual clinical trial sites (see "Risk Factors - Risks Relating to COVID-19" in our Annual report on Form 10-K).

The Company has presented preclinical scientific data in a number of poster presentations at scientific meetings in the past year.

At the 32nd EORTC-NCI-AACR Annual Symposium on Molecular Targets and Cancer Therapeutics ("ENA") on October 24th, 2020, an oral poster presentation titled, "The preclinical characterization of the N-terminal domain androgen receptor inhibitor, EPI-7386, for the treatment of prostate cancer", presented new information about EPI-7386 including: (i) in an *in vitro* cellular thermal shift assay (CETSA), EPI-7386 was shown to physically interact with the both the full-length and the splice variant (AR-V7) form of the androgen receptor ("AR") (ii) in an *in vitro* full-length AR-driven cellular model (LNCaP), RNAseq data was analyzed by pathway enrichment analysis. EPI-7386 demonstrates largely similar modulation of AR-regulated genes compared to enzalutamide, but with additional unique elements; and (iii) EPI-7386 exhibits superior activity to enzalutamide in the AR-V7-driven cellular models LNCaP95 and 22Rv1 by modulating AR-driven gene expression with or without the addition of an external androgen.

Previously, *in vitro* data had been presented demonstrating that EPI-7386 binds to the full-length androgen receptor and can inhibit the transcription of AR-regulated genes. The new data demonstrate that EPI-7386 can also physically interact with the splice variant form, AR-V7, of the androgen receptor and inhibit its activity. The importance of this interaction with AR-V7 is seen through the superior transcriptional inhibition of AR-regulated genes by EPI-7386 compared to enzalutamide in the AR-V7-driven cell models LNCaP95 and 22Rv1. Together, these data provide insights into mechanistic aspects related to the binding and utility of EPI-7386 against AR-V7 splice-variant driven prostate cancer models. The data supports the Company's rationale for studying EPI-7386 in men with prostate cancer resistant to current anti-androgens.

Advancing EPI-7386 through clinical development and regulatory approval in CRPC patients

The Company is conducting a Phase I clinical trial to determine the safety, tolerability, maximum tolerated dose, pharmacokinetics and potential therapeutic benefits of the drug in mCRPC patients. Depending on the number of cohorts enrolled, the Phase I clinical trial is expected to take nine to twelve months. The design of the Phase I clinical trial includes the standard three patients per dose cohort. Patients will be selected clinically, on the basis of having progressive metastatic CRPC as exemplified by rising PSA values and/or radiological disease progression despite latest generation anti-androgen treatment. However, all patients will be also be characterized biologically for underlying tumor genomic characteristics, for evidence of AR pathway activation and during the conduct of the trial, for dose-related biological, pharmacological and pharmacodynamic effects. Once the Phase I clinical trial is complete, the Company plans to review the data, including the safety, tolerability, evidence of efficacy and pharmacological and biomarker data. This information will inform the final size, design, timing and clinical as well as biological characteristics of the patients to be entered subsequent Phase II and additional clinical trials, including trials of combination aniten/lutamide therapy in earlier line patients.

On February 11, 2021, the Company presented preclinical and clinical pharmacology data from ESSA's Phase 1 clinical trial of EPI-7386 for the treatment of patients with metastatic castration-resistant prostate cancer ("mCRPC") at the 2021 American Society of Clinical Oncology Genitourinary ("ASCO GU") Cancers Symposium in an oral poster presentation titled, "Preclinical and clinical pharmacology of EPI-7386, an androgen receptor N-terminal domain inhibitor for castration-resistant prostate cancer". The poster is available on the Company website.

Data on the poster included a comparison of preclinical projections of EPI-7386 clinical pharmacokinetic parameters to the pharmacokinetic, safety and preliminary clinical data from the initial 200 mg cohort of patients enrolled in ESSA's multi-center, open-label, ascending multiple-dose Phase 1 study of EPI-7386 to treat patients with mCRPC who have become resistant to standard of care treatments. Patients participating in this trial have progressed on two or more approved systemic therapies for mCRPC, including at least one second generation antiandrogen therapy not necessarily in the metastatic disease setting. In this initial cohort of patients receiving the 200 mg once-daily dose, EPI-7386 was well-tolerated with no SAEs observed. The results from this cohort support ESSA's preclinical projections regarding the pharmacologic properties of EPI-7386 in patients. EPI-7386 was well-absorbed, demonstrated high exposure levels and was confirmed to have a long half-life of at least 24 hours. The predicted exposures of EPI-7386 in patients were similar to the Company's modeled projections and were still below optimal target exposures of EPI-7386 associated with anti-tumor activity in animal models. Although the 200 mg dose was suboptimal, one out of three patients who completed 12 weeks of therapy experienced a prostate specific antigen ("PSA") decline of more than 50 percent after three cycles of EPI-7386 therapy (12 weeks) with ongoing continued PSA declines continuing through six cycles of therapy, despite previously having failed enzalutamide and abiraterone acetate. ESSA recently completed the 28-Day safety evaluation period for the 400mg dose cohort and is currently dosing patients in the 600 mg cohort.

The Company believes these results from the initial clinical data are encouraging and suggest a favorable pharmacokinetic profile of EPI-7386 in patients. The Company believes the data demonstrate proof of concept by suggesting that EPI-7386, through its novel mechanism of action of targeting the N-terminal domain, may bypass the resistant mechanisms mCRPC patients may experience on current antiandrogen therapies. While early in the Phase 1 clinical study, the Company is encouraged to have seen early signs of biological activity and declining PSA levels in a multi-refractory patient at the initial 200 mg dose but recognizes that an accurate assessment of the full safety and tolerability profile as well as the potential clinical benefits to therapy with EPI-7386 will require longer observation of more patients treated at higher doses and anticipate providing more clinical data on the progress of the study in the second half of calendar 2021.

Developing a product candidate as an essential component of a new standard of care for the treatment of pre-CRPC and expanding usage earlier in the disease stage

An activated AR is required for the growth and survival of most prostate cancer. Unlike current anti-androgen therapies which can only inhibit full-length AR, NTD inhibition of AR-directed biology occurs both in full length AR and splice variant ARs. Therefore, the Company believes that the AR-NTD is an ideal target for next-generation anti-androgen hormone therapy. If ESSA's product candidate is successful in treating CRPC patients, it is reasonable to expect that such clinical candidate may be effective in treating earlier stage patients. Preclinical studies suggest particular value to the use of anitens in combination with the currently-widely used anti-androgens. As a result, the Company intends to conduct additional clinical studies potentially leading to the approval of EPI-7386 for use in prostate cancer patients at an earlier disease stage in combination with second-generation anti-androgens. The Company continues to develop *in vitro* and *in vivo* data in collaboration with academic and industry investigators in this regard and has recently announced a collaboration with Janssen Pharmaceutical to study EPI-7386 in combination clinical trials with abiraterone acetate/prednison, as well as with apalutamide. Preliminary data supporting this approach strongly indicates potential benefits to combining an NTD inhibitor, such as an Aniten compound, with an anti-androgen that works through inhibition of the LBD of the AR by directly blocking androgen binding (e.g. lutamides) or by inhibiting androgen synthesis (abiraterone acetate). Other emerging potential clinical applications for NTD inhibitors are in combination with other agents, such as poly ADP ribose polymerase ("PARP") inhibitors, as well as in the subset of metastatic breast cancer patients whose tumors have been demonstrated to have activation of the AR pathway.

Evaluating strategic collaborations to maximize value

The Company currently retains all commercial rights for its EPI and Aniten series drug portfolio. The Company continues to evaluate potential collaborations that could enhance the value of its prostate cancer program and allow it to leverage the expertise of such strategic collaborators. The first of these collaborations was announced recently, involving Janssen.

Future Clinical Development Program

Phase I/II Clinical Trial Design for treating CRPC patients

With the allowance by the FDA of the IND and clearance of the CTA by Health Canada for EPI-7386, the Company is conducting a Phase I clinical trial to determine the safety, tolerability, maximum tolerated dose, pharmacokinetics, and efficacy of the compound in CRPC patients at clinical sites in the US and Canada. In the Phase I study, it is expected the clinical trial will evaluate the safety, tolerability, pharmacokinetics, and maximum-tolerated dose of the compound, in multiple-dose escalations. The clinical trial is expected to enroll approximately 18 patients at multiple medical institutions in a standard 3+3 trial design with an approximate 10 additional patients enrolled in the dose expansion cohort. The Company is working with clinicals sites so patients can be enrolled ensuring compliance with COVID-19 risk management guidance as provided by FDA (see "*Risk Factors - Risks Relating to COVID-19*" in our Annual Report on Form 10-K). Learnings from the Phase I clinical trial of EPI-506 have been incorporated into the design and conduct of the Phase I study. The Company has included in the study design, for example, extensive biological characterization of the patients entered into the trial. If the Phase I portion of the clinical trial is successful, the Phase II portion of the clinical trial will evaluate activity in a larger group of biologically-characterized mCRPC patients.

Early Conduct of a Combination Phase I/II Clinical Trial

Given the evolution of prostate cancer therapeutics towards combination therapy strategies, the biological rationale for combining NTD and LBD inhibitors, and compelling early *in vitro* and preclinical animal model results, the Company intends to perform combination studies of the next-generation Aniten compound with current generation anti-androgens following the Phase 1 dose escalation and expansion studies. Since these combination studies will involve earlier lines of therapy i.e. often prior to receiving a late-stage anti-androgen, they will commence only after sufficient experience with safety, tolerability, and efficacy has been accumulated with single agent EPI-7386 therapy in later line of therapy patients. The Company currently estimates that these studies might commence within the third calendar quarter of 2021, and to that end the Company recently announced the signing of a collaboration agreement to conduct combination clinical trials with Janssen.

Phase III Clinical Trial

In order to ultimately obtain full single agent regulatory approval, the Company expects that at least one Phase III clinical trial will be required, most likely in patients similar to the population of mCRPC patients who will have been enrolled in the planned Phase I/II clinical trial. However, the results of the Phase I/II clinical trial may also suggest modification of the initial patient population based on anti-tumor response and biomarker assessment. In a Phase III clinical trial, the key end-point is expected to be progression-free survival or overall survival relative to patients receiving the standard-of-care. It is expected that such a Phase III clinical trial would be conducted at numerous sites around the world.

Competition

The competition in the prostate cancer market is very high, many of the companies against which we compete or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Several pharmaceutical therapies already have approved and many new molecules are being tested for their effect in this patient population. In addition, generic forms of Zytiga (abiraterone acetate) are now approved and commercially available in the U.S.

Currently approved therapies include:

GENERIC/PROGRAM NAME	BRAND NAME	COMPANY NAME(S)	STAGE
Enzalutamide	Xtandi	Astellas and Pfizer	Marketed
Abiraterone acetate	Zytiga	Johnson & Johnson	Marketed
Sipuleucel-T	Provenge	Valeant	Marketed
Docetaxel	n/a	Sanofi and various	Marketed
Cabazitaxel	Jevtana	Sanofi	Marketed
Radium-233	Xofigo	Bayer	Marketed
Apalutamide (ARN-509)	Erleada	Johnson & Johnson	Marketed
Darolutamide	Nubeqa	Bayer	Marketed
Pembrolizumab	Keytruda	Merck	Marketed
Olaparib	Lynparza	AstraZeneca	Marketed
Rucaparib	Rubraca	Clovis Oncology	Marketed

In this market, ESSA believes that its competitive position is strong because its product candidate, if successful, involves a mechanistically unique, differentiated approach to prostate cancer involving the therapeutic modality that has been shown to make the biggest difference to the survival of recurrent prostate cancer patients: blocking AR activation. Since EPI compounds have been shown to directly block the AR-NTD, they have the potential to bypass the AR-dependent resistance pathways (discussed above) that may develop as a result of treatment with current hormone-related therapies that target the AR LBD. If successful, ESSA believes this could represent a significant step forward in the treatment of prostate cancer. To ESSA's knowledge, no other antagonist to the AR-NTD is currently undergoing clinical trials for prostate cancer or any other indication. Other approaches to interfering with AR signaling include strategies to degrade the AR such as that being pursued by Arvinas, Inc.

Patents and Proprietary Rights

License Agreement with UBC and the BCCA

ESSA has in-licensed intellectual property embodied in issued patents, pending patents applications and know-how relating to compounds that modulate AR activity created through research work done at UBC and the BCCA (together, the "Licensors") under the direction of Dr. Raymond Andersen and Dr. Marianne Sadar, respectively. ESSA refers to these intellectual property rights as the "Licensed IP".

Pursuant to the License Agreement, ESSA has been granted a worldwide, exclusive license to develop and commercialize products based on the Licensed IP. ESSA paid a minimum annual royalty of C$40,000 in the 2014 calendar year, increasing to C$65,000 in each of 2015 and 2016 and C$85,000 in 2017, 2018, and 2019 and must continue to pay a minimum of C$85,000 for each year thereafter. For a First Compound entering clinical development, an additional C$50,000 and C$900,000 must be paid upon enrollment of a patient in a Phase II and Phase III clinical trial, respectively.

The Licensors may terminate the License Agreement upon ESSA's insolvency, or the License Agreement may be terminated by either party for certain material breaches by the other party. ESSA has already spent more than C$5,000,000 in connection with the commercialization of products relating directly to the Licensed IP, as required under the License Agreement. ESSA is required to allocate reasonable time to the development and commercialization of the Licensed IP and to use reasonable efforts to promote, market and sell products covered by the Licensed IP. The terms of the License Agreement required ESSA to issue to the Licensors, in lieu of payment of an initial license fee, 1,000,034 pre-Consolidation Common Shares. If ESSA develops products covered by the Licensed IP in the future, it will be required to pay certain development and regulatory milestone payments up to an aggregate of C$2.4 million for the first drug product developed under the license and up to an aggregate of C$510,000 for each subsequent product. ESSA must also pay the Licensors low single-digit royalties based on aggregate worldwide net sales of products covered by the Licensed IP and a percentage of sublicensing revenue in the low teens. ESSA is also required to reimburse costs incurred by the Licensors related to the prosecution and maintenance of patents embodying the Licensed IP. The License Agreement will expire on the later of 20 years after the date of the License Agreement or the expiry of the last issued patent included in the Licensed IP.

ESSA's Intellectual Property Strategy

Both ESSA and the broader pharmaceutical industry attach significant importance to patents for the protection of new technologies, products and processes. Accordingly, ESSA's success depends, in part, on its ability to obtain patents or rights thereto, to protect commercial secrets and carry on activities without infringing the rights of third parties. See "Risk Factors" in our Annual Report on Form 10-K. Where appropriate, and consistent with management's objectives, patents are pursued once concepts have been validated through appropriate laboratory work. To that end, ESSA will continue to seek patents in relation to those components or concepts that it perceives to be important.

Patent Applications

ESSA has licensed certain patent rights, with respect to some of its compounds that modulate AR activity, from the Licensors, jointly. ESSA has the right to acquire ownership of the licensed patents and patent applications upon specified payment to the Licensors, and providing that payments required under the License Agreement continue to be made.

ESSA currently has 16 pending and maintained patent families which cover multiple EPI- and Aniten structural classes of compounds with different structural motifs/analogues, that provide a strong and defensive intellectual property portfolio.

Regulatory Environment

The production and manufacture of ESSA's product candidate and potential future product candidates and its R&D activities are subject to regulation for safety, efficacy, quality and ethics by various governmental authorities around the world. In the United States, drugs and biological products are subject to regulation by the FDA. In Canada, these activities are regulated by the Food and Drugs Act and the rules and regulations thereunder, which are enforced by the TPD. Drug approval laws require registration of manufacturing facilities, carefully controlled research and testing of product candidates, government review and approval of experimental results prior to giving approval to sell drug products. Regulators also require that rigorous and specific standards such as cGMP, GLP and GCP are followed in the manufacture, testing and clinical development respectively of any drug product. See "Risk Factors" in our Annual Report on Form 10-K.

The process of obtaining regulatory approvals and the corresponding compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval may subject an applicant or sponsor to a variety of administrative or judicial sanctions, including refusal by the FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of enforcement letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by the FDA and the Department of Justice or other governmental entities.

An applicant seeking approval to market and distribute a new drug product in the United States must typically undertake the following:

- completion of extensive nonclinical, sometimes referred to as preclinical laboratory tests, and preclinical animal trials in compliance with applicable requirements for the humane use of laboratory animals and formulation studies, including GLPs;
- submission to the FDA of an IND, which must take effect before human clinical trials may begin;
- approval by an IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials according to the FDA's regulations commonly referred to as GCP regulations and any additional requirements for the protection of human research subjects and their health information, to establish the safety and efficacy of the proposed drug product for its intended use;
- preparation and submission to the FDA of a New Drug Application ("NDA");
- review of the product by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with cGMP requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- payment of user fees and securing FDA approval of the NDA; and
- compliance with any post-approval requirements, including Risk Evaluation and Mitigation Strategies ("REMS") and post-approval studies required by the FDA.

Preclinical Studies

Preclinical studies are conducted *in vitro* and in animals to evaluate pharmacokinetics, metabolism and possible toxic effects to provide evidence of the safety of the product candidate prior to its administration to humans in clinical studies and throughout development. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. The results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical studies, among other things, are submitted to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted.

Initiation of Human Testing

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written trial protocols detailing, among other things, the objectives of the trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to a proposed clinical trial and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. In Canada, this application is called a CTA. An IND/CTA application must be filed and accepted by the FDA or TPD, as applicable, before human clinical trials may begin. In addition, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the trial at least annually. The IRB must review and approve, among other things, the trial protocol and informed consent information to be provided to trial subjects. An IRB must operate in compliance with FDA regulations.

Two key factors influencing the rate of progression of clinical trials are the rate at which patients can be enrolled to participate in the research program and whether effective treatments are currently available for the disease that the drug is intended to treat. Patient enrollment is largely dependent upon the incidence and severity of the disease, the treatments available and the potential side effects of the drug to be tested and any restrictions for enrollment that may be imposed by regulatory agencies.

Phase I Clinical Trials

Phase I clinical trials for cancer therapeutics are typically conducted on a small number of patients to evaluate safety, dose limiting toxicities, tolerability, pharmacokinetics and to determine the dose for Phase II clinical trials in humans.

Phase II Clinical Trials

Phase II clinical trials typically involve a larger patient population than Phase I clinical trials and are conducted to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of a product candidate for specific targeted diseases and to determine dosage tolerance, optimal dosage and dosing schedule.

Phase III Clinical Trials

Phase III clinical trials typically involve testing an experimental drug on a much larger population of patients suffering from the targeted condition or disease – in ESSA's case, CRPC. These studies involve testing the experimental drug in an expanded patient population at geographically dispersed test sites (multi-center trials) to establish clinical safety and effectiveness. These trials also generate information from which the overall risk-benefit relationship relating to the drug can be determined.

In most cases FDA requires two adequate and well controlled Phase III clinical trials to demonstrate the efficacy of the drug. A single Phase III trial with other confirmatory evidence may be sufficient in rare instances where the trial is a large multicenter trial demonstrating internal consistency and a statistically very persuasive finding of a clinically meaningful effect on mortality, irreversible morbidity or prevention of a disease with a potentially serious outcome and confirmation of the result in a second trial would be practically or ethically impossible.

New Drug Application

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA, or the TPD as part of a New Drug Submission ("NDS"), requesting approval to market the drug product for one or more indications. The NDS or NDA is then reviewed by the applicable regulatory body for approval to market the drug.

The FDA conducts a preliminary review of an NDA within 60 days of its receipt and informs the sponsor by the 74th day after the FDA's receipt of the submission to determine whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to specified performance goals in the review process of NDAs. Most such applications are meant to be reviewed within ten months from the date of filing, and most applications for "priority review" products are meant to be reviewed within six months of filing. The review process may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections cover all facilities associated with an NDA submission, including drug component manufacturing (such as Active Pharmaceutical Ingredients), finished drug product manufacturing, and control testing laboratories. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP.

The cost of preparing and submitting an NDA is substantial. The submission of most NDAs is additionally subject to a substantial application user fee, currently exceeding $2,500,000 and the manufacturer or sponsor under an approved new drug application are also subject to significant annual program and establishment user fees. These fees are typically increased annually.

On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess the drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, significant changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

Orphan Designation and Exclusivity

ESSA may, in the future, seek orphan drug designation for its product candidates. Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition (generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for treatment of the disease or condition will be recovered from sales of the product). A company must request orphan product designation before submitting an NDA. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product with orphan status receives the first FDA approval for the disease or condition for which it has such designation, the product generally will receive orphan product exclusivity. Orphan product exclusivity means that the FDA may not approve any other applications for the same product for the same indication for seven years, except in certain limited circumstances. Competitors may receive approval of different products for the indication for which the orphan product has exclusivity and may obtain approval for the same product but for a different indication. If a drug or drug product designated as an orphan product ultimately receives marketing approval for an indication broader than what was designated in its orphan product application, it may not be entitled to exclusivity.

Developments

Recent Developments

On January 8, 2021, the Company issued 9,000 common shares for stock options exercised for gross proceeds of C$44,100.

On January 11, 2021, the Company issued 46,655 common shares for stock options exercised for gross proceeds of C$228,610 and 21,345 common shares for stock options exercised for gross proceeds of $72,262.

On January 13, 2021, the Company issued 34,716 common shares for stock options exercised for gross proceeds of $126,124.

On January 13, 2021, the Company announced a clinical collaboration with Janssen to evaluate EPI-7386 combination for patients with metastatic castration-resistant prostate cancer. Under the terms of the agreement, Janssen may sponsor and conduct up to two Phase 1/2 studies evaluating the safety, tolerability and preliminary efficacy of the combination of EPI-7386 and apalutamide as well as the combination of EPI-7386 with abiraterone acetate plus prednisone in patients with mCRPC who have failed a current second-generation antiandrogen therapy. Janssen will assume all costs associated with the studies, other than the manufacturing costs associated with the clinical drug supply of EPI-7386. The parties will form a joint oversight committee for the clinical studies, which are planned to start in 2021. ESSA will retain all rights to EPI-7386.

On January 20, 2021, the Company issued 15,000 common shares for stock options exercised for gross proceeds of C$73,500 and 15,000 common shares for stock options exercised for gross proceeds of $48,450.

On February 5, 2021, the Company issued 2,965 Common Shares upon the cashless exercise of 3,825 broker warrants.

On February 9, 2021, the Company issued 30,000 common shares for stock options exercised for gross proceeds of C$147,000.

On February 11, 2021, the Company presented preclinical and clinical pharmacology data from ESSA's Phase 1 clinical trial of EPI-7386 for the treatment of patients with metastatic castration-resistant prostate cancer ("mCRPC") at the 2021 American Society of Clinical Oncology Genitourinary ("ASCO GU") Cancers Symposium in an oral poster presentation titled, "Preclinical and clinical pharmacology of EPI-7386, an androgen receptor N-terminal domain inhibitor for castration-resistant prostate cancer,". The poster is available on the Company website.

Significant Business Developments for the Three Months Ended December 31, 2020

On October 14, 2020, the Company issued 1,493,504 Common Shares upon the cashless exercise of 1,493,504 pre-funded warrants.

On October 26, 2020, ESSA Pharma Inc. announced its strategic decision to voluntarily delist its Common Shares from the TSX-V.

On November 25, 2020, the Company filed a Registration Statement on Form S-3 with the SEC to replace the existing Registration Statement on Form F-3, which, once effective, will allow the Company to raise up to $200 million worth of the securities listed therein.

On December 3, 2020, the Company issued 42,207 Common Shares for stock options exercised for gross proceeds of $153,701.

ESSA has never been profitable and has incurred net losses since inception. ESSA's net losses were $6,528,704 and $4,613,273 for the three months ended December 31, 2020, and 2019 respectively. ESSA expects to incur losses for the foreseeable future, and it expects these losses to increase as it continues the development of, and seek regulatory approvals for, its product candidate. Because of the numerous risks and uncertainties associated with product development, ESSA is unable to predict the timing or amount of increased expenses or when, or if, it will be able to achieve or maintain profitability.

Selected Quarterly Financial Information

The following table sets forth ESSA's unaudited consolidated financial data for each of the last eight quarters, prepared in accordance with U.S. GAAP. The Company has not earned any revenues or declared dividends as of December 31, 2020:

	For the Quarters Ended			
	December 31, 2020	September 30, 2020	June 30, 2020	March 31, 2020
Research and development expense	$ 4,485,772	$ 2,236,680	$ 2,703,704	$ 4,618,436
General and administration	2,208,917	2,200,159	2,171,020	4,863,608
Comprehensive income (loss)	(6,528,704)	(4,553,342)	(4,924,828)	(9,353,927)
Basic and diluted earnings (loss) per share	(0.20)	(0.17)	(0.24)	(0.45)
Cash and cash equivalents	52,484,512	56,320,763	36,482,049	39,913,569
Short-term investments	22,016,344	22,011,337	-	-
Total assets	76,174,988	80,574,565	38,100,438	41,603,369
Long-term liabilities	38,246	127,376	76,762	40,477
Working capital	73,861,974	79,038,442	36,475,762	39,746,147

	For the Quarters Ended			
	December 31, 2019	September 30, 2019	June 30, 2019	March 31, 2019
Research and development expense	$ 2,587,148	$ 2,004,750	$ 1,951,084	$ 1,454,077
General and administration	2,139,165	1,246,426	1,208,591	1,757,638
Comprehensive income (loss)	(4,613,273)	(3,327,117)	(3,298,313)	(3,423,997)
Basic and diluted earnings (loss) per share	(0.22)	(0.23)	(0.52)	(0.54)
Cash and cash equivalents	45,934,420	53,322,723	4,874,410	8,597,639
Short-term investments	-	-	-	-
Total assets	47,168,317	54,573,093	6,866,899	9,402,541
Long-term liabilities	99,766	16,520	1,412,178	2,213,728
Working capital	45,527,165	48,724,264	281,688	5,371,772

Results of Operations for the Three Months Ended December 31, 2020 and 2019

There was no revenue in any of the periods ended as reported. The Company incurred a comprehensive loss of $6,528,704 for the three months ended December 31, 2020 compared to a comprehensive loss of $4,613,273 for the three months ended December 31, 2019. Variations in ESSA's expenses and net loss for the periods resulted primarily from the following factors:

Research and Development Expenditures

R&D expense included the following major expenses by nature:

	Three months ended December 31, 2020	Three months ended December 31, 2019
Clinical	$ 1,315,872	$ 101,143
Consulting	88,359	73,596
Legal patents and license fees	68,543	237,700
CMC	1,452,360	847,190
Other	7,349	41,262
Preclinical and data analysis	1,001,462	773,171
Salaries and benefits	261,049	345,198
Share-based payments	287,424	152,406
Travel and other	3,354	15,482
Total	$ 4,485,772	$ 2,587,148

The overall R&D expense for the three months ended December 31, 2020 was $4,485,772 compared to $2,587,148 for the three months ended December 31, 2019 and includes non-cash expense related to share-based payments expense of $287,424 (2019 - $152,406). R&D expense in the period ended December 31, 2019 was incurred primarily in preclinical research and IND-enabling work on the Company's next-generation Aniten compounds, and expenditure on chemistry and manufacturing of drug product at third party vendors, in anticipation of the Phase 1 clinical trial which commenced with the dosing of the first patient in July 2020.

The share-based payments expense of $287,424 (2019 - $152,406), which is a non-cash expense, relates to the value assigned to stock options and employee share purchase rights granted to key management and consultants of the Company. The expense is recognized in relation to the grant and vesting of these equity instruments, net of expiries and forfeitures, and allocated to research and development, general and administration and financing expenditures relative to the activity of the underlying optionee.

Clinical costs of $1,315,872 (2019 - $101,143) were generated in relation to expenditures with the Company's clinical research organizations conducting the Phase 1 clinical trial of EPI- 7386. In the prior period, the costs related to clinical consulting work in preparation for the IND filing in March 2020.

Preclinical and data analysis costs of $1,001,462 (2019 – $773,171) were incurred in the identification of the lead compound EPI-7386 in 2019 and the subsequent filing of the IND in 2020. In the current period, the amount includes pharmacokinetic data analysis on data from the clinical trial related to the Phase I study.

CMC costs of $1,452,360 (2019 - $847,190) included cGMP manufacturing of EPI 7386 drug supply to support the ongoing clinical trial. In the three months ended December 31, 2019, costs were incurred in formulation and chemistry work around the Company's pharmaceutical characteristics of EPI-7386.

Consulting costs increased to $88,359 for the three months ended December 31, 2020 (2019 - $73,596) relating to contract project management services. In the comparative period, costs were related to consulting fees for scientific advisors in connection with candidate selection and preparation of the IND filing, including contract project management services.

Salaries and benefits, related to preclinical and clinical staff, have decreased to $261,049 (2019 - $345,198) as a result of an additional employee in prior period.

Legal patents and license fees for the period totaled $68,543 (2019 - $237,700). The Company has adopted a tiered patent strategy to protect its intellectual property as the pharmaceutical industry places significant importance on patents for the protection of new technologies, products and processes. The costs reflect that ongoing investment and timing of associated maintenance costs. The Company anticipates that there will be continued investment into patent applications.

General and Administration Expenditures

General and administrative expenses include the following major expenses by nature:

	Three months ended December 31, 2020	Three months ended December 31, 2019
Amortization	$ 27,581	$ 27,580
Consulting and subcontractor fees	49,478	32,805
Director fees	93,500	92,500
Insurance	227,611	133,595
Investor relations	141,520	57,739
Office, insurance, IT and communications	54,655	50,232
Professional fees	332,485	195,118
Regulatory fees and transfer agent	37,844	10,320
Rent	16,071	15,644
Salaries and benefits	302,251	376,363
Share-based payments	917,561	1,101,215
Travel and other	4,364	46,054
Total	$ 2,208,917	$ 2,139,165

General and administration expenses decreased to $2,208,917 for the three months ended December 31, 2020 from $2,139,165 in the three months ended December 31, 2019 and includes non-cash expense related to share-based payments of $917,561 (2019 - $1,101,215). This non-cash expense relates to the value assigned to stock options and employees share purchase rights granted to key management and consultants of the Company. The expense is recognized in relation to the grant and vesting of these equity instruments, net of expiries and forfeitures, and allocated to research and development, general and administration and financing expenditures relative to the activity of the underlying optionee.

Director fees of $93,500 (2019 - $92,500) were incurred for remuneration paid to directors for attendance at meetings and participation in various committees during the period.

Salaries and benefits expense decreased to $302,251 (2019 - $376,363) as a result of some changes to benefits accruals and timing of related costs.

Insurance expense of $227,611 (2019 - $133,595) relates to increased cost of insurance coverage for directors and officers of the Company as a reporting issuer and publicly listed company in the United States, as well as general liability insurance. The Company has realized an increase in premiums which is in line with market trends.

Investor relations expense increased to $141,520 (2019 - $57,739) due to the cost of additional investor communications support engaged in the current period.

Professional fees of $332,485 (2019 - $195,118) were incurred for legal and accounting services in conjunction with increased corporate activities compared to activities in 2019. The Company also prepared for, and implemented changes with respect to its transition to a domestic issuer from foreign private issuer, including transition of financial statements to U.S. GAAP.

Financing costs

In the three months ended December 31, 2020, the Company incurred financing costs expense of $1,181 (2019 - $215,501). In the current period, the Company incurred a minimal amount finance accretion related to the operating lease. In the comparative period, the Company settled a long-term debt with Silicon Valley Bank which resulted in a non-recurrent finance charge of $211,079.

Liquidity and Capital Resources

ESSA is a clinical stage company and does not currently generate revenue.

As of December 31, 2020, the Company has working capital of $73,861,974 (September 30, 2020 - $79,093,604). Operational activities during the three months ended December 31, 2020 were financed mainly by proceeds from the acquisition of Realm, financing completed in August 2019 for gross proceeds of $36,000,000 and July 2020 Financing. At December 31, 2020, the Company had available cash reserves and short-term investments of $74,500,856 (September 30, 2020 - $78,332,100) to settle current liabilities of $2,035,377 (September 30, 2020 - $1,203,324). At December 31, 2020, the Company believed that it had sufficient capital to satisfy its obligations as they became due and execute its planned expenditures for more than twelve months.

ESSA's future cash requirements may vary materially from those now expected due to a number of factors, including the costs associated with future preclinical work and to take advantage of strategic opportunities, such as partnering collaborations or mergers and acquisitions activities. In the future, it may be necessary to raise additional funds. These funds may come from sources such as entering into strategic collaboration arrangements, the issuance of shares from treasury, or alternative sources of financing. However, there can be no assurance that ESSA will successfully raise funds to continue its operational activities. See "Risk Factors" in our Annual Report on Form 10-K.

Critical Accounting Policies and Estimates

The Company makes estimates and assumptions about the future that affect the reported amounts of assets and liabilities. Estimates and judgments are continually evaluated based on historical experience and other factors, including expectations of future events that are believed to be reasonable under the circumstances. In the future, actual experience may differ from these estimates and assumptions.

The effect of a change in an accounting estimate is recognized prospectively by including it in comprehensive income in the period of the change, if the change affects that period only, or in the period of the change and future periods, if the change affects both.

The critical accounting policies are those polices that require the most significant judgments and estimates in the preparation of our condensed consolidated interim financial statements. A summary of the critical accounting policies is presented in Note 2 of the annual consolidated financial statements for the year ended September 30, 2020 filed with the SEC and with the securities commissions in Alberta and Ontario on December 15, 2020.

Trend Information

ESSA is a clinical development stage company and does not currently generate revenue. The Company is focused on the development of small molecule drugs for the treatment of prostate cancer. The Company has acquired a license to certain Licensed IP. As of the date of this Quarterly Report on Form 10-Q, no products are in commercial production or use. The Company's financial success will be dependent upon its ability to continue development of its compounds through preclinical and clinical stages to commercialization.

Off-Balance Sheet Arrangement

ESSA has no material undisclosed off-balance sheet arrangements that have, or are reasonably likely to have, a current or future effect on its results of operations, financial condition, revenues or expenses, liquidity, capital expenditures or capital resources that is material to investors.

Outstanding Share Data

As of February 10, 2021, our authorized share capital consisted of an unlimited number of common shares, each without par value, of which 33,780,064 were issued and outstanding, and an unlimited number of preferred shares, each without par value, none of which were issued and outstanding. As of February 10, 2021, we had 7,775,648 common shares issuable pursuant to 7,775,648 common share purchase warrants pursuant to full cash exercise, 2,143,837 common shares issuable pursuant to 2,143,837 exercisable outstanding stock options, 4,624,470 common shares issuable pursuant to 4,624,470 outstanding options that were not exercisable at that date, and no outstanding restricted stock units.

JOBS Act

As a company with less than US$1.07 billion in revenue during the last fiscal year, ESSA qualifies as an "emerging growth company" pursuant to the JOBS Act. An emerging growth company may take advantage of specified exemptions from various requirements that are otherwise applicable generally to public companies in the United States.

The JOBS Act also permits an emerging growth company such as ESSA to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies. ESSA will not take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act for complying with new or revised accounting standards. This election is irrevocable. ESSA will remain an emerging growth company until the earliest of:

- the last day of the Company's fiscal year during which it has total annual gross revenues of at least US$1.07 billion;
- the last day of the Company's fiscal year following the fifth anniversary of the completion of an initial public offering;
- the date on which Company has, during the previous three-year period, issued more than US$1 billion in non-convertible debt securities; or
- the date on which the Company is deemed to be a "large accelerated filer" under the Exchange Act, which would occur if the market value of ESSA's Common Shares that are held by non-affiliates exceeds US$700 million as of the last business day of its most recently completed second fiscal quarter.

As a result of ESSA's status as an emerging growth company, the information that the Company provides shareholders may be less comprehensive than what you might receive from other public companies that are not emerging growth companies. When ESSA is no longer deemed to be an emerging growth company, ESSA will not be entitled to the exemptions provided in the JOBS Act.

Safe Harbor

See "*Cautionary Note Regarding Forward-Looking Statements*" in the introduction to this Quarterly Report.