Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

The following discussion should be read in conjunction with the attached financial statements and notes thereto. This Annual Report on Form 10-K, 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 Item 1A, "Risk Factors" of this 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 Annual Report on Form 10-K. We undertake no obligation to update forward-looking statements to reflect events or circumstances occurring after the date of this Annual Report on Form 10-K. 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 2021 as compared to fiscals 2020 and 2019 see Item 7 of our Annual Report on Form 10-K for the fiscal year ended September 30, 2021, filed with the SEC on November 18, 2021.

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 antiandrogen 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 antiandrogens. These antiandrogens 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.

General Development of the Business

Significant Business Developments for the Year Ended September 30, 2022

On October 31, 2022, the Company announced that Janssen Research and Development is suspending enrollment into the Phase 1 clinical study of EPI-7386 with apalutamide and EPI-7386 with abiraterone acetate plus prednisone in mCRPC patients as a result of operational recruitment challenges. Initial clinical activity was observed in some patients, with two of the three patients achieving a PSA reduction of 90% ("PSA90") within 12 weeks. The Company is in discussions with Janssen to supply abiraterone acetate and apalutamide for an ESSA-sponsored combination study.

On October 26, 2022, the Company announced the presentation of preclinical data for its lead first generation AR ANITen bAsed Chimera ("ANITAC"™) NTD degrader in a poster session at the 34th EORTC-NCI-AACR Annual Symposium on Molecular Targets and Cancer Therapeutics.

On October 26, 2022, the Company announced the presentation of updated clinical data from the first two cohorts of the Phase 1/2 study of ESSA's lead candidate EPI-7386 in combination with enzalutamide at the 2022 Prostate Cancer Foundation Scientific Retreat. In the multicenter, open-label Phase 1/2 dose escalation study, seven mCRPC patients naïve to second generation antiandrogens were enrolled in the first two cohorts, with escalating doses of EPI-7386 and a fixed 120 mg once a day (QD) dose of enzalutamide. The study permitted one prior line of chemotherapy. Pharmacokinetic results from these first two cohorts demonstrated that enzalutamide exposure was minimally impacted by EPI-7386 while exposures of EPI-7386 were reduced by coadministration with enzalutamide, but remained in the clinically relevant range as suggested by preclinical xenograft studies. The safety of the combination was favorable with a safety profile consistent

with second-generation antiandrogens and no dose limiting toxicities were observed. One of the patients in the first cohort discontinued after one cycle of dosing due to a strong CYP3A inducer concomitant medication which lowered exposures to both EPI-7386 and enzalutamide and was therefore not evaluable for efficacy. Anti-tumor activity in the remaining six patients enrolled demonstrated that four of six of these patients achieved a PSA90 by 12 weeks of dosing and five of six patients to date have achieved a PSA90.

On September 13, 2022, the Company appointed Philip Kantoff to its Board of Directors (the "Board").

On June 30, 2022, the Company announced the establishment of Automatic Securities Disposition Plans for its President and Chief Executive Officer, David R Parkinson and its Executive Vice President and Chief Operating Officer, Peter Virsik.

On June 27, 2022, the Company presented, by conference call and webcast, a clinical update on EPI-7386 monotherapy and combination therapy clinical development. The update on the Phase 1a dose escalation study showed initial data from 36 patients that demonstrated that EPI-7386 was well-tolerated, exhibited a favorable pharmacokinetic profile, and demonstrated initial anti-tumor activity in a heavily pretreated group of patients. The Company believes the favorable safety and tolerability profile, good pharmaceutical characteristics together with both antiandrogen biological and anti-tumor activity support the Company's decision to move into earlier lines of therapy and study EPI-7386 in combination with second-generation antiandrogens. The update also noted that ctDNA molecular analysis in the heavily pretreated population has provided a detailed profile of genetic alterations, which reveals the biological complexity of late-stage mCRPC patients and also allows for the continued refinement of the population of prostate cancer patients whose tumors are still primarily driven by the androgen receptor, and therefore most likely to respond to an androgen receptor inhibitor.

The update detailed that in the multi-center, open-label Phase 1a dose escalation study, 31 patients received EPI-7386 as oral tablets once a day (QD) in cohorts with 200 milligram increments from 200 milligrams up to 1000 milligrams. Patients in this QD group were heavily pretreated, with a median of seven lines of prior therapy for prostate cancer and four lines of therapy for mCRPC. Almost 60% of patients had been treated with prior chemotherapy. Patients entered the trial with rapidly progressive disease, as evidenced by a median PSA doubling time of only 2.1 months and a median ctDNA percent of 29%. Almost a third of the patients had lung, liver, or brain metastases, and an overlapping third of patients had overt neuroendocrine differentiation. The ctDNA analysis revealed that tumors in these patients had extensive non-AR associated genomic changes denoting the presence of multiple non-AR oncogenic drivers associated with late-stage prostate cancer. Subsequent to a protocol amendment, the experience was also presented for the five initial patients enrolled in a twice daily dose regimen in 400 mg and 600 mg BID cohorts. The amendment excluded patients who had been treated with more than three prior lines of therapy, excluded patients with visceral metastases, and permitted only one prior line of chemotherapy.

The key safety results from both QD and BID patients, as of June 1, 2022, showed that EPI-7386 was safe and well-tolerated at all dose levels and schedules tested, with no dose-limiting toxicities, treatment related adverse events were limited to Grade 1 or Grade 2, with one Grade 3 occurrence of anemia ultimately deemed unlikely to be treatment related, and that there was no apparent dose dependency in any of the side effects.

Antiandrogen response was assessed by changes in circulating PSA levels, changes in ctDNA levels, and radiographic changes in disease burden measured by both traditional RECIST criteria as well as by total lesion volumetric quantification using the AIQ Solutions platform.

The key response findings in both QD and BID patients, as of June 1, 2022, demonstrated that tumor volume decreased in five patients out of 10 patients who had measurable disease and were on therapy for more than 12 weeks. PSA decrease or PSA stabilization was observed in a clinical subset of patients with no visceral disease, fewer DNA genomic aberrations in non-AR oncogenic pathways, and fewer than 3 lines of therapy. This provides further information to support refining the monotherapy development program patient population. In 17 patients with measurable ctDNA levels at baseline, ctDNA declines were observed in patients harboring AR point mutations, AR gain/amplification and AR truncations, suggesting EPI-7386's potential activity against these tumors.

The update also described the planned Phase 1b study, the planned window of opportunity cohort and the status of the combination study of EPI-7386 with enzalutamide. The Phase 1b study will evaluate a patient population of mCRPC similar to the one treated under the Phase 1a BID cohort but with the additional exclusion of prior chemotherapy. Up to 12 patients per each dose/schedule (600 mg QD and either 400 mg or 600 mg BID) will be evaluated to gain additional information about safety, tolerability, exposure and anti-tumor activity of EPI-7386 in a less heavily pretreated patient population.

The update also described the planned window of opportunity cohort as part of the Phase 1b expansion in which a separate group of non-metastatic CRPC will be enrolled into a 12-week study with a clinical endpoint (i.e. PSA changes) to assess the anti-tumor activity of EPI-7386 in a patient population in which the disease is mainly AR-driven and the tumor biology has not been affected by second-generation antiandrogen therapy.

The clinical update also provided the status of the combination studies evaluating EPI-7386 in earlier lines of therapy in Phase 1/2 trials which combine EPI-7386 with approved second-generation antiandrogens. In the Phase 1/2 study being conducted by the Company of EPI-7386 in combination with Astellas Pharma Inc.'s and Pfizer Inc.'s AR inhibitor, enzalutamide, in patients with mCRPC who have not been treated with second-generation antiandrogens, the first cohort had cleared the 28 day DLT period with no safety issues and when reported the trial was currently enrolling the second cohort of patients. The preliminary data from the first cohort in the Phase 1/2 combination trial with enzalutamide suggests that the drugs can be combined safely and based upon clinical and preclinical data predicted to be active. The early data, in addition to preclinical studies, support EPI-7386's potential in combination with second-generation antiandrogens to suppress androgen receptor biology and induce a potent anti-tumor response.

The Company also described the anticipated initiation later in 2022 of a Phase 2 investigator-sponsored neoadjuvant study which will evaluate darolutamide compared to EPI-7386 + darolutamide in patients undergoing prostatectomy for high-risk localized prostate cancer.

At the AACR annual meeting on April 10, 2022, in a poster titled "Androgen receptor (AR) N-Terminal Domain degraders can degrade AR full length and AR splice variants in CRPC preclinical models," the Company presented preclinical data for its first generation of androgen receptor (AR) ANITen bAsed Chimera (ANITAC™) N-terminal domain (NTD) degraders. The preclinical data demonstrated the potential of ESSA's ANITAC degraders as a new approach to AR pathway inhibition. The intrinsically disordered nature of the NTD region of the AR has meant it has generally been considered undruggable. The preclinical studies have shown that through their unique ability to bind to the NTD of AR, ANITACs have the ability to inhibit NTD-mediated AR transcription while also degrading AR protein including resistant forms of AR which are commonly associated with CRPC. The preclinical results demonstrate that ANITAC degraders utilize the ubiquitin proteasome system and can degrade many forms of AR including full length, mutant, and splice variants which are often expressed in CRPC patients. Specifically, the ANITAC degraders show robust potency in inhibiting AR transcriptional activity driven by AR-FL, AR-V7, or AR-V567es. In addition, the orally-bioavailable ANITAC degraders exhibit high potency in inhibiting AR-dependent transcription and reducing viability of AR-dependent prostate cancer cells. The Company continues to design and test ANITAC degraders with a focus on improving selectivity.

On January 19, 2022, the Company announced the first patient dosed in the Company-sponsored Phase 1/2 study to evaluate the safety, tolerability and preliminary efficacy of ESSA's lead product candidate, EPI-7386, a first-in-class N-terminal domain androgen receptor inhibitor, in combination with Astellas and Pfizer Inc.'s ligand-binding domain androgen receptor inhibitor, enzalutamide, in patients with mCRPC. This combination trial investigates the potential clinical benefit of inhibiting the androgen receptor through two independent pathways in the treatment of patients with mCRPC who have not yet received treatment with a second-generation antiandrogen drug. In preclinical models, the combination of EPI-7386 with lutamides by simultaneously targeting both ends of the AR resulted in deeper and broader inhibition of androgen biology.

The Phase 1/2 clinical trial (NCT05075577) is a two part study. Phase 1 evaluates the safety and tolerability of the drug combination to establish the recommended Phase 2 range of doses for EPI-7386 and enzalutamide when dosed in combination. This Phase of the study is expected to enroll up to 30 mCRPC patients who have not yet been treated with second-generation antiandrogen therapies. As described below on June 27, 2022 the results of the initial experience with the first cohort were presented, demonstrating the safety and tolerability of the combination in this first cohort, along with

the accompanying pharmacokinetic and PSA reduction information. In Phase 2, single agent enzalutamide is compared to the combination of enzalutamide and EPI-7386 in the same patient population. The goal of Phase 2 is to evaluate the safety, tolerability and anti-tumor activity of EPI-7386 in combination with a fixed dose of enzalutamide compared with enzalutamide as a single agent. This part of the study is expected to enroll 120 mCRPC patients who have not yet been treated with second-generation antiandrogen therapies.

Financing and Capital

On February 22, 2021, the Company completed an underwritten public offering for aggregate gross proceeds of $149,999,985 (the "February 2021 Financing"). The Company issued a total of 5,555,555 common shares of the Company at a public offering price of $27.00 per share, which includes the underwriters having exercised their 30-day option to purchase an additional 724,637 common shares. In connection with the February 2021 Financing, the Company paid cash commissions of $8,999,999 and incurred other transaction costs of $150,498.

ESSA has never been profitable and has incurred net losses since inception. ESSA's net losses were $35,161,917 and $36,805,461 for the years ended September 30, 2022 and 2021, 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.

Results of Operations

The following table sets forth ESSA's consolidated statements of financial position and consolidated statements of loss and comprehensive loss as at and for the fiscal years ended September 30, 2022 and 2021:

(US$) Income Statement Data	Year Ended September 30, 2022	Year Ended September 30, 2021
Revenue	—	—
Research and development, net of recoveries	24,415,246	24,258,989
Financing costs	13,746	22,220
General and administration, net of recoveries	12,544,760	12,884,581
Total operating expenses	(36,973,752)	(37,165,790)
Comprehensive loss	(35,215,072)	(36,839,810)
Net loss, net of income tax	(35,161,917)	(36,805,461)
Balance Sheet Data		
Cash	57,076,475	137,825,024
Prepaids and other current assets	111,982,866	59,773,053
Deposits	259,455	259,455
Right-of-use assets	186,499	308,286
Total assets	169,505,295	198,165,818
Accounts payable and accrued liabilities	2,176,565	3,808,944
Income tax payable	—	—
Lease liabilities	210,252	330,970
Derivative liabilities	—	20,352
Shareholders' equity	167,118,478	194,005,552
Total liabilities and shareholders' equity	169,505,295	198,165,818

Results of Operations for the Fiscal Years Ended September 30, 2022 and 2021

There was no revenue in any of the fiscal years as reported. The Company incurred a comprehensive loss of $35,161,917 for the year ended September 30, 2022 compared to a comprehensive loss of $36,805,461 for the year ended September 30, 2021. 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:

	Year Ended September 30, 2022	Year Ended September 30, 2021
Clinical	$ 4,872,268	$ 4,597,114
Consulting	511,590	596,271
Legal patents and license fees	1,123,319	1,051,379
Manufacturing	2,946,412	6,867,397
Other	204,334	116,537
Preclinical and data analysis	8,134,161	4,760,269
Research grants and administration	-	157,080
Royalties	82,485	66,759
Salaries and benefits	2,073,188	1,731,852
Share-based payments	4,322,844	3,643,382
Travel and other	144,645	441,748
Impairment of CPRIT receivable	-	229,201
Total	$ 24,415,246	$ 24,258,989

The overall R&D expense for the year ended September 30, 2022 was $24,415,246 compared to $24,258,989 for the year ended September 30, 2021 and includes non-cash expense related to share-based payments expense of $4,322,844 (2021 - $3,643,382). R&D expense in 2022 reflects the ongoing clinical trial of EPI-7386.

The share-based payments expense of $4,322,844 (2021 - $3,643,382), which is a non-cash expense, relates to the value assigned to stock options and employee share purchase rights granted to key management personnel 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 $4,872,268 (2021 - $4,597,114) were generated in relation to expenditures associated with the Company's clinical research organizations conducting the Phase 1 clinical trial of EPI-7386.

Preclinical costs of $8,134,161 (2021 - $4,760,269) were generated in relation to expenditures for pharmacokinetic data analysis on data from the clinical trial related to the Phase 1 study and work on preclinical pipeline and Anitac compounds.

Manufacturing costs of $2,946,412 (2021 - $6,867,397) for the year ended September 30, 2022 includes amount for cGMP manufacturing of EPI 7386 drug supply to support the ongoing clinical trial as well as costs incurred in formulation and chemistry work around the Company's pharmaceutical characteristics of EPI-7386.

Consulting costs decreased to $511,590 (2021 - $596,271) for the year ended September 30, 2022 primarily resulting from contract project management services.

Salaries and benefits, related to preclinical and clinical staff, have increased to $2,073,188 (2021 - $1,731,852) as a result of an increased number of preclinical and clinical staff.

Legal patents and license fees were increased to $1,123,319 (2021 - $1,051,379). 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 the 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:

	Year Ended September 30, 2022	Year Ended September 30, 2021
Amortization	$ 264,698	$ 109,464
Consulting and subcontractor fees	185,292	218,262
Director fees	343,083	355,805
Insurance	2,088,637	943,848
Investor relations	577,350	646,058
Office, insurance, IT and communications	554,255	342,026
Professional fees	901,282	1,228,456
Regulatory fees and transfer agent	197,877	110,553
Rent	9,443	45,418
Salaries and benefits	3,710,999	3,036,894
Share-based payments	3,565,241	5,832,731
Travel and other	146,603	15,066
Total	$ 12,544,760	$ 12,884,581

General and administration expenses decreased to $12,544,760 for the year ended September 30, 2022 from $12,884,581 in the year ended September 30, 2021 and included non-cash expense related to share-based payments of $3,565,241 (2021 - $5,832,731). This 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.

Consulting and subcontractor fees of $185,292 (2021 - $218,262) were incurred for administrative and legal support in conjunction with corporate activities.

Insurance expense of $2,088,637 (2021 - $943,848) relates to increased cost of insurance coverage for directors and officers of the Company.

Professional fees of $901,282 (2021 - $1,228,456) were incurred for legal and accounting services in conjunction with ongoing corporate activities.

Salaries and benefits expense increased to $3,710,999 (2021 - $3,036,894) reflecting merit related salary adjustment and bonuses paid to employees and additional support staff costs.

Liquidity and Capital Resources

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

As at September 30, 2022, the Company had working capital of $166,748,942 (2021 - $193,668,414). Operational activities during the year ended September 30, 2022 were financed mainly by proceeds from a financing in July 2020 and the February 2021 Financing. At September 30, 2022, the Company had available cash reserves and short-term investments of $167,237,504 (2021 - $194,927,183) to settle current liabilities of $2,310,399 (2021 - $3,929,663). At September 30, 2022, 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. The Company expects its current cash runway to fund its operations and ESSA-sponsored clinical programs through 2025, including the Phase 1b monotherapy expansion and Window of Opportunity studies, a Phase 2 combination study with enzalutamide, additional cohorts in a Phase 1 study evaluating EPI-7386 with Janssen's antiandrogens, and an investigator-sponsored study of EPI-7386 and darolutamide.

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 Item 1A. elsewhere in this Annual Report.

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. Significant assumptions about the future and other sources of estimation uncertainty that management has made at the statement of financial position date, that could result in a material adjustment to the carrying amounts of assets and liabilities, in the event that actual results differ from assumptions that have been made that relate to the following key estimates:

Income tax

The determination of income tax is inherently complex and requires making certain estimates and assumptions about future events. Changes in facts and circumstances as a result of income tax audits, reassessments, changes to corporate structure and associated domiciling, jurisprudence and any new legislation may result in an increase or decrease the provision for income taxes. The value of deferred tax assets is evaluated based on the probability of realization; the Company has assessed that it is improbable that such assets will be realized and has accordingly not recognized a value for deferred taxes.

Share-based payments and compensation

The Company has applied estimates with respect to the valuation of shares issued for non-cash consideration. Shares are valued at the fair value of the equity instruments granted at the date of grant and the cost is recorded when the Company receives the goods or services.

The Company has applied estimates with respect to the valuation of pre-funded warrants issued for cash. Pre-funded warrants are valued at an amount equal to the cash proceeds received.

The Company measures the cost of equity-settled transactions with employees by reference to the fair value of the equity instruments at the date at which they are granted. Estimating fair value for share-based payment transactions requires determining the most appropriate valuation model, which is dependent on the terms and conditions of the grant. This estimate also requires determining the most appropriate inputs to the valuation model including the fair value of the underlying Common Shares, the expected life of the share option, volatility and dividend yield and making assumptions about them. The fair value of the underlying Common Shares is assessed as the most recent issuance price per common share for cash proceeds.

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 at the date of this Annual Report, 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.

Safe Harbor

See “Cautionary Note Regarding Forward-Looking Statements” in the introduction to this Annual Report.

Item 7A. Quantitative and Qualitative Disclosure About Market Risk

We are a smaller reporting company as defined by Rule 12b-2 of the Exchange Act and are not required to provide the information required under this item.