UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

☒ **Annual report pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934.**

For the Fiscal Year Ended December 31, 2023

or

☐ **Transition report pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934.**

For the transition period from _____ to _____

Commission File No. 001-34079

Ocuphire Pharma, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**11-3516358**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification
37000 Grand River Avenue, Suite 120 Farmington Hills, MI No.)	**48335**
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code: (248) 957-9024

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol	Name of each exchange on which registered
Common Stock, $0.0001 par value per share	**OCUP**	**The Nasdaq Stock Market LLC**

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days: Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company or an emerging growth company. See the definitions of ''large accelerated filer,'' ''accelerated filer,'' ''smaller reporting company'' and ''emerging growth company'' in Rule 12b-2 of the Exchange Act.

Large accelerated filer ☐	Accelerated filer ☐
Non-accelerated filer ☒	Smaller reporting company ☒
	Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. Yes ☐

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to § 240.10D-1(b). ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes ☐ No ☒

The aggregate market value of the common equity held by non-affiliates of the registrant on June 30, 2023, based on the closing price on that date of $4.34, was approximately $89,224,159. As of March 5, 2024, there were 24,813,370 shares of the registrant's common stock outstanding.

Documents Incorporated by Reference

Portions of the registrant's Definitive Proxy Statement to be filed with the Commission pursuant to Regulation 14A in connection with the registrant's 2024 Annual Meeting of Stockholders, to be filed subsequent to the date hereof, are incorporated by reference into Part III of this report. Such Definitive Proxy Statement will be filed with the Securities and Exchange Commission not later than 120 days after the conclusion of the registrant's fiscal year ended December 31, 2023.

Ocuphire Pharma, Inc.
Form 10-K

TABLE OF CONTENTS

[THIS PAGE INTENTIONALLY LEFT BLANK]

In this Annual Report on Form 10-K, unless otherwise specified, references to ''we,'' ''us,'' ''our,'' ''Ocuphire'' or ''the Company'' mean Ocuphire Pharma, Inc. Our financial statements are prepared in accordance with accounting principles generally accepted in the United States (''U.S. GAAP'').

FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements within the meaning of the safe harbor provisions of Section 27A of the Securities Act of 1933, as amended (the ''Securities Act''), and Section 21E of the Securities Exchange Act of 1934, as amended (the ''Exchange Act''). These forward-looking statements relate to us, our business prospects and our results of operations and are subject to certain risks and uncertainties posed by many factors and events that could cause our actual business, prospects and results of operations to differ materially from those anticipated by such forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those described under the heading ''Risk Factors'' included in this Annual Report on Form 10-K. Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this report. In some cases, you can identify forward-looking statements by the following words: ''anticipate,'' ''believe,'' ''continue,'' ''could,'' ''estimate,'' ''expect,'' ''intend,'' ''may,'' ''ongoing,'' ''plan,'' ''potential,'' ''predict,'' ''project,'' ''should,'' ''will,'' ''would'' or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. We undertake no obligation to revise any forward-looking statements in order to reflect events or circumstances that might subsequently arise. Readers are urged to carefully review and consider the various disclosures made by us in this report and in our other reports filed with the U.S. Securities and Exchange Commission (the ''SEC'') that advise interested parties of the risks and factors that may affect our business.

SUMMARY RISK FACTORS

Our business is subject to a number of risks, as fully described in ''Item 1A. Risk Factors'' in this Annual Report. The principal factors and uncertainties include, among others:

- We depend heavily on the success of our product pipeline and we (or our current or future strategic partners). Ocuphire and/or Viatris may never complete clinical development of, receive marketing approval for, or successfully commercialize, PS alone or as adjunctive therapy with low dose pilocarpine (LDP), APX3330, or any of our other product candidates. Moreover, if we (or our strategic partner) fail to adequately develop and commercialize APX3330 or PS, our business may be materially harmed.
- The results of previous clinical trials may not be predictive of future results, and the results of our current and planned clinical trials may not satisfy the requirements of the FDA or non-U.S. regulatory authorities.
- If we experience delays or difficulties in the enrollment of patients in clinical trials, our ability to conduct and complete clinical trials, and our ability to seek and receive necessary regulatory approvals, could be delayed or prevented.
- Changes in regulatory requirements or FDA guidance, or unanticipated events during our clinical trials, may result in changes to clinical trial protocols or additional clinical trial requirements, which could result in increased costs to us or delays in its development timeline.
- We or others could discover that our product candidates lack sufficient efficacy, or sufficient efficacy compared to competitor products or that they cause undesirable side effects that were not previously identified, which could delay or prevent regulatory approval or commercialization.
- Even if we receive marketing approval for our product candidates in the United States, we may never receive regulatory approval to market such product candidates outside of the United States.
- We face substantial competition and rapid technological change, which may result in others discovering, developing, or commercializing products before or more successfully than we do.
- We do not currently have any sales or marketing infrastructure in place and, if APX3330 is approved, we may face difficulties in establishing sales and marketing capabilities or engaging third parties to sell, market and distribute APX3330.
- Our future commercial success depends upon attaining significant market acceptance of our product candidates, if approved, among physicians, patients, third-party payors, and others in the medical community.

- If the FDA or a comparable foreign regulatory authority approves generic versions of our product candidates that receive marketing approval, or if such authorities do not grant our product candidates appropriate periods of exclusivity before approving generic versions of our products, the sales of our products could be adversely affected.
- We have not generated any revenue from sales of any products, and we expect to incur losses for the foreseeable future and may never achieve or maintain profitability.
- Our relatively short operating history may make it difficult for investors to evaluate our business to date and to assess our future viability.
- We will need substantial additional capital in the future. If additional capital is not available or is not available on acceptable terms (whether as a result of financial services industry changes, our financial performance or otherwise), we will have to delay, reduce or cease operations.
- Raising additional capital may cause dilution to our stockholders, restrict our operations, or require us to relinquish rights to our technologies or product candidates.
- Worldwide economic and social instability or adverse global economic conditions could adversely affect our revenue, financial condition, or results of operations.
- Our employees or our representatives may engage in misconduct or other improper activities, including violating applicable regulatory standards and requirements, which could significantly harm our business.
- Product liability lawsuits against us, or our suppliers and manufacturers, could cause us to incur substantial liabilities and could limit commercialization of any product candidate that we may develop.
- Federal legislation and actions by state and local governments could permit reimportation of drugs from foreign countries into the United States, which could adversely affect our operating results when the drugs are sold at lower prices in foreign countries.
- We rely on third parties to conduct our preclinical and clinical trials and perform other tasks for us. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or comply with regulatory requirements, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be harmed.
- We rely completely on third parties to supply and manufacture bulk drug substances and to formulate and package nonclinical and clinical drug supplies of our product candidates as well as to conduct analytical testing of drug substances and products in the manufacturing processes and we intend to rely on third parties to produce and test commercial supplies of our current and any future product candidates.
- We have entered and may enter into licensing arrangements for the development or sale of product candidates (such as the Viatris License Agreement (as defined below)) and may form or seek additional strategic alliances or enter into licensing arrangements in the future, including for APX3330. If we are unsuccessful in forming or maintaining these alliances on favorable terms, our business could be harmed and we may have to alter development, manufacturing and commercialization plans.
- If we engage in acquisitions, in-licensing or strategic partnerships, this may increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities and subject us to other risks.
- If we are unable to obtain and maintain sufficient patent protection for our product candidates, our competitors could develop and commercialize products or technology similar or identical to those of us, which would adversely affect our ability to successfully commercialize any product candidates we may develop, our business, results of operations, financial condition and prospects.
- If we do not obtain protection under the Hatch-Waxman Act and similar foreign legislation by extending the patent terms and obtaining data exclusivity for our product candidate, our business may be materially harmed.
- We may not be able to protect or practice our intellectual property rights throughout the world.

- Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment, and other requirements imposed by governmental agencies, and our patent protection could be reduced or eliminated for noncompliance with these requirements.
- We are dependent on our key personnel, and if we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.
- A variety of risks associated with operating internationally for us and our collaborators could adversely affect our business.
- Our business and operations would suffer in the event of system failures or unplanned events, including cyber incidents, network security breaches, service interruptions, or data corruption.
- We currently have a substantial number of shares subject to potential issuance associated with our Equity Line of Credit arrangement. The issuance or sale of shares under our ELOC arrangement would substantially increase the number of shares outstanding and result in dilution to our security holders. This might substantially decrease the market price of the common stock.
- We do not anticipate paying any cash dividends in the foreseeable future.
- If we fail to comply with the continued listing standards of the Nasdaq Capital Market, our common stock could be delisted. If it is delisted, our common stock and the liquidity of our common stock would be impacted.
- The market price of our common stock may fluctuate significantly.
- We may be subject to securities litigation, which is expensive and could divert management attention.

INDUSTRY AND MARKET DATA

In this Annual Report, we reference information, statistics and estimates regarding the medical devices and healthcare industries. We have obtained this information from various third-party sources, including industry and general publications, reports by market research firms and other sources. This information involves a number of assumptions and limitations, and we have not independently verified the accuracy or completeness of this information. Some data and other information are also based on the good faith estimates of management, which are derived from our research, review of internal surveys, general information discussed in the industry, and third-party sources. We believe that these external sources and estimates are reliable but have not independently verified them. The industries in which we operate are subject to a high degree of uncertainty, change, and risk due to a variety of factors, including those described in ‘‘Item 1A. Risk Factors.’’ These and other factors could cause results to differ materially from those expressed in this Annual Report and other publications.

PART I

ITEM 1. BUSINESS

Overview

Ocuphire Pharma, Inc. is a clinical-stage biopharmaceutical company focused on developing novel therapies for the treatment of unmet needs of patients with retinal and refractive eye disorders.

The Company's lead retinal product candidate, APX3330, is a small-molecule inhibitor of Ref-1 (reduction oxidation effector factor-1 protein). Ref-1 is a regulator of transcription factors such as HIF-1α and NF-κB. Inhibiting Ref-1 reduces levels of vascular endothelial growth factor (''VEGF'') and inflammatory cytokines which are known to play key roles in ocular angiogenesis and inflammation. APX3330 is an oral tablet administered once or twice per day in development for the treatment of diabetic retinopathy (''DR''). A Phase 2 study in subjects with DR or diabetic macular edema was completed and results were reported in January 2023. An End-of-Phase 2 (''EOP2'') meeting with the U.S. Food and Drug Administration (the ''FDA'') was held in October 2023 at which the Company obtained agreement on the registration endpoint supporting the advancement of APX3330 into future clinical trials. The Company submitted a special protocol assessment (''SPA'') to the FDA in February 2024 to seek agreement on the clinical trial protocol and statistical analysis plan and will share specifics on the study design parameters and anticipated timing if and when a SPA agreement is reached with the FDA.

DR affects approximately 10 million diabetics and is projected to impact over 14 million Americans by 2050. DR is classified as either Non-Proliferative Diabetic Retinopathy (''NPDR''), the early stage of the disease in which symptoms may be mild or non-existent or Proliferative Diabetic Retinopathy (''PDR'') which is the more advanced stage of diabetic eye disease that can be highly symptomatic with loss of vision. Approximately 8 million DR patients have NPDR that may progress to PDR, if left untreated. Despite the risk for visual loss associated with this disease, over 90% of NPDR patients currently receive no course of treatment apart from observation by their eye care specialist until they develop sight-threatening complications. This is due to various factors, including the treatment burden of the frequent eye injections required with currently approved therapies for this disease. APX3330, as an oral tablet, has the potential to be an early, non-invasive treatment for the approximately 8 million NPDR patients in the US.

The Company has also in-licensed APX2009 and APX2014, which are second-generation analogs of APX3330. The unique mechanism of action of this family of Ref-1 inhibitors of reducing angiogenesis and inflammation could potentially be beneficial in treating other retinal diseases such as age-related macular degeneration, geographic atrophy, and non-ophthalmic diseases.

In November 2022, the Company entered into a license and collaboration agreement (the ''Viatris License Agreement'') with FamyGen Life Sciences, Inc. (''Famy'') (acquired by and now known as Viatris, Inc. (''Viatris'') in January 2023) pursuant to which it granted Viatris an exclusive license to develop, manufacture, import, export and commercialize its refractive product candidate Phentolamine Ophthalmic Solution 0.75% (initially known as Nyxol) (''PS''). PS is a once-daily eye drop formulation of phentolamine mesylate designed to reduce pupil diameter and improve visual acuity. PS was approved by the FDA for the treatment for pharmacologically-induced mydriasis under the brand name RYZUMVI™ in September 2023. PS is currently in Phase 3 clinical trials for presbyopia (age-related blurry near vision). The VEGA-2 Phase 3 study in presbyopia achieved its primary endpoint and Viatris, our development and commercial partner, is expected to continue Phase 3 development in the first half of 2024. PS is also in Phase 3 for decreased vision under dim (mesopic or low) light conditions following keratorefractive surgery. On December 5, 2023, the Company received FDA Agreement Under Special Protocol Assessment for LYNX-2, a Phase 3 trial of PS for the treatment of decreased vision under dim (mesopic or low) light conditions following keratorefractive surgery and Viatris, our development and commercial partner, is expected to continue Phase 3 development in this indication in the first half of 2024.

Pursuant to the Viatris License Agreement, Ocuphire received an upfront cash payment of $35 million and a $10 million license agreement milestone payment for the NDA approval of RYZUMVI. In addition, Ocuphire is eligible to receive potential additional payments of up to $120 million, in the aggregate, upon achieving certain specified regulatory or net sales milestones. Ocuphire will also receive tiered royalties based on annual net sales of PS in and outside of the United States (with royalties ranging from percentages in the low double digits to the low twenties for annual net sales in the United States and percentages in the low double-digits for annual net sales outside of the United States). The Viatris License Agreement does not expire until terminated under the terms of the agreement.

Corporate History

In February 2018, Ocuphire Pharma, Inc. (prior to the Merger with Rexahn, ''Private Ocuphire'') was founded and subsequently merged in April 2018 with Ocularis Pharma, LLC, (the original innovator of phentolamine mesylate ophthalmic solution), and in January 2020 obtained from Apexian Pharmaceuticals, Inc. certain rights to its Ref-1inhibitor program, including APX3330 (see ''Apexian Sublicense Agreement'').

In November 2020, Private Ocuphire completed a reverse merger (the ''Merger'') into Rexahn Pharmaceuticals, Inc. (''Rexahn''), a publicly-traded company that had ceased its business of drug development activities, and simultaneously raised $20 million through an offering of common shares and warrants to purchase common shares. In connection with the Merger, Rexahn changed its name to Ocuphire Pharma, Inc. and has since conducted, as a public company, the business previously conducted by Private Ocuphire.

In November 2022, Ocuphire entered into the Viatris License Agreement, licensing its PS product to Viatris.

Many of Ocuphire's employees, directors, advisors and consultants have been involved in the development of PS and other ophthalmic drugs including approved products such as LUMIFY® marketed by Bausch & Lomb Incorporated, Zirgan® marketed by marketed by Bausch & Lomb Incorporated Durezol® marketed by Novartis, Upneeq® marketed by RVL Pharmaceuticals plc, Rhopressa® marketed by Alcon, Rocklatan® marketed by Alcon, Vyzulta® marketed by Bausch & Lomb Incorporated, Xiidra® marketed by Bausch & Lomb Incorporated, Cequa® marketed by Sun Pharmaceuticals Industries Limited, Iyuzeh™ marketed by Thea Pharma Inc., and Dextenza® marketed by Ocular Therapeutix, Inc. The management team, led by Chief Executive Officer (''CEO'') George Magrath, MS, MD, MBA, collectively has significant experience in operating pharmaceutical companies and discovering, developing, and commercializing treatments in multiple therapeutic areas.

Strategy

Ocuphire's goal is to build a leading biopharmaceutical company that discovers, develops, commercializes and/or out-licenses best-in-class therapies for patients and provides attractive solutions for physicians and payers. The key elements of Ocuphire's strategy to achieve its goal are the following:

- Advance the clinical development of our products.

For the APX3330 program, an End-of-Phase 2 (''EOP2'') meeting with the U.S. Food and Drug Administration (the ''FDA'') was held in October 2023 at which the Company obtained agreement on the registration endpoint supporting the advancement of APX3330 into future clinical trials. The Company submitted a SPA with the FDA in February 2024 and will provide further guidance on study design, cost and timelines if and when a SPA agreement is reached with the FDA.

For PS, Ocuphire entered into the Viatris License Agreement in November 2022, pursuant to which Viatris has exclusive rights to develop and commercialize PS. Pursuant to the Viatris License Agreement, Ocuphire continues to conduct development activities in the United States in partnership with Viatris, and is reimbursed by Viatris for such budgeted development activities. PS was approved by the FDA for the treatment for pharmacologically-induced mydriasis under the brand name RYZUMVI in September 2023 and is advancing Phase 3 trials for presbyopia and decreased vision under dim (mesopic or low) light conditions after keratorefractive surgery. Viatris has exclusive rights to pursue development and undertake commercialization efforts for PS outside of the United States.

- **Maintain and expand its intellectual property portfolio**. Ocuphire owns an exclusive worldwide sublicense for the Ref-1 Inhibitor program, including its product candidate APX3330, for all its ophthalmic and diabetic indications, and compositions and methods of use for Ref-1 pipeline candidates, including APX2009 and APX2014.

Ocuphire continues to explore additional opportunities to expand and extend this intellectual property protection, both in the U.S. and in other jurisdictions. Ocuphire owns an exclusive worldwide sublicense for the Ref-1 Inhibitor program, including its product candidate APX3330, for all its ophthalmic and diabetic indications, and compositions and methods of use for Ref-1 pipeline candidates, including APX2009 and APX2014. Ocuphire continues to explore additional opportunities to expand and extend this intellectual property protection, both in the U.S. and in other jurisdictions.

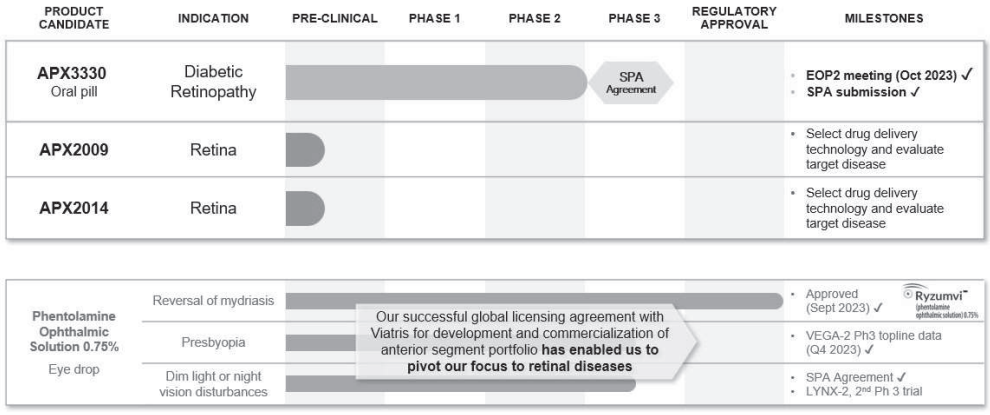
- **Maximize the value of APX3330 and PS.** Ocuphire may seek one or more partners to develop and commercialize APX3330 both in and/or outside of the United States.

RYZUMVI, now FDA approved and PS, if approved for presbyopia and decreased vision under dim (mesopic or low) light conditions after keratorefractive surgery, will be commercialized by the Viatris Eye Care Division in the U.S. and major non-U.S. markets pursuant to the Viatris License Agreement.

- **Evaluate in-licensing and acquisition opportunities**. Ocuphire's team is well qualified to identify and in-license or acquire clinical-stage assets and continually evaluates opportunities to expand and diversify its pipeline.

Ocuphire is continuing to develop APX3330 for multiple indications and may develop and commercialize on our own or seek a development and commercial partner for APX3330. Ocuphire is continuing the development PS with its partner Viatris for multiple indications. Ocuphire believes the two programs present similar potential advantages, including: (1) promising clinical data to date; (2) both small-molecule late-stage clinical candidates; (3) convenient dosing route and schedule; (4) potential for first-line or adjunctive therapy; and (5) significant commercial potential. FIGURE 1 below summarizes Ocuphire's current development pipeline of product candidates and their target indications and anticipated milestones:

FIGURE 1: Ocuphire Pipeline: Product Candidates and Indications Pipeline



Note: RYMZUMVI and 0.75% PS (Phentolamine Ophthalmic Solution) is the same as 1% PMOS (Phentolamine Mesylate Ophthalmic Solution). References to PS with both designations appear throughout this document, there is no difference in formulation between the two designations.

PS was approved by the FDA for the treatment for pharmacologically-induced mydriasis under the brand name RYZUMVI in September 2023 and is advancing in Phase 3 trials for treatment of presbyopia and decreased vision under dim (mesopic or low) light conditions after keratorefractive surgery. Ocuphire anticipates submitting supplemental NDAs for PS for treatment of presbyopia and decreased vision under dim (mesopic or low) light conditions after keratorefractive surgery and is advancing APX3330 towards an NDA in the future.

Overview of Eye Disease Market

Retinal (Back of the Eye) Disease Market

Retinal damage is one of the leading causes of blindness and continues to grow with aging and larger diabetic populations around the world. Diabetes is the leading cause of blindness among adults aged 20 – 74. According to the National Eye Institute, in the United States alone, over 10 million patients suffer from DR, a complication of diabetes in which chronically elevated blood sugar levels cause damage to blood vessels in the retina. An additional 750,000 patients suffer from diabetic macular edema (''DME''), one of the most common complications of diabetic retinopathy where the macula swells from fluid leaked from damaged blood vessels. The disease progression of both DR and DME involves abnormal vessel proliferation via VEGF signaling and inflammation. Ocuphire's APX3330 oral tablet recently completed a Phase 2 clinical trial for DR and has the potential to address this large DR market with a novel, dual mechanism of action of inhibiting VEGF, a modulator of angiogenesis, and inflammation. In addition, over 1 million patients in the United States suffer from wAMD. These retinal and choroidal vascular diseases, which cause damage to the macula, are leading causes of severe, permanent vision loss. Currently, there are several drugs on the market indicated for anti-VEGF therapy, including Lucentis® (ranibizumab), a monoclonal antibody marketed by Genentech, and EYLEA® (aflibercept), a recombinant fusion protein marketed by Regeneron

Pharmaceuticals, Inc., that have become the standard of care for treating severe forms of DME and wAMD amongst other retinal conditions. These injectable drugs are biologics with treatment administered in an ophthalmologist's office. Annual worldwide sales of Lucentis and EYLEA for all indications totaled over $13 billion in 2020 ($3.5 billion for Lucentis and over $10 billion for EYLEA).

Anterior (Front of the Eye) Segment Disease Market

There are approximately 100 million eye dilations in the United States and this number is expected to go up with the increasing aging and diabetic population that requires more frequent eye exams and procedures. Millions of Americans also suffer from various refractive errors.

Presbyopia, one such refractive error, is common in patients over the age of 40 years, which results in decreased ability to see objects at a near distance. This condition affects over 120 million Americans and usually requires reading glasses and/or contact lenses for focusing on near objects.

Further, according to GlobalData, approximately 38 million patients in the U.S. suffer from dim light or night vision disturbances caused by LASIK, night myopia, keratoconus, eye surgery, or the natural aging process. There is also a global trend in vision disturbances in younger individuals due to the overuse of smartphone screens.

Summary of APX3330 and PS

APX3330

APX3330 is a small molecule that specifically targets Apurinic/Apyrimidinic Endonuclease 1/Redox Factor-1 (APE-1/Ref-1, referred to as Ref-1),Ref-1, a dual function protein involved in the regulation of transcription factors critical to cell signaling. Ref-1 regulates inflammation, angiogenesis (blood vessel formation), and reduction-oxidation (redox) signaling, as well as DNA repair that is critical to normal function of neurons. By inhibiting redox activity and not DNA repair, APX3330 has been shown in preclinical studies to reduce angiogenesis and inflammation via modulation of several important proangiogenic and proinflammatory transcription factors such as NF-κB and HIF-1α and its downstream target, VEGF (Vascular Endothelial Growth Factor). These transcription factors are implicated in multiple pathways relevant to the pathophysiology of retinal and choroidal vascular diseases, including diabetic retinopathy (DR), diabetic macular edema (DME), wet age-related macular degeneration (wAMD) and geographic atrophy (GA).

Key attributes of Ocuphire's product candidate APX3330 include the following:

- **Potential to be the first oral therapy.** Compared to frequent intravitreal anti-VEGF injections, associated with ocular complications, twice a day oral administration of APX3330 could be a convenient, new preventative therapeutic option or adjunctive treatment option for large number of patients with retinal diseases, if approved.
- **Upstream target implicated in two validated pathways.** APX3330 is designed to modulate two validated cell signaling pathways (angiogenesis and inflammation) known to cause various retinal diseases. Moreover, the APX3330 mechanism of action is distinct in working upstream of the current anti-VEGF therapies, suggesting that it could complement anti-VEGF therapies and potentially reduce frequency of doctor visits and intravitreal injections.
- **Favorable tolerability profile.** In 12 completed Phase 1 and Phase 2 clinical trials, APX3330 was observed to be well-tolerated. The adverse events (''AEs'') were mostly infrequent and mild with transient pruritis being the most common.
- **Potential benefit of systemic administration.** As a systemic agent, APX3330 can be expected to treat bilateral binocular (both eyes) retinal vascular disease.
- **Oral tablet with scalable manufacturing process.** APX3330 is formulated as an oral tablet with favorable stability characteristics, and its active pharmaceutical ingredient is a small molecule with the advantages of standardized, scalable, and lower-cost manufacturing processes.

Ocuphire is initially pursuing APX3330 for the DR indication as first-line therapy and may explore opportunities for clinical benefit as monotherapy or adjunctive therapy for other retinal indications such as DME, wAMD, and GA:

- **DR**, the leading cause of vision loss in adults aged 20–74 years, which results from chronic elevations of glucose in the blood that leads to cell damage in the retina. Retinal key opinion leaders' feedback suggests that slowing of DR progression with an oral agent would be a useful treatment in patients with background DR and good visual function.
- **DME**, one of the most common complications of DR, in which vascular leakage causes swelling of the retinal macula and a loss of visual acuity.
- **wAMD**, a chronic eye disorder that causes visual distortions in the central part of one's vision, in which abnormal blood vessels leak fluid or blood into the macula, the part of the eye that is critical for central and color vision.
- **GA**, an advanced form of age-related macular degeneration (AMD) that leads to progressive and irreversible vision loss.

PS (phentolamine 0.75% ophthalmic solution)

PS, out-licensed to Viatris in 2022, is a once-daily, sterile, preservative-free eye drop formulation containing phentolamine mesylate, a reversible, non-selective alpha-1 and alpha-2 adrenergic antagonist that acts on the adrenergic nervous system and inhibits contraction of smooth muscle. Ocuphire submitted an NDA to the FDA in November 2022 under the 505(b)(2) pathway and PS was approved by the FDA for the treatment for pharmacologically-induced mydriasis under the brand name RYZUMVI in September 2023. RYZUMVI reverses the pharmacologically induced dilation of the pupils, where dilation leads to increased sensitivity to light and an inability to focus, making it difficult to read, work, and drive.

Viatris will continue to commercialize RYZUMVI for the treatment of pharmacologically-induced mydriasis. Ocuphire and Viatris are pursuing PS for the following additional indications under the Viatris License Agreement:

- Presbyopia, a condition in which the eye's lens loses elasticity, affecting its ability to focus on near objects. Presbyopia typically occurs after age 40 and most patients use reading glasses in order to read or see objects close to them. Vuity™ approved in October 2021, and QLOSI™ approved in October 2023 are the only two approved eye drops for the treatment of presbyopia.
- Decreased vision under dim (mesopic or low) light conditions after keratorefractive surgery, a condition in which peripheral imperfections (aberrations) of the cornea scatter light when the pupil opens wide in dim light. Patients experience glare, halos, starbursts, and decreased contrast sensitivity. decreased visual acuity under dim (mesopic) light conditions is a new indication with no approved therapies.

APX3330's Target Indications

Diabetic Retinopathy

Diabetic Retinopathy Overview

DR is an eye disease resulting from diabetes, affecting over 10 million patients in the U.S., in which chronically elevated blood sugar levels cause damage to blood vessels in the retina. It is the leading cause of vision loss in adults aged 20–74 years. There are two major types of DR:

- ***Non-proliferative DR, or NPDR.*** NPDR is an earlier stage of DR and can progress into more severe forms of DR over time if untreated and if exposure to elevated blood sugar levels persists.
- ***Proliferative DR, or PDR.*** PDR is a more advanced stage of DR than NPDR. It is characterized by retinal neovascularization and, if left untreated, leads to permanent damage and blindness.

Therapies for NPDR and PDR are distinct. For NPDR, treatment is usually directed at observation, lifestyle changes, and control of elevated blood sugars that led to progression of NPDR in the first place. Additionally, the current treatment paradigm is for physicians to wait and monitor early-stage DR/NPDR patients, with anti-VEGF or steroid injectable therapy or laser treatment reserved for patients who advance to proliferative DR or DME. In the Protocol S trial by the Diabetic Retinopathy Clinical Research Network, Lucentis was found to be noninferior to laser therapy in patients with PDR. Moreover, in 2018, from Regeneron's PANORAMA trial, EYLEA® reversed disease progression in patients with moderately severe to severe NPDR.

Limitations of Existing Treatments for DR

In DR (especially NPDR), despite the approvals of anti-VEGF therapeutics in recent years, the use of injectables is not adopted in practice as preferred treatment as the disease is asymptomatic and patients are reluctant to undergo injections or laser therapy.

In late-stage DR, intravitreal VEGF inhibitors are approved globally; however, these therapies rarely provide a complete solution to the underlying vascular problem associated with DR. Although these therapeutic agents have been successful for some patients, significant proportions of patients are resistant and refractory. Moreover, serious side effects including hemorrhage and intraocular infections are possible with intravitreal injections. Both Lucentis and EYLEA are also associated with increased risks of blood clots in the arteries. In addition, intravitreal injections require frequent visits to the ophthalmologist, usually on the order of every 4 weeks with a few anti-VEGF therapies in development that are working on increasing the time between injections (8 – 12 weeks).

Furthermore, retinal diseases are initially or over time bilateral, and thus treatments that only treat one eye, leave the other eye to remain untreated.

APX3330 Opportunity in DR

In addition to being characterized by abnormal increases in VEGF levels, recent scientific literature reports indicate that diabetic eye disease has an inflammatory component, unrelated to VEGF. Because inflammation and hypoxic signaling (VEGF production) play crucial roles in both vascular leakage and neovascularization of DR, treatments that impinge upon both pro-inflammatory and hypoxic signaling offer a promising therapeutic strategy. APX3330's target of Ref-1 (a protein associated with inflammation and immune response) may leverage this dual mechanism of action (or ''MOA'') to reduce the production and hence the quantity of VEGF while also preventing inflammatory damage. The MOA of APX3330 is differentiated from traditional anti-VEGF treatments in that it does not neutralize the elevated levels of VEGF, but rather brings VEGF levels to normal homeostatic levels, thereby making it an ideal treatment option to prevent progression or worsening in earlier stages of diabetic eye disease.

This potentially allows for improved response to DR treatment and may extend the duration between invasive treatments for late-stage retinal diseases (DME, wAMD). Moreover, as a potential orally administered product candidate twice a day, it has the potential to be a more convenient option at an earlier stage of disease especially for DR than intravitreal anti-VEGF injections, which are burdensome to patients and have a significant side effect profile including cataract formation, increased intraocular pressure, intraocular infections, and retinal detachments. Furthermore, as a systemic therapy, APX3330 offers the potential to treat both eyes while maintaining a favorable safety profile.

Potential Other Indications:

Diabetic Macular Edema

Diabetic Macular Edema Overview

DME is a common complication of DR where the macula swells with fluid leaked from damaged blood vessels as a result of worsening diabetic retinopathy. It is one of the most common reasons for blindness in diabetics, affecting approximately 750,000 patients. DME may cause blurriness in the center of vision, the appearance of straight lines as wavy, colors that look dull or washed out, or blind spots. The pathogenesis of DME involves vascular leakage, retinal ischemia, and release of vaso-proliferative growth factors and inflammatory mediators.

In DME, corticosteroids and anti-VEGF agents are used to treat vascular leakage, inflammation and hypoxia/angiogenesis. In patients whose disease has progressed to DR with DME, anti-VEGF agents are first line therapy followed by corticosteroids. Lucentis was approved for treatment of DME with a dosing regimen of a 0.3 mg injection approximately every four weeks. Similarly, EYLEA® was approved with a dosing regimen of a 2.0 mg injection approximately every four weeks.

In DME, intravitreal VEGF inhibitors are approved globally; however, these therapies rarely provide a complete solution to the underlying vascular problem associated with DME. Although these therapeutic agents have been successful for some patients, significant proportions of patients are resistant and refractory. Moreover, serious side effects including hemorrhage and intraocular infections are possible with intravitreal injections. Both Lucentis and

EYLEA are also associated with increased risks of blood clots in the arteries. In addition, intravitreal injections require frequent visits to the ophthalmologist, usually on the order of every 4 weeks with a few anti-VEGF therapies in development that are working on increasing the time between injections (8 – 12 weeks).

Furthermore, retinal diseases are initially or over time bilateral, and thus treatments that only treat one eye, leave the other eye to remain untreated.

Wet AMD

Age-Related Macular Degeneration (''AMD'') is a common eye condition affecting 11 million individuals in the U.S. and 196 million individuals globally, mostly over the age of 55 years. It is a progressive disease affecting the central portion of the retina, known as the macula, which is the region of the eye responsible for sharpness, central vision and color perception. wAMD is an advanced form of AMD characterized by neovascularization and fluid leakage under the retina. It is the leading cause of severe vision loss in patients over the age of 50 in the United States and EU. While wAMD represents only 10% of the number of cases of AMD overall, it is responsible for 90% of AMD-related severe vision loss. Untreated or undertreated wAMD results in further blood vessel leakage, fluid in the macula, and ultimately scar tissue formation, which can lead to permanent vision loss or even blindness as a result of the scarring and retinal deformation that occur during periods of non-treatment or undertreatment. Similar to severe DR and DME, current therapy for wAMD consists of intravitreal injections, mainly of Lucentis and EYLEA. The limitations of these therapies are described in the section above titled, ''Limitations of Existing Treatment for DR and DME''. Based on APX3330 targeting Ref-1 with a MOA of reducing overexpression of VEGF and inflammation, it has potential use in wAMD. Further, to enter the wAMD injectable market, Ocuphire is considering the utility of an intravitreal or sustained delivery formulation of APX3330 and its second-generation analogs, APX2009 and APX2014. APX2009 and APX2014 data suggest improved efficacy against the Ref-1 target compared to APX3330 (as published in the Journal of Pharmacology and Experimental Therapeutics).

GA

Geographic atrophy (''GA'') is an advanced form of AMD that leads to progressive and irreversible vision loss. AMD is the leading cause of permanent vision loss in people over the age of 65 in developed countries, and the risk of developing AMD increases with age. Based on published studies, approximately 1 million individuals have GA in the United States, and 5 million individuals have GA globally. In people with GA, photoreceptors, which are light sensitive cells, deteriorate in the macula, a central portion of the retina responsible for central vision and color perception. This damage starts as small spots that grow into larger patches. As the cells in the macula die, the person starts to lose vision. A person with early AMD may notice problems with reading or night vision. Eventually, if the disease progresses to advanced stages, permanent blind spots (scotomas) in the center of the visual field will develop. The cause of GA is thought to be multifactorial including inflammation, with numerous environmental and genetic risk factors. The dysregulation of the complement cascade, an important part of the body's immune system, plays a pivotal role. Excessive activation of the complement cascade results in destruction of healthy cells, which can lead to the onset or progression of many diseases including GA. SYFOVRE® and IZERVAY® are the only FDA approved treatments for GA and requires monthly or every other month intravitreal injections.

Product Candidates

APX3330

APX3330 (E3330) is an oral formulation administered twice a day and is designed to target multiple pathways relevant to retinal and choroidal vascular diseases, such as DR and DME, which, if left untreated, may progress to permanent visual acuity loss and eventual blindness. Mechanistic studies and prior clinical experience suggest that APX3330 is a promising candidate for clinical evaluation of its efficacy and safety in the treatment of these diseases, beginning with DR and DME.

In preclinical pharmacology studies in animal models or in vitro, APX3330 has demonstrated the ability to decrease angiogenesis and inflammation in the retina whether delivered orally, systemically, or directly into the eye via intravitreal injections. In humans, APX3330 was shown to be clinically well-tolerated in multiple Phase 1 and 2 trials with fewer than 10% of the patients experiencing mild, self-limiting side effects, such as nausea or diarrhea. In addition, it was shown that significant amounts of oral APX3330 reach the bloodstream concentrations in humans and higher than the levels in mice which showed effects in the retina.

Ocuphire is initially pursuing a moderate-to-severe NPDR indication. Additionally, Ocuphire may explore opportunities for clinical benefit as monotherapy or adjunctive therapy for other retinal indications such as DME, wAMD, and GA or other non-ophthalmic indications. Second-generation candidates, APX2009 and APX2014, may also be considered for intravitreal, oral or other injection routes of delivery for ophthalmic and non-ophthalmic indications.

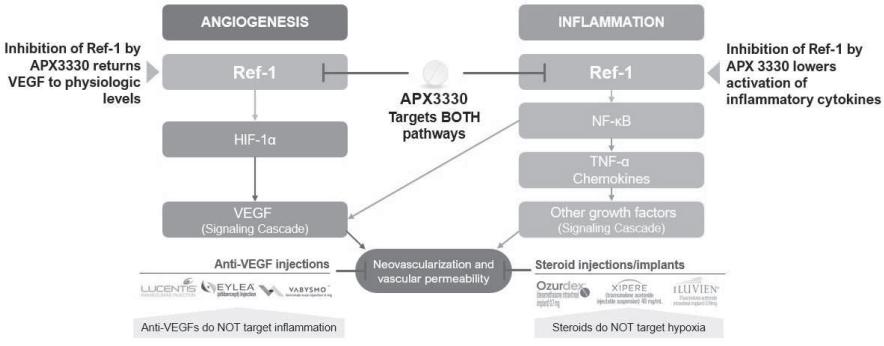
APX3330 Mechanism of Action

APX3330 is a selective small molecule that acts on the dual-functioning Apurinic/Apyrimidinic Endonuclease 1/Redox Effector Factor-1 (APE1/Ref-1) protein, referred to as Ref-1. This protein is implicated in both redox signaling and DNA repair. Because APX3330 selectively inhibits the redox function without affecting the molecule's ability to carry out DNA repair, normal cell function is left intact. Moreover, interference of Ref-1 activity with APX3330 blocks angiogenesis and inflammation by simultaneously decreasing the activity of several important transcription factors such as HIF-1α and NF-κB (see **FIGURE 2 below for a visual description**). HIF-1α regulates the expression of VEGF, a protein that is paramount for angiogenesis, and NF-κB is an upstream regulator of proteins involved in inflammatory processes such as TNFα and chemokines.

The development of DR/DME involves leakage from retinal vessels, lack of blood flow to the retina, and release of angiogenic growth factors and inflammatory mediators. The downstream targets of HIF-1α and NF-κB serve as key mediators of these disease features and are targets of current therapy for diabetic eye disease and wAMD. Rather than inhibiting the action of VEGF protein, APX3330 has been shown in preclinical models to inhibit its formation; this is a key potential distinction of APX3330 from the drugs currently approved or under development for DR such as Lucentis and EYLEA. APX3330's potential ability to inhibit the activity of these two transcription factors may mitigate the need for frequent intravitreal anti-VEGF or steroid injections.

APX3330 has a dual mechanism that decreases both abnormal angiogenesis and inflammation. APX3330 blocks pathways downstream of Ref-1. Blocking HIF-1α reduces VEGF signaling, and blocking NF-κB modulates VEGF, TNF-α and other inflammatory cytokine production. In contrast, anti-VEGF agents solely inhibit the actions of VEGF **(see FIGURE 2 below for a visual description)**.

FIGURE 2: APX3330 Dual Mechanism of Action in Validated Disease Pathways



Note: Eylea® is registered trademark of Regeneron and Lucentis® is registered trademark of Roche/Genentech, VABYSMO™ is a registered trademark of the Roche Group, OZURDEX® is registered trademark of Allergan, XIPERE® is registered trademark of Clearside Biomedical, Inc., ILUVIEN® is registered trademark of Alimera Sciences Inc.

APX3330 Clinical Experience Summary

APX3330 has been studied in over 375 healthy volunteers or patients with hepatitis or cancer or diabetic retinopathy, over 270 of whom were given the product candidate for an average of 75 days or more at up to 720mg per day dose. In these 12 Phase 1 and 2 non-ocular and ocular clinical trials, clinical data on safety and efficacy, effect upon the Ref-1 molecular target, and pharmacodynamic characteristics were collected. APX3330 showed favorable safety tolerability and biological efficacy.

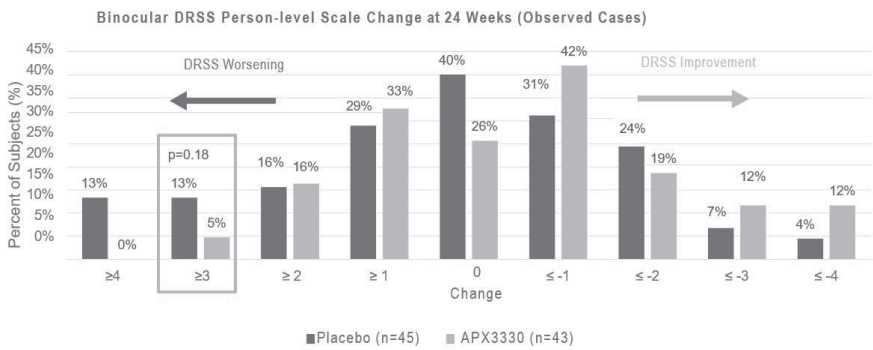
Across these 10 trials, it was found that APX3330 exhibited predictable PK that were consistent with the PK data obtained in nonclinical studies. In two studies it was found that meals have no impact on the PK of APX3330. APX3330 has been demonstrated to be well tolerated at doses up to 600 mg/day.

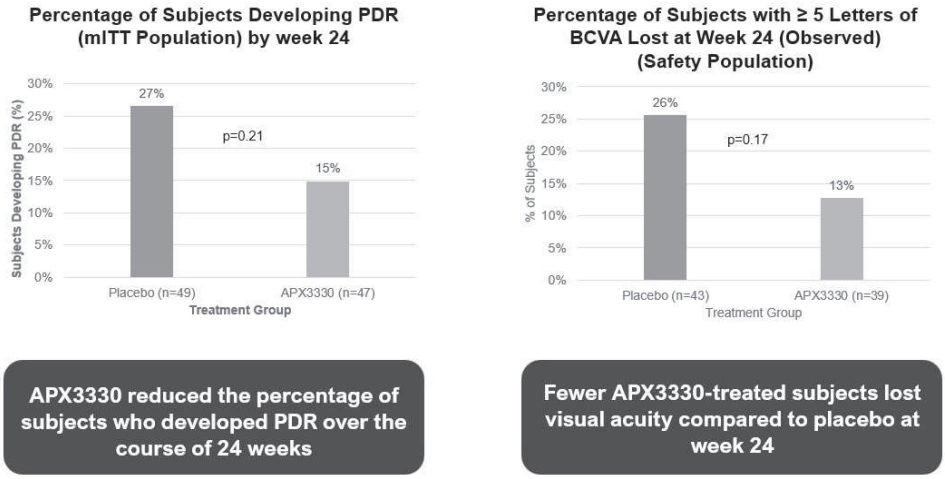
In the 75 patients receiving either placebo or APX3330 treatment in the five Phase 1 trials (CLN_0001, 2, 3, 4, and 8), five patients in the treatment arms experienced AEs (mild diarrhea at doses of 120 mg, 180 mg, or 240 mg/day). In the five Phase 2 trials of the 279 patients given APX3330, 40 (14%) had AEs, the majority of which were mild. In a Phase 1 trial for patients with adult solid tumors, APX_CLN_0011, patients received doses of APX3330 up to 720 mg/day. Two of six patients receiving 720 mg/day had a diffuse rash that was spontaneously reversible. Patients receiving doses up to 600 mg/day did not have any signs of acute toxicity. Of the 19 patients in the APX_CLN_0011 Phase 1 oncology trial, four patients had over 6 months of exposure, and three patients (at a dose of 600 mg/day) had over 300 days of exposure without any significant drug-related AEs.

APX3330 Phase 2b Trial in DR/DME Patients (ZETA-1) (Completed)

In August 2022 Ocuphire completed ZETA-1, a Phase 2b double-masked, randomized, placebo-controlled, multi-center trial in patients with DR and DME, which started in April 2021. 103 DR subjects were enrolled with 90% having NPDR (baseline DRSS of 47 or 53); mean baseline CST was 270 µm. This study evaluated the effect of 600 mg daily dose of APX3330 in treating patients with DR, including moderately severe NPDR to mild PDR, as well as patients with DME without loss of central vision. The primary endpoint was percent of patients with a ≥2 step improvement in Early Treatment of Diabetic Retinopathy Study (ETDRS) diabetic retinopathy severity scale (DRSS) at week 24 in the study eye. Key secondary endpoints at multiple time points included change in monocular and binocular DRSS, CST, and BCVA. Patient safety was assessed by AE monitoring, clinical laboratory evaluations, IOP, and vital sign assessments. The ZETA-1 trial did not meet the primary endpoint in the study eye; however, the trial demonstrated the potential for clinically meaningful prevention of progression of diabetic retinopathy when evaluating both eyes. In contrast to intravitreal injections which treat a single eye, systemic drugs treat both eyes, and thus the response of both eyes needs to be considered. Patients treated with APX3330 were less likely to worsen in DR severity compared to placebo. In ZETA-1 trial, 13% patients in placebo group compared to 5% in APX3330 group (p=0.18) worsened by ≥ 3 step on binocular person-level scale from baseline at week 24 with a baseline binocular DRSS level 47, 53, or 61 (FIGURE 3). Additional efficacy endpoints were directionally favorable to support the biological effect of APX3330 in slowing the progression of DR and preserving vision. Visual acuity was stable with APX3330, and a trend was seen with fewer APX3330 treated patients losing 5 or more letters of distance vision compared to placebo patients (13% vs 26%, p=0.17) (FIGURE 3).

FIGURE 3: Percentage of Subjects with Progression of DR, PDR and Vision Loss at Week 24





APX3330 showed a favorable safety profile. Of the treatment-emergent serious AEs, 14 were considered unrelated to study medication, 11 in the placebo group and 3 in the APX3330 group. Two subjects in each group withdrew due to an AE, where one placebo subject had OU DME worsening considered treatment related. Overall, there were 211 AEs (91 APX3330, 120 placebo) in 64 subjects (29 APX3330, 35 placebo). Only 31 of these AEs were considered drug-related (14 APX3330, 17 placebo). All treatment related AEs were mild or moderate in severity. There were no adverse treatment effects on any other characteristics of the ophthalmic examination or on any assessments of systemic safety (**FIGURE 4**).

FIGURE 4: ZETA-1 Safety Overview

	Placebo (n=52)	APX3330 (n=51)
Total AEs	120	91
Subjects with AEs	35 (67%)	29 (57%)
Treatment-related AEs	17 (14%)	14 (15%)
Serious AEs	11 (9%)	3 (3%)
Withdrawals due to AEs	1 (2%)	2 (4%)
Deaths	1 (2%)	0 (0%)
AEs in > 5 % of Subjects*		
Ocular AEs		
DME	5 (10%)	2 (4%)
DR	6 (12%)	1 (2%)
Vitreous detachment	3 (6%)	0 (0%)
Cataract	1 (2%)	3 (6%)
Non-ocular AEs		
Pruritus	1 (2%)	6 (12%)
Rash	1 (2%)	3 (6%)
COVID-19	5 (10%)	1 (2%)

*Preferred term within organ class
AE, adverse event; DME, diabetic macular edema, DR, diabetic retinopathy.
APX3330 SAEs: Dyskinesia, transient ischemic attack, chest pain
Placebo SAEs: Vertigo, asthenia, multiple organ dysfunction, bradycardia, coronary artery disease, cholelithiasis, COVID-19 pneumonia, cellulitis, respiratory failure, skin ulcer, peripheral embolism
AEs – withdrawal from APX3330: Presyncope, dyspnea; placebo: DME (both eyes)

APX3330 Safety Profile

- Limited AEs; most were mild
- Ocular AEs similar between APX3330 and placebo
- Lower incidence of clinical DME/DR worsening with APX3330
- Pruritis was mild and resolved without APX3330 dose de-escalation or discontinuation
- **Patients with DR continued routine medications to manage comorbid conditions**

12* Phase 1 & Phase 2 trials

Exposure in Humans **>10,000** subject days at 600mg/day

APX3330 – Ten Phase 1 and 2 Trials - Eisai (APX CLN 0001-0010)

Under the sponsorship of Eisai Co., Ltd., 10 clinical trials were conducted involving healthy volunteers as well as patients with chronic hepatitis diseases (i.e., Type C, B, alcohol-induced) in Japan with the intent of developing a TNF-α blocking agent. At the time of their clinical trials, the molecular target of APX3330 had not been confirmed and was not known to be the Ref-1 protein.

Across these 10 trials, it was found that APX3330 exhibits predictable pharmacokinetics that were consistent with the pharmacokinetic data obtained in non-clinical studies. In addition, there was a lack of significant acute toxicity at doses up to 600 mg/day. APX3330 has been demonstrated to be well-tolerated. Moreover, in two studies it was found that meals have no impact on the product candidate's pharmacokinetics. Safety tolerability measures showed no changes in vital signs and no changes in clinical laboratory values. The only adverse events observed included diarrhea and rash, each of which occurred in less than 5% of patients and were mild.

APX3330 Clinical Development Plan

For APX3330, the IND application for APX3330 to pursue retinal choroidal vascular diseases was submitted to the FDA Division of Ophthalmology in December 2018 and is in effect (IND 142152). APX3330 also has an IND with the FDA Division of Oncology for the treatment of pancreatic cancer (IND 125360). APX3330 has completed 12 trials (6 Phase 1 and 6 Phase 2 trials), mostly related to patients with liver disease, patients with solid tumors and diabetic retinopathy. Ocuphire conducted an EOP2 meeting with the FDA and shared the outcome of the meeting in October 2023 which stated the agreement on the registration program including confirmation of the primary endpoint for registration of a systemic agent for DR. The company has submitted a SPA to the FDA.

Potential Clinical Plans for APX3330:

Potential clinical plans for APX3330 will be based on the Phase 2 safety, tolerability and efficacy results of APX3330 in patients with DR/DME reported in January 2023 and the outcome from the EOP2 meeting with the FDA in October 2023 to confirm registration endpoints to finalize the design of the future trials for APX3330 as first-line therapy in DR in addition to defining the chronic safety exposure trial and any further animal toxicology studies necessary prior to an NDA submission. Ocuphire may explore opportunities for clinical benefit as monotherapy or adjunctive therapy for other retinal indications such as DME, wAMD, and GA.

PS

PS Mechanism of Action

PS is a once-daily sterile eye drop formulation of phentolamine mesylate designed to reduce pupil diameter and improve visual acuity. The active pharmaceutical ingredient of PS, phentolamine mesylate, is a non-selective alpha-1 and alpha-2 adrenergic antagonist that inhibits activation of the smooth muscle of the iris, reducing pupil diameter. Unlike phentolamine, cholinergic agonists (such as pilocarpine, carbachol and aceclidine) work on the iris sphincter muscle to reduce the pupil diameter, and are associated with side effects given the engagement of the ciliary muscle such as headaches, brow aches and retinal detachments and have limited use in patients with high myopia. PS shares many of the attributes of existing ophthalmic eye drops, including a convenient route of administration and cost-effective manufacturing process, with the potential advantage of once-daily dosing.

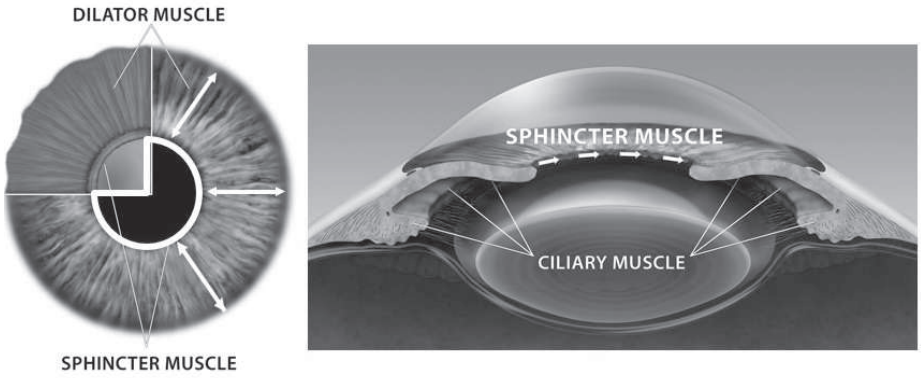
PS is a relatively non-selective alpha-1 and alpha-2 adrenergic antagonist. Dilation of the pupil is primarily controlled by the radial iris dilator muscles surrounding the pupil; these muscles are activated by the alpha-1 adrenergic receptors. Phentolamine reversibly binds to these receptors on the iris dilator muscle, thereby reducing pupil diameter. Phentolamine directly antagonizes the mydriatic effect of an α-1 adrenergic agonist, and indirectly reverses mydriasis induced by muscarinic antagonist effects on the iris sphincter muscle. Alpha-1 antagonists bind to the receptors to inhibit the pupillary response and reduce dilation (**FIGURE 5**). Phentolamine mesylate is the active ingredient in two injectable FDA-approved drugs, Regitine and OraVerse, as described previously.

For the treatment of pharmacologically-induced mydriasis indication, mydriasis is achieved either by stimulating the iris dilator muscle with the use of alpha agonists (e.g., phenylephrine), or by blocking the iris sphincter muscle with the use of muscarinic antagonists (e.g., tropicamide). PS, either by directly antagonizing the alpha-1 agonist or by indirectly antagonizing the pupil dilation effect of muscarinic blocking, may expedite the reversal of mydriasis prior to natural reversal.

For presbyopic patients, to overcome the lens' inability to change shape (accommodation) and focus light from near objects, pupil diameter reduction to a small size will allow light to come in the eye only in a near straight direction and increase the depth of focus (the ''pinhole effect''). Ocuphire believes that it is possible to reach a target 2 mm to 3 mm optimal pupil diameter by relaxing the dilator iris muscle with PS and contracting the iris sphincter muscle with a muscarinic agonist such as a low dose pilocarpine. This could result in an optimal depth of focus and near vision clarity without the assistance of lenticular accommodation.

Lastly, for the dim light vision disturbances, it is proposed that a moderate miotic effect by application of PS might mitigate night vision difficulties, a large portion of which are caused by imperfections or aberrations present on the periphery of the cornea. Therefore, the effects of these imperfections can be reduced or eliminated by reducing the pupil size to a smaller diameter, knowing that a smaller pupil blocks what would be unfocused, aberrant rays of light on the retina.

FIGURE 5: PS's Mechanism of Action



PS Clinical Experience Summary

PS has been assessed in twelve investigator-initiated and company-sponsored Phase 1, Phase 2, and Phase 3 clinical trials. Across all trials, over 700 adult patients have been exposed to at least one dose of phentolamine ophthalmic solution. Clinical trial data from Phase 2 and Phase 3 trials were presented at the annual American Academy of Ophthalmology (AAO), Association for Research in Vision and Ophthalmology (ARVO), or American Society of Cataract and Refractive Surgery (ASCRS) meetings. Results of VEGA-2 trial may be presented at future medical conferences.

VEGA PROGRAM Presbyopia Indication for PS

PS Presbyopia: Phase 3 VEGA-2 Trial (Completed)

VEGA-2 (NYXP-301) was a double-masked, randomized, placebo-controlled multi-center trial of PS, placebo and with adjunctive LDP compared with vehicle (placebo) in presbyopic patients. Three hundred thirty-three subjects were randomized to one of 4 treatment groups in 2 stages.

The primary efficacy endpoint was met. The data from this study may be presented at future medical conferences.

Phase 2 VEGA-1 Trial (Completed)

VEGA-1 (NYXP-201) was a double-masked, randomized, placebo-controlled, multi-center trial of PS and LDP compared with vehicle (placebo) ophthalmic solution in presbyopic patients. A total of 150 patients were randomized 3:2:2:3 to one of four treatment groups. The primary efficacy endpoint for this study was met. The data from this study was presented at several medical conferences in 2021 and 2022.

LYNX PROGRAM – Decreased Vision Under Dim (Mesopic or Low) Light Conditions After Keratorefractive Surgery Indication for PS

PS: Phase 3 LYNX-1 Trial (Completed)

LYNX-1 (NYXDLD-301) was a Phase 3 double-masked, randomized, placebo-controlled, multi-center study of PS compared with placebo ophthalmic solution in patients with dim light vision disturbances at multiple sites in the U.S. In this trial, 145 patients who experienced vision impairment under dim light conditions were randomized to receive either PS or placebo. Each subject was randomized 1:1 to treatment with PS or placebo ophthalmic solution and stratified by iris color (light/dark irides). Treatment was self-administered in each eye QD at or near bedtime for 14 days.

At Day 8 (primary endpoint), a statistically significantly greater percent of subjects treated with PS in the mITT Population had study eyes with ≥ 15 letters improvement from baseline in mLCVA compared with placebo treatment (13% vs 3%, respectively; p=0.0459). A significantly greater percentage of subjects treated with PS also had study eyes with ≥ 15 letters improvement from baseline in mLCVA compared with placebo treatment at Day 15 (21% vs 3%, respectively; p=0.0042) PS demonstrated favorable safety and tolerability in this study.

PS Nonclinical Toxicology Studies

As part of a comprehensive nonclinical toxicity program, Ocuphire conducted single and repeated-dose toxicity studies of phentolamine mesylate drug substance in rabbits and beagle dogs. There were no PS-related histopathologic ocular pathology findings.

Nonclinical information (pharmacological properties, general and reproductive toxicology) for phentolamine mesylate is described in the literature in connection with other approved phentolamine drug products and formulations, and was reviewed by the FDA in the approval process of the market applications for RYZUMVI, Oraverse and Regitine.

PS Clinical Development Plan

Ocuphire is developing PS in partnership with Viatris. For PS, the investigational new drug (IND) application was submitted to the FDA Division of Ophthalmology in July 2011 and is in effect (IND 70499). In November 2022, Ocuphire submitted an NDA for PS for the treatment of pharmacologically induced-mydriasis and was approved in September 2023. PS has completed 12 trials (3 Phase 1 trials, 5 Phase 2 trials and 4 Phase 3 trials), mostly in young and older healthy volunteers in reversal of pharmacologically induced mydriasis, presbyopia, dim light disturbance and glaucoma patients. In December 2023, Ocuphire received SPA agreement with the FDA for PS for decreased vision under dim (mesopic or low) light conditions after keratorefractive surgery.

PS Potential Clinical Plans

Ocuphire and its partner, Viatris, VEGA-3 (NYXP-302) trial is planned as a double-masked, randomized, placebo-controlled, multicenter trial in approximately 545 patients with presbyopia. This second registration trial will evaluate efficacy and safety of PS similar to VEGA-2 and include similar primary and key secondary endpoints and analysis, with assessment of tachyphylaxis and an optional extension for a total of 48 weeks. Viatris, our development and commercial partner, is expected to continue Phase 3 development in the first half of 2024.

Based on the positive results of the first Phase 3 trial, LYNX-1, Ocuphire and its partner, Viatris, are planning a similar second registration trial for PS in up to 200 subjects for the treatment of decreased vision under dim (mesopic or low) light conditions after keratorefractive surgery. Viatris, our development and commercial partner, is expected to continue Phase 3 development in the first half of 2024.

Future In-Licensing and Acquisition Opportunities

Ocuphire continually evaluates product candidates based on scientific merit, patent protection, regulatory pathways, and commercial opportunity.

Sales and Marketing

The company maintains discussions with a range of ophthalmic drug companies regarding development and commercialization of APX3330, including co-development, distribution, license, or mergers and acquisitions. As part of the pre-commercialization planning, Ocuphire has started market development activities, which include engaging with key opinion leaders as well as increased visibility and presence at retina, ophthalmology and optometry medical and industry conferences.

In November 2022, Ocuphire entered into a licensing agreement with Viatris for the development and commercialization of all PS indications in the U.S. and ex-U.S. markets (excluding certain countries in Asia).

Manufacturing

For APX3330, PS, and for other product candidates that will be developed in the future, Ocuphire's contract manufacturers are currently producing, and will produce, its bulk drug substances and drug products for use in Ocuphire's preclinical studies and clinical trials, utilizing reliable and reproducible synthetic processes and common manufacturing techniques.

Pursuant to the Viatris License Agreement, Ocuphire intends to transfer commercial manufacturing responsibilities for PS to Viatris. Ocuphire does not have any long-term agreements but Ocuphire or its development partners intend to secure such arrangements for drug substances or drug products as appropriate, and currently uses purchase orders with multiple manufacturers. Ocuphire is qualifying its selected manufacturers to provide bulk drug

substances and drug products in conjunction with the NDA regulatory submission to the FDA. Ocuphire plans to continue to rely upon contract manufacturers and, potentially, collaboration partners to manufacture commercial quantities of its drug substances and drug products, if approved for marketing by the applicable regulatory authorities. Ocuphire does not own or operate, and currently has no plans to establish, any manufacturing facilities.

APX3330

APX3330 is an oral formulation of a small molecule drug substance that is synthesized from readily available raw materials and using conventional chemical processes. The APX3330 drug substance has been optimized to a new form. Process and analytical development of APX3330 drug substance and drug product is being finalized, and their production scaled-up under cGMP regulatory requirements. Previously, the APX3330 drug product manufacturer has performed pharmaceutical development to support the cGMP manufacturing campaign for tablets of 60 mg and 120 mg dose strengths, the latter being used in prior clinical trials. Ocuphire has reformulated the drug product and increased the dose strength to 300 mg for convenient once or twice a day dosing. Ocuphire is also planning additional stability studies for future lots of both the drug substance and drug product of APX3330 in order to establish expiry of the new tablet strength, formulation, and to support regulatory approval and commercial stage.

PS

The proprietary formulation of PS is a sterile, preservative-free, isotonic, buffered aqueous solution containing phentolamine mesylate, mannitol, and sodium acetate. The drug substance phentolamine mesylate USP is a small molecule that can be manufactured by reliable and reproducible synthetic processes from readily available starting materials. Ocuphire currently obtains the active pharmaceutical ingredient for PS from a single supplier in Italy and is presently taking steps to develop a second source, but is working with Viatris to determine the long-term commercial manufacturing strategy. All lots of drug substance phentolamine mesylate and PS drug product used in clinical trials are manufactured under current good manufacturing practices (cGMP), a quality-system regulating manufacturing, with processes registered by the supplier with FDA in an active Drug Master File (DMF). PS was previously packaged in a single-use bottle with cap served as the container closure system for Phase 1 and 2 clinical trials. Ocuphire transitioned the container closure system to an industry standard, single-use preservative-free blow-fill-seal (''BFS'') container for PS, which is being formulated and filled by a leading U.S. manufacturer. PS eye drops in the BFS container are classified by FDA as a drug-device combination product. The current manufacturing process has been scaled to a commercial capacity. PS has demonstrated stability at 5°C refrigerated for a minimum of two years. Ocuphire is performing additional stability studies on lots of both the drug substance phentolamine mesylate and the drug product of PS in order to establish expiry dating and to support regulatory submissions and commercial manufacturing. To supply eventual global markets and to avoid reliance on a single facility, Ocuphire and its partner Viatris are evaluating the establishment of second-source manufacturing facilities for drug substance and drug product.

Apexian Sublicense Agreement

On January 21, 2020, Ocuphire entered into a sublicense agreement with Apexian pursuant to which it in-licensed patents and other intellectual property relating to the APX3330 product candidate and second-generation product candidates owned by Apexian, and intellectual property that Apexian in-licensed from Eisai, including certain study reports, manufacturing and analytical records, data, know-how, technical and other proprietary information relating to APX3330. This intellectual property constitutes a Ref-1 Inhibitor program focused on developing therapeutic applications to treat disorders related to ophthalmic and diabetes mellitus conditions. The lead compound in the Ref-1 Inhibitor program is APX3330, which Ocuphire intends to develop as an oral tablet therapeutic to treat DR and DME, and potentially wAMD. See ''*Ocuphire Management's Discussion and Analysis of Financial Condition and Results of Operations—Contractual Obligations and Commitments—Apexian Sublicense Agreement*'' for more details regarding the Apexian Sublicense Agreement.

Intellectual Property

APX3330

As of December 31, 2023, the patent estate that Ocuphire has in-licensed for APX3330 and related compounds contains nine U.S. patents and two pending U.S. non-provisional patent applications, as well as issued patents in Europe, Japan, Canada, China, and Australia, and pending patent applications in Europe, Japan, Canada, and South

Korea. The license is for the use and commercialization of APX3330 and related composition of matter compounds covered by the subject patents and patent applications in the field of human health uses for ophthalmic and diabetes mellitus indications.

In-licensed U.S. patent 9,040,505 has claims to methods of treating diabetic retinopathy and other diseases using, for example, APX3330 and is scheduled to expire in year 2030. Counterpart patents have issued in Europe, Japan, Australia, and Canada, which are scheduled to expire in year 2028, and there is a related pending U.S. patent application with method of treatment claims that, if issued as a patent, would expire in year 2028. Pending U.S. application 18/341,077 and pending applications in Europe, Japan, Canada, South Korea have claims to methods of treating wAMD and other diseases using, for example, APX3330, APX2009, or APX2014. Patents, if granted, based on these pending patent applications would expire in year 2039. The U.S. and certain foreign countries permit extension of patent term for up to five years to compensate for patent term lost during the government regulatory review process for a new medicine. If U.S. patent 9,040,505 qualifies for the full five years of patent term extension, the expiration of U.S. patent 9,040,505 would be in year 2035. Whether U.S. patent 9,040,505 qualifies for the full five years of patent term extension depends in part on the date of FDA approval for the new medicine.

Ocuphire in-licenses one U.S. patent directed to methods of treating certain retinal disease using APX2014, whereby this U.S. patent is scheduled to expire in year 2030. Ocuphire also in-licenses patent applications in the U.S. and Canada directed to a combination therapy composition comprising an APE1/REF-1 inhibitor, such as APX3330, and a second therapeutic agent, and methods of using such combination therapy to treat retinal diseases and/or treat other indications are pending in the U.S. and Canada. Patents, if granted, based on these applications would expire in year 2038. In-licensed patent applications directed to use of an APE1/REF-1 inhibitor, such as APX3330, in monotherapy or combination therapy to reduce neuronal sensitivity and/or treat other indications are pending in Europe, Japan, and Canada, whereby patents, if granted based on these applications, would expire in year 2038. This same patent family includes one in-licensed U.S. patent directed to methods using APX3330 to treat inflammation and pain as part of a combination therapy.

U.S. patents that Ocuphire has in-licensed to derivatives of APX3330 include U.S. patents 9,089,605; 9,193,700; 9,877,936; 10,154,973; 11,160,770; 11,648,226; and 11,723,886. These U.S. patents are schedule to expire from 2029 to 2032. Foreign patents that Ocuphire has in-licensed to derivatives of APX3330 include patents in Europe, Japan, Australia, China, and Canada that are scheduled to expire between the years 2028 to 2039.

In addition to patents and patent applications that Ocuphire has in-licensed, as of December 31, 2023, Ocuphire owns a patent application that is pending in the U.S., Europe, Japan, Australia, Canada and other countries and directed to methods of treating diabetic retinal diseases using APX3330. Patents, if granted, based on the foregoing patent applications would expire in year 2042. Additionally, Ocuphire owns one pending international patent application with counterpart patent applications pending in the U.S., Taiwan, and Argentina directed to APX3330 salts and esters, compositions comprising an APX3330 salt or ester and therapeutic uses of APX3330 salts and esters. A patent granted on the foregoing patent applications would expire in year 2043. Ocuphire also owns one pending U.S. provisional patent application directed to additional therapeutic methods using APX3330 in patients with diabetic retinal disease, and one U.S. provisional patent application directed to additional therapeutic methods using new generation molecules APX2009 or APX2014, whereby any patents, if granted, from an application filed based on these provisional patent applications would expire in year 2044.

PS

Ocuphire's patent estate includes patents and patent applications to forms of phentolamine mesylate, formulations containing phentolamine mesylate, methods of using phentolamine mesylate, and methods of manufacturing phentolamine mesylate. Ocuphire primarily protects its intellectual property through a combination of patents and patent applications on inventions, trademark protection on Ocuphire's product name, and trade secret protection as Ocuphire deems appropriate. Ocuphire owns all of the worldwide rights to PS for all indications, but has out-licensed certain rights to PS pursuant to the Viatris License Agreement.

As of December 31, 2023, Ocuphire's patent estate relating to PS contains twelve U.S. patents, nine pending U.S. non-provisional patent applications, as well as issued patents in Australia, Canada, Europe, Japan, and Mexico and pending patent applications in Australia, Canada, Europe, Japan, China, and other foreign countries.

Ocuphire's U.S. Patents 9,795,560; 10,278,918; 10,772,829; 11,090,261 and 11,844,858 and counterpart Australian Canadian, European, and Japanese patents each contain composition of matter claims to aqueous

phentolamine mesylate formulations and are scheduled to expire in year 2034. In the same patent family, Ocuphire also has 1 pending U.S. patent application with additional claims to aqueous phentolamine mesylate formulations, whereby a patent, if granted, would expire in year 2034. The patents and patent applications cover the current clinical formulation for the PS product.

Ocuphire's U.S. Patent Nos. 9,089,560; 9,789,088; 11,000,509 and 11,717,510 contain claims directed to methods of improving visual performance using, for example, phentolamine mesylate and are scheduled to expire in year 2034. Counterpart patents have issued in Australia, Canada, Europe, and Japan, which are scheduled to expire in year 2034. In the same patent family, Ocuphire also has 1 pending U.S. patent application with additional claims to methods of improving visual performance using, for example, phentolamine mesylate, whereby a patent, if granted, based on this pending application would expire in year 2034. The patents and patent applications cover uses of the current clinical formulation for the PS product.

Ocuphire has patent applications pending in the U.S., Australia, Canada, China, Europe, and Japan directed to treating glaucoma and other medical disorders using phentolamine mesylate. Patents, if granted, based on these pending applications would expire in year 2039.

Ocuphire's U.S. Patent 10,993,932 contains claims directed to methods of treating presbyopia using phentolamine mesylate with adjunctive pilocarpine and is scheduled to expire in year 2039. Ocuphire's U.S. Patent 11,400,077 contains claims directed to methods of treating mydriasis using phentolamine mesylate and is scheduled to expire in year 2039. In the same patent family as U.S. Patent Nos. 10,993,932 and 11,400,077, Ocuphire has four pending U.S. patent applications, two of which have claims to treating presbyopia and the other two U.S. applications have claims to treating mydriasis. Counterpart patent applications are pending in Australia, Canada, China, Europe, Japan, and other foreign countries, whereby a patent, if granted, based on these pending U.S. and foreign patent applications would expire in year 2039.

Ocuphire's U.S. Patent 11,566,005 contains claims directed to high-purity phentolamine mesylate as composition of matter, methods to make phentolamine mesylate from phentolamine and methods for inhibiting contraction of smooth muscle of a subject's iris, improving visual contrast sensitivity or visual acuity, treating a dim light or night vision disturbance, treating or reversing pharmacologically induced mydriasis, and treating presbyopia, with phentolamine mesylate. Counterpart patent applications are pending in the U.S., Europe, Japan, and other foreign countries. This U.S. patent and other patents, if granted on the foregoing patent applications are projected to expire in year 2042. Ocuphire also has one patent application that is pending in China and directed to methods for making high purity phentolamine mesylate and compositions comprising phentolamine mesylate. A patent granted on this Chinese application would expire in year 2041, In addition, Ocuphire has a patent application that is pending in Europe directed to particular phentolamine mesylate crystal forms and their use. A patent granted on this European patent application would expire in year 2043. Ocuphire also has a pending patent application in the U.S., Europe, Japan, and other foreign countries directed to additional methods for treating mydriasis and glaucoma, whereby any foreign patents, if granted, based on the foregoing patent applications would expire in year 2042.

Ocuphire also owns an issued patent in Mexico that is scheduled to expire in year 2025 and has claims to ophthalmic formulations.

Ocuphire has registered trademark protection in the United States for the NYXOL® and a pending U.S. federal trademark application for RYZUMVI.

Additional Patent Term Information

As background, the patent term is typically 20 years from the date of filing a non-provisional application. In the United States, a patent's term may be lengthened several ways. First, patent term adjustment (PTA) compensates a patentee for administrative delays by the USPTO in granting a patent. Second, in certain instances, a patent term extension (PTE) can be granted to recapture a portion of the term effectively lost as a result of the FDA regulatory review period, as provided under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Act. This restoration period cannot be longer than 5 years for approval of a drug, and the total patent term, including the restoration period, must not exceed 14 years following FDA approval. Only patent(s) applicable to an approved drug is (are) eligible for the PTE and the application for the extension must be submitted prior to the expiration of the patent and within 60 days from market approval. Independent of patent protection, in the United States, the Hatch-Waxman Act provides a 5-year period of non-patent data exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity (NCE). Under this provision,

APX3330 may be eligible for up to 5 years of data and market exclusivity under the Hatch-Waxman Act, because it is considered an NCE as the FDA has not previously approved any other drug containing the active ingredient of APX3330.

In Europe, under the Data Exclusivity Directive, pharmaceutical companies may receive up to 11 years to market their product without risk of competition. In Japan, under the Pharmaceuticals Act of Japan, the market authorization holder, based on the length of a required study period reexamination, may have up to 10 years before a generic can enter the market. Further, the expiration date of certain patents may be extended for up to a maximum of 5 additional years to accommodate for time spent seeking government approval to market a new medicine, in those countries that permit extension of patent term to accommodate for time spent seeking government approval to market a new medicine.

Ocuphire also protects its proprietary information through written agreements. Ocuphire's employees, consultants, contractors, partners and other advisors are required to execute nondisclosure and assignment of invention agreements upon commencement of employment or engagement. In addition, Ocuphire protects its proprietary information through written confidentiality agreements with outside parties who may come into possession of Ocuphire's confidential information.

Competition

There is intense competition within the pharmaceutical industry. While Ocuphire believes that RYZUMVI and its current product candidates, APX3330 and PS, are well-positioned for development in each indication, Ocuphire or its development partners will face competition from both branded and generic pharmaceutical companies as well as products that are currently in development. Many of these companies have significantly greater financial and human resources and experience in drug development, R&D, and commercialization. These competitors compete with Ocuphire in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient enrollment for clinical trials as well as acquiring products, product candidates or other technologies complementary to Ocuphire program. Smaller and other early-stage companies may also prove to be significant competitors if they choose to partner with large, established companies.

Government Regulation and Product Approvals

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union (EU), extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of pharmaceutical products. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

The EMA is a decentralized agency governed by an independent management board responsible for the evaluation, supervision, and safety monitoring of medicines in the EU. The Medicines and Healthcare products Regulatory Agency (MHRA) regulates medicines, medical devices, and blood components in the United Kingdom (UK) and serves as a similar function to the EMA in the EU, following the exit of the UK from the EU in Brexit. The Japanese Pharmaceuticals and Medical Devices Agency serves a similar function to the FDA in the United States and is an independent administrative institution. The National Medical Products Administration (NMPA) is the Chinese agency for regulating drugs and medical devices (formerly the China Food and Drug Administration or CFDA).

Review and Approval of Drugs in the United States

In the United States, the FDA regulates drug products under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. The failure to comply with applicable requirements under the FDCA and other applicable laws at any time during the product development process, approval process or after approval may subject an applicant and/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 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 preclinical laboratory tests, animal studies and formulation studies in compliance, as applicable, with the Animal Welfare Act and FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an IND, which must take effect before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, and other applicable regulations to establish the safety and efficacy of the proposed drug product for each proposed indication;
- manufacturing, packaging, labelling, and distribution of drug substances and drug products consistent with the FDA's Good Manufacturing Practice (GMP) regulations which are utilized in the GLP non-clinical and GCP clinical studies to investigate the drug candidate;
- development of product label, package inserts, and prescriber information that is intended to be used and included with the commercial product;
- preparation and submission to the FDA of an 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 current Good Manufacturing Practices, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data;
- payment of user fees, if appropriate, and securing FDA approval of the NDA; and
- compliance with any post-approval requirements, including Risk Evaluation and Mitigation Strategies, or REMS, and post-approval studies required by the FDA.

Preclinical Studies

Preclinical studies include laboratory evaluation of the purity and stability of the manufactured drug substance or active pharmaceutical ingredient and the formulated drug or drug product, as well as *in vitro* and *in vivo* animal studies to assess the safety and activity of the drug for initial testing in humans and to establish a rationale for therapeutic use. 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 trials, among other things, are submitted to the FDA as part of an IND. Some long-term preclinical testing, such as long-term repeat-dose toxicology studies, may continue after the IND is submitted.

Companies usually must complete some long-term preclinical testing, such as long-term repeat-dose toxicology studies, and must also develop additional information about the chemistry and physical characteristics of the investigational product and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the candidate product and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the candidate product does not undergo unacceptable deterioration over its shelf life.

The IND and IRB Processes

An IND is an exemption from the FDCA that allows an unapproved drug to be shipped in interstate commerce for use in an investigational clinical trial. In support of a request for an IND, applicants must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In

addition, the results of preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. An IND goes into effect 30-days after its filing, unless during this 30-day period the FDA raises concerns or questions and imposes a clinical hold.

A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. For example, a specific protocol or part of a protocol is not allowed to proceed, while other protocols may do so. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following issuance of a clinical hold or partial clinical hold, an investigation may only resume after the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed. The FDA may also place a clinical hold or partial clinical hold on a trial after a clinical trial has begun.

A sponsor may choose, but is not required, to conduct a foreign clinical trial under an IND. When a foreign clinical trial is conducted under an IND, all FDA IND requirements must be met unless waived. When the foreign clinical trial is not conducted under an IND, the sponsor must ensure that the trial complies with certain FDA regulatory requirements in order to use the trial as support for an IND or application for marketing approval, including that such trials must be conducted in accordance with GCP, including review and approval by an independent ethics committee, or IEC, and obtaining informed consent from patients. The GCP requirements in the final rule encompass both ethical and data integrity standards for clinical studies. The FDA's regulations are intended to help ensure the protection of human patients enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

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 exercise continuing supervision over the trial. The IRB must review and approve, among other things, the trial protocol and informed consent information to be provided to trial patients. An IRB must operate in compliance with FDA regulations. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the trial. Suspension or termination of development during any phase of clinical trials can occur if it is determined that the participants or patients are being exposed to an unacceptable health risk. Other reasons for suspension or termination may be made by Ocuphire based on evolving business objectives and/or competitive climate.

Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on its ClinicalTrials.gov website.

Human Clinical Trials in Support of an NDA

Clinical trials involve the administration of the investigational product to human patients or healthy volunteers under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research patients 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 inclusion and exclusion criteria, the objectives of the trial, the tests to be conducted on study participants, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated.

Human clinical trials are typically conducted in 3 sequential phases, but the phases may overlap.

- *Phase 1*. The drug is initially introduced into healthy human subjects or, in certain indications such as cancer, patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.

- *Phase 2*. The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- *Phase 3*. The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product and to provide adequate information for the labeling of the product.

Reports detailing activities under, and the status of, an IND must be submitted at least annually to the FDA. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the drug; and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

Sponsors may reach a Special Protocol Assessment (SPA) agreement with respect to the design of clinical trials. The FDA's SPA process is designed to facilitate the FDA's review and approval of drugs and biologics by allowing the FDA to evaluate the proposed design and size of certain clinical or animal studies, including clinical trials that are intended to form the primary basis for determining a product candidate's efficacy. Upon specific request by a clinical trial sponsor, the FDA will evaluate the protocol and respond to a sponsor's questions regarding protocol design and scientific and regulatory requirements. The FDA aims to complete SPA reviews within 45 days of receipt of the request. The FDA ultimately assesses whether specific elements of the protocol design of the trial, such as entry criteria, dose selection, endpoints and/or planned analyses, are acceptable to support regulatory approval of the product with respect to the effectiveness of the indication studied. All exchanges between the FDA and the sponsor regarding an SPA must be clearly documented in an SPA letter or the minutes of a meeting between the sponsor and the FDA.

Although the FDA may agree to an SPA, an SPA agreement does not guarantee approval of a product. Even if the FDA agrees to the design, execution, and analysis proposed in protocols reviewed under the SPA process, the FDA may revoke or alter its agreement in certain circumstances. In particular, an SPA agreement is not binding on the FDA if public health concerns emerge that were unrecognized at the time of the SPA agreement, other new scientific concerns regarding product safety or efficacy arise, the sponsor company fails to comply with the agreed upon trial protocols, or the relevant data, assumptions or information provided by the sponsor in a request for the SPA change or are found to be false or omit relevant facts.

In addition, even after an SPA agreement is finalized, the SPA agreement may be modified, and such modification will be deemed binding on the FDA review division, except under the circumstances described above, if the FDA and the sponsor agree in writing to modify the protocol. Generally, such modification is intended to improve the study. The FDA retains significant latitude and discretion in interpreting the terms of the SPA agreement and the data and results from any study that is the subject of the SPA agreement. Moreover, if the FDA revokes or alters its agreement under the SPA, or interprets the data collected from the clinical trial differently than we do, the FDA may not deem the data sufficient to support an application for regulatory approval.

Concurrent with clinical trials, companies often complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, must develop methods for testing the identity, strength, quality, purity, and potency of the final drug. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

Submission of an NDA to the FDA

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical studies and clinical trials, 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 requesting approval to market the drug product for one or more indications. Under federal law, the submission of most NDAs is subject to an application user fee. The sponsor of an approved NDA is also subject to an annual prescription drug program fee. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for drugs with orphan designation and a waiver for certain small businesses. 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, and the sponsor receives a Refuse to File Notice. 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 certain performance goals in the review process of NDAs. The goal for review of most standard applications is within 10 months from the date of filing, and for ''priority review'' products the review goal is within 6 months of filing. The review process may be extended by the FDA 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 (''PAIs'') may 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 at the commercial scale. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP.

In addition, as a condition of approval, the FDA may require an applicant to develop a Risk Evaluation and Mitigation Strategies (''REMS''). REMS uses risk minimization strategies to ensure that the benefits of the product outweigh the potential risks. REMS can include medication guides, physician communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU may include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The FDA may require a REMS at the time of approval or post-approval if it becomes aware of a serious risk associated with use of the product. The requirement for a REMS can materially affect the potential market and profitability of a product.

The FDA may refer an application for a novel drug to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Fast Track, Breakthrough Therapy, and Priority Review Designations

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are referred to as fast-track designation, breakthrough therapy designation, and priority review designation.

Specifically, the FDA may designate a product for Fast Track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For Fast Track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a Fast Track product's application before the application is complete. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing a Fast Track application does not begin until the last section of the application is submitted. In addition, the Fast Track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Second, a product may be designated as a Breakthrough Therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to Breakthrough Therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; and assigning a cross-disciplinary project lead for the review team.

Third, the FDA may designate a product for Priority Review if it is a product that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed product represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from 10 months to 6 months.

The FDA's Decision on an NDA

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 may issue an approval letter. The FDA has committed to reviewing such resubmissions in 2 or 6 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, including REMS, 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 (such as annual reports and quarterly safety reports for the first 3 years), product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most 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 user fee requirements for any marketed products, 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. All promotional materials must be submitted to FDA prior to the time of their first use. 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 drug samples at the federal level and sets minimum standards for the registration and regulation of drug sample 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.

Section 505(b)(2) NDAs

NDAs for most new drug products are based on 2 adequate and well-controlled clinical trials which must contain substantial evidence of the safety and efficacy of the proposed new product. These applications are submitted under Section 505(b)(1) of the FDCA. The FDA is, however, authorized to approve an alternative type of NDA under Section 505(b)(2) of the FDCA. This type of application allows the applicant to rely, in part, on the FDA's previous findings of safety and efficacy for a similar product, or published literature. Specifically, Section 505(b)(2) applies to an NDA for a drug for which the investigations to show whether the drug is safe and effective and relied upon by the applicant for approval of the application ''were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.''

Thus, Section 505(b)(2) authorizes the FDA to approve an NDA based in part on safety and effectiveness data that were not developed by the applicant. Section 505(b)(2) may provide an alternate and potentially more expeditious pathway to FDA approval for new or improved formulations or new uses of previously approved products. If the Section 505(b)(2) applicant can establish that reliance on the FDA's previous approval is scientifically appropriate, the applicant may eliminate the need to conduct certain preclinical studies or clinical trials of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new drug candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress authorized the FDA to approve generic drugs that are the same as drugs previously approved by the FDA under the NDA provisions of the statute. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. In support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference-listed drug, or RLD.

Specifically, in order for an ANDA to be approved, the FDA generally must find that the generic version is a duplicate to the RLD with respect to the active ingredients, the route of administration, the dosage form, conditions of use and the strength of the drug. The FDA must also determine that the generic drug is ''bioequivalent'' to the innovator drug. Under the statute, a generic drug is required to be bioequivalent to an RLD.

Upon approval of an ANDA, the FDA indicates whether the generic product is ''therapeutically equivalent'' to the RLD in its publication Approved Drug Products with Therapeutic Equivalence Evaluations, also referred to as the Orange Book. Clinicians and pharmacists often consider a therapeutic equivalent generic drug to be fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA's designation of therapeutic equivalence often results in substitution of the generic drug without the knowledge or consent of either the prescribing clinicians or patient.

Under the Hatch-Waxman Amendments, the FDA may not approve an ANDA until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity. For the purposes of this provision, a new chemical entity, or NCE, is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval.

The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period applies to the condition(s) of use for which the new clinical investigation was conducted, and often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication. Three-year exclusivity would be available for a drug product that contains a previously approved active moiety, provided the statutory requirement for a new clinical investigation is satisfied. Unlike five-year NCE exclusivity, an award of three-year exclusivity does not block the FDA from accepting ANDAs seeking approval for generic versions of the drug as of the date of approval of the original drug product.

Hatch-Waxman Patent Certification and the 30-Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or an approved method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an ANDA applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval. To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would.

Specifically, the applicant must certify with respect to each patent that: (1) the required patent information has not been filed, (2) the listed patent has expired, (3) the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or (4) the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the ANDA or 505(b)(2) application will not be approved until all the listed patents claiming the referenced product have expired (other than method of use patents involving indications for which the applicant is not seeking approval).

If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months after the receipt of the Paragraph IV notice, expiration of the patent, or a decision in the infringement case that is favorable to the ANDA applicant.

To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would. As a result, approval of a Section 505(b)(2) NDA can be stalled until all the listed patents claiming the referenced product have expired, until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired, and, in the case of a Paragraph IV certification and subsequent patent infringement suit, until the earlier of 30 months, settlement of the lawsuit or a decision in the infringement case that is favorable to the Section 505(b)(2) applicant.

505(b)(2) and NCE Data Exclusivity in U.S.

In the United States, the Hatch-Waxman Act provides a 3-year period of non-patent data exclusivity within the United States to the first applicant to gain approval through a 505(b)(2) application seeking regulatory approval of, for example, a new indication, dosage, or strength of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigation and does not prohibit the FDA from approving an ANDA for drugs containing the original active agent. Under this provision, PS for use in treating presbyopia, mydriasis, or decreased vision under dim (mesopic or low) lighting conditions after keratorefractive surgery may be eligible for 3 years of data exclusivity under the Hatch-Waxman Act.

In the United States, the Hatch-Waxman Act provides period of 5-years of non-patent data exclusivity for a new drug containing a new chemical entity. For the purposes of this provision, a new chemical entity, or NCE, is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval.

Pediatric Studies and Exclusivity

Under the Pediatric Research Equity Act of 2003, an NDA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the drug product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. With enactment of the Food and Drug Administration Safety and Innovation Act or FDASIA, in 2012, sponsors must also submit pediatric trial plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric trial or studies the applicant plans to conduct, including trial objectives and design, any deferral or waiver requests, and other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in FDASIA. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional 6 months to the term of any patent or regulatory exclusivity, including orphan exclusivity. This 6-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, the latest statutory or regulatory period of exclusivity or patent covering the product is extended by 6 months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application.

Orphan Drug Designation and Exclusivity

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 drug exclusivity. Orphan drug exclusivity means that the FDA may not approve any other applications for the same product for the same indication for 7 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.

Patent Term Restoration and Extension

A patent claiming a new drug product may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to 5 years for patent term lost during product development and the FDA regulatory review. The restoration period granted is typically one-half the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved drug product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple drugs for which approval is sought can only be extended in connection with one of the approvals. The U.S. Patent and Trademark Office reviews and approves the application for any patent term extension or restoration in consultation with the FDA. Ocuphire cannot provide any assurance that any patent term extension with respect to any U.S. patent will be obtained and, if obtained, the duration of such extension, in connection with any of its product candidates.

Review and Approval of Drug Products in the European Union

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of products. Whether or not it obtains FDA approval for a product, Ocuphire would need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. The approval process ultimately varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Procedures Governing Approval of Drug Products in the European Union

Pursuant to the European Clinical Trials Directive, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the member states. Under this system, an applicant must obtain approval from the competent national authority of a European Union member state in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial after a competent ethics committee has issued a favorable opinion. Clinical trial application must be accompanied by an investigational medicinal product dossier with supporting information prescribed by the European Clinical Trials Directive and corresponding national laws of the member states and further detailed in applicable guidance documents.

To obtain marketing approval of a product under European Union regulatory systems, an applicant must submit a marketing authorization application, or MAA, either under a centralized or decentralized procedure. The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all European Union member states. The centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional.

Under the centralized procedure, the Committee for Medicinal Products for Human Use, or the CHMP, established at the European Medicines Agency, or EMA, is responsible for conducting the initial assessment of a product. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. In this circumstance, the EMA ensures that the opinion of the CHMP is given within 150 days.

The decentralized procedure is available to applicants who wish to market a product in various European Union member states where such product has not received marketing approval in any European Union member states before. The decentralized procedure provides for approval by one or more other, or concerned, member states of an assessment of an application performed by one-member state designated by the applicant, known as the reference member state. Under this procedure, an applicant submits an application based on identical dossiers and related materials, including a draft summary of product characteristics, and draft labeling and package leaflet, to the reference member state and concerned member states. The reference member state prepares a draft assessment report and drafts of the related materials within 210 days after receipt of a valid application. Within 90 days of receiving the reference member state's assessment report and related materials, each concerned member state must decide whether to approve the assessment report and related materials.

If a member state cannot approve the assessment report and related materials on the grounds of potential serious risk to public health, the disputed points are subject to a dispute resolution mechanism and may eventually be referred to the European Commission, whose decision is binding on all member states.

Within this framework, manufacturers may seek approval of hybrid medicinal products under Article 10(3) of Directive 2001/83/EC. Hybrid applications rely, in part, on information and data from a reference product and new data from appropriate pre-clinical tests and clinical trials. Such applications are necessary when the proposed product does not meet the strict definition of a generic medicinal product, or bioavailability studies cannot be used to demonstrate bioequivalence, or there are changes in the active substance(s), therapeutic indications, strength, pharmaceutical form or route of administration of the generic product compared to the reference medicinal product. In such cases the results of tests and trials must be consistent with the data content standards required in the Annex to the Directive 2001/83/EC, as amended by Directive 2003/63/EC.

Hybrid medicinal product applications have automatic access to the centralized procedure when the reference product was authorized for marketing via that procedure. Where the reference product was authorized via the decentralized procedure, a hybrid application may be accepted for consideration under the centralized procedure if the applicant shows that the medicinal product constitutes a significant therapeutic, scientific or technical innovation, or the granting of a community authorization for the medicinal product is in the interest of patients at the community level.

Clinical Trial Approval in the European Union

Requirements for the conduct of clinical trials in the European Union including Good Clinical Practice, or GCP, are set forth in the Clinical Trials Directive 2001/20/EC and the GCP Directive 2005/28/EC. Pursuant to Directive 2001/20/EC and Directive 2005/28/EC, as amended, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the E.U. member states. Under this system, approval must be obtained from the competent national authority of each E.U. member state in which a trial is planned to be conducted. To this end, a CTA is submitted, which must be supported by an investigational medicinal product dossier, or IMPD, and further supporting information prescribed by Directive 2001/20/EC and Directive 2005/28/EC and other applicable guidance documents. Furthermore, a clinical trial may only be started after a competent ethics committee has issued a favorable opinion on the clinical trial application in that country.

In April 2014, the E.U. passed the new Clinical Trials Regulation (EU) No 536/2014. The new Clinical Trials Regulation, which will replace the Clinical Trials Directive, introduces a complete overhaul of the existing regulation of clinical trials for medicinal products in the E.U., including a new coordinated procedure for authorization of clinical trials that is reminiscent of the mutual recognition procedure for marketing authorization of medicinal products, and increased obligations on sponsors to publish clinical trial results. The entry into application of the Clinical Trials Regulation has been delayed. The Clinical Trials Directive may be replaced with the new Clinical

Trials Regulation in late 2022. The new Clinical Trials Regulation aims to simplify and streamline the approval of clinical trials in the European Union. The main characteristics of the regulation include: a streamlined application procedure via a single entry point, the E.U. portal; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures that will spare sponsors from submitting broadly identical information separately to various bodies and different member states; a harmonized procedure for the assessment of applications for clinical trials, which is divided into two parts (Part I is assessed jointly by all member states concerned, and Part II is assessed separately by each member state concerned); strictly defined deadlines for the assessment of clinical trial applications; and the involvement of the ethics committees in the assessment procedure in accordance with the national law of the member state concerned but within the overall timelines defined by the Clinical Trials Regulation.

Periods of Authorization and Renewals

Marketing authorization is valid for five years in principle and the marketing authorization may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the authorizing member state. To this end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal. Any authorization which is not followed by the actual placing of the drug on the European Union market (in case of centralized procedure) or on the market of the authorizing member state within three years after authorization ceases to be valid (the so-called sunset clause).

Data and Market Exclusivity in the European Union

In the European Union, new chemical entities qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. This data exclusivity, if granted, prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic (abbreviated) application for eight years, after which generic marketing authorization can be submitted, and the innovator's data may be referenced, but not approved for two years. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity and the sponsor is able to gain the prescribed period of data exclusivity, another company nevertheless could also market another version of the product if such company can complete a full MAA with a complete database of pharmaceutical test, preclinical tests and clinical trials and obtain marketing approval of its product.

Orphan Drug Designation and Exclusivity

Regulation 141/2000 provides that a drug shall be designated as an orphan drug if its sponsor can establish: that the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the European Community when the application is made, or that the product is intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition in the European Community and that without incentives it is unlikely that the marketing of the drug in the European Community would generate sufficient return to justify the necessary investment. For either of these conditions, the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the European Community or, if such method exists, the drug will be of significant benefit to those affected by that condition.

Regulation 847/2000 sets out criteria and procedures governing designation of orphan drugs in the European Union. Specifically, an application for designation as an orphan product can be made any time prior to the filing of an application for approval to market the product. Marketing authorization for an orphan drug leads to a ten-year period of market exclusivity. This period may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan drug designation, for example because the product is sufficiently profitable not to justify market exclusivity. Market exclusivity can be revoked only in very selected cases, such as consent from the marketing authorization holder, inability to supply sufficient quantities of the product,

demonstration of ''clinically relevant superiority'' by a similar medicinal product, or, after a review by the Committee for Orphan Medicinal Products, requested by a member state in the fifth year of the marketing exclusivity period (if the designation criteria are believed to no longer apply). Medicinal products designated as orphan drugs pursuant to Regulation 141/2000 shall be eligible for incentives made available by the European Community and by the member states to support research into, and the development and availability of, orphan drugs.

Regulatory Requirements after Marketing Authorization

As in the United States, both marketing authorization holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA and the competent authorities of the individual EU Member States both before and after grant of the manufacturing and marketing authorizations. The holder of an EU marketing authorization for a medicinal product must, for example, comply with EU pharmacovigilance legislation and its related regulations and guidelines which entail many requirements for conducting pharmacovigilance, or the assessment and monitoring of the safety of medicinal products. The manufacturing process for medicinal products in the European Union is also highly regulated and regulators may shut down manufacturing facilities that they believe do not comply with regulations. Manufacturing requires a manufacturing authorization, and the manufacturing authorization holder must comply with various requirements set out in the applicable EU laws, including compliance with EU cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients.

In the European Union, the advertising and promotion of approved products are subject to EU Member States' laws governing promotion of medicinal products, interactions with clinicians, misleading and comparative advertising and unfair commercial practices. In addition, other legislation adopted by individual EU Member States may apply to the advertising and promotion of medicinal products. These laws require that promotional materials and advertising in relation to medicinal products comply with the product's Summary of Product Characteristics, or SmPC, as approved by the competent authorities. Promotion of a medicinal product that does not comply with the SmPC is considered to constitute off-label promotion, which is prohibited in the European Union.

Healthcare Reform

The healthcare industry in the United States, including the pharmaceutical sector, is highly regulated and subject to frequent substantial changes. Any significant efforts from the federal or state governments to change how healthcare is provided or funded within the United States could have a material impact on Ocuphire's business. Currently, the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act (collectively, the ''ACA'') is the seminal legislation that has had, and continues to have, substantial impact on the healthcare industry. The ACA was intended to expand access to health insurance coverage for uninsured individuals while containing the overall cost of healthcare services. The ACA hasbeen subject to reform through legislation, Executive Orders, and judicial challenges. For example, the Tax Cuts and Jobs Act of 2017 included a provision that repealed the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the ''individual mandate.'' Further, the Consolidated Appropriations Act of 2020 fully repealed the ACA's mandated ''Cadillac'' tax on certain high-cost employer-sponsored health coverage and the medical device excise tax on non-exempt medical devices, and eliminated the health insurer tax. The Bipartisan Budget Act of 2018 (''BBA'') amended the ACA to increase from 50% to 70% the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the ''donut hole.'' Under the Inflation Reduction Act (''IRA''), this coverage gap will be eliminated beginning January 1, 2025. The IRA also requires pharmaceutical manufacturers to pay 10% of the negotiated price of brands, biologics, and biosimilar products, when Medicare Part D beneficiaries are in the initial coverage phase, and 20% of the negotiated price during the catastrophic phase of Medicare Part D coverage. On June 17, 2021, the US Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the law. It is unclear how future actions before the Supreme Court, other such litigation, and the healthcare reform measures of the Biden administration will impact the ACA.

Provisions in the ACA impacting Ocuphire's potential drug candidates include:

- A special, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, although this fee would not apply to sales of certain products approved exclusively for orphan indications;
- Expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- Expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program (''MDRP'') by increasing the minimum rebate for both branded and generic drugs and revising the definition of ''average manufacturer price,'' or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices and extending rebate liability to prescriptions for individuals enrolled in Medicare Advantage plans; addressed a new methodology by which rebates owed by manufacturers under the MDRP are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- Expanded the types of entities eligible for the 340B drug discount program;
- A new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and
- Established the Center for Medicare and Medicaid Innovation within the Centers of Medicare and Medicaid Services (''CMS'') to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

There may be additional legislative changes, including potential repeal and replacement of certain provisions of the ACA. While the timing and scope of any potential future legislation to repeal and replace ACA provisions is highly uncertain in many respects, it is also possible that some of the ACA provisions that generally are not favorable for the research-based pharmaceutical sector could also be repealed along with ACA coverage expansion provisions.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013, and, due to subsequent legislative amendments, will remain in effect through the first six months of the FY 2032 sequestration order, unless additional Congressional action is taken (with the exception of a temporary suspension, and later a temporary reduction, instituted during the COVID-19 pandemic that expired on July 1, 2022).

In addition, there has been heightened governmental scrutiny in the U.S. of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. For example, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which temporarily increased premium tax credit assistance for individuals eligible for subsidies under the ACA for 2021 and 2022 and removed the 400% federal poverty level limit that otherwise applies for purposes of eligibility to receive premium tax credits. The IRA extended this increased tax credit assistance and removal of the 400% federal poverty limit through 2025.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. For example, several state laws require disclosures to state agencies and/or commercial purchasers with respect to price increases and new product launches that exceed certain pricing thresholds as identified in the relevant statutes. Some of these laws and regulations contain ambiguous requirements that government officials have not yet clarified. Given the lack of clarity in the laws and their implementation, our reporting actions could be subject to the penalty provisions of the pertinent

federal and state laws and regulations. Some states have also established prescription drug affordability boards that are tasked with identifying certain high-cost prescription products that may pose affordability challenges for consumers and payers, conducting cost reviews on such products, and, in some circumstances, imposing upper payment limits on such products.

Policy changes, including potential modification or repeal of all or parts of the ACA or the implementation of new health care legislation, could result in significant changes to the health care system, which may prevent us from being able to generate revenue, attain profitability or commercialize our drugs. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand or lower pricing for our product candidates, or additional pricing pressures.

Healthcare Frauds & Abuse and Compliance Laws and Regulations

There are other healthcare-related fraud and abuse and compliance laws and regulations that extensively govern how pharmaceutical companies, like Ocuphire, are operated and regulate activities related to pharmaceutical products. These laws and regulations may require administrative guidance to implement. Failure to comply could subject the company to legal and/or administrative actions, which may include substantial fines and/or penalties; orders to stop non-compliant activities; criminal charges; warning letters; product recalls or seizures; delays in product approvals; exclusion from participation in government reimbursement programs or contracts as well as limitations on conducting business in applicable jurisdictions.

Applicable federal and state healthcare laws and regulations include:

- The federal Anti-Kickback Statute, which is a criminal law that prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Violations of the federal Anti-Kickback Statute can result in significant civil monetary penalties and criminal fines, as well as imprisonment and exclusion from participation in government health care programs;
- The federal civil False Claims Act, which may be enforced through civil whistleblower or qui tam actions and imposes significant civil penalties, treble damages and potential exclusion from government health care programs against individuals or entities for, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or for making a false record or statement material to an obligation to pay the federal government or for knowingly and improperly avoiding, decreasing or concealing an obligation to pay money to the federal government. Further, a violation of the federal Anti-Kickback Statute can serve as a basis for liability under the federal civil False Claims Act. There is also the federal Criminal False Claims Act, which is similar to the federal Civil False Claims Act and imposes criminal liability on those that make or present a false, fictitious or fraudulent claim to the federal government;
- The federal Civil Monetary Penalties Law, which authorizes the imposition of substantial civil monetary penalties against an entity that engages in activities including, among others (1) knowingly presenting, or causing to be presented, a claim for services not provided as claimed or that is otherwise false or fraudulent in any way; (2) arranging for or contracting with an individual or entity that is excluded from participation in federal health care programs to provide items or services reimbursable by a federal health care program; (3) violations of the federal Anti-Kickback Statute; or (4) failing to report and return a known overpayment;
- The federal payment transparency tracking and reporting requirements known as the federal Physician Payments Sunshine Act, implemented as the Open Payments Program, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, among others, to track and report annually to CMS, within the United States Department of Health and Human Services (''HHS''), information related to payments and other transfers of value made by that entity to US-licensed physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), physician assistants, nurse

practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists, certified nurse midwives, and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to timely, accurately, and completely submit the required information for all payments, transfers of value and ownership or investment interests may result in civil monetary penalties;

- The federal Health Insurance Portability and Accountability Act of 1996 (''HIPAA'') which imposes criminal and civil liability for, among other things, executing or attempting to execute a scheme to defraud any healthcare benefit program, including any third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statements or representations, or making false statements relating to healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, which mandates, among other things, the adoption of uniform standards for the electronic exchange of information in common health care transactions as well as standards relating to the privacy and security of individually identifiable health information. These standards require the adoption of administrative, physical and technical safeguards to protect such information. In addition, many states have enacted comparable laws addressing the privacy and security of health information, some of which are more stringent than HIPAA. Failure to comply with these laws can result in the imposition of significant civil and criminal penalties;

- State laws that require the reporting of certain pricing information, including information pertaining to and justifying price increases, prohibit prescription drug price gouging; or impose payment caps on certain pharmaceutical products deemed by the state to be ''high cost''; and

- Analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures.

- Additionally, we expect our products, if and when approved, may be eligible for coverage under Medicare, the federal health care program that provides health care benefits to the aged and disabled. Specifically, we expect our products would be primarily reimbursed under Medicare Part D, which provides an outpatient prescription drug benefit for Medicare beneficiaries. Medicare Part D is implemented through private insurance plans under contractual arrangements between the plans and the federal government. Similar to pharmaceutical coverage through private health insurance, Part D plans develop formularies, impose utilization controls (such as prior authorization, step therapy, and quantity limits), and negotiate discounts from drug manufacturers. Because of this, the list of prescription drugs covered by Part D plans varies by plan. However, with limited exceptions, individual plans are required by statute to cover certain therapeutic categories and classes of drugs or biologics and to have at least two drugs in each unique therapeutic category or class. Our products may also be covered and reimbursed under other government programs, including those discussed below:

- The MDRP requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of the Department of Health and Human Services as a condition for states to receive federal matching funds for the manufacturer's outpatient drugs furnished to Medicaid patients. Under the MDRP, manufacturers must pay a rebate to each state Medicaid program for quantities of products utilized on an outpatient basis (with some exceptions) that are dispensed to Medicaid beneficiaries and paid for by a state Medicaid program. MDRP rebates are calculated using a statutory formula,

state-reported utilization data, and pricing data that are calculated and reported by manufacturers on a monthly and quarterly basis to CMS. These data include the AMP and, in the case of single source and innovator multiple source products, the best price for each drug.

- The 340B drug pricing program requires participating manufacturers to agree to charge statutorily-defined covered entities no more than the 340B ''ceiling price'' for the manufacturer's covered outpatient drugs. These 340B covered entities include health care organizations that have certain federal designations or receive funding from specific federal programs, including Federally Qualified Health Centers, Ryan White HIV/AIDS Program grantees, and certain types of hospitals and specialized clinics, as well as certain hospitals that serve a disproportionate share of low-income patients. The ACA expanded the 340B program to also include certain children's hospitals, certain free-standing cancer hospitals, critical access hospitals, certain rural referral centers and certain sole community hospitals, each as defined by ACA. The 340B ceiling price is calculated using a statutory formula, which is based on the AMP and rebate amount for the covered outpatient drug as calculated under the MDRP, and in general, products subject to the MDRP are also subject to the 340B ceiling price calculation and discount requirement. Any changes to the definition of Medicaid AMP and the Medicaid rebate amount also could affect our 340B ceiling price calculation for our products and could negatively impact our results of operations.
- Federal law further requires that for a company to be eligible to have its products paid for with federal funds under the MDRP and Medicare Part B programs, as well as to be purchased by certain federal agencies and grantees, it also must participate in the Department of Veterans Affairs (''VA'') Federal Supply Schedule (''FSS'') pricing program. To participate, manufacturers are required to enter into an FSS contract and other agreements with the VA for any covered drugs. Under these agreements, manufacturers must make such products available to the ''Big Four'' federal agencies—the VA, the Department of Defense (''DoD''), the Public Health Service (including the Indian Health Service), and the Coast Guard—at pricing that is capped pursuant to a statutory federal ceiling price (''FCP''), formula set forth in Section 603 of the Veterans Health Care Act of 1992 (''VHCA''). The FCP is based on a weighted average non-federal average manufacturer price (''Non-FAMP''), which manufacturers are required to report on a quarterly and annual basis to the VA.
- Any failure to comply with price reporting and rebate payment obligations under federal healthcare programs could negatively impact our financial results. Civil monetary penalties can be applied if we are found to have knowingly submitted any false price information to the government, if we are found to have made a misrepresentation in the reporting of our average sales price, or if we fail to submit the required price data on a timely basis. Such conduct also could provide a basis for other potential liability under other federal laws such as the False Claims Act.

Healthcare Reimbursement

Healthcare providers and third-party payors play a primary role in recommending and prescribing pharmaceutical products that are granted regulatory approval. If our potential drug candidates receive regulatory approval, successful commercialization of the products may depend, in part, on obtaining and maintaining adequate reimbursement levels with third-party payors, including commercial health insurers, managed care organizations, and government health programs in the United States such as Medicare and Medicaid. However, a growing trend in the United States healthcare industry and elsewhere is cost containment.

Recently, there has been greater scrutiny from governmental bodies over how pharmaceutical manufacturers and distributors set prices for their products. This has resulted in congressional inquiries as well as other proposed and enacted legislation designed to (i) bring more transparency to product pricing, (ii) limit coverage and reimbursement for drugs and other medical products, and (iii) reform government health program reimbursement within the healthcare system as a whole. While proposed reform measures will require the U.S. Congress to pass legislation to become effective, President Biden's administration and the U.S. Congress have each indicated that they will continue to seek new legislative and/or administrative measures to control drug costs.

For example, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which included among its provisions a sunset of the provision in the ACA that capped pharmaceutical manufacturers' rebate liability under the MDRP. Under the ACA, manufacturers' rebate liability was previously capped at 100% of the average manufacturer price for a covered outpatient drug. As of January 1, 2024, manufacturers' MDRP rebate liability is no longer capped, potentially resulting in a manufacturer paying more in MDRP rebates than it receives

on the sale of certain covered outpatient drugs. . Additionally, on October 14, 2022 President Biden issued an Executive Order on Lowering Prescription Drug Costs for Americans, which instructed the Secretary of the Department of Health and Human Services to consider whether to select for testing by the CMS Innovation Center new health care payment and delivery models that would lower drug costs and promote access to innovative drug therapies for beneficiaries enrolled in the Medicare and Medicaid programs. On February 14, 2023, the Department of Health and Human Services issued a report in response to the October 14, 2022, Executive Order, which, among other things, selects three potential drug affordability and accessibility models to be tested by the CMS Innovation Center. Specifically, the report addresses: (1) a model that would allow Part D Sponsors to establish a ''high-value drug list'' setting the maximum co-payment amount for certain common generic drugs at $2; (2) a Medicaid-focused model that would establish a partnership between CMS, manufacturers, and state Medicaid agencies that would result in multi-state outcomes-based agreements for certain cell and gene therapy drugs; and (3) a model that would adjust Medicare Part B payment amounts for Accelerated Approval Program drugs to advance the developments of novel treatments.

Furthermore, on August 16, 2022, President Biden signed the IRA into law. The IRA includes several provisions that may potentially impact our business, including provisions that (i) create a $2,000 cap on out-of-pocket expenses for Medicare Part D beneficiaries beginning in 2025, (ii) impose new manufacturer discount obligations for all drugs in Medicare Part D, (iii) allow the U.S. government establish a ''maximum fair price'' for a fixed number of pharmaceutical and biological products covered under Medicare Parts B and D following a price negotiation process with CMS; (iv) require companies to pay rebates to Medicare for drug prices that increase faster than inflation, CMS has also taken steps to implement the IRA, including: on June 30, 2023, issuing guidance detailing the requirements and parameters of the first round of price negotiations, to take place during 2023 and 2024, for products subject to the ''maximum fair price'' provision that would become effective in 2026; on August 29, 2023, releasing the initial list of ten drugs subject to price negotiations; on November 17, 2023, releasing guidance outlining the methodology for identifying certain manufacturers eligible to participate in a phase-in period where discounts on applicable products will be lower than those required by the Medicare Part D Manufacturer Discount Program; and on December 14, 2023, releasing a list of 48 Medicare Part B products that had an adjusted coinsurance rate based on the inflationary rebate provisions of the IRA for the time period of January 1, 2024 to March 31, 2024. It remains to be seen how these drug pricing initiatives will affect the broader pharmaceutical industry.. The effect of IRA on our business and the healthcare industry in general is not yet known.

In addition, individual states in the United States have also become increasingly active in passing laws and implementing regulations designed to control pharmaceutical product pricing, including reimbursement constraints, discounts, restrictions on certain product access, marketing cost disclosure and transparency measures and, in some cases, mechanisms to encourage importation from other countries and bulk purchasing.

Human Capital Resources

As of December 31, 2023, Ocuphire had fourteen full-time employees, with the following assignments: three engaged in clinical research and development activities, one of whom holds a Ph.D. degree, five engaged in research and development activities and also business development and finance, and six engaged in finance, human resources, and administrative support. Ocuphire plans to continue to utilize expert consultants and contract organizations to support execution of the day-to-day operations. None of Ocuphire's employees are represented by labor unions or covered by collective bargaining agreements.

Ocuphire believes that it maintains good relations with its employees.

Available Information

The Company's Internet address is www.ocuphire.com. We make available free of charge through our investor relations website, ir.ocuphire.com/sec-filings, copies of our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, as soon as reasonably practicable after such documents are electronically filed with, or furnished to, the SEC. The information contained on our website is not included as a part of, or incorporated by reference into, this Report.

ITEM 1A. RISK FACTORS

An investment in our securities has a high degree of risk. Before you invest you should carefully consider the risks and uncertainties described below and the other information in this Annual Report. Any of the risks and uncertainties set forth herein could materially and adversely affect our business, results of operations and financial condition, which in turn could materially and adversely affect the trading price or value of our securities. Additional risks not currently known to us or which we consider immaterial based on information currently available to us may also materially adversely affect us. As a result, you could lose all or part of your investment.

Risks Related to the Commercialization and Development of Our Product Candidates

We depend heavily on the success of our product pipeline. If we (or our strategic partner) fail to adequately commercialize RYZUMVI or develop and commercialize APX3330 or PS, our business will be materially harmed.

Our business depends on the successful clinical development, regulatory approval and commercialization of APX3330 and Phentolamine Ophthalmic Solution 0.75% Eye Drops ''PS''. Viatris is our strategic partner for the commercialization of FDA-approved RYZUMVI and for the further development and commercialization, if FDA-approved, of PS. APX300 is still in clinical development. We have invested a significant portion of our efforts and financial resources in the development of APX3330, RYZUMVI, and PS, and we (or our strategic partner) expect to invest a significant portion of our efforts and financial resources in the development and commercialization of APX3330, RYZUMVI and PS in the future. There remains a significant risk that we or Viatris will fail to successfully develop and commercialize RYZUMVI or our product candidates. We cannot accurately predict when or if APX3330 will prove effective or safe in humans or whether it will receive marketing approval. Our ability to generate product revenues depends heavily on the continued commercialization of RYZUMVI and obtaining marketing approval for and commercializing APX3330 and PS (together, ''our product candidates'').

The research, testing, manufacturing, labeling, approval, sale, marketing and distribution of a drug product are subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries, where regulations may differ. We are not permitted to market our product candidates in the United States until we receive approval of an NDA from the FDA or in any foreign countries until we receive the requisite approval from such countries. Before obtaining regulatory approval for the commercial sale of our product candidates for a particular indication, we must demonstrate through nonclinical testing and clinical trials that the applicable product candidate is safe and effective for use in that target indication. This process can take many years and may be followed by post-marketing studies and surveillance together which will require the expenditure of substantial resources beyond the proceeds raised in our equity and debt financings to date. Of the large number of drugs in development in the United States, only a small percentage of drugs successfully complete the FDA regulatory approval process and are commercialized. Accordingly, even if we are able to complete development and FDA approval of our product candidates, we cannot assure you that our product candidates will be approved or commercialized, widely accepted in the marketplace, or more effective than other commercially available alternatives. If we are unable to successfully develop and commercialize additional product candidates, or successfully continue to commercialize RYZUMVI, our commercial opportunity will be limited. The success of APX3330, RYZUMVI and PS could be impacted by several factors, including the following:

- delays in the launch or difficulties in the widespread commercialization of RYZUMVI (currently the launch is anticipated in the first half of 2024);
- delays in, termination, or numerous unforeseen events during, or as a result of, manufacturing or clinical trials;
- obtaining unfavorable results from nonclinical and clinical studies for our product candidates;
- the cost of clinical trials being greater than anticipated;
- the willingness of patients or medical investigators to follow our clinical trial protocols and the number of patients willing to participate;
- delays in applying for and receiving marketing and NDA approvals from applicable regulatory authorities for our product candidates;
- other government or regulatory delays and changes in regulatory requirements, policy and guidelines may require us to perform additional clinical trials or use substantial additional resources to obtain regulatory approval;

- issues with making arrangements with third-party manufacturers for commercial quantities of RYZUMVI and our product candidates and receiving regulatory approval of our manufacturing processes and our third-party manufacturers' facilities from applicable regulatory authorities;
- establishing sales, marketing, and distribution capabilities and launching commercial sales of RYZUMVI and our product candidates, if and when approved, whether alone or in collaboration with others;
- acceptance of RYZUMVI and our product candidates by patients, the medical community, and third-party payors;
- effectively competing with other therapies, including the existing standard-of-care;
- maintaining a continued acceptable safety profile of RYZUMVI and our product candidates following approval;
- obtaining and maintaining coverage and adequate reimbursement from third-party payors;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity;
- protecting our rights in our intellectual property portfolio related to RYZUMVI and our product candidates; and
- our ability to fulfill requests for additional data regarding our product candidates.

In addition, under the Apexian License Agreement, Ocuphire has rights to certain compounds for use in ophthalmic and diabetic diseases. Ocuphire does not control the development of these compounds in other non-ophthalmic indications.

Viatris has exclusive global rights to commercialize RYZUMVI and PS in key global markets. Viatris' failure to timely develop or commercialize these products would have a material adverse effect on our business and operating results.

We granted Viatris an exclusive right to commercialize RYZUMVI and PS in key global markets. Additionally, we granted Viatris the exclusive right and license to develop RYZUMVI and PS outside of the United States. The collaboration with Viatris may not be successful due to several factors, including the following:

- Viatris may not be able to manufacture our products in a timely or cost-effective manner;
- Viatris may not timely perform its obligations under the Viatris License Agreement;
- Viatris may fail to effectively commercialize our products;
- Viatris may not be able to sublicense RYZUMVI or PS to one or more suitable parties outside the United States; or
- Contractual disputes or other disagreements between us and Viatris, including those regarding the development, manufacture, sub licensure and commercialization of our products, interpretation of the License Agreement, and ownership of proprietary rights. Viatris may select a new development partner for RYZUMVI and PS in the U.S. upon 90 days' notice to Ocuphire.

Any of the foregoing could adversely impact the likelihood and timing of any payments we are eligible to receive under the Viatris License Agreement. The Company will be reliant on Viatris to drive the commercialization and sales of our products. If Viatris does not perform its obligations under the Viatris License Agreement, this could result in a material adverse effect on our business, results of operations and prospects and would likely cause our stock price to decline

The results of previous clinical trials may not be predictive of future results, and the results of our current and planned clinical trials may not satisfy the requirements of the FDA or non-U.S. regulatory authorities.

The results from the prior nonclinical studies and clinical trials for APX3330 and PS discussed elsewhere in this Annual Report may not necessarily be predictive of the results of future nonclinical studies or clinical trials. Even if we are able to complete our planned clinical trials of our product candidates according to our current development timeline, the results from our prior clinical trials of our product candidates may not be replicated in these future trials. Many companies in the pharmaceutical and biotechnology industries (including those with greater resources and

experience than us) have suffered significant setbacks in late-stage clinical trials after achieving positive results in early-stage development, and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, nonclinical findings made while clinical trials were underway or safety or efficacy observations made in clinical trials, including previously unreported adverse events (''AEs''). Moreover, nonclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in nonclinical studies and clinical trials nonetheless have failed to obtain FDA approval. If we fail to produce adequate results reflecting adequate efficacy and safety in our clinical trials of any of our product candidates, the development timelines, regulatory approvals, and commercialization prospects for our product candidates, as well as Ocuphire's business and financial prospects, would be adversely affected. Further, Ocuphire's product candidates may not be approved even if they achieve their respective primary endpoints in additional Phase 3 registration trials. The FDA or non-U.S. regulatory authorities may disagree with our trial designs or our interpretation of data from nonclinical studies and clinical trials. In addition, any of these regulatory authorities may change requirements for the approval of a product candidate even after reviewing and providing comments or advice on a protocol for a clinical registration trial that has the potential to result in approval by the FDA or another regulatory authority.

For instance, although we have reached an SPA agreement with FDA for a Phase 3 study for PS for decreased vision under dim (mesopic or low) light conditions after keratorefractive surgery and plan to seek a SPA agreement for studies to support approval of APX3330, the FDA may ultimately require additional studies for approval.

The FDA's SPA process is designed to facilitate the FDA's review and approval of drugs and biologics by allowing the FDA to evaluate the proposed design and size of certain clinical or animal studies, including clinical trials that are intended to form the primary basis for determining a product candidate's efficacy. Upon specific request by a clinical trial sponsor, the FDA will evaluate the protocol and respond to a sponsor's questions regarding protocol design and scientific and regulatory requirements. The FDA aims to complete SPA reviews within 45 days of receipt of the request. The FDA ultimately assesses whether specific elements of the protocol design of the trial, such as entry criteria, dose selection, endpoints and/or planned analyses, are acceptable to support regulatory approval of the product with respect to the effectiveness of the indication studied. All exchanges between the FDA and the sponsor regarding an SPA must be clearly documented in an SPA letter or the minutes of a meeting between the sponsor and the FDA.

Although the FDA may agree to an SPA, an SPA agreement does not guarantee approval of a product. Even if the FDA agrees to the design, execution, and analysis proposed in protocols reviewed under the SPA process, the FDA may revoke or alter its agreement in certain circumstances. In particular, an SPA agreement is not binding on the FDA if public health concerns emerge that were unrecognized at the time of the SPA agreement, other new scientific concerns regarding product safety or efficacy arise, the sponsor company fails to comply with the agreed upon trial protocols, or the relevant data, assumptions or information provided by the sponsor in a request for the SPA change or are found to be false or omit relevant facts.

In addition, even after an SPA agreement is finalized, the SPA agreement may be modified, and such modification will be deemed binding on the FDA review division, except under the circumstances described above, if the FDA and the sponsor agree in writing to modify the protocol. Generally, such modification is intended to improve the study. The FDA retains significant latitude and discretion in interpreting the terms of the SPA agreement and the data and results from any study that is the subject of the SPA agreement. Moreover, if the FDA revokes or alters its agreement under the SPA, or interprets the data collected from the clinical trial differently than we do, the FDA may not deem the data sufficient to support an application for regulatory approval.

Furthermore, any of these regulatory authorities may also approve our product candidates for fewer or more limited indications than we request or may grant approval contingent on the performance of costly post-marketing clinical trials. Before obtaining regulatory approvals for the commercial sale of any product candidate for any target indication, we must demonstrate with substantial evidence gathered in nonclinical studies and adequate and well-controlled clinical studies, and, with respect to approval in the United States, to the satisfaction of the FDA, that the product candidate is safe and effective for use for that target indication. We cannot assure you that the FDA or non-U.S. regulatory authorities would consider our planned clinical trials to be sufficient to serve as the basis for approval of our product candidates for any indication. The FDA and non-U.S. regulatory authorities retain broad discretion in evaluating the results of our clinical trials and in determining whether the results demonstrate that our product candidates are safe and effective. If we are required to conduct clinical trials of our product candidates in

addition to those we have planned prior to approval, we may need substantial additional funds, and cannot assure you that the results of any such outcomes trial or other clinical trials will be sufficient for approval. Furthermore, if our current and planned nonclinical and clinical trials do not satisfy the requirements of the FDA or non-U.S. regulatory authorities, our business may be materially harmed.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our ability to conduct and complete those clinical trials, and our ability to seek and receive necessary regulatory approvals, could be delayed or prevented.

We or our future collaborators may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or analogous regulatory authorities outside the United States. Patient enrollment can be affected by many factors, including:

- severity of the disease under investigation;
- availability and efficacy of medications already approved for the disease under investigation;
- eligibility criteria and visit schedule for the trial in question;
- competition for eligible patients with other companies conducting clinical trials for product candidates seeking to treat the same indication or patient population;
- our payments for conducting clinical trials;
- perceived risks and benefits of the product candidate under study;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment;
- proximity and availability of clinical trial sites for prospective patients; and
- the ability of patients to participate in clinical trials during any public health emergencies.

Our inability to enroll a sufficient number of patients for our clinical trials or retain sufficient enrollment through the completion of our trials would result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates and cause our stock price to decline.

We or others could discover that our product candidates lack sufficient efficacy, or sufficient efficacy compared to competitor products or that they cause undesirable side effects that were not previously identified, which could delay or prevent regulatory approval or commercialization.

Because both APX3330 and PS have been tested in relatively small patient populations, at a limited range of daily doses up to 720 mg and up to 0.75% Phentolamine Ophthalmic Solution (which is the same as 1.0% Phentolamine Mesylate Ophthalmic Solution) respectively, and for limited durations to date, it is possible that our clinical trials have or will indicate an apparent positive effect of APX3330 or PS that is greater than the actual positive effect, if any, or that additional and unforeseen side effects may be observed as its development progresses. The discovery that either APX3330 or PS lacks sufficient efficacy, or that they cause undesirable side effects (including side effects not previously identified in our completed clinical trials), could cause us or regulatory authorities to interrupt, delay, or discontinue clinical trials, and could result in the denial of regulatory approval by the FDA or other non-U.S. regulatory authorities for any or all targeted indications.

The discovery that our product candidates lack sufficient efficacy or that they cause undesirable side effects that were not previously identified could prevent us from commercializing such product candidates and generating revenues from sales. In addition, if we receive marketing approval for our product candidates and we or others later:

- discover that they are less effective, or identify undesirable side effects caused by our product candidates:
- regulatory authorities may withdraw their approval of the product;
- we may be required to recall the product, change the way this product is administered, conduct additional clinical trials, or change the labeling or distribution of the product (including REMS);

- additional restrictions may be imposed on the marketing of, or the manufacturing processes for, the product;
- we may be subject to fines, injunctions, or the imposition of civil or criminal penalties;
- we could be sued and held liable for harm caused to patients;
- the product may be rendered less competitive and sales may decrease; or
- our reputation may suffer generally among both clinicians and patients.

Any one or a combination of these events could prevent us from achieving or maintaining market acceptance of the affected product candidate or could substantially increase the costs and expenses of commercializing the product candidate, which in turn could delay or prevent us from generating significant, or any, revenues from the sale of the product candidate.

Changes in regulatory requirements or FDA guidance, or unanticipated events during our clinical trials, may result in changes to clinical trial protocols or additional clinical trial requirements, which could result in increased costs to us or delays in development timelines.

Changes in regulatory requirements or FDA guidance, or unanticipated events during our clinical trials, may require us to amend clinical trial protocols or the FDA may impose additional clinical trial requirements. Amendments to our clinical trial protocols would require resubmission to the FDA and IRBs for review and approval, and may adversely impact the cost, timing or successful completion of a clinical trial. If we experience delays completing, or if we terminate, any trials, or if we are required to conduct additional clinical trials, the commercial prospects for our product candidates may be harmed and our ability to generate product revenues may be delayed.

If we fail to receive regulatory approval for any of our planned indications for our product candidates or fail to develop additional product candidates, our commercial opportunity will be limited.

We are initially focused on the development of our product candidates for our target indications, DR, the reversal of pharmacologically-induced mydriasis, treatment of presbyopia, and decreased vision under dim (mesopic or low) lighting conditions after keratorefractive surgery. RYZUMVI has been approved for the treatment of pharmacologically-induced mydriasis. However, we cannot assure you that we will be able to obtain regulatory approval of our product candidates for any other indication, or successfully commercialize our product candidates, following approval. If we do not receive regulatory approval for, or successfully commercialize, our product candidates for one or more of our targeted or other indications, our commercial opportunity will be limited.

Even if we do receive regulatory approval for, or successfully commercialize, our product candidates, they will be subject to ongoing regulatory review and critique. This ongoing review and critique may cause the loss of regulatory approval.

We may pursue clinical development of additional acquired or in-licensing product candidates. Developing, obtaining regulatory approval for and commercializing additional product candidates will require substantial additional funding beyond the net proceeds of our completed equity and debt financings, and are prone to the risks of failure inherent in drug product development. We cannot assure you that we will be able to successfully advance any additional product candidates through the development process.

We have limited drug research and discovery capabilities and may need to acquire or license product candidates from third parties, raise additional capital, or shift capital resources to expand our product candidate pipeline.

We currently have limited drug research and discovery capabilities. Accordingly, if we are to expand our pipeline beyond our product pipeline candidates, we may need to acquire or license product candidates from third parties, or either raise additional capital or shift capital resources to fund such expansion. We would face significant competition in seeking to acquire or license promising product candidates, may not be able to raise additional capital, or may divert capital resources from other areas of the Company that may then face material consequences from less funding. Many of our competitors for such promising product candidates may have significantly greater financial resources and more extensive experience in nonclinical testing and clinical trials, obtaining regulatory approvals, and manufacturing and marketing pharmaceutical products, and thus, may be a more attractive option to a potential licensor than us. If we are unable to acquire or license additional promising product candidates, raise additional capital, or shift capital resources, we may not be able to expand our product candidate pipeline.

If we are able to acquire or license other product candidates, such license agreements will likely impose various obligations upon us, and our licensors may have the right to terminate the license thereunder in the event of a material breach or, in some cases, at will. A termination of a future license could result in our loss of the right to use the licensed intellectual property, which could adversely affect our ability to develop and commercialize a future product candidate, if approved, as well as harm our competitive business position and our business prospects.

We may expend our limited resources to pursue a particular indication and fail to capitalize on indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we are currently focusing only on development programs that we identify for specific indications for our product candidates. As a result, we may forego or delay pursuit of opportunities for other indications, or with other potential product candidates that later prove to have greater commercial potential. Due to changes or failure to accurately predict the size of the addressable market, among other reasons, our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs for specific indications or future product candidates may not yield any commercially viable product. If we do not accurately evaluate the commercial potential or target market for our product candidates, we may not gain approval or achieve market acceptance of that candidate, and our business and financial results will be harmed.

Risks Related to Our Financial Position and Need for Additional Capital

We have not generated any revenue from sales of any products, expect to incur losses for the foreseeable future and may never achieve or maintain profitability.

Our only product approved for commercial sale is RYZUMVI, which we expect will be launched in the first half of 2024 by Viatris, our commercialization partner. We do not anticipate generating any additional product revenue, unless and until our product candidates receive the regulatory approvals necessary for commercialization in one or more jurisdictions. Our ability to generate revenue depends on a number of factors, including our ability to:

- the successful launch and widespread commercialization of RYZUMVI;
- obtain favorable results from and complete the nonclinical and clinical development of our product candidates for their planned indications, including successful completion of additional clinical trials for these indications;
- submit applications to regulatory authorities for both product candidates and receive timely marketing approvals in the United States and foreign countries;
- establish and maintain commercially viable supply and manufacturing relationships with third parties that can provide adequate, in both amount and quality, products and services to support clinical development and meet the market demand for RYZUMVI and our product candidates that we develop, if approved;
- establish sales and marketing capabilities to effectively market and sell our product candidates in the United States or other markets, either alone or with a pharmaceutical partner;
- address any competing products and technological and market developments;
- obtain coverage and adequate reimbursement for customers and patients from government and third-party payors for RYZUMVI and our product candidates that we develop; and
- achieve market acceptance of RYZUMVI and our product candidates.

Furthermore, as of December 31, 2023, we had an accumulated deficit of $81.5 million. We have funded our operations primarily through issuance of promissory notes and convertible notes in private placements, and then common stock and warrants after becoming a publicly-traded company, and more recently, through fees and a milestone payment received under the Viatris License Agreement. We have devoted substantially all of our financial resources and efforts to the clinical development of our product candidates. Even assuming we obtain additional regulatory approval for one or more of our product candidates, we expect it to be several years before APX3330 [and PS] is potentially ready for commercialization, and our product candidates may not gain market acceptance or achieve commercial success. We may not achieve profitability soon after generating product revenue, if ever, and may be unable to continue operations without continued funding.

To become and remain profitable from our product candidates, we must develop and eventually commercialize a product with market potential. This will require us to be successful in a range of challenging activities, including completing nonclinical testing and clinical trials, obtaining regulatory approval for a product candidate, manufacturing, marketing, and selling any drug for which it may obtain regulatory approval and satisfying any post-marketing requirements. We anticipate incurring significant costs associated with these activities. We are in the early stages of most of these activities. We may never succeed in these activities and, even if we do, we may never generate revenues that are significant or large enough to achieve profitability.

If we do achieve profitability from our product candidates, we may not be able to sustain or increase profitability on an annual basis. Our failure to become or remain profitable from our product candidates may decrease our value and could impair our ability to raise capital, maintain our research and development efforts, expand our business, or continue our operations.

Our relatively short operating history may make it difficult for investors to evaluate the success of our business to date and to assess our future viability.

We are a clinical-stage company, and our operations to date have been limited to organizing and staffing our company, business planning, raising capital, and developing our product candidates. We have not yet demonstrated our ability to manufacture a product at commercial scale or conduct sales and marketing activities necessary for successful product commercialization.

Additionally, there is no operating history on which investors may evaluate our business and our prospects. Investment in a clinical stage company such as ours is inherently subject to many risks. These risks and difficulties include challenges in accurate financial planning as a result of: (a) accumulated losses; (b) uncertainties resulting from a relatively limited time period in which to develop and evaluate business strategies as compared to companies with longer operating histories; (c) compliance with regulations required to commence sales on future products; (d) reliance on third parties for clinical, manufacturing, analytical laboratory work, nonclinical, regulatory, commercialization or other activities; (e) financing the business; and (f) meeting the challenges of the other risk factors described herein. We have no operating history upon which investors may base an evaluation of our performance; therefore, we are subject to all risks incident to the creation and development of a new business. There can be no assurance that we can realize our plans on our projected timetable in order to reach sustainable or profitable operations.

Adverse developments affecting the financial services industry could negatively affect our current and projected business operations and our financial condition and results of operations.

Although we assess our banking relationships as we believe necessary or appropriate, our access to funding sources and other credit arrangements in amounts adequate to finance or capitalize our current and projected future business operations could be significantly impaired by factors that affect us, the financial institutions with which we have arrangements directly, or the financial services industry or economy in general. These factors could include, among others, events such as liquidity constraints or failures, the ability to perform obligations under various types of financial, credit or liquidity agreements or arrangements, disruptions or instability in the financial services industry or financial markets, or concerns or negative expectations about the prospects for companies in the financial services industry. These factors could involve financial institutions or financial services industry companies with which we have financial or business relationships, but could also include factors involving financial markets or the financial services industry generally. The results of events or concerns that involve one or more of these factors could include a variety of material and adverse impacts on our current and projected business operations and our financial condition and results of operations. These could include, but may not be limited to, the following:

- Delayed access to deposits or other financial assets or the uninsured loss of deposits or other financial assets;
- Loss of access to revolving existing credit facilities or other working capital sources and/or the inability to refund, roll over or extend the maturity of, or enter into new credit facilities or other working capital resources;
- Potential or actual breach of contractual obligations that require us to maintain letters or credit or other credit support arrangements; or
- Termination of cash management arrangements and/or delays in accessing or actual loss of funds subject to cash management arrangements.

In addition, investor concerns regarding the U.S. or international financial systems could result in less favorable commercial financing terms, including higher interest rates or costs and tighter financial and operating covenants, or systemic limitations on access to credit and liquidity sources, thereby making it more difficult for us to acquire financing on acceptable terms or at all. Any decline in available funding or access to our cash and liquidity resources could, among other risks, adversely impact our ability to meet our operating expenses, financial obligations or fulfill our other obligations, result in breaches of our financial and/or contractual obligations or result in violations of federal or state wage and hour laws. Any of these impacts, or any other impacts resulting from the factors described above or other related or similar factors not described above could have material adverse impacts on our liquidity and our current and/or projected business operations and financial condition and results of operations. In addition, any further deterioration in the macroeconomic economy or financial services industry could lead to losses or defaults by parties with whom we conduct business, which in turn, could have a material adverse effect on our current and/or projected business operations and results of operations and financial condition. For example, a party with whom we conduct business may fail to make payments when due, default under their agreements with us, become insolvent or declare bankruptcy. Any bankruptcy or insolvency, or the failure to make payments when due, of any counterparty of ours, or the loss of any significant relationships, could result in material losses to us and may material adverse impacts on our business.

We will need substantial additional capital in the future. If additional capital is not available, we will have to delay, reduce or cease operations.

We will need to raise additional capital to continue to fund the further development of our product candidates and operations. Our future capital requirements may be substantial and will depend on many factors including:

- the scope, size, rate of progress, results, and costs of researching and developing our product candidates, and initiating and completing our nonclinical studies and clinical trials;
- the cost, timing and outcome of our efforts to obtain further marketing approval for our product candidates in the United States and other countries, including to fund the preparation and filing of NDAs with the FDA for our product candidates and to satisfy related FDA requirements and regulatory requirements in other countries;
- the number and characteristics of any additional product candidates we develop or acquire, if any;
- our ability to establish and maintain collaborations on favorable terms, if at all;
- the amount of revenue, if any, from commercial sales, should our product candidates receive marketing approval;
- the costs associated with commercializing our product candidates, if we receive marketing approval, including the cost and timing of developing sales and marketing capabilities or entering into strategic collaborations to market and sell our product candidates;
- the cost of manufacturing our product candidates or products we successfully commercialize; and
- the costs associated with general corporate activities, such as the cost of filing, prosecuting and enforcing patent claims and making regulatory filings.

Changing circumstances may cause us to consume capital significantly faster than we currently anticipate. Because the outcome of any clinical trial is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development, regulatory approval and commercialization of our product candidates. Additional financing may not be available when we need it, or may not be available on terms that are favorable to us. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. If adequate funds are unavailable to us on a timely basis, or at all, we may not be able to continue the development of our product candidates, or commercialize our product candidates, if approved, unless we find a strategic partner.

Worldwide economic and social instability or adverse global economic conditions could adversely affect our revenue, financial condition, or results of operations.

The health of the global economy, and the equity and credit markets in particular, as well as the stability of the social fabric of our society, affects our business and operating results. For example, the equity and credit markets may be adversely affected by current conflicts in Europe and the Middle East, negative trends in the real estate and other

sectors in China, and measures taken in response thereto. If the equity and credit markets are not favorable, we may be unable to raise additional financing when needed or on favorable terms. Our vendors and development partners may experience financial difficulties or be unable to borrow money to fund their operations, which may adversely impact their ability to purchase our products or to pay for our products on a timely basis, if at all. Any weak or declining economy or political disruption, including international trade disputes, could also strain our manufacturers or suppliers, possibly resulting in supply disruption, or cause our customers to delay making payments for our potential products. In addition, adverse economic conditions, such as recent supply chain disruptions and labor shortages and persistent inflation, have affected, and may continue to adversely affect our suppliers' ability to provide our manufacturers with materials and components, which may negatively impact our business. These economic conditions make it more difficult for us to accurately forecast and plan our future business activities.

Furthermore, a general slowdown in the global economy, including a recession, or in a particular region or industry, an increase in trade tensions with U.S. trading partners, inflation or a tightening of the credit markets could negatively impact our business, financial condition and liquidity. Adverse global economic conditions have from time to time caused or exacerbated significant slowdowns in the industries and markets in which we operate, which have adversely affected our business and results of operations. Macroeconomic weakness and uncertainty also make it more difficult for us to accurately forecast revenue, gross margin and expenses, and may make it more difficult to raise or refinance debt.

Any of the foregoing could seriously harm our business, and we cannot anticipate all of the ways in which the political or economic climate and financial market conditions could seriously harm our business.

Raising additional capital may cause dilution to our stockholders, restrict our operations, or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity and debt financings as well as potential strategic collaborations and licensing arrangements. We do not have any committed external source of funds. Debt financing or preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. Thus, raising additional capital may not be able to be achieved, even if desired, and if possible to raise additional capital, it may not be done so on terms that are desirable. If we raise funds through strategic collaborations or marketing, distribution, or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. This may reduce the value of our common stock.

Risks Related to Government Regulation

Even if we receive marketing approval for our product candidates in the United States, we may never receive regulatory approval to market such product candidates outside of the United States.

In addition to the United States, we intend to seek regulatory approval to market our product candidates in Europe, Japan, Canada, and Australia, and potentially other markets. If we pursue additional product candidates in the future, we may seek regulatory approval of such product candidates outside the United States. In order to market any product outside of the United States, however, we must establish and comply with the numerous and varying safety, efficacy and other regulatory requirements of these other countries. Approval procedures vary among countries and can involve additional product candidate testing and additional administrative review periods. The time required to obtain approvals in other countries might differ from that required to obtain FDA approval. The marketing approval processes in other countries may include all of the risks detailed above regarding FDA approval in the United States as well as other risks. In particular, in many countries outside of the United States, products must receive pricing and reimbursement approval before the product can be commercialized. Obtaining this approval can result in substantial delays in bringing products to market in such countries. Marketing approval in one country does not ensure marketing approval in another, but a failure or delay in obtaining marketing approval in one country may have a negative effect on the regulatory process in others. Failure to obtain marketing approval in other countries or any delay or other setback in obtaining such approval would impair our ability to market our product candidates in such foreign markets. Any such impairment would reduce the size of our potential market, which could have an adverse impact on our business, results of operations and prospects.

Even if we obtain further marketing approval for our product candidates, such product candidates could be subject to post-marketing, obligations, restrictions or withdrawal from the market, and we may be subject to substantial penalties if we fail to comply with regulatory requirements or experience unanticipated problems with a product following approval.

Any product candidate for which we, or our future collaborators, obtain marketing approval in the future, as well as the manufacturing processes, post-approval studies and measures, labeling, advertising, and promotional activities for such drug, among other things, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the drug may be marketed or to the conditions of approval, including the requirement to implement a REMS, which could include requirements for a restricted distribution system.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of a product candidate. The FDA and other agencies, including the Department of Justice, closely regulate and monitor the post-approval marketing and promotion of drugs to ensure that they are manufactured, marketed, and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we, or any future collaborator, does not market a product candidate for which it receives marketing approval for only its approved indications, we, or the collaborator, may be subject to warnings or enforcement action for off-label promotion. Violation of the Federal Food, Drug, and Cosmetic Act (''FDC Act'') and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs, may lead to investigations or allegations of violations of federal or state healthcare fraud and abuse laws and state consumer protection laws

In addition, later discovery of previously unknown AEs or other problems with our product candidates or our manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- litigation involving patients taking our drugs;
- restrictions on such drugs, manufacturers, or manufacturing processes;
- restrictions on the labeling or marketing of a drug;
- restrictions on drug distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the drugs from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- product recall or public notification or medical product safety alerts to healthcare professionals;
- fines, restitution, or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- damage to relationships with any potential collaborators;
- unfavorable press coverage and damage to our reputation;
- refusal to permit the import or export of drugs;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

Legislative reform or changes in the regulatory environment affecting our business may increase the difficulty and cost for obtaining marketing approval of our product candidates, or otherwise affect the pricing and commercial viability of or product candidates.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of a product candidate, restrict or regulate post-approval activities and affect our ability, or the ability of our future collaborators, to profitably sell any drug for which we, or they, obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and cause downward pressure on the price that we, or our future collaborators, may charge for any approved drug.

For example, in March 2010, the United States Congress enacted the Patient Protection and Affordable Care Act (''ACA''), and the Health Care and Education Reconciliation Act, or the Healthcare Reform Act, which expanded health care coverage through Medicaid expansion and the implementation of the individual mandate for health insurance coverage and which included changes to the coverage and reimbursement of drug products under government healthcare programs.

There have also been efforts by federal and state government officials or legislators to implement measures to regulate prices or payment for pharmaceutical products, including legislation on drug importation. Recently, there has been considerable public and government scrutiny of pharmaceutical pricing and proposals to address the perceived high cost of pharmaceuticals. There have also been recent state legislative efforts to address drug costs, which generally have focused on increasing transparency around drug costs or limiting drug prices. General legislative cost control measures may also affect reimbursement for our product candidates. The Budget Control Act, as amended, resulted in the imposition of 2% reductions in Medicare (but not Medicaid) payments to providers in 2013 and will remain in effect through 2027 unless additional Congressional action is taken. Any significant spending reductions affecting Medicare, Medicaid or other publicly funded or subsidized health programs that may be implemented and/or any significant taxes or fees that may be imposed on us could have an adverse impact on results of operations. Adoption of new legislation at the federal or state level could affect demand for, or pricing of, our current or future products if approved for sale. We cannot, however, predict the ultimate content, timing or effect of any changes to the Healthcare Reform Act or other federal and state reform efforts. There is no assurance that federal or state health care reform will not adversely affect our future business and financial results.

There have been judicial and congressional challenges and amendments to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future, as well as efforts to repeal and replace it. In addition, other legislative changes have been proposed and adopted since the ACA was enacted. These new laws have resulted in additional reductions in Medicare and other healthcare funding and otherwise may affect the prices we may obtain for any product candidate for which marketing approval is obtained. Any reduction in reimbursement from Medicare or other government-funded programs may result in a similar reduction in payments from private payors. Moreover, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our drugs.

Further, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap for single source and innovator multiple source drugs, beginning January 1, 2024. In addition, Congress is considering additional health reform measures, such as capping the costs for prescription drugs covered by Medicare Part D and by setting the annual out-of-pocket limit at $2,000 beginning in 2024, as part of other health reform initiatives. Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance, or interpretations will be changed, or what the impact of such changes on the marketing approvals of a product candidate, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval or subject us or our future collaborators to more stringent drug labeling and post-marketing testing and other requirements. More recently, President Biden signed the Inflation Reduction Act of 2022 into law in August of 2022, which, among other things, requires manufacturers to pay rebates to Medicare if prices increase faster than inflation for products used by Medicare beneficiaries.

Our relationships with healthcare providers and third-party payors will be subject to applicable fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, and diminished profits and future earnings, among other penalties and consequences.

Healthcare providers and third-party payors will play a primary role in the recommendation and prescription of any product candidate for which we obtain marketing approval. Our current and future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell, and distribute product candidates for which we obtain marketing approval. Restrictions and obligations under applicable federal and state healthcare laws and regulations include the following. For additional detail on potentially applicable laws, see the section titled ''Part I, Item 1 – Business – Healthcare Fraud and Abuse and Compliance Laws and Regulations.'' Certain state and foreign laws also govern the privacy and security of health information in ways that differ from each other and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our current and future business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations, or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal, and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, disgorgement, individual imprisonment, contractual damages, reputational harm, diminished profits and future earnings, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil, and administrative sanctions, including exclusions from government funded healthcare programs. Defending against any such actions can be costly, time-consuming, and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired.

We are subject to U.S. and certain foreign export and import controls, sanctions, embargoes, anti-corruption laws, and anti-money laundering laws and regulations. Compliance with these legal standards could impair our ability to compete in domestic and international markets. We could face criminal liability and other serious consequences for violations which could harm our business.

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls, the U.S. Foreign Corrupt Practices Act of 1977, as amended, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, contractors, and other partners from authorizing, promising, offering, or providing, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector. We may engage third parties for clinical trials outside of the United States, to sell our products abroad once we enter a commercialization phase, and/or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, contractors, and other partners, even if we do not explicitly authorize or have actual knowledge of such activities. Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences.

Our employees or representatives may engage in misconduct or other improper activities, including violating applicable regulatory standards and requirements, which could significantly harm our business.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to:

- comply with the regulations of the FDA and applicable non-U.S. regulators;
- provide accurate information to the FDA and applicable non-U.S. regulators;

- comply with healthcare fraud and abuse laws and regulations in the United States and abroad;
- report financial information or data accurately; or
- disclose unauthorized activities to us.

In particular, sales, marketing, and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing, and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs, and other business arrangements. Employee misconduct could also involve the improper use of, including trading on, information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity, including employee compliance training, may be ineffective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant civil, criminal, and administrative penalties, damages, fines, exclusion from government funded healthcare programs such as Medicare and Medicaid, disgorgement, individual imprisonment, contractual damages, reputational harm, diminished profits and future earnings, and the curtailment or restructuring of our operations.

The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. If found to have improperly promoted off-label uses, we may become subject to significant liability.

The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription products. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product's approved labeling. If we receive marketing approval for our product candidates for a certain indication, physicians may nevertheless prescribe such products to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may become subject to significant liability. The federal government has levied large civil and criminal fines against companies for improper promotion and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. If we cannot successfully manage the promotion of our product candidates, if approved, we could become subject to significant liability, which would adversely affect our business and financial condition.

Changes to U.S. tax laws and state tax laws, such as those impacting our ability to use our net operating loss carryforwards and certain other tax attributes, may adversely affect our financial condition or results of operations and create the risk that we may need to adjust our accounting for these changes.

We have incurred substantial losses during our history and do not expect to become profitable in the near future, and we may never achieve profitability. Unused federal net operating losses, or NOLs, for taxable years beginning before January 1, 2018 may be carried forward to offset future taxable income, if any, until such unused NOLs expire. Under current law, federal NOLs incurred in taxable years beginning after December 31, 2017, can be carried forward indefinitely, but the deductibility of such federal NOLs is limited to 80% of taxable income. It is uncertain if and to what extent various states will conform to the federal tax laws.

In addition, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, if a corporation undergoes an ''ownership change,'' generally defined as a greater than 50 percentage point change (by value) in its equity ownership by certain stockholders over a three-year period, the corporation's ability to use its pre-change NOLs and other pre-change tax attributes (such as research tax credits) to offset its post-change income or taxes may be limited. We may have experienced ownership changes in the past and may experience ownership changes in the future as a result of subsequent shifts in our stock ownership (some of which shifts are outside our control). As a result, if we earn net taxable income, our ability to use our pre-change NOLs to offset such taxable income will be subject to limitations. Similar provisions of state tax law may also apply to limit our use of accumulated state tax attributes. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. As a result, even if we attain profitability, we may be unable to use a material portion of our NOLs and other tax attributes, which could adversely affect our future cash flows or results of operations.

The accounting treatment of additional changes in U.S. or state tax law changes is complex, and changes may affect both current and future periods. Consistent with guidance from the SEC, our consolidated financial statements reflect our estimates of the tax effects of the current tax laws and regulation.

Risks Related to Commercialization of Our Product Candidates

We face substantial competition and rapid technological change, which may result in others discovering, developing, or commercializing products before or more successfully than we do.

The development and commercialization of new drug products is highly competitive. We expect to face competition with respect to our product candidates, if approved, and will face competition with respect to any future product candidates that we may seek to develop or commercialize from major pharmaceutical companies, specialty pharmaceutical companies, biotechnology companies, universities and other research institutions, and government agencies worldwide. The ophthalmic therapies market is highly competitive and dynamic. Our success will depend, in part, on our ability to obtain a share of the market for our planned indications.

Other pharmaceutical companies may develop therapies for the same indications that would compete with RYZUMVI or our product candidates, if approved, and that would not infringe the claims of our in-licensed patents, pending patent applications, or other proprietary rights, which could adversely affect our business and results of operations.

Our competitors may develop products that are more effective, safer, more convenient, or less costly than any that we are developing, or that would render our product candidates obsolete or non-competitive. Our competitors may also render our technologies obsolete by advances in existing technological approaches or the development of new or different approaches, potentially eliminating the advantages in our drug discovery process. Our competitors may also obtain marketing approval from the FDA or other regulatory authorities for their products more rapidly than we obtain approval for our products, which could result in our competitors establishing a strong market position before we are able to enter the market. Further information on competition is described in ‘‘Item 1, Business’’ in this Annual Report.

Many of our competitors have significantly greater name recognition, financial resources, and expertise in research and development, manufacturing, nonclinical 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. Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These companies compete with us in recruiting, hiring, and retaining qualified scientific and management personnel, engaging contract service providers, manufacturers and consultants, establishing clinical trial sites, recruiting patients for clinical trials, and entering into strategic transactions, as well as in acquiring technologies complementary to, or necessary for, our programs.

We do not currently have any sales or marketing infrastructure in place and may face difficulties in establishing sales and marketing capabilities or engaging third parties to sell, market and distribute APX3330.

We do not have any sales or marketing infrastructure and have no capabilities in place at the present time for the sale, marketing, or distribution of pharmaceutical products. To achieve commercial success for any approved product for which we retain sales and marketing responsibilities, we must either develop a sales and marketing organization or outsource part or all of these functions to other third parties. The Viatris License Agreement covers the commercialization of RYZUMVI and PS, if approved, but we do not have a similar agreement for APX3330.

There are risks involved with us both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time-consuming, which could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred the costs of the commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our product candidates on our own include:

- the inability to recruit and retain adequate numbers of effective sales and marketing personnel or enter into distribution agreements with third parties;
- the inability of sales personnel to obtain access to physicians or educate an adequate number of physicians as to the benefits of our products;

- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines;
- unforeseen costs and expenses associated with creating an independent sales and marketing organization; and
- the inability to obtain sufficient coverage and reimbursement from third-party payors and governmental agencies.
- If we enter into arrangements with third parties to perform sales, marketing, and distribution services, our product revenues or the profitability of these product revenues to us are likely to be lower than if we were to market and sell a product that we developed ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market any product candidate or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market a drug effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

Our future commercial success depends upon attaining significant market acceptance of RYZUMVI and our product candidates, if approved, among physicians, patients, third-party payors, and others in the medical community.

RYZUMVI and our product candidates, even if they do receive marketing approval, may nonetheless fail to gain sufficient market acceptance by physicians, patients, healthcare payors, or others in the medical community. If RYZUMVI and our product candidates do not achieve an adequate level of acceptance, we may not generate significant product revenues and may not become profitable. The degree of market acceptance for RYZUMVI and our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- efficacy and potential advantages compared to alternative treatments;
- the ability to offer our product for sale at competitive prices;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- any restrictions on the use of our product together with other medications;
- interactions of our product with other medicines patients are taking;
- inability of certain types of patients to take our product;
- demonstrated ability to treat patients and, if required by any applicable regulatory authority in connection with the approval for target indications as compared with other available therapies;
- the relative convenience and ease of administration as compared with other treatments available for approved indications;
- the prevalence and severity of any adverse side effects;
- limitations or warnings contained in the labeling approved by the FDA;
- availability of alternative treatments already approved or expected to be commercially launched in the near future;
- the effectiveness of our sales and marketing strategies;
- our ability to increase awareness through marketing efforts;
- guidelines and recommendations of organizations involved in research, treatment and prevention of various diseases that may advocate for alternative therapies;
- our ability to obtain sufficient third-party coverage and adequate reimbursement;
- the willingness of patients to pay out-of-pocket in the absence of third-party coverage; and
- physicians or patients may be reluctant to switch from existing therapies even if potentially more effective, safe or convenient.

We have not yet sold any of our products. We cannot assure investors that there is a sufficient market demand for our products. Achieving market acceptance for our products will require substantial marketing efforts and

expenditure of funds to create awareness and demand by participants in the industry. We have not conducted any independent market research to determine the extent of any demand that exists for the products to be provided by us and there is no guarantee that a sufficient interest in the market will exist for the products and services being produced by, or for, us. Any lack of sufficient demand for the products contemplated to be provided by us will have a material adverse effect on us.

If the FDA or a comparable foreign regulatory authority approves generic versions of RYZUMVI or our product candidates that receive marketing approval, or if such authorities do not grant our product candidates appropriate periods of exclusivity before approving generic versions of our products, the sales of our products could be adversely affected.

Once an NDA is approved, the product covered thereby becomes a ''reference listed drug'' in the FDA's publication, ''Approved Drug Products with Therapeutic Equivalence Evaluations.'' Manufacturers may seek approval of generic versions of reference listed drugs through submission of abbreviated new drug applications (''ANDAs'') in the United States. In support of an ANDA, a generic manufacturer need not conduct clinical studies. Rather, the applicant generally must show that its product has the same active ingredient(s), dosage form, strength, route of administration, and conditions of use or labeling as the reference listed drug (''RLD'') and that the generic version is bioequivalent to the RLD, meaning it is absorbed in the body at the same rate and to the same extent. Generic products may be significantly less costly to bring to market than the RLD, and companies that produce generic products are generally able to offer them at lower prices. Thus, following the introduction of a generic drug, a significant percentage of the sales of any branded product or RLD may be lost to the generic product.

The FDC Act provides a period of five years of non-patent exclusivity for a new drug containing a new chemical entity (''NCE''). Specifically, in cases where such exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification that a patent covering the reference listed drug is either invalid or will not be infringed by the generic product, in which case the applicant may submit its application four years after approval of the RLD. It is unclear whether the FDA will treat the active ingredients in its product candidates as NCEs and, therefore, afford them five years of NCE exclusivity if they are approved. If any product we develop does not receive five years of NCE exclusivity, we may nonetheless be eligible for three years of exclusivity. Competition that our product candidates would face from generic versions could materially and adversely impact our future revenue, profitability, and cash flows and substantially limit our ability to obtain a return on the investments we have made in any such product candidate.

Even if we (or our partners) are able to commercialize RYZUMVI and our product candidates, our profitability will likely depend in significant part on third-party reimbursement practices, which, if unfavorable, would harm our business.

Our (or our partners) ability to commercialize RYZUMVI and our product candidates successfully will depend in part on the extent to which coverage and adequate reimbursement will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for certain medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that coverage will be available for any product candidate that we commercialize and, if coverage is available, whether the level of reimbursement will be adequate. Assuming we obtain coverage for our product candidates, if approved, by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. Patients who are prescribed medications for the treatment of their conditions, and their prescribing physicians, generally rely on third-party payors to reimburse all or some of the costs associated with their prescription drugs. Patients are unlikely to use a product candidate, if approved, unless coverage is provided and reimbursement is adequate to cover all or a significant portion of the cost of its products. Therefore, coverage and adequate reimbursement are critical to new product acceptance. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval. Furthermore, drug pricing and access policies in the United States and internationally may change and negatively impact our product candidates' commercial viability. Proposed policy changes, including the potential for Medicare to negotiate with drug manufacturers, may limit our ability to competitively price our product candidates, if approved. There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the

purposes for which a product candidate is approved by the FDA or similar regulatory authorities outside the United States. Moreover, eligibility for reimbursement does not imply that any product will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale, and distribution. Interim reimbursement levels for a new product, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the product and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost medicines, and may be incorporated into existing payments for other services. Net prices for products may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of medicines from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. However, there is no uniform policy requirement for coverage and reimbursement for drug products among third-party payors in the United States. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. As a result, the coverage determination process is often time-consuming and costly, and it will require us to provide scientific and clinical support for the use of our products to each payor separately. There is no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Any inability to promptly obtain coverage and profitable payment rates from government-funded or private payors for any approved products that we develop could have an adverse effect on our operating results, our ability to raise capital needed to commercialize products, and our overall financial condition.

Product liability lawsuits against us, or our suppliers and manufacturers, could cause us to incur substantial liabilities and could limit commercialization of any product candidate that we may develop.

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any products that we may develop. Product liability claims might be brought against us by patients, healthcare providers, or others selling or otherwise coming into contact with our product candidates during product testing, manufacturing, marketing, or sale. For example, we may be sued under allegations that a product candidate caused injury or that the product was otherwise unsuitable. Any such product liability claims may include allegations of manufacturing or design defects, failure to warn of dangers inherent in the product, such as interactions with alcohol or other drugs, negligence, or breach of warranty. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against claims that our product candidate caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidate that we are developing;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- increased FDA warnings on product labels;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- distraction of management's attention from our primary business;
- loss of revenue;
- the inability to commercialize any product candidate that we may develop;
- the initiation of investigations by regulators; and
- the inability to take advantage of limitations on product liability lawsuits that apply to generic drug products, which could increase our exposure to liability for products deemed to be dangerous or defective.

Our product liability and/or clinical trial insurance coverage may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage as we expand clinical trials and if we successfully commercialize our product candidates. Insurance coverage is increasingly expensive, and we may not be able to obtain product liability insurance on commercially reasonable terms or for a sufficient amount to satisfy liabilities that may arise.

Similarly, we may be a party to, or may be otherwise responsible for, pending or threatened lawsuits or other claims related to products purchased from our manufacturers and suppliers. Although we intend to require our providers to have product liability insurance, the ability to obtain such coverage and the sufficiency thereof is uncertain. Such cases and claims may raise difficult and complex factual and legal issues and may be subject to many uncertainties and complexities, including, but not limited to, the facts and circumstances of each particular case or claim, the jurisdiction in which each suit is brought, and differences in applicable law. Such litigation could result in additional expense and exposure in excess of our anticipated reserves, especially if such matters are not covered by insurance. Upon resolution of any pending legal matters or other claims, we may incur charges in excess of established reserves. Product liability lawsuits and claims, safety alerts or product recalls in the future, regardless of their ultimate outcome, could have a material adverse effect on the business and reputation and on our ability to attract and retain customers and strategic partners. The business, profitability and growth prospects could suffer if we face such negative publicity.

If we or our third-party manufacturers fail to comply with environmental or health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have an adverse effect on the success of our business.

Our research and development activities involve the controlled use of potentially hazardous substances, including chemical and biological materials, by ourselves and our third-party manufacturers. Our manufacturers are subject to federal, state, and local laws and regulations in the United States and abroad governing laboratory procedures and the use, manufacture, storage, handling, and disposal of medical and hazardous materials. Although we believe that our manufacturers' procedures for using, handling, storing, and disposing of these materials comply with legally prescribed standards, we cannot eliminate the risk of contamination or injury resulting from medical or hazardous materials. As a result of any such contamination or injury, we may incur liability, or federal, state, city, or local authorities may curtail our use of these materials and interrupt our business operations. In the event of an accident, we could be held liable for damages or fined, and such liability or fines could exceed our resources. We do not have insurance for liabilities arising from medical or hazardous materials. Although we maintain workers' compensation insurance for costs and expenses that we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. Compliance with applicable environmental and health and safety laws and regulations is expensive, and current or future environmental regulations may impair our research, development, and production efforts, which could harm our business, prospects, financial condition, or results of operations.

Risks Related to Our Reliance on Third Parties

We rely on third parties to conduct our nonclinical and clinical trials and perform other tasks for us. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or comply with regulatory requirements, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be harmed.

We rely on third-party CROs and other third parties to assist in managing, monitoring, and otherwise carrying out our nonclinical studies and clinical trials. We expect to continue to rely on third parties, such as CROs, clinical data management organizations, medical institutions, and clinical investigators, to conduct our nonclinical studies and clinical trials in the future. We compete with many other companies for the resources of these third parties.

As a result, we will have limited control over the conduct, timing, and completion of these nonclinical studies and clinical trials and the management of data developed through the nonclinical studies and clinical trials. We have experienced in the past, and may experience in the future, schedule disruptions due to events affecting the performance of third parties on which we rely. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Additionally, other unexpected natural events and disruptions in the supply chain and operations may affect the ability of third parties to fulfill their obligations to us. Outside parties may have staffing difficulties;

- fail to comply with contractual obligations;
- experience regulatory compliance issues;
- undergo changes in ownership or management;
- undergo changes in priorities or become financially distressed; or
- form relationships with other entities, some of which may be our competitors.

These factors may adversely affect the willingness or ability of third parties to conduct our clinical trials and may subject us to unexpected cost increases that are beyond our control.

While our reliance on these third parties for research and development activities will reduce our control over these activities, it will not relieve us of our responsibilities and requirements. For example, the FDA requires us to comply with standards, commonly referred to as good clinical practices (''GCP''), for conducting recording, and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity, and confidentiality of clinical trial participants are protected.

Problems with the timeliness or quality of the work of any CRO may lead us to seek to terminate our relationship with any such CRO and use an alternative service provider. Making this change may be costly or delay our clinical trials, and contractual restrictions may make such a change difficult or impossible. If we must replace any CRO that is conducting our clinical trials, our clinical trials may have to be suspended until we find another CRO that offers comparable services. The time that it would take us to find alternative organizations may cause a delay in the commercialization of our product candidates, or it may cause us to incur significant expenses to replicate any lost data. Although we do not believe that any CRO on which we would rely would offer services that are not available elsewhere, we may be difficult to find a replacement organization that can conduct our clinical trials in an acceptable manner and at an acceptable cost. Any delay in or inability to complete our clinical trials could significantly compromise our ability to secure regulatory approval for our product candidates and preclude our ability to commercialize our product candidates, thereby limiting or preventing our ability to generate sales revenue.

Further, requirements related to clinical trials continue to evolve, which may require additional oversight, greater costs, and/or delay. In 2023, FDA published guidance documents related to informed consent and GCPs that may present additional requirements to CROs.

In August 2023, FDA published a guidance document, Informed Consent, Guidance for IRBs, Clinical Investigators, and Sponsors, which supersedes past guidance and finalizes draft guidance on informed consent. Further, in December 2023, FDA published a final rule, Institutional Review Board Waiver or Alteration of Informed Consent for Minimal Risk Clinical Investigations, which allows exceptions from informed consent requirements when a clinical investigation poses no more than minimal risk to the human subject and includes appropriate safeguards to protect the rights, safety, and welfare of human subjects. These guidance documents present evolving requirements for informed consent which may affect recruitment and retention of patients in clinical trials. Effects on recruitment and retention of patients may hinder or delay a clinical trial, which may increase costs and delay clinical programs.

Additionally, in June 2023, FDA published a draft guidance, E6(R3) Good Clinical Practice (GCP), which seeks to unify standards for clinical trial data for ICH member countries and regions. Changes to data requirements may cause FDA or comparable foreign regulatory authorities to disagree with data from preclinical studies or clinical trials, and may require further studies.

We rely completely on third parties to supply and manufacture bulk drug substances and to formulate and package nonclinical and clinical drug supplies of our product candidates as well as to conduct analytical testing of drug substances and products in the manufacturing processes and we intend to rely on third parties to produce and test commercial supplies of our current and any future product candidates.

We do not currently have, nor do we plan to acquire, the infrastructure or capability to internally manufacture our clinical drug supply of product candidates for use in the conduct of our nonclinical studies and clinical trials. We lack the internal resources and the capability to manufacture any product candidates on a clinical or commercial scale. The process of manufacturing drug products is complex, highly regulated, and subject to several risks. For example, the facilities used by our contract manufacturers to manufacture and conduct analytical testing of the active pharmaceutical ingredient (or drug substance) and final drug product for product candidates must be inspected by the FDA and other comparable foreign regulatory agencies in connection with our submission of an NDA or relevant foreign regulatory submission to the applicable regulatory agency. In addition, the manufacturing of drug substance or product is susceptible to product loss due to contamination, equipment failure, improper installation or operation of equipment, or vendor or operator error. Moreover, the manufacturing facilities in which product candidates are made could be adversely affected by equipment failures, labor shortages, natural disasters, power failures, or other factors. Manufacturing timelines may be negatively affected by material shortages, construction delays and supply chain challenges due to, among other factors, global supply chain shortages.

Further, requirements related to the manufacturing of ophthalmic products may evolve, which may require modifications to our current manufacturing processes. In December 2023, FDA published a revised draft guidance, Quality Considerations for Topical Ophthalmic Drug Products, which focuses on quality considerations for ophthalmic drug products intended for topical delivery in and around the eye. Updated quality considerations may cause delay to adapt to new requirements and may also increase costs associated with manufacturing.

We do not control the manufacturing and testing processes of our contract manufacturers and analytical labs, and are completely dependent on them to comply with current good manufacturing practices (''cGMP'') for manufacture and good lab practices (''GLP'') of both active drug substances and finished drug products. If our contract manufacturers and analytical labs cannot successfully manufacture and test materials that conform to our specifications and the strict regulatory requirements of the FDA or applicable foreign regulatory agencies, we will not be able to secure and/or maintain regulatory approval for our products. In addition, we have no control over our contract manufacturers' and analytical labs' ability to maintain adequate quality control, quality assurance, and qualified personnel. Failure to satisfy the regulatory requirements for the production and testing of those materials and products may affect the regulatory clearance of our contract manufacturers' and analytical labs' facilities generally. If the FDA or a comparable foreign regulatory agency does not approve these facilities for the manufacture and testing of product candidates, or if it withdraws its approval in the future, we may need to find alternative manufacturing and testing facilities, which would adversely impact our ability to develop, obtain regulatory approval for, or market product candidates. Furthermore, all of our contract manufacturers and analytical labs are engaged with other companies to supply and/or manufacture and/or test materials or products for such companies, which exposes our manufacturers to regulatory and sourcing risks for the production of such materials and products. To the extent practicable, we have attempted to identify more than one supplier. However, some raw materials are available only from a single source or only one supplier has been identified, even in instances where multiple sources exist.

We have relied and will rely upon third-party manufacturers and testing labs in the United States and overseas for the manufacture and testing of APX3330 and PS for nonclinical and clinical testing purposes and intend to continue to do so in the future for APX3330, PS, and any other product candidates, including for commercial purposes. If our third-party manufacturers and analytical labs are unable to supply or test drug substance and/or drug product on a commercial basis, we may not be able to successfully produce and market product candidates, if approved, or we could be delayed in doing so. For instance, we presently rely on one supplier in Italy for the drug substance for PS, and one manufacturer in India for APX3330 drug substance. If there is any delay or problem with the manufacture of these drug substances or if there is a delay in producing finished drug product from these drug substances, the development and PS, the possible approval of our product candidates and potential commercial launch may be delayed or otherwise adversely affected. We will rely on comparison of product specifications (identity, strength, quality, and potency) to demonstrate equivalence of the current drug substance and/or drug product to the drug substance and/or drug product used in previously completed nonclinical and clinical testing. If we are unable to demonstrate such equivalence, we may be required to conduct additional nonclinical and/or clinical testing of our product candidates. Due to these and other potential problems, we are exploring the possibility of establishing additional sources of supply, with U.S. manufacturers, for the active pharmaceutical ingredients of both APX3330 and PS. Establishing these additional sources, including qualifying their manufacturing processes and demonstrating the equivalence of their products, may be costly, time-consuming, and difficult to effectuate, and may delay our research and development activities. Even if we could transfer manufacturing to a different third party, any shift would likely be expensive and time consuming, particularly since the new facility would need to comply with the necessary regulatory requirements and we would need FDA approval before using or selling any products manufactured at that facility. If we must replace any manufacturer, our research and development activities may have to be suspended until we find another manufacturer that offers comparable services. The time that it takes us to find alternative organizations may cause a delay in the development and commercialization of product candidates.

We have entered and may enter into licensing arrangements for the development or sale of product candidates (such as the Viatris License Agreement) and may form or seek additional strategic alliances or enter into licensing arrangements in the future. If we are unsuccessful in forming or maintaining these alliances on favorable terms, our business could be harmed.

We have entered into and may form or seek additional strategic alliances, create joint ventures or collaborations or enter into additional licensing arrangements with third parties that we believe will complement or augment our development and commercialization efforts with respect to product candidates (such as the Viatris License Agreement). Any of these relationships may require us to incur non-recurring and other charges, increase our near- and long-term expenditures, or issue securities that dilute our existing stockholders, which may disrupt our

management and business. Our likely collaborators include large, mid-size, regional, or national pharmaceutical companies and biotechnology companies. If we enter into any such arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of product candidates. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. We cannot be certain that, following a strategic transaction or license, we will achieve the revenue or specific net income that justifies such transaction. Collaborations involving product candidates pose the following risks to us:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding, or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials, or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidate if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more attractive than ours;
- a collaborator with marketing and distribution rights to one or more product candidates may not commit sufficient resources to the marketing or distribution of any such product candidate;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- disputes may arise between us and collaborators that result in the delay or termination of research, development, or commercialization of our product candidates, or in litigation or arbitration that diverts management attention and resources;
- we may lose certain valuable rights under circumstances identified in our collaborations, including if we undergo a change of control;
- collaborations may be terminated and such terminations may create a need for additional capital to pursue further development or commercialization of the applicable product candidates;
- collaborators may learn about our discoveries and use this knowledge to compete with us in the future;
- the results of collaborators' nonclinical or clinical studies could harm or impair other development programs;
- there may be conflicts between different collaborators that could negatively affect those collaborations and potentially others;
- the number and nature of our collaborations could adversely affect our attractiveness to potential future collaborators or acquirers;
- collaboration agreements may not lead to development or commercialization of our product candidate in the most efficient manner or at all. If a present or future collaborator of us were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program under such collaboration could be delayed, diminished, or terminated; and
- collaborators may be unable to obtain the necessary marketing approvals.

If future collaboration partners fail to develop or effectively commercialize product candidates for any of these reasons, such product candidates may not be approved for sale and our sales of such product candidates, if approved, may be limited, which would have an adverse effect on our operating results and financial condition.

If we are not able to establish new collaborations for APX3330 on commercially reasonable terms, we may have to alter our development, manufacturing, and commercialization plans.

We face significant competition in attracting collaborators for development, manufacturing or commercialization plans. We already have a collaboration with Viatris for the development and commercialization of RYZUMVI and PS. Whether we reach a definitive agreement for collaboration for APX3330 will depend, among other things, upon our assessment of the proposed collaborator's resources, expertise, and evaluation of a number of factors related to the associated product candidate, as well as the terms and conditions of the proposed collaboration. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which may exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available for collaborations and whether such a collaboration could be more attractive than one with us. We may not be able to enter into these agreements on commercially reasonable terms, or at all.

Much of the potential revenue from future commercial collaborations may consist of contingent payments, such as payments for achieving regulatory milestones or royalties payable on sales of our product candidate, if approved. The milestone and royalty revenue that we may receive under these collaborations would depend upon our collaborators' ability to successfully develop, introduce, market and sell our product candidate, if approved. In addition, collaborators may decide to enter into arrangements with third parties to commercialize products developed under collaborations related to our product candidates, which could reduce the milestone and royalty revenue received, if any.

We may also be restricted under existing collaboration agreements from entering into future agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate collaborations on a timely basis and on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay our development program or that of one or more of our other development programs, delay our potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidate or bring us to market and generate product revenue.

If we engage in acquisitions, in-licensing or strategic partnerships, this may increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities and subject us to other risks.

We may engage in various acquisitions and strategic partnerships, including licensing or acquiring complementary products, intellectual property rights, technologies, or businesses. Any acquisition or strategic partnership may entail numerous risks, including:

- increased operating expenses and cash requirements;
- the assumption of indebtedness or contingent liabilities;
- the issuance of our equity securities which would result in dilution to our stockholders;
- assimilation of operations, intellectual property, products and product candidates of an acquired company, including difficulties associated with integrating new personnel;
- the diversion of management's attention from our existing product candidates and initiatives in pursuing such an acquisition or strategic partnership;

- retention of key employees, the loss of key personnel, and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing products or product candidates and regulatory approvals; and
- our inability to generate revenue from acquired intellectual property, technology and/or products sufficient to meet our objectives or even to offset the associated transaction and maintenance costs.

In addition, if we undertake such a transaction, we may incur large one-time expenses and acquire intangible assets that could result in significant future amortization expense.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain sufficient patent protection for our product candidates, our competitors could develop and commercialize products or technology similar or identical to those of us, which would adversely affect our ability to successfully commercialize any product candidates we may develop, our business, results of operations, financial condition and prospects.

We and our licensors have sought to protect our proprietary position by filing patent applications in the U.S. and abroad related to our novel technologies and product candidates.

Our pending and future patent applications may not result in patents being issued which protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. In particular, during prosecution of any patent application, the issuance of any patents based on the application may depend upon our ability to generate additional pre-clinical or clinical data that support the patentability of our proposed claims. We may not be able to generate sufficient additional data on a timely basis, or at all.

The patent prosecution process is expensive and time-consuming, and we and our future licensors, licensees, or collaboration partners may not be able to prepare, file, and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we or any future licensors, licensees, or collaboration partners may fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. We and our licensors' patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent is issued from such applications, and then only to the extent the issued claims cover the technology.

We cannot assure you that any of our patents have matured, or that any of our pending patent applications will mature, into issued patents that will include, claims with a scope sufficient to protect our product candidates. Others have developed technologies that may be related or competitive to our approach, and may have filed or may file patent applications and may have received or may receive patents that overlap or conflict with our patent applications, for example by claiming the same compounds, methods or formulations or by claiming subject matter that could dominate the patents that we owns or in-licenses. The patent positions of biotechnology and pharmaceutical companies, including our patent position, involve complex legal and factual questions, and, therefore, the issuance, scope, validity, and enforceability of any patent claims that we may obtain cannot be predicted with certainty. Patents, if issued, may be challenged, deemed unenforceable, invalidated, or circumvented. U.S. patents and patent applications may also be subject to interference proceedings, *ex parte* reexamination, or *inter partes* review proceedings, supplemental examination and challenges in district court. Patents may be subjected to opposition, post-grant review, or comparable proceedings in various national and regional patent offices. These proceedings could result in either loss of the patent or denial of the patent application or loss or reduction in the scope of one or more of the claims of the patent or patent application. In addition, such interference, re-examination, opposition, post-grant review, *inter partes* review, supplemental examination, or revocation proceedings may be costly or time-consuming. Thus, any patents that we may own or exclusively license may not provide any protection against competitors. Furthermore, an adverse decision in an interference proceeding can result in a third party receiving the patent right sought by us, which in turn could affect our ability to develop, market or otherwise commercialize our product candidates.

Furthermore, the issuance of a patent, while presumed valid, is not conclusive as to its validity or its enforceability and it may not provide us with adequate proprietary protection or competitive advantages against competitors with similar products. Competitors may also be able to design around our patents. Other parties may develop and obtain patent protection for more effective technologies, designs, or methods. We may not be able to

prevent the unauthorized disclosure or use of any technical knowledge or trade secrets by consultants, vendors, former employees, or current employees. The laws of some foreign countries do not protect proprietary rights to the same extent as do the laws of the United States, and we may encounter significant problems in protecting our proprietary rights in these countries. If these developments were to occur, they could have a material adverse effect on our sales.

Our ability to enforce our patent rights depends on our ability to detect infringement. It is difficult to detect infringers who do not advertise the components that are used in their products. Moreover, it may be difficult or impossible to obtain evidence of infringement in a competitor's or potential competitor's product. Any litigation to enforce or defend our patent rights, if any, even if we were to prevail, could be costly and time-consuming and would divert the attention of management and key personnel from our business operations. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded if we were to prevail may not be commercially meaningful.

In addition, proceedings to enforce or defend our patents could put our patents at risk of being invalidated, held unenforceable, or interpreted narrowly. Such proceedings could also provoke third parties to assert claims against us, including that some or all of the claims in one or more of our patents are invalid or otherwise unenforceable. If, in any proceeding, a court invalidated or found unenforceable our patents covering our product candidates, our financial position and results of operations would be adversely impacted. In addition, if a court found that valid, enforceable patents held by third parties covered our product candidates, our financial position and results of operations would also be adversely impacted.

The degree of future protection for our proprietary rights is uncertain, and we cannot ensure that:

- any of our patents, or any of our pending patent applications, if issued, will include claims having a scope sufficient to protect our product candidates;
- any of our pending patent applications will result in issued patents;
- we will be able to successfully commercialize our product candidates, if approved, before our relevant patents expire;
- we were the first to make the inventions covered by each of our patents and pending patent applications;
- we were the first to file patent applications for these inventions;
- others will not develop similar or alternative technologies that do not infringe our patents;
- any of our patents will be valid and enforceable;
- any patents issued to us will provide a basis for an exclusive market for our commercially viable products, will provide us with any competitive advantages or will not be challenged by third parties;
- we will develop additional proprietary technologies or product candidates that are separately patentable; or
- our commercial activities or products will not infringe upon the patents of others.

Patents have a limited lifespan. The natural expiration of a patent is generally 20 years after its effective filing date. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. Given the extensive period of time between patent filing and regulatory approval for a product candidate, the time during which we can market a product candidate under patent protection is listed, and our patent may expire before we obtain such approval. Without patent protection for our product candidates, we may be vulnerable to competition from generic versions of our product candidates, which may affect the profitability of our product candidates.

Furthermore, obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment, and other requirements imposed by governmental agencies, and our patent protection could be reduced or eliminated for noncompliance with these requirements. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment or other provisions during the patent application process. In addition, periodic maintenance and annuity fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in

accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market, which would have an adverse effect on our business.

It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Maintaining patents in the U.S. is an expensive process and it is even more expensive to maintain patents and patent applications in foreign countries. As a result, it is possible that we and our licensors will fail to maintain such patents thereby reducing the rights of our portfolio. The patent position of pharmaceutical, biotechnology, and medical device companies generally is highly uncertain, involves complex legal and factual questions, and has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability, and commercial value of our and our licensors' patent rights are highly uncertain. Our and our licensors' pending and future patent applications may not result in patents being issued which protect our technology or products, or which effectively prevent others from commercializing competitive technologies and products.

If we do not obtain protection under the Hatch-Waxman Act and similar foreign legislation by extending the patent terms and obtaining data exclusivity for our product candidate, our business may be materially harmed.

Depending upon the timing, duration of regulatory review, and date of FDA marketing approval of our or other product candidates, if any, one of such U.S. patents may be eligible for patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Act. The Hatch-Waxman Act provides for a patent restoration term, or patent term extension, of up to five years as compensation for the time the product is under FDA regulatory review. The duration of patent term extension is calculated based on the time spent in the regulatory review process. In the future, we may plan to seek patent term extension for one or more of our patents related to our RYZUMVI or other product candidates. However, we may not be granted an extension because of, for example, failing to apply within the applicable deadline, expiration of relevant patents prior to obtaining approval, or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be shorter or less than what we request. If we are unable to obtain patent term extension or the term of any such extension is less than we request, our revenue could be reduced, possibly materially.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

In 2011, the United States enacted wide-ranging patent reform legislation with the America Invents Act (''AIA''). An important change introduced by the AIA is that, as of March 16, 2013, the United States transitioned to a ''first-to-file'' system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. A third party that files a patent application in the USPTO after that date but before we could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by the third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application, but circumstances could prevent us from promptly filing patent applications on our inventions. Among some of the other changes introduced by the AIA are changes that limit where a patentee may file a patent infringement suit and providing opportunities for third parties to challenge any issued patent in the USPTO. This applies to all of our U.S. patents, even those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. The AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. Additionally, the U.S. Supreme Court's holdings in several patent cases in recent years, such as Association for Molecular Pathology v. Myriad Genetics, Inc. (Myriad I), Mayo Collaborative Services v. Prometheus Laboratories, Inc., and Alice Corporation Pty. Ltd. v. CLS Bank International, have narrowed the scope of patent protection available in certain circumstances or weakened the rights of patent owners in certain situations. In addition to increasing uncertainty about our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the

federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

We may not be able to protect or practice our intellectual property rights throughout the world.

In jurisdictions where we have not obtained patent protection, competitors may use our intellectual property to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but where it is more difficult to enforce a patent as compared to the United States. Competitor products may compete with our product candidates in jurisdictions where we do not have issued or granted patents or where our issued or granted patent claims or other intellectual property rights are not sufficient to prevent competitor activities in these jurisdictions. The legal systems of certain countries, particularly certain developing countries, make it difficult to enforce patents and such countries may not recognize other types of intellectual property protection, particularly that relating to pharmaceuticals. This could make it difficult for us to prevent the infringement of our patents or marketing of competing products in violation of our proprietary rights generally in certain jurisdictions. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business. The laws of some jurisdictions do not protect intellectual property rights to the same extent as the laws in the United States, and many companies have encountered significant difficulties in protecting and defending such rights in such jurisdictions. If we, or any future licensor, encounters difficulties in protecting, or is otherwise precluded from effectively protecting, the intellectual property rights important for our business in such jurisdictions, the value of these rights may be diminished and we may face additional competition from others in those jurisdictions. Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we, or any licensor, is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position in the relevant jurisdiction may be impaired and our business and results of operations may be adversely affected.

We may become involved in lawsuits to protect or enforce our patents and other intellectual property rights, which could be expensive, time consuming, and unsuccessful.

Competitors may infringe on our patents, the patents of our licensing partners, or other intellectual property rights. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming. In addition, in an infringement proceeding, a court may decide that our patent is invalid or unenforceable, or may refuse to stop the other party from using the technology on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded.

Litigation proceedings may fail and, even if successful, may be costly and a distraction to our management and other employees. We may not be able to prevent, alone or with our collaborators, misappropriation of our proprietary rights, particularly in countries where the laws may not protect those rights as fully as in the United States.

In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, we could have a substantial adverse effect on the price of our common stock.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have an adverse effect on the success of our business.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights and intellectual property of third parties. The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. We may in the future become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our

medicines and technology, including interference or derivation proceedings, post-grant reviews, *inter partes* reviews, or other procedures before the USPTO or other similar procedures in foreign jurisdictions. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our medicines and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, we could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us. We could be forced, including by court order, to cease developing and commercializing the infringing technology or medicine. In addition, we could be held liable for substantial monetary damages, potentially including treble damages and attorneys' fees, if found to have willfully infringed. A finding of infringement could prevent us from commercializing a product candidate or force us to cease some of our business operations, which could harm our business. Alternatively, we may need to redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business. The cost to us of any litigation or other proceeding relating to patent or other proprietary rights, even if resolved in our favor, could be substantial and may result in substantial costs and distraction to our management and other employees. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could delay our research and development efforts and limit our ability to continue our operations.

We may be subject to damages resulting from claims that our employees or we have wrongfully misappropriated their intellectual property of their former employers.

Our employees and consultants have been previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we are not aware of any claims currently pending against us, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information or intellectual property of the former employers of our employees. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management. If we fail in defending such claims, in addition to paying money claims, we may lose valuable intellectual property rights or personnel. A loss of key personnel or their work product could detract from our ability to develop or commercialize our product candidates.

If we are not able to adequately prevent disclosure of trade secrets and other proprietary information, the value of any product we may pursue could be significantly diminished.

While it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own.

Our and their assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property. We may rely upon trade secrets, know-how, and continuing technological innovation to develop and maintain our competitive position. However, trade secrets are difficult to protect. We rely in part on confidentiality agreements with our employees, consultants, outside scientific collaborators, sponsored researchers, contract manufacturers, vendors, and other advisors to protect our trade secrets and other proprietary information. These agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. In addition, we cannot guarantee that we have executed these agreements with each party that may have or has had access to trade secrets. If a party breaches an agreement and discloses our proprietary information, including our trade secrets, we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive, and time consuming, and the outcome is unpredictable. In addition, some courts in and outside of the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they disclose such trade secrets, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to, or independently developed by, a competitor or other third party, our competitive position would be harmed.

Obtaining and maintaining our trademark protection depends on approval from the USPTO and other foreign government agencies, and third parties may challenge, infringe, or otherwise weaken our trademark rights.

We have obtained registration of the ''RYZUMVI'' trademark in the United States. We have not yet registered trademarks for any other product candidates in any jurisdiction (other than ''Nyxol'', which we are no longer using). If we do not secure and maintain registrations for our trademarks, we may encounter more difficulty in enforcing them against third parties than we otherwise would, which could affect our business. When we file trademark applications for a product candidate, those applications may not be allowed for registration, and registered trademarks may not be obtained, maintained, or enforced. During trademark registration proceedings in the United States and foreign jurisdictions, we may receive rejections. We are given an opportunity to respond to those rejections, but may not be able to overcome such rejections. In addition, the SPTO and comparable agencies in many foreign jurisdictions allow third parties opportunities to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks and our trademarks may not survive such proceedings. In addition, any proprietary name we propose to use with a future product candidate in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed drug names, including an evaluation of potential for confusion with other drug names. If the FDA objects to any proposed proprietary drug name for any product candidate, we may be required to expend significant additional resources in an effort to identify a suitable substitute proprietary drug name that would qualify under applicable trademark laws, not infringe the existing rights of third parties, and be acceptable to the FDA. If we register any of our trademarks, our trademarks or trade names may be challenged, infringed, circumvented, declared generic, or determined to infringe on other marks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively, and our business may be adversely affected.

We may enter into collaborations, in-licensing arrangements, joint ventures, strategic alliances or partnerships with third parties that may not result in the development of commercially viable products or the generation of significant future revenues.

We may enter into certain license or other collaboration agreements in the future. Such agreements may impose various diligence, milestone payment, royalty, insurance or other obligations on us. If we fail to comply with such obligations, our licensor or collaboration partners may have the right to terminate the relevant agreement, in which event we would not be able to develop or market the products covered by such licensed intellectual property. Moreover, disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our product candidates, technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under our collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property; and
- the priority of invention of patented technology.

In addition, the agreements under which intellectual property or technology is licensed from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates, which could have a material

adverse effect on our business, financial conditions, results of operations, and prospects. In addition, we cannot be certain that the preparation, filing, prosecution and maintenance activities by any future licensors have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents and other intellectual property rights.

We depend on intellectual property sublicensed from third parties (such as Apexian Pharmaceuticals, Inc. for product candidates ("Apexian") for our APX3330 product candidate under development) and our additional pipeline candidates, and the termination of, or reduction or loss of rights under, this sublicense would harm our business.

We entered into a sublicense agreement with Apexian (as amended, the ''Apexian Sublicense Agreement'') to in-license patents and other intellectual property relating to the APX3330 product candidate and second-generation product candidates owned by Apexian, and intellectual property that Apexian in-licensed from Eisai Co., Ltd. (''Eisai'') including certain study reports, manufacturing and analytical records, data, know-how, technical and other proprietary information relating to APX3330. We may, in the future, enter into additional sublicense agreements of the same or a similar nature for APX3330 or other product candidates. The rights granted under sublicense agreements, such as the Apexian Sublicense Agreement, are and may be subject to various milestone payment, royalty, insurance or other obligations on us, and may be revocable under certain circumstances including if we cease to do business, fail to make the payments due thereunder, commit a material breach of the agreement that is not cured within a certain time period after receiving written notice or fail to meet certain specified development and commercial timelines. Termination of sublicense agreements, such as the Apexian Sublicense Agreement, may result in us having to negotiate a new or reinstated agreement, which may not be available to us on equally favorable terms, or at all, which may mean we are unable to develop or commercialize APX3330 and second-generation assets. We do not have total control over the preparation, filing, prosecution and maintenance of patents and patent applications covering the technology that we license under sublicense agreements, including the Apexian Sublicense Agreement.

Under the Sublicense Agreement, Indiana University Research and Technology Corp. (''IURTC''), the owner of the patents licensed to Apexian and sublicensed to us, maintains the right to control all prosecution and maintenance of such patents. Therefore, we cannot always be certain that these patents and patent applications will be prepared, filed, prosecuted and maintained in a manner consistent with the best interests of our business. Although we have a right to have our comments considered in connection with, and have agreed to bear the costs of, the prosecution and maintenance of the licensed patents, if IURTC fails to prosecute and maintain such patents, or loses rights to those patents or patent applications as a result of its control of the prosecution activities, the rights we have licensed may be reduced or eliminated, and our right to develop and commercialize any of our product candidates that are the subject of such licensed rights could be adversely affected. Similar reductions of rights or terminations may occur with regards to future sublicense agreements. Further, if Apexian breaches its license agreement with IURTC and fails to cure such breach within a 60-day cure period, IURTC may terminate such license agreement with Apexian, in which case, our license shall also terminate and we will lose all rights under the license agreement with Apexian.

While the Apexian Sublicense Agreement provides that Apexian must cooperate with us to remedy and cure Apexian's breach of the license agreement with IURTC in order to prevent the termination of such license agreement, we cannot guarantee that such efforts will be successful in preventing the termination of the license agreement between Apexian and IURTC. Similarly, if Apexian breaches its license agreement with Eisai and fails to cure such breach within a 60-day cure period, Eisai may terminate such license agreement with Apexian, in which case, our sublicense rights under such license shall also terminate. While we do not have any material obligations under the license agreement between Eisai and Apexian, Apexian has certain confidentiality and payment obligations that, if not met, could result in breach of the Eisai license agreements.

Under Apexian's license agreement with IURTC, any act or omission by us that would be a breach of the license agreement with IURTC if imputed to Apexian is deemed to be a breach by Apexian of such license agreement and cause for termination, including, in particular, any breach by us of our payment, reporting, audit, and indemnification obligations.

Expansion through obtaining rights to product candidates and approved products through acquisitions may not be successful.

We may acquire the rights to other products, product candidates, or technologies in the future. The future growth of our business may depend in part on our ability to acquire the rights to approved products, additional product candidates, or technologies. However, we may be unable to acquire the rights to any such products, product

candidates, or technologies from third parties. The acquisition of pharmaceutical products is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire products, product candidates, or technologies that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources, and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to acquire the rights to the relevant product, product candidate, or technology on terms that would allow us to make an appropriate return on our investment. Furthermore, we may be unable to identify suitable products, product candidates, or technologies within our area of focus. If we are unable to successfully obtain rights to suitable products, product candidates or technologies, our ability to pursue this element of our strategy could be impaired.

Risks Related to Our Employee Matters and Managing Growth

We are dependent on our key personnel, and if we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.

We are highly dependent on our management, scientific, and medical personnel, including George Magrath, MD, MBA, MS, Chief Executive Officer and Board Director. We have entered into employment agreements with our executive officers, but any employee may terminate his or her employment with us. The loss of the services of any of our executive officers, other key employees or consultants, or other scientific and medical advisors in the foreseeable future might impede the achievement of our research, development, and commercialization objectives. If we fail to retain key personnel and are unable to hire highly qualified replacements, we may not be able to meet key objectives, such as meeting financial goals, and maintaining or expanding our business. We rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. Recruiting and retaining qualified scientific personnel and business and commercial personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific personnel from universities and research institutions. Failure to succeed in clinical trials may also make it more challenging to recruit and retain qualified scientific personnel.

We expect that we will need to develop and expand a number of corporate functions in our company (including sales, marketing, and distribution teams), and, as a result, we may encounter difficulties in managing this development and expansion, which could disrupt our operations.

As of March 1, 2024, we had 17 full-time employees, and we expect to increase our number of employees and the scope of our operations as we further the clinical development of our product candidates. To manage our anticipated development and expansion, we must continue to implement and improve our managerial, operational, and financial systems, expand our facilities, and continue to recruit and train additional qualified personnel. Also, our management may need to divert a disproportionate amount of our attention away from our day-to-day activities and devote a substantial amount of time to managing these development activities. Due to our limited resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. This may result in weaknesses in our infrastructure, and give rise to operational mistakes, loss of business opportunities, loss of employees, or reduced productivity among remaining employees. The physical expansion of our operations may lead to significant costs and may divert financial resources from other projects, such as the development of product candidates. If our management is unable to effectively manage our expected development and expansion, our expenses may increase more than expected, our ability to generate or increase our revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize product candidates, if approved, and compete effectively will depend, in part, on our ability to effectively manage our future development and expansion.

A variety of risks associated with operating internationally for us and our collaborators could adversely affect our business.

In addition to our U.S. operations, we may pursue international operations in the future and would face risks associated with such global operations, including possible unfavorable regulatory, pricing and reimbursement, legal, political, tax, and labor conditions, which could harm our business. We plan to conduct clinical trials outside of the United States. We are subject to numerous risks associated with international business activities, including:

- compliance with differing or unexpected regulatory requirements for our product candidates;
- different medical practices and customs affecting acceptance of our product candidates, if approved, or any other approved product in the marketplace;
- language barriers;
- the interpretation of contractual provisions governed by foreign law in the event of a contract dispute;
- difficulties in staffing and managing foreign operations, and an inability to control commercial or other activities where it is relying on third parties;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- potential liability under the Foreign Corrupt Practice Act of 1977 or comparable foreign regulations;
- production shortages resulting from any events affecting raw material supply or manufacturing capability abroad;
- foreign government taxes, regulations, and permit requirements;
- U.S. and foreign government tariffs, trade restrictions, price and exchange controls, and other regulatory requirements;
- economic weakness, including inflation, natural disasters, war, events of terrorism, or political instability in particular foreign countries;
- fluctuations in currency exchange rates, which could result in increased operating expenses and reduced revenues;
- compliance with tax, employment, immigration, and labor laws, regulations, and restrictions for employees living or traveling abroad;
- changes in diplomatic and trade relationships; and
- challenges in enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States.

If we experience any of these risks, our sales in non-U.S. jurisdictions may be harmed, our results of operations would suffer, and our reputation and business prospects would be negatively impacted.

Our business and operations would suffer in the event of system failures or unplanned events, including cyber incidents, network security breaches, service interruptions, or data corruption.

Despite the implementation of security measures, our internal computer systems and those of our current and future contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war, and telecommunications and electrical failures. In March 2021, we were the victim of a business email compromise. This fraud did not cause any losses to us. If another such event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our product candidates could be delayed. We may be required to expend significant resources, fundamentally change our business activities and practices, or modify our operations, including our clinical trial activities, or information technology in an effort to protect against security breaches and to mitigate, detect and remediate actual or potential vulnerabilities. Furthermore, failure to protect our information technology

infrastructure against cyber incidents, network security breaches, service interruptions, or data corruption could materially disrupt our operations and adversely affect our business, operating results, or the effectiveness of our internal controls over financial reporting. Furthermore, any unplanned event, such as flood, fire, explosion, tornadoes, earthquake, extreme weather condition, medical epidemics, power shortage, telecommunications failure, cybersecurity incidents, network security breaches, service interruptions, or data corruption other natural or manmade accidents or incidents, or pandemics, that result in us being unable to fully utilize the facilities, may have an adverse effect on our ability to operate our business, particularly on a daily basis, and have significant negative consequences on its financial and operating conditions. Loss of access to these facilities may result in increased costs, delays in the development of our product candidates, or interruption of our business operations.

Risks Related to Ownership of Our Common Stock

We currently have a substantial number of shares of common stock subject to potential issuance associated with our Equity Line of Credit arrangement. The issuance or sale of shares under our ELOC arrangement would substantially increase the number of shares outstanding and result in dilution to our security holders. This might substantially decrease the market price of the common stock.

We have a substantial number of shares of our common stock that may be issued in the future.

- In connection with our equity line of credit, or ELOC, arrangement, we issued Lincoln Park Capital Fund, LLC 246,792 shares of our common stock.
- Under our ELOC arrangement, we can sell up to $50,000,000 worth of our Common Stock over the thirty-six month term of the ELOC arrangement, to Lincoln Park Capital, LLC, beginning only after certain conditions set forth in the Purchase Agreement have been satisfied.

To the extent that shares of common stock are issued or sold under our ELOC arrangement, dilution to our security holders may occur. The issuance of these additional securities may have an adverse effect on the market price of our securities.

We do not anticipate paying any cash dividends in the foreseeable future.

The current expectation is that we will retain our future earnings, if any, to fund the development and growth of our business. As a result, capital appreciation, if any, of our common stock will be investors' sole source of gain, if any, for the foreseeable future.

If we fail to comply with the continued listing standards of the Nasdaq Capital Market, our common stock could be delisted. If it is delisted, the liquidity of our common stock would be impacted.

The continued listing of our common stock on Nasdaq is contingent on our continued compliance with a number of listing standards. There is no assurance that we will remain in compliance with these standards. Delisting from Nasdaq would adversely affect our ability to raise additional financing through the public or private sale of equity securities, significantly affect the ability of investors to trade our securities and negatively affect the value and liquidity of our common stock. Delisting also could limit our strategic alternatives and attractiveness to potential counterparties and have other negative results, including the potential loss of employee confidence, the loss of institutional investors or interest in business development opportunities. In addition, if our common stock is delisted from the Nasdaq Capital Market and the trading price remains below $5.00 per share, trading in our common stock might also become subject to the requirements of certain rules promulgated under the Exchange Act, which require additional disclosure by broker-dealers in connection with any trade involving a stock defined as a ''penny stock'' (generally, any equity security not listed on a national securities exchange or quoted on Nasdaq that has a market price of less than $5.00 per share, subject to certain exceptions).

The market price of our common stock may fluctuate significantly.

The market price of our common stock may fluctuate significantly in response to factors, some of which are beyond our control, such as:

- the announcement of new products or product enhancements by us or our competitors;
- changes in our relationships with our licensors or other strategic partners;
- developments concerning intellectual property rights and regulatory approvals;

- variations in ours and our competitors' results of operations;
- substantial sales of shares of our common stock due to the release of lock-up agreements;
- the announcement of clinical trial results;
- the announcement of potentially dilutive financings;
- changes in earnings estimates or recommendations by securities analysts;
- changes in the structure of healthcare payment systems;
- developments and market conditions in the pharmaceutical and biotechnology industries, including due to the COVID-19 pandemic; and
- the results of clinical trials of APX3330, PS, or any other product candidate that we may develop.

Further, the stock market, in general, and the market for biotechnology companies, in particular, have experienced extreme price and volume fluctuations. As a result of this volatility, investors may not be able to sell their securities at a profit. Continued market fluctuations could result in extreme volatility in the price of our common stock, which may be unrelated or disproportionate to our operating performance and which could cause a decline in the value of our common stock and result in substantial losses for purchasers of our common stock.

We may be subject to securities litigation, which is expensive and could divert management attention.

The market price of our common stock may be volatile, and in the past companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and direct our management's attention from other business concerns, which could seriously harm our business.

ITEM 1B. UNRESOLVED STAFF COMMENTS

Not applicable.

ITEM 1C. CYBERSECURITY

Risk Management and Strategy

The Company has adopted a cybersecurity risk management program that includes processes designed to identify, assess, manage, and monitor risks from cybersecurity threats. We have integrated cybersecurity risk management into our broader risk management framework to promote a company-wide culture of cybersecurity awareness and risk management. Those processes include conducting an assessment of internal and external threats to the security, confidentiality, integrity and availability of Company data and systems along with other material risks to Company operations, at least annually and whenever there are material changes to the Company's systems or operations, and responding to risks identified. The Company's cybersecurity and risk management program is based on National Institute of Standards and Technology (NIST) frameworks. As part of our risk management process, the Company also engages outside providers to conduct periodic security assessments. As part of our third-party risk management program, we conduct assessments of vendor cybersecurity risks, including risks associated with our cloud vendors and other third parties.

Cybersecurity Threats

As of the date of this report, we have not identified any risks from a cybersecurity threat or incident that we believe has or is reasonably likely to have a material effect on our business strategy, results of operations, or financial condition. Despite our continuing efforts, we cannot guarantee that our cybersecurity safeguards will prevent breaches or breakdowns of our or our third-party service providers' information technology systems, particularly in the face of continually evolving cybersecurity threats and increasingly sophisticated threat actors. For more information, see Item 1A Risk Factors, "*Our business and operations would suffer in the event of system failures or unplanned events, including cyber incidents, network security breaches, service interruptions, or data corruption*."

Governance

The cybersecurity risk management program, including the prevention, detection, mitigation, and remediation of cybersecurity incidents, is led by the Company's Finance organization, including the Senior Vice President of Finance and the Senior Director of Finance. Both of these individuals have experience in overseeing our cybersecurity and information technology programs and have held similar oversight functions in prior roles. We rely heavily on information technology consultants for advice and expertise on monitoring evolving industry standards and to monitor our compliance with applicable policies. The Senior Vice President of Finance reports on cybersecurity matters to the Company's Audit Committee at least annually, as well as any time there are material changes to the Company's systems or operations and material updates are shared at each regular meeting of the full Board. The Senior Vice President of Finance also reports to the Company's Chief Executive Officer and other members of our senior management as appropriate. These reports may feature an overall assessment of the Company's compliance with the Company's cybersecurity policies and include topics such as risk assessment, risk management and control decisions, service provider arrangements, test results, security incidents and responses, and recommendations for changes and updates to policies and procedures. In addition, the results of any external reviews on our cybersecurity program are reported to senior management and the Audit Committee.

ITEM 2. PROPERTIES

Our headquarters is currently located in Farmington Hills, Michigan, and consists of approximately 1,600 square feet of leased office space under a lease that expires on December 31, 2024. We may extend our current space or require additional space and facilities as our business expands, and we believe that suitable additional and alternative spaces will be available in the future on commercially reasonable terms.

ITEM 3. LEGAL PROCEEDINGS

From time to time, we are subject to litigation and claims arising in the ordinary course of business. Although the results of litigation and claims cannot be predicted with certainty, as of the date of this filing, we do not believe we are party to any claim or litigation, the outcome of which, if determined adversely to us, would individually or in the aggregate be reasonably expected to have a material adverse effect on our business or financial condition. Regardless of the outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Market Information

Our shares of common stock trade on the Nasdaq Capital Market under the symbol ''OCUP''.

Holders

As of March 5, 2024, there were approximately 75 holders of record of our common stock. The number of holders of record is based on the actual number of holders registered on the books of our transfer agent and does not reflect holders of shares in ''street name'' or persons, partnerships, associations, corporations, or other entities identified in security position listings maintained by depository trust companies.

Dividend Policy

We have not paid any cash dividends on our common stock since our inception and do not anticipate paying any cash dividends in the foreseeable future. We currently plan to retain our earnings, if any, to provide funds for the expansion of our business.

Recent Sales of Unregistered Securities

None.

ITEM 6. [RESERVED]

Not applicable.

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and the related notes included elsewhere in this Annual Report. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Annual Report, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a clinical-stage biopharmaceutical company focused on developing novel therapies for the treatment of unmet needs of patients with retinal and refractive eye disorders.

APX3330

Our lead retinal product candidate, APX3330, is a small-molecule inhibitor of Ref-1 (reduction oxidation effector factor-1 protein). Ref-1 is a regulator of transcription factors such as HIF-1α and NF-kB. Inhibiting Ref-1 reduces levels of vascular endothelial growth factor (''VEGF'') and inflammatory cytokines which are known to play key roles in ocular angiogenesis and inflammation. APX3330 is an oral tablet administered once or twice per day in development for the treatment of diabetic retinopathy (''DR'').

DR affects approximately 10 million diabetics and is projected to impact over 14 million Americans by 2050. DR is classified as either Non-Proliferative Diabetic Retinopathy ('' NPDR''), the early stage of the disease in which symptoms may be mild or non-existent or Proliferative Diabetic Retinopathy (''PDR''), which is the more advanced stage of diabetic eye disease that can be highly symptomatic with loss of vision. Approximately 8 million DR patients have NPDR that may progress to PDR if left untreated. Despite the risk for visual loss associated with this disease, over 90% of NPDR patients currently receive no course of treatment apart from observation by their eye care specialist until they develop sight-threatening complications. APX3330, as an oral tablet, has the potential to be an early, non-invasive treatment for the 8 million NPDR patients in the US.

In January 2023, we reported top-line efficacy and safety results from the ZETA-1 Phase 2 trial conducted in 103 subjects (51 treated with 600 mg daily dose of APX3330) in DR, including moderately severe and severe NPDR and mild PDR, as well as patients with diabetic macular edema without loss of central vision. Although administration of APX3330 daily did not meet the study's primary endpoint of percentage of patients with a ≥ 2-step improvement in Early Treatment of Diabetic Retinopathy Study (''ETDRS'') diabetic retinopathy severity scale (''DRSS'') in the study eye at week 24 compared to placebo, efficacy was seen on the ≥3-step worsening on a binocular DRSS Person Scale. Prevention or slowing of progression of DR to vision-threatening complication such as PDR is a clinically meaningful endpoint. APX3330 also demonstrated favorable safety and tolerability in diabetic patients. An End-of-Phase 2 (''EOP2'') meeting with the U.S. Food and Drug Administration (the ''FDA'') was held in October 2023 at which we obtained agreement on the registration endpoint of ≥3-step worsening on a binocular DRSS Person Scale. APX3330 demonstrated favorable safety and tolerability in the ZETA-1 trial. Ocuphire submitted a Special Protocol Assessment (''SPA'') to the FDA in February 2024 to seek agreement on the clinical trial protocol and statistical analysis plan and will share specifics on the study design parameters and anticipated timing if and when a SPA agreement is reached with the FDA.

We also in-licensed APX2009 and APX2014, which are second-generation analogs of APX3330. The unique mechanism of action of this family of Ref-1 inhibitors of reducing angiogenesis and inflammation could potentially be beneficial in treating other retinal diseases such as age-related macular degeneration, geographic atrophy, and non-ophthalmic diseases.

We are currently evaluating local delivery routes of APX3330 and its second-generation analogs (APX2009 and APX2014) in addition to the systemic (oral) route as part of its pipeline expansion in retinal therapies.

RYZUMVI and Phentolamine Ophthalmic Solution 0.75% (PS)

In November 2022, we entered into a license and collaboration agreement (the ''the Viatris License Agreement'') with FamyGen Life Sciences, Inc. (acquired by Viatris, Inc. (''Viatris'') in January 2023), pursuant to which we granted Viatris an exclusive license to develop, manufacture, import, export and commercialize (i) our

refractive product candidate Phentolamine Ophthalmic Solution 0.75%, formerly known as Nyxol (''PS''), for treating (a) reversal of pharmacologically-induced mydriasis, (b) decreased vision under mesopic (low) light conditions after keratorefractive surgery, and (c) presbyopia, and (ii) PS and low dose pilocarpine for treating presbyopia (together, the ''PS Products'') worldwide except for certain countries and jurisdictions in Asia (the ''Viatris Territory''). PS was approved by the FDA for the treatment for pharmacologically-induced mydriasis under the brand name RYZUMVI in September 2023, which triggered a $10 million milestone payment under the Viatris License Agreement.

Under the terms of the Viatris License Agreement, Ocuphire, in partnership with Viatris, will develop the PS Products in the United States. Viatris will reimburse us for budgeted costs related to the development of the PS Products through FDA approval. Viatris will be responsible for developing the PS Products in countries and jurisdictions in the Viatris Territory outside of the United States.

PS is a once-daily eye drop formulation of phentolamine mesylate designed to reduce pupil diameter and improve visual acuity. PS can potentially be used across multiple indications such as treatment of pharmacologically-induced mydriasis (''RM'') (dilation of the pupil), presbyopia (age-related blurry near vision) and decreased vision under mesopic (low) light conditions after keratorefractive surgery. PS has been studied in a total of 12 clinical trials (3 Phase 1, 5 Phase 2 and 4 Phase 3) in a total of over 1100 study participants (with over 650 PS-treated) and has demonstrated promising clinical data across the three targeted refractive indications.

We reported positive top-line data from multiple late-stage clinical trials for PS in reversal of pharmacologically induced mydriasis, presbyopia and dim light disturbances. The VEGA-2 Phase 3 study in presbyopia achieved its primary endpoint and Viatris, our development and commercial partner, is expected to continue Phase 3 development in the first half of 2024. For decreased vision under mesopic (low) light conditions following keratorefractive surgery, we received FDA agreement under Special Protocol Assessment for LYNX-2, a Phase 3 Trial of PS. Viatris, our development and commercial partner, is expected continue Phase 3 development in this indication in the first half of 2024.

Strategic Outlook

We intend to continue to explore opportunities to acquire additional assets, expand current pipeline to other retinal indications with APX3330, APX2009 and APX2014, and to seek strategic partners for late-stage development, regulatory preparation and commercialization of APX3330 in key global markets. To date, our primary activities have been conducting research and development activities, performing business and financial planning, recruiting personnel and raising capital. We have only one product, RYZUMVI, approved for sale that may generate royalties based on sales by Viatris, and we do not expect to consistently generate significant revenues, other than license and collaborations revenue, unless and until the FDA or other regulatory authorities approve, and we successfully commercialize, APX3330 or PS for other indications. Until such time, if ever, as we can consistently generate substantial product revenue, we expect to finance our cash needs through a combination of equity and debt financings as well as through collaborations, strategic alliances and licensing arrangements.

Through December 31, 2023, we have funded our operations primarily through equity financings that totaled $63.3 million in gross proceeds, of which $21.15 million was received in connection with the merger (''Merger'') with Rexahn Pharmaceuticals, Inc. (''Rexahn'') and through the issuance of convertible notes in private placements that totaled $8.5 million in gross proceeds net cash. In addition, we have received license fee and milestone payments of $45.0 million in the aggregate and reimbursement for costs related to development, all in connection with the Viatris License Agreement.

Our net loss was $10.0 million for the year ended December 31, 2023 as compared to a net income of $17.9 million for the year ended December 31, 2022. As of December 31, 2023, we had an accumulated deficit of $81.5 million. Furthermore, we anticipate that our expenses will increase as we:

- continue clinical trials for APX3330, PS and for any other product candidate in our future pipeline;
- continue nonclinical studies for APX3330, APX2009 and APX2014, PS and for any other product candidate in our future pipeline;
- develop additional product candidates that we identify, in-license or acquire;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- contract to manufacture our product candidates;

- maintain, expand and protect our intellectual property portfolio;
- hire additional staff, including clinical, scientific, operational and financial personnel, to execute our business plan;
- add operational, financial and management information systems and personnel to support our product development and potential future commercialization efforts;
- continue to operate as a public company; and
- establish on our own or with partners, a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain regulatory approval.

Our net income (loss) will likely continue to fluctuate significantly from quarter to quarter and year to year, depending on the timing of our nonclinical studies, clinical trials, expenditures on other research and development activities (and reimbursement thereof), and from potential milestone payments received from and revenue earned under the Viatris License Agreement or any other license and collaboration agreements that we enter into, and potential payments that may become payable from time to time under the Apexian Sublicense Agreement.

Recent Developments

Clinical Milestones

APX3330

In January 2023, we announced top-line efficacy and safety results from ZETA-1, a Phase 2b trial of APX3330 in diabetic retinopathy patients. In ZETA-1, APX3330 demonstrated favorable safety and tolerability and exhibited efficacy in slowing or prevention of DR worsening on a binocular DRSS Person Scale. The FDA agreed this was an approvable registration endpoint at our EOP2 meeting.

PS

In January 2023, we announced the initiation of the VEGA-2 Phase 3 pivotal trial, the first of two Phase 3 registration trials intended to support a presbyopia indication for PS alone and PS with LDP. The VEGA-2 Phase 3 study achieved its primary endpoint and Viatris, our development and commercial partner, is expected to continue Phase 3 development in the first half of 2024.

Regulatory Update

In September 2023, we announced FDA approval of PS under the brand name RYZUMVI for the treatment of RM. In connection with this approval, we received a $10 million milestone payment under the Viatris License Agreement.

In November 2023, we announced the outcome of the EOP2 meeting with the FDA, at which we obtained agreement on the registration endpoint supporting the advancement of APX3330. Ocuphire submitted a SPA to the FDA in February 2024 to seek agreement on the clinical trial protocol and statistical analysis plan and will share specifics on the study design parameters and anticipated timing if and when a SPA agreement is reached with the FDA.

In January 2024, we announced that we received agreement from the FDA under a SPA for the clinical trial protocol and planned statistical analysis of the LYNX-2 Phase 3 trial to evaluate PS for the proposed indication for the treatment of decreased visual acuity under dim (mesopic) light conditions after keratorefractive surgery. Viatris, our development and commercial partner, is expected to continue Phase 3 development in the first half of 2024.

CEO Transition

On April 19, 2023, the Company terminated the employment of Mina Sooch, the former President and Chief Executive Officer of the Company, and appointed Richard Rodgers as the Company's interim President and Chief Executive Officer. On June 8, 2023, the Company entered into a Separation and Release Agreement with Ms. Sooch.

On November 1, 2023, the Company announced the appointment of George Magrath, M.D., M.B.A., M.S., as Chief Executive Officer and member of the Board of Directors. As a result of such appointment, Richard Rodgers, who was serving as Interim President and Chief Executive Officer, resigned from such positions and remains on the Board.

Purchase Agreement with Lincoln Park Capital Fund, LLC ("Lincoln Park")

On August 10, 2023, we entered into a common stock purchase agreement (the ''Purchase Agreement'') with Lincoln Park, which provides that, upon the terms and subject to the conditions and limitations set forth therein, Ocuphire has the sole right, but not the obligation, to direct Lincoln Park to purchase up to $50 million of shares of our common stock, par value $0.0001 (the ''Common Stock''), from time to time over the 30-month term of the Purchase Agreement. Concurrently with entering into the Purchase Agreement, Ocuphire also entered into a registration rights agreement with Lincoln Park (the ''Registration Rights Agreement''), pursuant to which we agreed to register the resale of the shares of our Common Stock that have been and may be issued to Lincoln Park under the Purchase Agreement pursuant to a registration statement. Upon the execution of the Purchase Agreement, we issued 246,792 shares of Common Stock to Lincoln Park as consideration for its commitment to purchase shares of our Common Stock under the Purchase Agreement. Lincoln Park has agreed not to cause or engage in any manner whatsoever in any direct or indirect short selling or hedging of our Common Stock.

Financial Operations Overview

License and Collaborations Revenue

License and collaborations revenue to date was derived from a one-time non-refundable payment related to a license transfer, an additional milestone payment and reimbursement of expenses earned under the Viatris License Agreement, and to a much lesser degree, from license agreements with BioSense Global LLC (''BioSense'') and Processa Pharmaceuticals, Inc. (''Processa'') in connection with the Rexahn RX-3117 drug compound. We anticipate that we will recognize revenue as we earn reimbursement for research and development services in connection with the Viatris License Agreement and we may earn additional revenues from potential milestone and royalty payments from the agreements with Viatris, BioSense, Processa, or from other license agreements entered into the future; however, the attainment of milestones or level of sales required to earn royalty payments is highly uncertain for the reasons explained below.

To date, outside of the license and collaborations revenue referenced above, we do not expect to generate significant revenue unless or until our partner, Viatris, commercializes RYZUMVI, or regulatory approval is obtained, and commercialization begins for APX3330 or PS for indications other than RM. If we fail to complete the development of APX3330, PS, or any other product candidate we may pursue in the future, in a timely manner, or fail to obtain regulatory approval, our ability to generate significant revenue would be compromised.

Operating Expenses

Ocuphire's operating expenses are classified into two categories: general and administrative and research and development.

General and Administrative Expenses

General and administrative expenses consist primarily of personnel-related costs, including salaries, benefits and stock-based compensation costs, for personnel in functions not directly associated with research and development activities. Other significant costs include insurance coverage for directors and officers and other property and liability exposures, legal fees relating to intellectual property and corporate matters, professional fees for accounting and tax services, other services provided by business consultants and legal settlements.

Research and Development Expenses

To date, our research and development expenses have related primarily to the clinical stage development of APX3330 and PS. Research and development expenses consist of costs incurred in performing research and development activities, including compensation, benefits and stock-based compensation costs for research and development employees and costs for consultants, costs associated with nonclinical studies and clinical trials, regulatory activities, manufacturing activities to support clinical activities, license fees, nonlegal patent costs, fees paid to external service providers that conduct certain research and development, and an allocation of overhead expenses.

Pursuant to the Viatris License Agreement, our budgeted research and development expenses related to the development of PS are fully reimbursed by Viatris. However, all research and development costs, including those related to PS, are expensed as incurred, and costs incurred by third parties are expensed as the contracted work is

performed. We accrue for costs incurred as the services are being provided by monitoring the status of the study or project, and as the invoices are received from our external service providers. We adjust our accrual as actual costs become known. Research and development activities are central to our business model.

We expect that APX3330 and PS will have higher development costs during the later stages of clinical development, as compared to costs incurred during their earlier stages of development, primarily due to the increased size and duration of the later-stage clinical trials and associated nonclinical studies. We expect our research and development expenses to increase over the next several years. However, it is difficult for us to determine with certainty the duration, costs and timing to complete our current or future nonclinical programs and clinical trials of APX3330, PS, and other product candidates.

Financing costs

Financing costs consist of issuance costs attributed to an equity line financing with Lincoln Park discussed further below.

Interest Expense

Interest expense consists of interest costs on principal related to a short-term loan (related to financing an insurance policy) during the period it was outstanding and which was fully repaid in May 2022.

Fair value change in derivative liabilities

The fair value change in derivative liabilities consists of the fair value change of the derivative liability associated with our equity line financing during the periods the equity line financing is outstanding. In addition, the fair value change of the warrant liabilities associated with the Rexahn warrants, while outstanding, was also included in this line item.

Other Income (Expense), net

Other income (expense), net includes interest earned from cash and cash equivalent investments, realized and unrealized gains (losses) from equity investments and reimbursements in connection with grants and other sources when they occur. In addition, other income (expense), net also includes payments when made by us in connection with the Contingent Value Rights Agreement (the ''CVR Agreement'') with former Rexahn shareholders.

Provision for Income Taxes

Provision for income taxes consists of federal and state income taxes in the United States, as well as deferred income taxes and changes in related valuation allowance reflecting the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Currently, a full valuation allowance has been provided on the net deferred tax assets as of December 31, 2023 and 2022 given the uncertainty of future taxable income and other related factors impacting the realizability or our remaining net deferred tax assets.

Results of Operations

The following table summarizes our operating results for the periods indicated (in thousands):

	For the Year Ended December 31,		
	2023	**2022**	**Change**
License and collaborations revenue	$ 19,049	$39,850	$(20,801)
Operating expenses:			
General and administrative	11,959	7,269	4,690
Research and development	17,653	14,355	3,298
Total operating expenses	29,612	21,624	7,988
(Loss) income from operations	(10,563)	18,226	(28,789)

	For the Year Ended December 31,		
	2023	2022	Change
Financing costs	(1,328)	—	(1,328)
Interest expense	—	(9)	9
Fair value change in derivative liabilities	80	—	80
Other income (expense), net	1,837	(14)	1,851
(Loss) income before income taxes	(9,974)	18,203	(28,177)
Provision for income taxes	(12)	(315)	303
Net (loss) income	$(9,986)	$17,888	$(27,874)

Comparison of Years Ended December 31, 2023 and 2022

License and Collaborations Revenue

License and collaborations revenue was $19.0 million for the year ended December 31, 2023 compared to $39.8 million for the year ended December 31, 2022. Revenue during 2023 was derived in part from a milestone payment of $10.0 attributed to the FDA's approval of PS, under brand name RYZUMVI for the treatment of pharmacologically induced mydriasis. The $10 million milestone payment was previously constrained by the Company with regard to its inclusion in the initial aggregate transaction price associated with the Viatris License Agreement. Lastly, the balance of the revenue recognized during calendar year 2023 related to the output of research and development services in connection with the Viatris License Agreement. Revenue during calendar year 2022 was derived from the Viatris License Agreement in the fourth quarter associated largely with the transfer of a perpetual, sub-licensable license to develop, manufacture, import, export and commercialize the PS Products, and to a lesser extent, from the reimbursement of research and development services.

General and Administrative

General and administrative expenses for the year ended December 31, 2023 were $12.0 million compared to $7.3 million for the year ended December 31, 2022. The $4.7 million increase was attributed to payroll related costs of $1.4 million primarily attributable to severance costs associated with the departure of our former Chief Executive Officer in the amount of $1.2 million, stock-based compensation of $1.4 million, other personnel related costs of $0.3 million, professional services of $0.8 million, legal support of $0.6 million, and business development activities and other costs of $0.2 million on a net basis. General and administrative expenses included $2.4 million and $1.1 million in stock-based compensation expense during the years ended December 31, 2023, and 2022, respectively.

Research and Development

The following table illustrates the components of our research and development expenses for the periods presented (in thousands):

	For the Year Ended December 31,		
	2023	2022	Change
External costs:			
Phentolamine Ophthalmic Solution 0.75% ("PS")	$ 9,983	$ 8,962	$1,021
APX 3330	4,818	3,047	1,771
Unallocated	678	647	31
Total external cost	15,479	12,656	2,823
Internal costs:			
Employee related expenses	2,148	1,637	511
Facilities, supplies and other	26	62	(36)
Total internal costs	2,174	1,699	475
Total research and development expenses	$17,653	$14,355	$3,298

Research and development expenses for the year ended December 31, 2023 were $17.7 million compared to $14.4 million for the year ended December 31, 2022. The $3.3 million increase was primarily attributable to increased clinical costs of $0.4 million for the PS VEGA-2 trial, increased manufacturing and toxicology activities of approximately $2.5 million for APX3330 and PS, higher payroll costs of $0.7 million including stock-based compensation, and other operating expenses of $0.3 million, offset by a decrease in regulatory activities $0.6 million. Pursuant to the Viatris License Agreement, our budgeted research and development expenses related to the development of the PS Products are fully reimbursed by Viatris. Research and development expenses included $1.1 million and $0.7 million in stock-based compensation expense during the years ended December 31, 2023 and 2022, respectively.

Financing costs

Financing costs for the year ended December 31, 2023 of $1.3 million was comprised of issuance costs attributed to the equity line financing with Lincoln Park described further below. We did not have any financing costs during the year ended December 31, 2022.

Interest Expense

Interest expense for the year ended December 31, 2022 of $9,000 was comprised of interest on principal related to a short-term loan (related to financing an insurance policy). We did not have any interest expense during the year ended December 31, 2023.

Fair value change in derivative liabilities

The fair value change in derivative liabilities was attributed to the equity line financing, described further below, was a gain of $80,000 for the year ended December 31, 2023 attributed to the fluctuations in our common stock fair value and the number of potential shares of common stock issuable at the various discount tiers under the equity line financing. Lastly, the fair value change of the warrant liabilities associated with the Rexahn warrants was also included in this line item, but was de minimis during the years ended December 31, 2023 and 2022. The last of the Rexahn warrants classified as liabilities expired in April 2023 unexercised.

Other Income (Expense), net

During the year ended December 31, 2023, Ocuphire had other income, net of $1.8 million related primarily to interest income in connection with our cash and cash equivalents on-hand.

During the year ended December 31, 2022, we had other expense, net of $14,000 stemming from net unrealized losses attributed to our short-term investments of $170,000 and realized currency losses of approximately $3,000, offset largely by interest income of $159,000 related to cash and cash equivalents.

Provision for Income Taxes

Provision for income taxes consisted of federal and state income taxes in the United States in the amount of $12,000 and $315,000 for the years ended December 31, 2023 and 2022, respectively, resulting from our net taxable income after the application of net operating loss carryforwards and research credits.

Liquidity and Capital Resources

Capital Resources

As of December 31, 2023, our principal sources of liquidity consisted of cash and cash equivalents of $50.5 million. We believe that our cash on hand at the end of 2023 will be sufficient to fund our operations for at least twelve months beyond the date of this filing. As of December 31, 2023, our cash and cash equivalents were invested primarily in cash deposits and cash equivalent investments at two large financial institutions.

Historical Capital Resources

Our primary source of cash to fund our operations has been various equity offerings in the amount of $63.3 million and the issuance of convertible notes in the amount of $8.5 million, inclusive of the promissory notes exchanged for Ocuphire convertible notes (the ‘‘Ocuphire Convertible Notes’’). In addition, we received a one-time

non-refundable cash payment of $35.0 million during the fourth quarter of 2022, a $10.0 million milestone payment during the fourth quarter of 2023, and have received reimbursement for costs related to development since the fourth quarter of 2022, all in connection with the Viatris License Agreement.

Lincoln Park Purchase Agreement

On August 10, 2023, we entered into a common stock purchase agreement with Lincoln Park Capital Fund, LLC (''Lincoln Park'') for an equity line financing (the ''Purchase Agreement''). The Purchase Agreement provides that, subject to the terms and conditions set forth therein, we have the sole right, but not the obligation, to direct Lincoln Park to purchase up to $50 million of shares of the Company's common stock from time to time over the 30-month term of the Purchase Agreement. Concurrently with entering into the Purchase Agreement, we also entered into a Registration Rights Agreement, pursuant to which we agreed to register the resale of the shares of our common stock that have been and may be issued to Lincoln Park under the Purchase Agreement pursuant to a registration statement. Upon the execution of the Purchase Agreement, we issued 246,792 shares of the Company's common stock to Lincoln Park as consideration for its commitment to purchase shares of our common stock under the Purchase Agreement. Lincoln Park has agreed not to cause or engage in any manner whatsoever in any direct or indirect short selling or hedging of our common stock. In addition to the commitment shares referenced above, a total of 1,300,000 shares of common stock were sold under the Purchase Agreement for gross proceeds through December 31, 2023 in the amount of $4.5 million. No shares of common stock were sold under the Purchase Agreement prior to the third quarter of 2023.

At-The-Market Program

On January 10, 2024, we filed a Form S-3 shelf registration under the Securities Act which was declared effective by the SEC on January 23, 2024 under which the Company may offer and sell, from time to time in our sole discretion, securities having an aggregate offering price up to $175 million. On March 11, 2021, we entered into a sales agreement with JonesTrading Institutional Services LLC (''JonesTrading'') under which we may offer and sell, from time to time at our sole discretion, to or through JonesTrading, acting as agent and/or principal, shares of our common stock having an aggregate offering price of up to $40 million (the ''ATM''). A total of 6,045,316 shares of common stock were sold under the ATM since its inception for gross proceeds through December 31, 2023 in the amount of $22.7 million.

Registered Direct Offering

On June 4, 2021, we entered into a placement agency agreement with A.G.P./Alliance Global Partners (''AGP''). Pursuant to the terms of the placement agency agreement, AGP on June 8, 2021, sold an aggregate of 3,076,923 shares of our common stock and warrants to purchase 1,538,461 shares of our common stock (the ''RDO Warrants'') at an offering price of $4.875 per share and 0.50 RDO Warrants, for gross proceeds of $15.0 million, before deducting AGP's fees and related offering expenses in the amount of $1.1 million. The purchase agreement contains customary representations, warranties and agreements by Ocuphire, customary conditions to closing, indemnification obligations of Ocuphire, other obligations of the parties and termination provisions.

The RDO Warrants have an exercise price of $6.09 per share, are exercisable upon the initial issuance date of June 8, 2021, and will expire five years following the initial exercise date. Subject to limited exceptions, a holder of a RDO Warrant will not have the right to exercise any portion of its RDO Warrants if the holder, together with its affiliates, would beneficially own in excess of 4.99% (or, at the election of a holder prior to the date of issuance, 9.99%) of the number of shares of common stock outstanding immediately after giving effect to such exercise; provided, however, that upon prior notice to us, the holder may increase or decrease the beneficial ownership limitation, provided further that in no event shall the beneficial ownership limitation exceed 9.99%. As of December 31, 2023, 1,538,461 RDO Warrants were still outstanding. The offering of the securities was made pursuant to our effective shelf registration statement on Form S-3.

Pre-Merger Financing

Securities Purchase Agreement

On June 17, 2020, Private Ocuphire, Rexahn and certain investors entered into a Securities Purchase Agreement, which was amended and restated in its entirety on June 29, 2020 (as amended and restated, the ''Securities Purchase Agreement''). Pursuant to the Securities Purchase Agreement, the investors invested a total of $21.15 million in cash,

including $300,000 invested by directors of Private Ocuphire, and one director of Rexahn, upon closing of the Merger (the ''Pre-Merger Financing''). Pursuant to the Pre-Merger Financing, (i) Private Ocuphire issued and sold to the investors shares of common stock of Private Ocuphire (the ''Initial Shares''), which converted pursuant to the exchange ratio in the Merger into an aggregate of 1,249,996 shares (the ''Converted Initial Shares'') of common stock, (ii) Private Ocuphire deposited into escrow, for the benefit of the investors, additional shares of common stock of Private Ocuphire (the ''Additional Shares''), which converted pursuant to the exchange ratio in the Merger into an aggregate of 3,749,992 shares of common stock (the ''Converted Additional Shares''), which Converted Additional Shares were delivered (or became deliverable) to the investors on November 19, 2020, and (iii) we agreed to issue to each investor on the tenth trading day following the consummation of the Merger (x) Series A Warrants representing the right to acquire shares of common stock equal to the sum of (A) the Converted Initial Shares purchased by the investor, (B) the Converted Additional Shares delivered or deliverable to the investor, without giving effect to any limitation on delivery contained in the Securities Purchase Agreement and (C) the initial number of shares of common stock, if any, underlying the Series B Warrants issued to the investor and (y) additional warrants to purchase shares of common stock.

Waiver Agreements

Effective February 3, 2021, each investor that invested in the Pre-Merger Financing (each, a ''Holder'') entered into a Waiver Agreement with the Company (collectively, the ''Waiver Agreements''). Pursuant to the Waiver Agreements, the Holders and Ocuphire agreed to waive certain rights, finalize the exercise price and number of Series A Warrants and Series B Warrants, eliminate certain financing restrictions, extend the term of certain leak-out agreements, and, in the case of certain Holders, grant certain registration rights for the shares underlying the warrants.

The Waiver Agreements provide for the permanent waiver of the full ratchet anti-dilution provisions, contained in the Series A Warrants (as certain of the anti-dilution provisions had previously caused liability accounting treatment for the Series A Warrants). Upon the effective date of the Waiver Agreement, the Series A Warrants were reclassified to equity.

Pursuant to the Waiver Agreements, the number of shares underlying all of the Series B Warrants was fixed to 1,708,335 in the aggregate with respect to all Holders.

Series A Warrants

The Series A Warrants were issued on November 19, 2020 at an initial exercise price of $4.4795 per share, were immediately exercisable upon issuance and have a term of five years from the date of issuance. The Series A Warrants are exercisable for 5,665,838 shares of common stock in the aggregate (without giving effect to any limitation on exercise contained therein). As of December 31, 2023, 5,665,838 Series A Warrants were still outstanding.

At issuance, the Series A Warrants contained certain provisions that could have resulted in a downward adjustment of the initial exercise price and an upward adjustment in the number of shares underlying the warrants if Ocuphire were to have issued or sold, or made an agreement to issue or sell, any shares of common stock for a price lower than the exercise price then in effect. Pursuant to the terms of the Waiver Agreements, these provisions are no longer in effect.

Series B Warrants

The Series B Warrants had an exercise price of $0.0001, were exercisable upon issuance and would have expired on the day following the later to occur of (i) the Reservation Date (as defined therein) or (ii) the date on which the investor's Series B Warrants would have been exercised in full (without giving effect to any limitation on exercise contained therein). The Series B Warrants were initially exercisable for 665,836 shares of common stock in the aggregate (without giving effect to any limitation on exercise contained therein) and ultimately became exercisable for 1,708,335 shares of common stock upon execution of the Waiver Agreements. As of December 31, 2023, none of the Series B Warrants remained outstanding.

At issuance, the Series B Warrants contained certain provisions that could have resulted in the issuance of additional Series B Warrants depending on the dollar volume-weighted average prices of a share of Common Stock during a 45-trading day reset period. Pursuant to the terms of the Waiver Agreements, those provisions were no longer in effect.

Ocuphire Convertible Notes

From May 2018 through March 2020, we issued the Ocuphire Convertible Notes for aggregate gross proceeds of $8.5 million, inclusive of the promissory notes exchanged for Ocuphire Convertible Notes. The final closing of the Ocuphire Convertible Notes occurred on March 10, 2020. The Ocuphire Convertible Notes had an interest rate of 8% per annum. On November 4, 2020, all of Ocuphire's outstanding notes were converted into 977,128 shares of Ocuphire common stock in connection with the completion of the Merger.

Cash Flows

The following table summarizes our cash flows for the periods indicated (in thousands):

	For the Year Ended December 31,	
	2023	**2022**
Net cash (used in) provided by operating activities	$(1,112)	$14,314
Net cash used in investing activities	—	—
Net cash provided by financing activities	8,979	3,786
Net increase in cash and cash equivalents	$ 7,867	$18,100

Cash Flow from Operating Activities

For the year ended December 31, 2023, cash used by operating activities of $1.1 million was attributable to net loss of $10.0 million, partially offset by $4.8 million in non-cash operating expenses and offset by a net cash source of approximately $4.1 million resulting from the change in Ocuphire's operating assets and liabilities. The non-cash expenses consisted principally of stock-based compensation of $3.5 million, non-cash financing costs of $1.2 million in connection with the equity line financing and $0.2 million of issuance costs reclassified to financing activities, offset by a fair value gain attributed to the derivative liability of $ 0.1 million. The change in operating assets and liabilities was primarily attributable to our decrease in our accounts receivable and contract asset associated with the Viatris License Agreement of $2.5 million and to a lesser extent from the increase in our accounts payable and accrued expenses of $1.2 million and a decrease in our prepaid expenses of $0.4 million associated with the fluctuations of Ocuphire's operating expenses.

For the year ended December 31, 2022, cash provided by operating activities of $14.3 million was attributable to net income of $17.9 million, partially offset by $2.0 million in non-cash operating expenses and offset by a net cash use of approximately $5.6 million resulting from the change in Ocuphire's operating assets and liabilities. The non-cash expenses consisted largely of stock-based compensation of $1.8 million and a net unrealized loss in our short-term investments of $0.2 million. The change in operating assets and liabilities was primarily attributable to our increase in our accounts receivable and contract asset associated with the Viatris License Agreement of $4.9 million and to a lesser extent from the decrease in our accounts payable and accrued expenses and increases in our prepaid expenses in the aggregate of $0.7 million associated with the fluctuations of Ocuphire's operating expenses.

Cash Flow from Investing Activities

There were no investing activities during the periods presented.

Cash Flow from Financing Activities

Net cash provided by financing activities during the year ended December 31, 2023 was $9.0 million that consisted principally of proceeds received from the Purchase Agreement and ATM, net of issuance costs, in the amount of $4.3 million and $4.6 million, respectively.

Net cash provided by financing activities during the year ended December 31, 2022 was $3.8 million that consisted principally of proceeds received from the ATM, net of issuance costs, in the amount of $4.3 million, offset in part by payments made on the short-term loan of $0.5 million.

Liquidity and Capital Resource Requirements

As of December 31, 2023, we had cash and cash equivalents of $50.5 million. License and collaborations revenue inception to date was derived from a one-time non-refundable payment of $35 million, a milestone payment of $10 million and reimbursement and expected reimbursement of expenses earned under the Viatris License

Agreement and, to a much lesser degree, from license agreements with BioSense Global LLC (''BioSense'') and Processa Pharmaceuticals, Inc. (''Processa'') in connection with the Rexahn RX-3117 drug compound. We anticipate that we will recognize revenue as we earn reimbursement for research and development services in connection with the Viatris License Agreement and we may earn additional revenues from future potential milestone and royalty payments from the agreements with Viatris, BioSense, Processa, or from other license agreements entered into in the future; however, the attainment of milestones or level of sales required to earn royalty payments is highly uncertain for the reasons explained below.

To date, outside of the license and collaborations revenue referenced above, we do not expect to generate significant revenue unless or until our partner, Viatris, commercializes RYZUMVI, or regulatory approval is obtained and commercialization begins for APX3330 or PS for indications other than RM. If we fail to complete the development of APX3330, PS or any other product candidate we may pursue in the future, in a timely manner, or fail to obtain regulatory approval for any of such product candidates, our ability to generate significant revenue would be compromised.

In addition, on August 10, 2023, we entered into the Purchase Agreement with Lincoln Park, which provides that we have the sole right, but not the obligation, to direct Lincoln Park to purchase up to $50 million of shares of our common stock, from time to time over the 30-month term of the Purchase Agreement. The Purchase Agreement was executed to compliment the ATM. Concurrently with entering into the Purchase Agreement, we also entered into a Registration Rights Agreement with Lincoln Park, pursuant to which we agreed to register the resale of the shares of our common stock that have been and may be issued to Lincoln Park under the Purchase Agreement pursuant to a registration statement. We filed a prospectus supplement to our Registration Statement (File No. 333-252715) on August 11, 2023 with the SEC. Per the terms of the Purchase Agreement, we will be unable to sell shares of our common stock to Lincoln Park if the sale price falls below $0.25 per share. Therefore, there is no assurance that we will have full access to the facility during the term of the Purchase Agreement.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation, warrants or other preferences that adversely affect your rights as a common stockholder. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through future collaborations, strategic alliances or licensing arrangements with pharmaceutical partners, we may have to relinquish valuable rights to our technologies, future revenue streams or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or through collaborations, strategic alliances or licensing arrangements when needed, we may be required to delay, limit, reduce or terminate our product development, future commercialization efforts, or grant rights to develop and market our product candidates that we would otherwise prefer to develop and market ourselves.

Future Capital Requirements

Pursuant to the Viatris License Agreement, our budgeted research and development expenses related to the development of PS are fully reimbursed by Viatris. The development of APX3330 is subject to numerous uncertainties, and we have based these estimates on assumptions that may prove to be substantially different than what we currently anticipate and could result in cash resources being used sooner than what we currently expect. Additionally, the process of advancing early-stage product candidates and testing product candidates in clinical trials is costly, and the timing of progress in these clinical trials is uncertain. Our ability to successfully transition to profitability will be dependent upon achieving a level of product sales adequate to support our cost structure. We cannot give any assurance that we will ever be profitable or generate positive cash flow from operating activities.

Contractual Obligations and Commitments

Facility Lease

We lease a facility under a non-cancellable operating lease that expires on December 31, 2024, as amended, for a base rent in the amount of $3,000 per month.

Apexian Sublicense Agreement

On January 21, 2020, we entered into the Apexian Sublicense Agreement, pursuant to which we obtained exclusive worldwide patent and other intellectual property rights that constitute a Ref-1 Inhibitor program relating to therapeutic applications to treat disorders related to ophthalmic and diabetes mellitus conditions. The lead

compound in the Ref-1 Inhibitor program is APX3330, which is currently in development as an oral tablet therapeutic to treat DR in patients with NPDR. The mechanism of action of Ref-1 inhibitors (e.g., APX3330, APX2009 and APX2014) of reducing angiogenesis and inflammation could potentially be beneficial in treating other retinal diseases such as diabetic macular edema (''DME''), wet age-related macular degeneration (''wAMD'') and geographic atrophy (''GA'') as well as non-ophthalmic indications. Ocuphire is currently evaluating local delivery routes in addition to the systemic (oral) route as part of its pipeline expansion into retina and non-ophthalmic indications.

In connection with the Apexian Sublicense Agreement, we issued 843,751 shares of our common stock to Apexian and certain of Apexian's affiliates.

We agreed to make one-time milestone payments under the Apexian Sublicense Agreement for each of the first ophthalmic indication and the first diabetes mellitus indication. These milestone payments include (i) payments for specified developmental and regulatory milestones (including completion of the first Phase 2 trial (if such trial meets a primary endpoint) and the first Phase 3 pivotal trial in the United States, and filing and achieving regulatory approval from the FDA for the first New Drug Application for a compound) totaling up to $11 million in the aggregate and (ii) payments for specified sales milestones of up to $20 million in the aggregate, each of which net sales milestone payments is payable once, upon the first achievement of such milestone.

Additionally, we also agreed to make royalty payments equal to a single-digit percentage of our net sales of products covered by the patents under the Apexian Sublicense Agreement. None of the milestone or royalty payments were triggered as of the date of this Annual Report.

Other Commitments

In the course of normal operations, we entered into cancellable purchase commitments with our suppliers for various key research, clinical and manufacturing services. The purchase commitments covered by these arrangements are subject to change based on our research and development efforts.

Other Funding Requirements

As noted above, certain of our cash requirements relate to the funding of our ongoing research and development of APX3330, inclusive of any potential milestone and royalty obligations under our intellectual property licenses. See ''Part I, Item 1—Business—Potential Clinical Plans for APX3330—PS Potential Clinical Plans—Future In-Licensing and Acquisition Opportunities—Manufacturing—Apexian Sublicense Agreement— Review and Approval of Drugs in the United States'' of this Annual Report for a discussion of design, development, pre-clinical and clinical activities that we may conduct in the future, including expected cash expenditures required for some of those activities, to the extent we are able to estimate such costs.

Our other cash requirements within the next twelve months include accounts payable, accrued expenses, purchase commitments and other current liabilities. Our other cash requirements greater than twelve months from various contractual obligations and commitments may include operating leases and contractual agreements with third-party service providers for clinical research, product development, manufacturing, commercialization, supplies, payroll, equipment maintenance, and audits for periods into calendar year 2024. Refer to Note 3 – Commitments and Contingencies included in ''Part II, Item 8 – Financial Statements and Supplementary Data'' of this Annual Report for further detail of our lease obligation and license agreements with regard to the timing of expected future payments.

We expect to satisfy our short-term and long-term obligations through cash on hand, from future equity and debt financings, and from reimbursement payments, potential milestone and royalty payments under the Viatris License Agreement and any future collaborations and license agreements, until we generate an adequate level of revenue from commercial sales to cover expenses, if ever.

Critical Accounting Policies and Estimates

Our financial statements are prepared in accordance with U.S. GAAP. These accounting principles require us to make estimates and judgments that can affect the reported amounts of assets and liabilities as of the date of the financial statements as well as the reported amounts of revenue and expense during the periods presented. We believe that the estimates and judgments upon which we rely are reasonably based upon information available to us at the time that we make these estimates and judgments. To the extent that there are material differences between these

estimates and actual results, our financial results will be affected. The accounting policies that reflect our more significant estimates and judgments and which we believe are the most critical to aid in fully understanding and evaluating our reported financial results are described below.

Our significant accounting policies are discussed in Note 1—Company Description and Summary of Significant Accounting Policies, included in ''Part II, Item 8 – Financial Statements and Supplementary Data'' of this Annual Report. We believe that the following accounting policies and estimates are the most critical to aid in fully understanding and evaluating our reported financial results. These estimates require our most difficult, subjective, or complex judgments because they relate to matters that are inherently uncertain. We have reviewed these critical accounting policies and estimates and related disclosures with the Audit Committee of our Board of Directors. We have not made any material changes to date, nor do we believe there is a reasonable likelihood of a material future change to the accounting methodologies for the areas described below.

License and Collaborations Revenue

We account for license and collaborations revenue in accordance with the provisions of the Financial Accounting Standards Board (''FASB'') Accounting Standards Codification (''ASC'') 606, *Revenue from Contracts with Customers*. The guidance provides a unified model to determine how revenue is recognized. We have entered into license and collaboration agreements which have revenue recognition implications. We recognize license and collaborations revenue by first allocating the transaction price of a contract to each performance obligation under the contract based on its stand-alone price. The stand-alone price of each performance obligation is based on its fair value utilizing a discounted cash flow approach, taking into consideration assumptions, including projected worldwide net profit for each of the respective programs based on probability assessments, projections based on internal forecasts, industry data, and information from other guideline companies within the same industry and other relevant factors. We do not expect to have in the future, significant variable consideration adjustments related to our existing license and collaborations revenue recognized. For discussion about the determination of license and collaborations revenue, see Note 9—License and Collaboration Agreements included in ''Part II, Item 8 – Financial Statements and Supplementary Data'' of this Annual Report.

Stock-based Compensation

We account for stock-based compensation in accordance with the provisions of ASC 718, Compensation — Stock Compensation. Accordingly, compensation costs related to equity instruments granted are recognized at the grant date fair value based on a Black-Scholes model which is not subject to remeasurement. We record equity instrument forfeitures when they occur. For discussions about the application of grant date fair value associated with our stock-based compensation, see Note 6—Stock-based Compensation included in ''Part II, Item 8 – Financial Statements and Supplementary Data'' of this Annual Report.

Income Tax Assets and Liabilities

A full valuation allowance has been provided on our net deferred tax assets given the uncertainty of future taxable income and other related factors impacting the realizability of our remaining net deferred tax assets. For additional information, see Note 11—Income Taxes included in ''Part II, Item 8 – Financial Statements and Supplementary Data'' of this Annual Report.

Contingencies

We are subject to numerous contingencies arising in the ordinary course of business, including obligations related to certain license agreements. For additional information, see Note 3—Commitments and Contingencies included in ''Part II, Item 8 – Financial Statements and Supplementary Data'' of this Annual Report.

Recent Accounting Pronouncements

From time to time the FASB, or other standard-setting bodies, issue new accounting pronouncements. Where applicable, we adopt these new standards according to the specified effective dates. Unless otherwise disclosed in the notes to the financial statements appearing in this Annual Report, we believe that the impact of any recently issued standard(s) that are not yet effective will not have a material impact on our financial position or results of operations upon adoption. See Note 1, ''Company Description and Summary of Significant Accounting Policies,'' included in ''Part II, Item 8 – Financial Statements and Supplementary Data'' of this Annual Report for a more in-depth discussion of recently issued accounting standard(s).

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Not applicable.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

The information required by this item is included in this Annual Report beginning on page 95 and is incorporated herein by reference.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

As required by Rule 13a-15(b) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, under the direction of the Chief Executive Officer and the Chief Financial Officer, our principal executive officer and principal financial officer, respectively, we have evaluated our disclosure controls and procedures as defined in Rule 13a-15(e) or 15d-15(e) as of the end of the period covered by this Annual Report. Based on this evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that our disclosure controls and procedures were effective as of the end of the period covered by this Annual Report.

Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting to provide reasonable assurance regarding the reliability of our financial reporting and the preparation of financial statements for external purposes in accordance with U.S. generally accepted accounting principles. Internal control over financial reporting includes those policies and procedures that: (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of our assets; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with U.S. generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorizations of our management and Board; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the financial statements.

Our management, including our Chief Executive Officer and Chief Financial Officer, recognizes that our internal control over financial reporting cannot prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. The design of a control system must reflect the fact that there are resource constraints, and the benefits of controls must be considered relative to their costs. Further, because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud, if any, have been detected. The design of any system of controls is based in part on certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions.

Management, with the participation of the Chief Executive Officer and Chief Financial Officer, assessed our internal control over financial reporting as of December 31, 2023, the end of our fiscal year. Management based its assessment on criteria established in Internal Control—Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on that evaluation, management has concluded that the Company's internal control over financial reporting was effective as of December 31, 2023.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) that occurred during the quarter ended December 31, 2023 which have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

None.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

Not applicable.

PART III

We will file a definitive Proxy Statement for our 2024 Annual Meeting of Stockholders (the ''2024 Proxy Statement'') with the SEC, pursuant to Regulation 14A, not later than 120 days after the end of our fiscal year. Accordingly, certain information required by Part III has been omitted under General Instruction G(3) to Form 10-K. Only those sections of the 2024 Proxy Statement that specifically address the items set forth herein are incorporated by reference.

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by Item 10 is hereby incorporated by reference to the sections of the 2024 Proxy Statement under the captions ''Board and Committee Information'', ''Delinquent Section 16(a) Reports'', and ''Proposal No. 1 – Election of Directors,'' ''Executive Officers''.

ITEM 11. EXECUTIVE COMPENSATION

The information required by Item 11 is hereby incorporated by reference to the sections of the 2024 Proxy Statement under the captions ''Executive Compensation'' and ''Proposal No. 1 – Election of Directors – Non-Employee Director Compensation.''

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required by Item 12 is hereby incorporated by reference to the sections of the 2024 Proxy Statement under the captions ''Security Ownership of Certain Beneficial Owners and Management'' and ''Executive Compensation – Securities Authorized for Issuance under Equity Compensation Plans.''

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by Item 13 is hereby incorporated by reference to the sections of the 2024 Proxy Statement under the captions ''Certain Relationships and Related-Party Transactions'' and ''Board and Committee Information.''

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The information required by Item 14 is hereby incorporated by reference to the sections of the 2024 Proxy Statement under the caption ''Proposal No. 2 – Ratification of Independent Registered Public Accounting Firm.''

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

The following documents are filed as a part of this Annual Report on Form 10-K:

(a) Financial Statements: The financial statements filed as part of this report are listed in Part II, Item 8.

(b) Financial Statement Schedules: The schedules are either not applicable or the required information is presented in the financial statements or notes thereto.

(c) Exhibits: The following exhibits are incorporated by reference or filed as part of this Annual Report on Form 10-K:

EXHIBIT NUMBER	DESCRIPTION OF DOCUMENT
3.1	Amended and Restated Certificate of Incorporation of the Registrant (incorporated by reference to Appendix G to the Registrant's Definitive Proxy Statement on Schedule 14A, filed on April 29, 2005).
3.2	Certificate of Amendment of Amended and Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K, filed on May 5, 2017).
3.3	Certificate of Amendment of Amended and Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K, filed on August 30, 2018).
3.4	Certificate of Amendment of Amended and Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K, filed on April 12, 2019).
3.5	Certificate of Amendment of Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K, filed on November 6, 2020).
3.6	Certificate of Amendment of Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K, filed on November 6, 2020).
3.7	Second Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.3 to the Registrant's Current Report on Form 8-K, filed on November 6, 2020).
3.8	First Amendment to Second Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K filed on June 10, 2022).
3.9	Second Amendment to Second Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K filed on June 17, 2022).
3.10	Third Amendment to Second Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K filed on June 2, 2023).
4.1	Form of Common Stock Purchase Warrant (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K, filed on October 13, 2017).
4.2	Form of Common Stock Purchase Warrant (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K, filed on October 19, 2018).
4.3	Form of Common Stock Purchase Warrant (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K, filed on January 25, 2019).
4.4	Form of Series A/B Warrants (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K, filed on July 1, 2020).
4.5	Description of Securities (incorporated by reference to Exhibit 4.11 to the Registrant's Annual Report on Form 10-K, filed on March 11, 2021).
4.6	Form of Warrant to purchase shares of common stock (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K/A, filed on June 7, 2021).
4.7	Form of Indenture (incorporated by reference to Exhibit 4.13 to the Registrant's Registration Statement on Form S-3, filed on January 10, 2024).

EXHIBIT NUMBER	DESCRIPTION OF DOCUMENT
4.8	Form of Common Stock Warrant Agreement and Warrant Certificate (incorporated by reference to Exhibit 4.15 to the Registrant's Registration Statement on Form S-3, filed on January 10, 2024).
4.9	Form of Preferred Stock Warrant Agreement and Warrant Certificate (incorporated by reference to Exhibit 4.16 to the Registrant's Registration Statement on Form S-3, filed on January 10, 2024).
4.10	Form of Debt Securities Warrant Agreement and Warrant Certificate (incorporated by reference to Exhibit 4.17 to the Registrant's Registration Statement on Form S-3, filed on January 10, 2024).
10.1*++	Amended and Restated Employment Agreement by and among the Company and Mina Sooch, effective as of November 5, 2020 (incorporated by reference to Exhibit 10.27 to the Registrant's Registration Statement on Form S-4 (File No. 333-239702), filed on September 30, 2020).
10.1.1*	First Amendment to the Amended and Restated Employment Agreement by and among the Company and Mina Sooch, effective as of March 26, 2023 (incorporated by reference to Exhibit 10.1.1 to the Registrant's Annual Report on Form 10-K, filed on March 30, 2023).
10.1.2*	Separation and Release Agreement, dated as of June 8, 2023, by and between Ocuphire Pharma, Inc. and Mina Sooch (incorporated by reference to Exhibit 10.3 to the Registrant's Quarterly Report on Form 10-Q, filed on August 11, 2023).
10.2*	Amended and Restated Employment Agreement by and among the Company and Bernhard Hoffmann, effective as of November 5, 2020 (incorporated by reference to Exhibit 10.29 to the Registrant's Registration Statement on Form S-4 (File No. 333-239702), filed on September 30, 2020).
10.2.1*	First Amendment to the Amended and Restated Employment Agreement by and among the Company and Bernhard Hoffmann, effective as of March 26, 2023 (incorporated by reference to Exhibit 10.2.1 to the Registrant's Annual Report on Form 10-K , filed on March 30, 2023).
10.3*	Form of Indemnification Agreement (incorporated by reference to Exhibit 10.30 to the Registrant's Registration Statement on Form S-4 (File No. 333-239702), filed on September 30, 2020).
10.4++	Sublicense Agreement, dated as of January 21, 2020, by and between Ocuphire Pharma, Inc. and Apexian Pharmaceuticals, Inc (incorporated by reference to Exhibit 10.31 to the Registrant's Registration Statement on Form S-4 (File No. 333-239702), filed on September 30, 2020).
10.4.1	First Amendment to Sublicense Agreement, dated as of June 4, 2020, by and between Apexian Pharmaceuticals, Inc. and Ocuphire Pharma, Inc (incorporated by reference to Exhibit 10.32 to the Registrant's Registration Statement on Form S-4 (File No. 333-239702), filed on September 30, 2020).
10.5	Lease Agreement, dated as of May 19, 2019, by and between Ocuphire Pharma, Inc. and Duke & Duke, LP (incorporated by reference to Exhibit 10.33 to the Registrant's Registration Statement on Form S-4 (File No. 333-239702), filed on September 30, 2020).
10.5.1	First Amendment to Lease Agreement, dated as of October 29, 2019, by and between Ocuphire Pharma, Inc. and Duke & Duke, LP (incorporated by reference to Exhibit 10.34 to the Registrant's Registration Statement on Form S-4 (File No. 333-239702), filed on September 30, 2020).
10.5.2	Second Lease Amendment, dated as of November 17, 2020, by and between the Company and Duke & Duke (incorporated by reference to Exhibit 10.43 to the Registrant's Annual Report on Form 10-K, filed on March 11, 2021).
10.5.3	Third Lease Amendment, dated as of September 9, 2021, by and between the Company and Duke & Duke (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q, filed on November 12, 2021).
10.5.4	Fourth Lease Amendment, dated as of October 17, 2022, by and between the Company and Duke & Duke (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q, filed on November 4, 2022).
10.5.5**	Fifth Lease Amendment, dated as of November 29, 2023, by and between the Company and Duke & Duke.
10.6*	Ocuphire Pharma, Inc. 2018 Equity Incentive Plan, dated as of April 9, 2018 (incorporated by reference to Exhibit 10.35 to the Registrant's Registration Statement on Form S-4 (File No. 333-239702), filed on September 30, 2020).

EXHIBIT NUMBER	DESCRIPTION OF DOCUMENT
10.6.1*	First Amendment to 2018 Equity Incentive Plan, dated as of December 23, 2019 (incorporated by reference to Exhibit 10.36 to the Registrant's Registration Statement on Form S-4 (File No. 333-239702), filed on September 30, 2020).
10.6.2*	Form of Option Agreement issuable under the Ocuphire Pharma, Inc. 2018 Equity Incentive Plan (incorporated by reference to Exhibit 10.37 to the Registrant's Registration Statement on Form S-4 (File No. 333-239702), filed on September 30, 2020).
10.7*	Ocuphire Pharma, Inc. 2020 Equity Incentive Plan (incorporated by reference to Annex D to the Registrant's Registration Statement on Form S-4 (File No. 333-239702), filed on September 30, 2020).
10.7.1*	Form of Restricted Stock Unit Grant Notice issued under the Ocuphire Pharma, Inc. 2020 Equity Incentive Plan (incorporated by reference to Exhibit 10.7.1 to the Registrant's Annual Report on Form 10-K (File No. 001-34079), filed on March 30, 2023).
10.7.2*	Form of Stock Option Grant Notice issued under the Ocuphire Pharma, Inc. 2020 Equity Incentive Plan (incorporated by reference to Exhibit 10.7.2 to the Registrant's Annual Report on Form 10-K (File No. 001-34079), filed on March 30, 2023).
10.8++	Contingent Value Rights Agreement, dated as of November 5, 2020, by and among the Company, Shareholder Representative Services LLC and the Olde Monmouth Stock Transfer Co., Inc. (incorporated by reference to Exhibit 10.4 to the Registrant's Current Report on Form 8-K, filed on November 6, 2020).
10.9*	Ocuphire Pharma, Inc. 2021 Inducement Plan (incorporated by reference to Exhibit 10.41 to the Registrant's Annual Report on Form 10-K, filed on March 11, 2021)
10.9.1*	Form of Stock Option Grant Notice issued under the Ocuphire Pharma, Inc. 2021 Inducement Plan (incorporated by reference to Exhibit 10.9.1 to the Registrant's Annual Report on Form 10-K (File No. 001-34079), filed on March 30, 2023).
10.10*	Employment Agreement dated November 11, 2020, by and between the Company and Amy Rabourn (incorporated by reference to Exhibit 10.42 to the Registrant's Annual Report on Form 10-K, filed on March 11, 2021)
10.10.1*	First Amendment to the Employment Agreement by and among the Company and Amy Rabourn, effective as of March 26, 2023 (incorporated by reference to Exhibit 10.10.1 to the Registrant's Annual Report on Form 10-K (File No. 001-34079), filed on March 30, 2023).
10.11	Capital on Demand™ Sales Agreement, dated March 11, 2021 between the Company and JonesTrading Institutional Services LLC (incorporated by reference to Exhibit 1.1 to the Registrant's Current Report on Form 8-K, filed on March 11, 2021).
10.12	Form of Purchase Agreement, dated as of June 4, 2021, by and among Ocuphire Pharma, Inc. and the purchasers identified on the signature pages thereto (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K/A, filed on June 7, 2021).
10.13++	Processa License Agreement dated June 16, 2021 (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, filed on June 23, 2021).
10.14++	Viatris (f/k/a Famy Life Sciences) License and Collaboration Agreement dated November 6, 2022 (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, filed on November 7, 2022).
10.15*	Consulting Agreement dated April 8, 2022, by and between the Company and Jay Pepose (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q, filed on May 13, 2022).
10.15.1*	First Amendment to the Consulting Agreement dated September 19, 2022, by and between the Company and Jay Pepose (incorporated by reference to Exhibit 10.15.1 to the Registrant's Annual Report on Form 10-K (File No. 001-34079), filed on March 30, 2023).
10.15.2*	Amendment No. 2 to the Consulting Agreement dated December 1, 2022, by and between the Company and Jay Pepose (incorporated by reference to Exhibit 10.15.2 to the Registrant's Annual Report on Form 10-K (File No. 001-34079), filed on March 30, 2023).
10.16	Amended and Restated Non-Employee Director Compensation Policy dated July 1, 2022 (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q, filed on August 12, 2022).

EXHIBIT NUMBER	DESCRIPTION OF DOCUMENT
10.17	Interim President and CEO Consulting Letter Agreement by and between Ocuphire Pharma, Inc. and Richard Rodgers, dated April 20, 2023 (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q filed on May 15, 2023).
10.18*	Non-Employee Director Compensation Policy (incorporated by reference to Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q filed on May 15, 2023).
10.19*	Second Amended and Restated Non-Employee Director Compensation Policy (incorporated by reference to Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q filed on May 15, 2023).
10.20	Purchase Agreement, dated as of August 10, 2023, by and between Ocuphire Pharma, Inc. and Lincoln Park Capital Fund, LLC (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, filed on August 11, 2023).
10.21	Registration Rights Agreement, dated as of August 10, 2023, by and between Ocuphire Pharma, Inc. and Lincoln Park Capital Fund, LLC (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K, filed on August 11, 2023).
10.22*	Employment Agreement entered into on October 31, 2023 by and between Ocuphire Pharma, Inc. and George Magrath (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, filed on November 1, 2023).
10.23*	Form of Restricted Stock Unit Award and Form of Award Agreement (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K, filed on November 1, 2023).
10.24*	First Amendment to 2021 Inducement Plan (incorporated by reference to Exhibit 10.3 to the Registrant's Current Report on Form 8-K, filed on November 1, 2023).
10.25	Amended and Restated Employment Agreement, dated as of April 24, 2023, by and between Ocuphire Pharma, Inc. and Ronil Patel (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, filed on December 6, 2023).
10.26*	First Amendment to Amended and Restated Employment Agreement, dated as of December 1, 2023, by and between Ocuphire Pharma, Inc. and Ronil Patel (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K, filed on December 6, 2023).
10.27*	Employment Agreement, dated February 13, 2024, by and between the Company and Nirav Jhaveri (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, filed on February 16, 2024).
10.28*	First Amendment to Employment Agreement, entered into on February 16, 2024, by and between the Company and Nirav Jhaveri (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K, filed on February 16, 2024).
10.29*	Offer Letter entered into on November 20, 2023 by and between Ocuphire Pharma, Inc. and Joseph Schachle (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, filed on November 27, 2023).
21.1	Subsidiaries of the Registrant.
23.1	Consent of Ernst & Young, LLP.
31.1	Certification of Principal Executive Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2	Certification of Principal Financial Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as adopted pursuant to section 302 of the Sarbanes-Oxley Act of 2002.
32.1	Certification of Principal Executive Officer and Principal Financial Officer pursuant to Rules 13a-14(b) and 15d-14(b) promulgated under the Securities Exchange Act of 1934 and 18 U.S.C. Section 1350, as adopted pursuant to section 906 of The Sarbanes-Oxley Act of 2002.
97**	Compensation Recovery Policy.
101.INS	Inline XBRL Instance Document (the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document).
101.SCH	Inline XBRL Taxonomy Extension Schema Document.

EXHIBIT NUMBER	DESCRIPTION OF DOCUMENT
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (formatted as inline XBRL and contained in Exhibit 101)

---

* Indicates management contract or compensatory plan.

** Indicates exhibits that are being filed herewith.

\+ Certain schedules and exhibits have been omitted pursuant to Item 601(b)(2) of Regulation S-K. A copy of any omitted schedule and/or exhibit will be furnished to the SEC upon request.

++ Portions of this exhibit have been omitted in compliance with Item 601 of Regulation S-K.

ITEM 16. FORM 10-K SUMMARY

None

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

INDEX TO FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors
of Ocuphire Pharma, Inc.

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Ocuphire Pharma, Inc. (the Company) as of December 31, 2023 and 2022, the related statements of comprehensive (loss) income, changes in stockholders' equity and cash flows for each of the two years in the period ended December 31, 2023, and the related notes (collectively referred to as the ''financial statements''). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2023 and 2022, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2023, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matters

Critical audit matters are matters arising from the current period audit of the financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. We determined that there are no critical audit matters.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2018.

Detroit, Michigan
March 8, 2024

Ocuphire Pharma, Inc.
Balance Sheets
(in thousands, except share amounts and par value)

	As of December 31,	
	2023	**2022**
Assets		
Current assets:		
Cash and cash equivalents	$ 50,501	$ 42,634
Accounts receivable	926	1,298
Contract assets and unbilled receivables (Note 9)	1,407	3,552
Prepaids and other current assets	1,099	1,453
Short-term investments	15	49
Total current assets	53,948	48,986
Property and equipment, net	—	6
Total assets	$ 53,948	$ 48,992
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 2,153	$ 1,069
Accrued expenses	1,815	1,684
Derivative liability	74	—
Total current liabilities	4,042	2,753
Total liabilities	4,042	2,753
Commitments and contingencies (Note 3 and Note 7)		
Stockholders' equity:		
Preferred stock, par value $0.0001; 10,000,000 shares authorized as of December 31, 2023 and 2022; no shares issued and outstanding at December 31, 2023 and 2022	—	—
Common stock, par value $0.0001; 75,000,000 shares authorized as of December 31, 2023 and 2022; 23,977,491 and 20,861,315 shares issued and outstanding at December 31, 2023 and 2022, respectively	2	2
Additional paid-in capital	131,370	117,717
Accumulated deficit	(81,466)	(71,480)
Total stockholders' equity	49,906	46,239
Total liabilities and stockholders' equity	$ 53,948	$ 48,992

See accompanying notes.

Ocuphire Pharma, Inc.
Statements of Comprehensive (Loss) Income
(in thousands, except share and per share amounts)

	For the Year Ended December 31,	
	2023	2022
License and collaborations revenue	$ 19,049	$ 39,850
Operating expenses:		
General and administrative	11,959	7,269
Research and development	17,653	14,355
Total operating expenses	29,612	21,624
(Loss) income from operations	(10,563)	18,226
Financing costs (Note 8)	(1,328)	—
Interest expense (Note 4)	—	(9)
Fair value change in derivative liabilities	80	—
Other income (expense), net	1,837	(14)
(Loss) income before income taxes	(9,974)	18,203
Provision for income taxes	(12)	(315)
Net (loss) income	(9,986)	17,888
Other comprehensive (loss) income, net of tax	—	—
Comprehensive (loss) income	$ (9,986)	$ 17,888
Net (loss) income per share (Note 10):		
Basic	$ (0.46)	$ 0.90
Diluted	$ (0.46)	$ 0.87
Number of shares used in per share calculations:		
Basic	21,589,821	19,931,080
Diluted	21,589,821	20,597,212

See accompanying notes.

Ocuphire Pharma, Inc.
Statements of Changes in Stockholders' Equity
(in thousands, except share amounts)

	Common Stock		Additional Paid–In Capital	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount			
Balance at December 31, 2021	18,845,828	$ 2	$111,588	$(89,368)	$22,222
Issuance of common stock in connection with the at-the-market program	1,848,980	—	4,428	—	4,428
Issuance costs	—	—	(133)	—	(133)
Exercise of Series B warrants	60,832	—	—	—	—
Stock-based compensation	81,366	—	1,807	—	1,807
Exercise of stock options	24,309	—	27	—	27
Net and comprehensive income	—	—	—	17,888	17,888
Balance at December 31, 2022	20,861,315	2	117,717	(71,480)	46,239
Issuance of common stock in connection with the at-the-market program and purchase agreement	2,964,238	—	10,249	—	10,249
Issuance costs	—	—	(136)	—	(136)
Exercise of Series B warrants	17,869	—	—	—	—
Stock-based compensation	106,600	—	3,510	—	3,510
Exercise of stock options	27,469	—	30	—	30
Net and comprehensive loss	—	—	—	(9,986)	(9,986)
Balance at December 31, 2023	23,977,491	$ 2	$131,370	$(81,466)	$49,906

See accompanying notes.

Ocuphire Pharma, Inc.
Statements of Cash Flows
(in thousands)

	For the Year Ended December 31,	
	2023	2022
Operating activities		
Net (loss) income	$ (9,986)	$17,888
Adjustments to reconcile net (loss) income to net cash (used in) provided by operating activities:		
Stock-based compensation	3,510	1,807
Depreciation	6	4
Fair value change in derivative liabilities	(80)	—
Financing costs	1,328	—
Unrealized loss from short-term investments	34	170
Change in assets and liabilities:		
Accounts receivable	372	(1,298)
Contract assets and unbilled receivables	2,145	(3,552)
Prepaid expenses and other assets	354	(139)
Accounts payable	1,082	(515)
Accrued expenses	123	(51)
Net cash (used in) provided by operating activities	(1,112)	14,314
Investing activities		
Transaction costs in connection with asset acquisition	—	—
Net cash used in investing activities	—	—
Financing activities		
Proceeds from issuance of common stock	9,227	4,428
Issuance costs attributed to common stock	(278)	(131)
Payments made on short-term loan principal	—	(538)
Exercise of stock options and Series B warrants	30	27
Net cash provided by financing activities	8,979	3,786
Net increase in cash and cash equivalents	7,867	18,100
Cash and cash equivalents at beginning of period	42,634	24,534
Cash and cash equivalents at end of period	$50,501	$42,634
Supplemental disclosure of cash flow information:		
Cash paid for income taxes	$ 344	$ —
Cash paid for interest	$ —	$ 9
Supplemental non-cash financing transactions:		
Non-cash issuance of common stock in connection with equity purchase agreement	$ 1,022	$ —
Value of derivative established in connection with the equity purchase agreement	$ 154	$ —
Unpaid issuance costs	$ 10	$ 2

See accompanying notes.

1. Company Description and Summary of Significant Accounting Policies

Nature of Business

Ocuphire Pharma, Inc. (the ''Company'' or ''Ocuphire'') is a clinical-stage biopharmaceutical company focused on developing novel therapies for the treatment of unmet needs of patients with retinal and refractive eye disorders. The Company's headquarters is located in Farmington Hills, Michigan.

The Company's lead retinal product candidate, APX3330, is a small-molecule inhibitor of Ref-1 (reduction oxidation effector factor-1 protein). Ref-1 is a regulator of transcription factors such as HIF-1α and NF-kB. Inhibiting Ref-1 reduces levels of vascular endothelial growth factor (''VEGF'') and inflammatory cytokines which are known to play key roles in ocular angiogenesis and inflammation. APX3330 is an oral tablet administered once or twice per day in development for the treatment of diabetic retinopathy (''DR''). A Phase 2 study in subjects with DR or diabetic macular edema was completed and results were reported in January 2023. An End-of-Phase 2 (''EOP2'') meeting with the U.S. Food and Drug Administration (the ''FDA'') was held in October 2023 at which the Company obtained agreement on the registration endpoint supporting the advancement of APX3330 into future clinical trials. Ocuphire submitted a Special Protocol Assessment (''SPA'') to the FDA in February 2024 to seek agreement on the clinical trial protocol and statistical analysis plan.

The Company has also in-licensed APX2009 and APX2014, which are second-generation analogs of APX3330. The unique mechanism of action of this family of Ref-1 inhibitors of reducing angiogenesis and inflammation could potentially be beneficial in treating other retinal diseases such as age-related macular degeneration, geographic atrophy, and non-ophthalmic diseases.

In November 2022, the Company entered into a license and collaboration agreement (the ''Viatris License Agreement'') with FamyGen Life Sciences, Inc. (''Famy'') (acquired by Viatris, Inc. (''Viatris'') in January 2023) pursuant to which it granted Viatris an exclusive license to develop, manufacture, import, export and commercialize its refractive product candidate Phentolamine Ophthalmic Solution 0.75%, formerly known as Nyxol (''PS''). PS is a once-daily eye drop formulation of phentolamine mesylate designed to reduce pupil diameter and improve visual acuity. PS was approved by the FDA for the treatment for pharmacologically-induced mydriasis under the brand name RYZUMVI in September 2023. The VEGA-2 Phase 3 study in presbyopia achieved its primary endpoint. PS is currently in Phase 3 clinical trials for presbyopia (age-related blurry near vision). On December 5, 2023, the Company received FDA Agreement Under Special Protocol Assessment for LYNX-2, a Phase 3 Trial of PS for the treatment of decreased Visual Acuity under dim (mesopic) light conditions following keratorefractive surgery.

Reverse Merger with Rexahn

On June 17, 2020, Ocuphire, Rexahn Pharmaceuticals, Inc. (''Rexahn'') and Razor Merger Sub, Inc., a Delaware corporation and wholly-owned subsidiary of Rexahn (''Merger Sub''), entered into an Agreement and Plan of Merger and Reorganization, as amended on June 29, 2020 (as amended, the ''Merger Agreement''), pursuant to which, among other things, and subject to the satisfaction or waiver of certain conditions set forth in the Merger Agreement, Merger Sub merged with and into Ocuphire, with Ocuphire continuing as a wholly-owned subsidiary of Rexahn and the surviving corporation of the merger (the ''Merger''). The Merger closed on November 5, 2020. Upon completion of the Merger, Rexahn changed its name to Ocuphire Pharma, Inc. and changed its ticker symbol on the Nasdaq Capital Market (''Nasdaq'') to ''OCUP''.

Basis of Presentation

The accompanying financial statements have been prepared in accordance with accounting standards generally accepted in the United States of America (''GAAP'').

The Company does not have any subsidiaries or other entities that require consolidation for financial statement reporting purposes.

Liquidity

The accompanying financial statements have been prepared on the basis that the Company will continue as a going concern. From its inception, the Company has devoted substantially all of its efforts to drug development and conducting clinical trials.

As of December 31, 2023, the Company had $50.5 million in cash and cash equivalents. The Company believes its current available cash and cash equivalents will be sufficient to fund the Company's planned expenditures and meet its obligations for at least twelve months from the date of issuance of these financial statements.

In the future, the Company may need to raise additional funds until it is able to generate sufficient revenues to fund its development activities. The Company's future operating activities, coupled with its plans to raise capital or issue debt financing, may provide additional liquidity in the future, however these actions are not solely within the control of the Company and the Company is unable to predict the outcome of these actions to generate the liquidity ultimately required.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ from those estimates.

Segment Information

Operating segments are components of an enterprise for which separate financial information is available and is evaluated regularly by the Company's chief operating decision maker in deciding how to allocate resources and assessing performance. The Company's chief operating decision maker is its Chief Executive Officer or such person functioning in such role. The Company's Chief Executive Officer views the Company's operations and manages its business in one operating segment, which is the business of development of products related to vision performance and health. Accordingly, the Company has a single reporting segment.

Cash and Cash Equivalents

The Company considers all highly liquid investments with an original maturity of 90 days or less at the time of deposit to be cash equivalents.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to a concentration of credit risk consist of cash and cash equivalents. Management follows approved policies established by its Board of Directors to reduce credit risk associated with the Company's cash deposit and investment accounts. Pursuant to these policies, the Company limits its exposure through the kind, quality and concentration of its investments. The Company's cash and cash equivalents are held or managed by two financial institutions in the United States. As of December 31, 2023, the Company had cash equivalents of $50.2 million that were not eligible for coverage by Federal Deposit Insurance Corporation (''FDIC''). These balances are invested in funds whose assets consist almost entirely of securities issued by the U.S. Treasury or guaranteed by the U.S. government.

Short-term Investments

The Company determines the appropriate classification of its investments in debt and equity securities at the time of purchase and records them on a settlement date basis. The Company's short-term investments are comprised of equity securities, which in accordance with the fair value hierarchy described below are recorded at fair value using Level l inputs on the balance sheets. Subsequent changes in fair values are recorded in other income (expense), net on the statements of comprehensive (loss) income. The Company classifies investments available to fund current operations as current assets on its balance sheets. The Company did not recognize any impairments on its investments to date through December 31, 2023.

Revenue Recognition

The Company follows the provisions of Accounting Standards Codification (''ASC'') 606, *Revenue from Contracts with Customers*. The guidance provides a five-step model to determine how revenue is recognized. The Company has entered into license agreements which have revenue recognition implications (See Note 9 – License and Collaboration Agreements).

In determining the appropriate amount of revenue to be recognized, the Company performs the following steps: (i) identification of the contracts with a customer; (ii) determination of the performance obligations in the contract; (iii) measurement of the transaction price, including potential constraints on variable consideration; (iv) allocation of the transaction price to the performance obligations based on estimated stand-alone selling prices; and (v) recognition of revenue when (or as) the Company satisfies a performance obligation.

A performance obligation is a promise in a contract to transfer a distinct good or service to the customer and is the unit of account in ASC 606. Performance obligations may include license rights, development and other services. Significant management judgment is required to determine the level of effort required under an arrangement and the period over which the Company expects to complete its performance obligations under the arrangement. If the Company cannot reasonably estimate when its performance obligations are either completed or become inconsequential, then revenue recognition is deferred until the Company can reasonably make such estimates. Revenue is then recognized over the remaining estimated period of performance using the cumulative catch-up method.

As part of the accounting for these arrangements, the Company must develop assumptions that require judgment to determine the stand-alone selling price of each performance obligation identified in the contract. The Company uses key assumptions to determine the stand-alone selling price, which may include forecasted revenues, development timelines, reimbursement rates for personnel costs, discount rates and probabilities of technical and regulatory success. The Company allocates the total transaction price to each performance obligation based on the relative standalone selling prices of the promised goods or service underlying each performance obligation.

Licenses of intellectual property and research and development services: If the license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenues from non-refundable, up-front fees allocated to the license when the license is transferred to the customer, and the customer can use and benefit from the license. For licenses that are bundled with other obligations, such as research and development services, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, up-front fees. For research and development services that are distinct from a license transfer obligation, the Company determines whether the services are satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from such services. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Milestone payments: At the inception of each arrangement that includes milestone payments, the Company evaluates whether the milestones are considered probable of being achieved and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the value of the associated milestone (such as a regulatory submission) is included in the transaction price. Milestone payments that are not within the control of the Company, such as approvals from regulators, are not considered probable of being achieved until such contingency occurs (such as receipt of those approvals).

Royalties: For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (a) when the related sales occur, or (b) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied).

Contract Assets and Unbilled Receivables

The Company recognizes contract assets and unbilled receivables when goods or services are transferred to the customer before the customer pays or before reimbursement for payment is billed or due, excluding any amounts presented as an account receivable. The Company recorded contract assets and unbilled receivables in connection with a license and collaboration agreement (See Note 9 – License and Collaboration Agreements).

Accounts Receivable and Allowances for Credit Losses

The Company records a provision for credit losses, when appropriate, based on historical experience, current conditions and reasonable supportable forecasts. In estimating the allowance for credit losses, the Company

considers, among other factors, the estimate of credit losses over the remaining expected life of the asset, primarily using historical experience and current economic conditions that could affect the collectability of the balances in the future. Account balances are charged off against the allowance when the Company believes that it is probable that the receivable will not be recovered. Actual write-offs may be in excess of the Company's estimated allowance. The Company has not incurred any bad debt expense to date and no allowance for credit losses has been recorded during the periods presented.

General and Administrative Expenses

General and administrative expenses consist primarily of personnel-related costs, including salaries, benefits and stock-based compensation costs, for personnel in functions not directly associated with research and development activities. Other significant costs include insurance coverage for directors and officers and other property and liability exposures, legal fees relating to intellectual property and corporate matters, professional fees for accounting and tax services, other services provided by business consultants and legal settlements.

Research and Development

Research and development expenses consist of costs incurred in performing research and development activities, including compensation, benefits and stock-based compensation costs for research and development employees and costs for consultants, costs associated with nonclinical studies and clinical trials, regulatory activities, manufacturing activities to support clinical activities, license fees, nonlegal patent costs, fees paid to external service providers that conduct certain research and development, and an allocation of overhead expenses. Research and development expenses include costs that are reimbursed under the Viatris License Agreement (See Note 9 – License and Collaboration Agreements).

Financing costs

Financing costs consist of issuance costs attributed to an equity line financing facility with Lincoln Park (See Note 8 – Stockholders' Equity).

Interest Expense

Interest expenses were attributed to interest on principal related to a short-term loan during the period it was outstanding. The short-term loan was fully repaid in May 2022.

Other Income (Expense), net

Other income (expense), net includes interest earned from cash and cash equivalent investments, realized and unrealized gains (losses) from equity investments and reimbursements in connection with grants and other sources when they occur. In addition, this line item includes payments made by the Company in connection with the Contingent Value Rights Agreement discussed further below with former Rexahn shareholders.

Stock-Based Compensation

The Company accounts for stock-based compensation in accordance with the provisions of the Financial Accounting Standards Board (''FASB'') ASC 718, *Compensation — Stock Compensation*. Accordingly, compensation costs related to equity instruments granted are recognized at the grant date fair value. The Company records forfeitures when they occur. Stock-based compensation arrangements to non-employees are accounted for in accordance with the applicable provisions of ASC 718.

Derivative Liability

The Company evaluates all features contained in financing agreements to determine if there are any embedded derivatives that require separation from the underlying agreement under ASC 815 – *Derivatives and Hedging*. An embedded derivative that requires separation is accounted for as a separate liability from the host agreement. The separated embedded derivative is accounted for separately on a fair market value basis. The Company records the fair value changes of a separated embedded derivative at each reporting period in the statements of comprehensive (loss)

income under the fair value change in derivative liability line item. The Company determined that certain features under an equity line financing (See Note 8 — Stockholders' Equity) collectively qualified as an embedded derivative. The derivative was accounted for separately from the underlying equity line financing agreement.

Fair Value Measurements

The Company follows accounting guidance that emphasizes that fair value is a market-based measurement, not an entity-specific measurement. Fair value is defined as ''the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date.'' Fair value measurements are defined on a three-level hierarchy:

- Level 1 inputs: Unadjusted quoted prices for identical assets or liabilities in active markets;
- Level 2 inputs: Quoted prices for similar assets and liabilities in active markets, quoted prices in markets that are not active, or inputs which are observable, whether directly or indirectly, for substantially the full term of the asset or liability; and
- Level 3 inputs: Unobservable inputs in which there is little or no market data available, which requires management to develop its own assumptions in pricing the asset or liability.

As of December 31, 2023 and 2022, the fair values of cash and cash equivalents, accounts receivable, contract assets and unbilled receivables, prepaid and other current assets, accounts payable, and accrued expenses approximated their carrying values because of the short-term nature of these assets or liabilities. The fair value of the short-term investments, while outstanding, were based on observable Level 1 inputs in the form of quoted market prices from a major stock exchange. The fair value of the derivative liability associated with the equity line financing facility (See Note 8 – Stockholders' Equity) was based on cash flow models discounted at current implied market rates representing expected returns by market participants for similar instruments and are based on Level 3 inputs as well the Company's underlying stock price and associated volatility, expected term of the financing and market interest rates. The fair value of the warrant liabilities, while outstanding, were based on a Black-Scholes option model using Level 3 inputs. There were no transfers between fair value hierarchy levels during the years ended December 31, 2023 and 2022.

The fair value of financial instruments measured on a recurring basis is as follows (in thousands):

	As of December 31, 2023			
Description	**Total**	**Level 1**	**Level 2**	**Level 3**
Assets:				
Short-term investments	$15	$15	$—	$—
Total assets at fair value	$15	$15	$—	$—
Liabilities:				
Derivative liability	$74	$—	$—	$74
Total liabilities at fair value	$74	$—	$—	$74

	As of December 31, 2022			
Description	**Total**	**Level 1**	**Level 2**	**Level 3**
Assets:				
Short-term investments	$49	$49	$—	$—
Total assets at fair value	$49	$49	$—	$—

The following table provides a roll-forward of short-term investments and derivative liabilities measured at fair value on a recurring basis using observable Level 1 and Level 3 inputs, as applicable, for the years ended December 31, 2023 and 2022 (in thousands):

	2023	2022
Short-term investments		
Balance as of beginning of period	$ 49	$ 219
Unrealized loss	(34)	(170)
Balance as of end of period	$ 15	$ 49

	2023	2022
Derivative liabilities		
Balance as of beginning of period	$ —	$—
Purchase agreement execution	154	—
Unrealized gain	(80)	—
Balance as of end of period	$ 74	$—

Rexahn Warrants

The fair value of the warrant liabilities associated with the Rexahn warrants was de minimis during the periods presented. The last of the Rexahn warrants classified as liabilities expired in April 2023 unexercised. See Note 2 – Merger for additional background.

There were no financial instruments measured on a non-recurring basis for any of the periods presented.

Recent Accounting Pronouncements

In June 2016, the FASB issued Accounting Standards Update (''ASU'') 2016-13, *Financial Instruments – Credit Losses*. The ASU sets forth a current expected credit loss (CECL) model which requires the Company to measure all expected credit losses for financial instruments held at the reporting date based on historical experience, current conditions, and reasonable supportable forecasts. This replaces the existing incurred loss model and is applicable to the measurement of credit losses on financial assets measured at amortized cost and applies to some off-balance sheet credit exposures. The Company adopted this ASU on January 1, 2023 and it did not have a significant impact on its financial statements.

In August 2020, FASB issued ASU 2020-06, *Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity's Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity's Own Equity*, which, among other things, provides guidance on how to account for contracts on an entity's own equity. This ASU eliminates the beneficial conversion and cash conversion accounting models for convertible instruments. It also amends the accounting for certain contracts in an entity's own equity that are currently accounted for as derivatives because of specific settlement provisions. In addition, this ASU modifies how particular convertible instruments and certain contracts that may be settled in cash or shares impact the diluted earnings per share computation. The amendments in this ASU are effective for public business entities that meet the definition of an SEC filer, excluding entities eligible to be smaller reporting companies as defined by the SEC, for fiscal years beginning after December 15, 2021, including interim periods within those fiscal years. For all other entities, the amendments are effective for fiscal years beginning after December 15, 2023, including interim periods within those fiscal years. The Company adopted this ASU on January 1, 2023 and the adoption did not have a material impact on its financial statements.

In November 2023, the FASB issued ASU 2023-07 - *Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures*, which enhances reportable segment disclosure requirements, primarily through disclosures of significant segment expenses. This ASU is effective for fiscal years beginning after December 15, 2023, including interim periods within those fiscal years, with early adoption permitted. The guidance must be applied retrospectively to all prior periods presented. The Company is currently evaluating the impact of adoption of this guidance on its financial statements.

In December 2023, the FASB issued ASU 2023-09 *Income Taxes (Topic 740): Improvements to Income Tax Disclosures*, which enhances income tax disclosures primarily related to the rate reconciliation and income taxes paid information. This guidance also includes certain other amendments to improve the effectiveness of income tax disclosures. This ASU is effective for fiscal years beginning after December 15, 2024, including interim periods within those fiscal years and should be applied on a prospective basis, with retrospective application permitted. The Company is currently evaluating the impact of adoption of this guidance on its financial statements.

2. Merger

On November 5, 2020, the Company completed the Merger transaction with Rexahn. In connection with the Merger, the Company, Shareholder Representatives Services LLC, as representative of the Rexahn stockholders prior to the Merger, and Olde Monmouth Stock Transfer Co., Inc., as the rights agent, entered into a Contingent Value Rights Agreement (the ''CVR Agreement'').

Pursuant to the terms of the Merger and the CVR Agreement, Rexahn stockholders of record as of immediately prior to the effective time of the Merger received one contingent value right (''CVR'') for each share of Rexahn common stock held.

Each CVR entitles such holders to receive, for each calendar quarter (each, a ''CVR Payment Period'') during the 15-year period after the closing (the ''CVR Term''), an amount equal to the following:

- 90% of all payments received by Rexahn or its affiliates during such CVR Payment Period from or on behalf of BioSense Global LLC (''BioSense'') pursuant to that certain License and Assignment Agreement, dated as of February 25, 2019, by and between BioSense and Rexahn, as amended by Amendment No. 1, dated August 24, 2019, and as further amended by Amendment No. 2, dated March 10, 2020, minus certain permitted deductions;
- 90% of all payments received by Rexahn or its affiliates during such CVR Payment Period from or on behalf of Zhejiang HaiChang Biotechnology Co., Ltd. (''HaiChang'') pursuant to that certain Exclusive License Agreement, dated as of February 8, 2020, by and between HaiChang and Rexahn, minus certain permitted deductions; and
- 75% of the sum of (i) all cash consideration paid by a third party to Rexahn or its affiliates during the applicable CVR Payment Period in connection with the grant, sale or transfer of rights to Rexahn's pre-closing intellectual property (other than a grant, sale or transfer of rights involving a sale or disposition of the post-Merger combined company) that is entered into during the 10-year period after the closing (''Parent IP Deal''), plus (ii) with respect to any non-cash consideration received by Rexahn or its affiliates from a third party during the applicable CVR Payment Period in connection with any Parent IP Deal, all amounts received by Rexahn or its affiliates for such non-cash consideration at the time such non-cash consideration is monetized by Rexahn or its affiliates, minus (iii) certain permitted deductions.

The CVRs are not transferable, except in certain limited circumstances, will not be certificated or evidenced by any instrument, will not accrue interest and will not be registered with the SEC or listed for trading on any exchange. The CVR Agreement will continue in effect until the later of the end of the CVR Term and the payment of all amounts payable thereunder. As of December 31, 2023, no payments subject to the CVR had been received beyond those previously reported in the second and third quarters of calendar year 2021. In addition, no milestones had been accrued as there were no potential milestones yet considered probable beyond those previously reported.

Former Rexahn Warrants

Following the closing of the Merger, 231,433 outstanding, unexercised Rexahn warrants to purchase common stock remained outstanding, the majority of which were subsequently repurchased according to the terms of the original warrant agreements. As of December 31, 2023, 58,597 of the Rexahn warrants remained outstanding with an exercise price of $38.40 per share with an average remaining contractual life of 0.1 years and were accounted for and classified as equity.

3. Commitments and Contingencies

Apexian Sublicense Agreement

On January 21, 2020, the Company entered into a sublicense agreement with Apexian Pharmaceuticals, Inc., pursuant to which it obtained exclusive worldwide patent and other intellectual property rights. In exchange for the patent and other intellectual rights, the Company agreed to certain milestone payments and royalty payments on future sales (See Note 7 — Apexian Sublicense Agreement). As of December 31, 2023, there was sufficient uncertainty with regard to any future cash milestone payments under the sublicense agreement that no liabilities were recorded related to the sublicense agreement.

Facility Leases

The Company has a short-term, non-cancellable facility lease (the ''HQ Lease'') for its headquarters. The HQ Lease qualified for the short-term lease exception under ASC 842, *Leases*. The monthly base rent for the HQ Lease is approximately $3,000. The rent expense associated with the HQ Lease amounted to $36,000 and $39,000 during the years ended December 31, 2023 and 2022, respectively. The total remaining expected rental payments under the HQ Lease amount to $36,000 through its current expiration date of December 31, 2024.

Other

In the ordinary course of business, from time to time, the Company may be subject to a broad range of claims and legal proceedings that relate to contractual allegations, patent infringement and other claims. In addition, the Company from time to time may be potentially committed to reimburse third parties for costs incurred associated with business development related transactions upon the achievement of certain milestones. The Company establishes accruals when applicable for matters and commitments which it believes losses are probable and can be reasonably estimated. To date, no loss contingency for such matters and potential commitments have been recorded. Although it is not possible to predict with certainty the outcome of these matters or potential commitments, the Company is of the opinion that the ultimate resolution of these matters and potential commitments will not have a material adverse effect on its results of operations or financial position.

4. Supplemental Balance Sheet Information

Prepaid and Other Current Assets

Prepaid and other current assets consist of the following (in thousands):

	December 31,	
	2023	2022
Prepaids	$ 997	$1,373
Other	102	80
Total prepaids and other current assets	$1,099	$1,453

Property and Equipment, net

Property and equipment held for use by category are presented in the following table (in thousands):

	December 31,	
	2023	2022
Equipment	$ 20	$ 20
Furniture	5	5
Total property and equipment	25	25
Less accumulated depreciation	(25)	(19)
Property and equipment, net	$ —	$ 6

Depreciation expense was $6,000 and 4,000 during the years ended December 31, 2023 and 2022, respectively.

Accrued Expenses

Accrued expenses consist of the following (in thousands):

	December 31,	
	2023	**2022**
Income taxes	$ —	$ 315
Payroll	753	782
Professional services	591	208
R&D services and supplies	400	212
Other	71	167
Total	$1,815	$1,684

Short-Term Loan

The Company entered into an unsecured short-term loan (the ''Loan'') agreement in the amount of $0.6 million in November 2021 related to financing an insurance policy. The Loan was payable in six monthly installments of $108,000 beginning in December 2021. The Loan had an annual interest rate of 5.5% per annum. Interest expense in the amount of $9,000 was recognized in connection with the Loan during the year ended December 31, 2022. The final payment on the Loan was made in May 2022.

5. Related Party Transactions

On April 8, 2022, Ocuphire entered into a consulting agreement for medical advisory services with Jay Pepose, a director of the Company. The consulting agreement provided for $10,000 a month in cash payments, effective as of April 1, 2022. Additionally, on April 8, 2022, in connection with the consulting arrangement, Dr. Pepose received a stock option grant for 50,000 options, of which 25% vested on March 31, 2023, with the remainder vesting in equal monthly installments over 36 months. The consulting agreement was amended on September 19, 2022 to provide for vesting acceleration for stock-based awards in the event of a change in control. The consulting agreement was also amended effective December 1, 2022 to increase the cash payment to $25,000 per month.

The Company incurred related consulting expenses of $300,000 and $105,000 during the years ended December 31, 2023 and 2022, respectively. As of December 31, 2023 and 2022, $25,000 and $25,000 of the related consulting expenses were unpaid, respectively.

On April 19, 2023, Ocuphire appointed Richard Rodgers, a director of the Company, as interim President and Chief Executive Officer. In connection with his appointment, Ocuphire and Mr. Rodgers entered into a letter agreement concerning Mr. Rodgers's services (the ''Letter Agreement''). The Letter Agreement provided that Mr. Rodgers (i) was to receive a $40,000 monthly salary, and (ii) is eligible for a potential prorated bonus at the discretion of Ocuphire's Board of Directors, at the end of his term as interim President and Chief Executive Officer. Mr. Rodgers also received 50,000 restricted stock units under the Company's 2020 Equity Incentive Plan which will vest 12 months following the grant date. The Company incurred related expenses of $255,000 during the year ended December 31, 2023. As of December 31, 2023, $100,000 of the related expenses were unpaid related to a prorated bonus.

6. Stock-based Compensation

Stock-based compensation expense was included in general and administrative and research and development costs as follows in the accompanying statements of comprehensive (loss) income for the periods indicated below (in thousands):

	December 31,	
	2023	**2022**
General and administrative	$2,435	$1,060
Research and development	1,075	747
Total stock-based compensation	$3,510	$1,807

Inducement Plan

On February 22, 2021, the Company adopted the Ocuphire Pharma, Inc. 2021 Inducement Plan (the ''Inducement Plan'') which was amended on November 1, 2023, pursuant to which the Company reserved 2,325,258 shares of its common stock to be used exclusively for grants of awards to individuals who were not previously employees or directors of the Company, as an inducement material to the individual's entry into employment with the Company within the meaning of Rule 5635(c)(4) of the Nasdaq Listing Rules.

2020 Equity Incentive Plan

In November 2020, the stockholders of the Company approved the 2020 Equity Incentive Plan (the ''2020 Plan'') for stock-based awards. Under the 2020 Plan, (i) 1,000,000 new shares of common stock were reserved for issuance and (ii) up to 70,325 additional shares of common stock may be issued, consisting of (A) shares that remain available for the issuance of awards under prior equity plans and (B) shares of common stock subject to outstanding stock options or other awards covered by prior equity plans that have been cancelled or expire on or after the date that the 2020 Plan became effective. Under the 2020 Plan, the shares reserved automatically increase on January 1 of each year, for a period of not more than ten years from the date the 2020 Plan is approved by the stockholders of the Company, commencing on January 1, 2021 and ending on (and including) January 1, 2030, by an amount equal to 5% of the shares of common stock outstanding as of December 31st of the preceding calendar year. The 2020 Plan permits the grant of incentive and nonstatutory stock options, appreciation rights, restricted stock, restricted stock units, performance stock and cash awards, and other stock-based awards.

2018 Equity Incentive Plan

Prior to the 2020 Plan, the Company had adopted a 2018 Equity Incentive Plan (the ''2018 Plan'') in April 2018 under which 1,175,000 shares of the Company's common stock were reserved for issuance to employees, directors and consultants. Upon the effective date of the 2020 Plan, no additional shares were available for issuance under the 2018 Plan.

Stock Options

During the years ended December 31, 2023 and 2022, 1,768,116 and 893,305 stock options were granted to officers, directors, employees and consultants, respectively, generally vesting over a five (5) to forty-eight (48) month period. The Company recognized $2.5 million and $1.7 million in stock-based compensation expense related to stock options during the years ended December 31, 2023 and 2022, respectively. Stock-based compensation expense during the year ended December 31, 2023 included a one-time charge of $0.4 million attributed to the modification of the Company's former Chief Executive Officer's stock options with respect to their exercisability provisions.

During the years ended December 31, 2023 and 2022, 27,469 and 24,309 stock options were exercised, respectively, with an intrinsic value of $70,000 and $59,000, respectively. The following table summarizes the Company's stock option plan activity:

	Number of Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (years)	Aggregate Intrinsic Value[(1)] (in thousands)
Outstanding at December 31, 2021	2,096,836	$2.97	8.20	$2,795
Granted	893,305	$2.64		
Exercised	(24,309)	$1.09		
Forfeited/Cancelled	(29,788)	$6.21		
Outstanding at December 31, 2022	2,936,044	$2.87	7.82	$3,314
Granted	1,768,116	$3.20		
Exercised	(27,469)	$1.09		
Forfeited/Cancelled	(266,433)	$3.66		

	Number of Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (years)	Aggregate Intrinsic Value[(1)] (in thousands)
Outstanding at December 31, 2023	4,410,258	$2.98	7.81	$2,385
Vested and expected to vest at December 31, 2023	4,410,258	$2.98	7.81	$2,385
Vested and exercisable at December 31, 2023	2,519,673	$2.77	6.72	$ 607

(1) The aggregate intrinsic value is calculated as the difference between the exercise price of the underlying options and the fair value of our common stock as of December 31, 2023 and 2022 of $3.01 and $3.53 per share, respectively.

The weighted average fair value per share of options granted during the years ended December 31, 2023 and 2022 was $2.53 and $2.06, respectively. The Company measures the fair value of stock options with service-based vesting criteria to employees, directors and consultants on the date of grant using the Black-Scholes option pricing model. The Company does not have adequate history to support an internal calculation of volatility and expected term. As such, the Company has used a weighted average volatility considering the volatilities of several guideline companies.

For purposes of identifying similar entities (guideline companies), the Company considered characteristics such as industry, length of trading history, and stage of life cycle. The average expected life of the options was based on the contractual term for agreements that allow for exercise of vested options through the end of the contractual term upon termination of continuous service, and for all other agreements, was based on the mid-point between the vesting date and the end of the contractual term according to the ''simplified method'' as described in Staff Accounting Bulletin 110. The risk-free interest rate is determined by reference to implied yields available from U.S. Treasury securities with a remaining term equal to the expected life assumed at the date of grant. The Company records forfeitures when they occur. The assumed dividend yield was based on the Company's expectation of not paying dividends in the foreseeable future.

The weighted average assumptions used in the Black-Scholes option pricing model are as follows during the years ended December 31, 2023 and 2022:

	2023	2022
Expected stock price volatility	96.0%	97.4%
Expected life of options (years)	6.1	5.8
Expected dividend yield	0%	0%
Risk free interest rate	4.2%	2.3%

During the years ended December 31, 2023 and 2022, 834,818 and 488,621 stock options vested, respectively. The weighted average fair value per share of options vesting during the years ended December 31, 2023 and 2022 was $2.41 and $3.29, respectively. During the years ended December 31, 2023 and 2022, 266,433 and 29,788 stock options were forfeited, respectively.

Restricted Stock Units

During the year ended December 31, 2023, the Company granted an aggregate of 936,156 restricted stock units (''RSUs''), respectively, to certain officers and employees under the 2020 Plan. The weighted average grant date per unit fair value of the RSUs granted during the year ended December 31, 2023 was $3.37. The vesting period of the RSUs range from a six month to four year period with vesting tranches on a quarterly, semi-annual and annual basis, subject to the recipient's continued service on such dates. There were no RSUs granted during the year ended December 31, 2022.

During the year ended December 31, 2023, 33,614 RSUs vested and 100,842 RSUs were forfeited, attributed solely to the departure of the Company's former Chief Executive Officer. The total expense for the year ended December 31, 2023 related to the RSUs was $0.7 million.

A summary of RSU activity is as follows for the year ended December 31, 2023:

	Number of Shares
Non-vested at December 31, 2022	—
Granted	936,156
Forfeited	(100,842)
Vested	(33,614)
Non-vested at December 31, 2023	801,700

Common Stock Issued for Services

The Company granted common stock for services in the amount of 72,986 and 74,396 shares of common stock during the years ended December 31, 2023 and 2022, respectively, with a weighted grant date fair value of $3.77 and $2.04 per share, respectively, to board members during those periods, respectively, who elected to receive their board retainers in the form of stock for services. The stock-based compensation related to these services amounted to $275,000 and $154,000 during the years ended December 31, 2023 and 2022, respectively.

General

Unrecognized stock-based compensation cost was $6.4 million as of December 31, 2023. The unrecognized stock-based compensation cost is expected to be recognized over a weighted average period of 1.8 years. As of December 31, 2023, 1,528,003 shares in the aggregate were available for future issuance under the 2020 Plan and Inducement Plan.

7. Apexian Sublicense Agreement

On January 21, 2020, the Company entered into a sublicense agreement (as amended on June 4, 2020, the ''Apexian Sublicense Agreement'') with Apexian, pursuant to which it obtained exclusive worldwide patent and other intellectual property rights that constitute a Ref-1 Inhibitor program relating to therapeutic applications to treat disorders related to ophthalmic and diabetes mellitus conditions. The lead compound in the Ref-1 Inhibitor program is APX3330, which the Company intends to develop as an oral tablet therapeutic to treat diabetic retinopathy initially, and potentially later to treat diabetic macular edema, geographic atrophy and age-related macular degeneration. In connection with the Apexian Sublicense Agreement, the Company issued a total of 891,422 shares of its common stock to Apexian and to certain affiliates of Apexian in calendar year 2020. As a result of the common stock issued pursuant to the Apexian Sublicense Agreement, Apexian is considered by Ocuphire to be a related party.

The Company also agreed to make one-time milestone payments under the Apexian Sublicense Agreement for each of the first ophthalmic indication and the first diabetes mellitus indication for the development and regulatory milestones, and once for each of several sales milestones. These milestone payments include (i) payments for specified developmental and regulatory milestones (including completion of the first Phase 2 trial and the first Phase 3 pivotal trial in the United States, and filing and achieving regulatory approval from the FDA for the first New Drug Application for a compound) totaling up to $11 million in the aggregate and (ii) payments for specified sales milestones of up to $20 million in the aggregate, which net sales milestone payments are payable once, upon the first achievement of such milestone. Lastly, the Company also agreed to make a royalty payment equal to a single-digit percentage of its net sales of products associated with the covered patents under the Apexian Sublicense Agreement. If it is not terminated pursuant to its terms, the Apexian Sublicense Agreement shall remain in effect until expiration of the last to expire of the covered patents.

None of the milestone or royalty payments, were triggered or deemed probable as of December 31, 2023.

8. Stockholders' Equity

Lincoln Park Purchase Agreement

On August 10, 2023, the Company entered into a common stock purchase agreement with Lincoln Park Capital Fund, LLC (''Lincoln Park'') for an equity line financing (the ''Purchase Agreement''). The Purchase Agreement provides that, subject to the terms and conditions set forth therein, the Company has the sole right, but not the

obligation, to direct Lincoln Park to purchase up to $50 million of shares of the Company's common stock from time to time over the 30-month term of the Purchase Agreement. Concurrently with entering into the Purchase Agreement, the Company also entered into a registration rights agreement with Lincoln Park (the ''Registration Rights Agreement''), pursuant to which the Company agreed to register the resale of the shares of the Company's common stock that have been and may be issued to Lincoln Park under the Purchase Agreement pursuant to a registration statement. Upon the execution of the Purchase Agreement, the Company issued 246,792 shares of the Company's common stock to Lincoln Park with a fair value of $1.0 million as consideration for its commitment to purchase shares of the Company's common stock under the Purchase Agreement which was recorded as a component of financing costs in the accompanying statements of comprehensive (loss) income during the year ended December 31, 2023. Lincoln Park has agreed not to cause or engage in any manner whatsoever in any direct or indirect short selling or hedging of the Company's common stock.

In addition to the commitment shares referenced above, a total of 1,300,000 shares of the Company's common stock were sold under the Purchase Agreement for net proceeds through December 31, 2023 in the amount of $4.5 million. Lastly, the Company incurred issuance costs of $152,000, consisting of investor expense reimbursement and legal costs, during the year ended December 31, 2023 which were recorded as a component of financing costs in the accompanying statements of comprehensive (loss) income during the year ended December 31, 2023. No shares of the Company's common stock were sold under the Purchase Agreement prior to the third quarter of 2023.

Under the Purchase Agreement on any business day selected by the Company, the Company may direct Lincoln Park to purchase up to 50,000 shares of its common stock on such business day (or the purchase date) (a ''Regular Purchase''), provided that the closing sale price of the Company's common stock on Nasdaq on the applicable purchase date is not below $0.25 and subject to other adjustments. A Regular Purchase may be increased to up to (i) 60,000 shares if the closing sale price of the Company's common stock on Nasdaq is not below $5.00 on the applicable purchase date and (ii) 70,000 shares if the closing sale price of the Company's common stock on Nasdaq is not below $7.50 on the applicable purchase date. The Company may direct Lincoln Park to purchase shares in Regular Purchases as often as every business day. The purchase price per share for each such Regular Purchase will be equal to the lesser of:

- the lowest sale price for the Company's common stock on Nasdaq on the purchase date of such shares; and
- the average of the three (3) lowest closing sale prices for the Company's common stock on Nasdaq during the ten (10) consecutive business days prior to the purchase date of such shares.

In addition, the Company may also direct Lincoln Park, on any business day on which the Company has submitted a Regular Purchase notice for the maximum amount allowed for such Regular Purchase, to purchase an additional amount of the Company's common stock (an ''Accelerated Purchase'') of up to the lesser of:

- three (3) times the number of shares purchased pursuant to such Regular Purchase; and
- 30% of the aggregate shares of the Company's common stock traded on Nasdaq during all or, if certain trading volume or market price thresholds specified in the Purchase Agreement are crossed on the applicable Accelerated Purchase date, the portion of the normal trading hours on the applicable Accelerated Purchase date prior to such time that any one of such thresholds is crossed (the ''Accelerated Purchase Measurement Period'').

The purchase price per share for each such Accelerated Purchase will be equal to 96.5% of the lower of:

- the closing sale price of the Company's common stock on Nasdaq on the applicable Accelerated Purchase date; and
- the volume-weighted average price of the Company's common stock on Nasdaq during the applicable Accelerated Purchase Measurement Period on the applicable Accelerated Purchase date.

The Company may also direct Lincoln Park, on any business day on which an Accelerated Purchase has been completed and all of the shares to be purchased thereunder have been delivered to Lincoln Park in accordance with the Purchase Agreement, to purchase an additional amount of the Company's common stock (an ''Additional Accelerated Purchase'') as described in the Purchase Agreement.

The pricing and settlement provisions in the Purchase Agreement result in the recognition of a derivative liability accounted for on a fair value basis under the provisions of ASC 815 - *Derivatives and Hedging*. A Monte Carlo simulation model was used to estimate future stock pricing and purchase activity to determine the fair value of the derivative liability as of the August 10, 2023 commencement date and again as of December 31, 2023. As of August 10, 2023 and December 31, 2023, the inputs used to determine fair value of the derivative liability included the Company's Nasdaq closing stock price of $4.14 and $3.01 per share, respectively, a stock volatility rate of 82.5% and 77.5%, respectively, an expected term of 2.5 years and 2.1 years, respectively, and a risk-free interest rate of 4.6% and 4.2%, respectively. Lastly, the fair value of the derivative liability took into account future purchase decisions based on economic considerations and relevant stock issuance rules/limitations. The fair value change in the derivative liability was recorded in the fair value change in derivative liabilities line item in the accompanying statements of comprehensive (loss) income during the year ended December 31, 2023.

At-The-Market Program

On February 4, 2021, Ocuphire filed a Form S-3 shelf registration under the Securities Act of 1933 which was declared effective by the SEC on February 12, 2021 (the ''2021 Shelf'') under which the Company may offer and sell, from time to time in its sole discretion, securities having an aggregate offering price of up to $125 million. In connection with the 2021 Shelf, on March 11, 2021, Ocuphire entered into a sales agreement with JonesTrading Institutional Services LLC (''JonesTrading'') under which the Company may offer and sell, from time to time at its sole discretion, to or through JonesTrading, acting as agent and/or principal, shares of its common stock having an aggregate offering price of up to $40 million (the ''2021 ATM''). During the years ended December 31, 2023 and 2022, 1,417,446 and 1,848,980 shares of common stock were sold under the ATM for aggregate gross proceeds in the amount of $4.7 million and $4.4 million, respectively, before deducting issuance expenses, including the placement agent's fees, legal and accounting expenses, in the amount of $136,000 and $133,000, respectively. See Note 13 – Subsequent Events.

Registered Direct Offering

On June 4, 2021, the Company entered into a placement agency agreement for a registered direct offering (''RDO'') with A.G.P./Alliance Global Partners (''AGP''). Pursuant to the terms of the placement agency agreement, AGP on June 8, 2021 sold an aggregate of 3,076,923 shares of the Company's common stock and warrants to purchase 1,538,461 shares of the Company's common stock (the ''RDO Warrants'') at an offering price of $4.875 per one share and 0.50 RDO Warrants, for gross proceeds of approximately $15.0 million, before AGP's fees and related offering expenses in the amount of approximately $1.1 million. The proceeds were allocated between the relative fair values of common stock and warrants at the sale date. The purchase agreement contains customary representations, warranties and agreements by the Company, customary conditions to closing, indemnification obligations of the Company, other obligations of the parties and termination provisions. The RDO was made pursuant to the Company's 2021 shelf registration.

The RDO Warrants have an exercise price of $6.09 per share, are exercisable from the initial issuance date of June 8, 2021, and will expire five years following the initial issuance date. As of December 31, 2023, 1,538,461 RDO Warrants were outstanding.

Subject to limited exceptions, a holder of a RDO Warrant will not have the right to exercise any portion of its RDO Warrants if the holder, together with its affiliates, would beneficially own in excess of 4.99% (or, at the election of a holder prior to the date of issuance, 9.99%) of the number of shares of the Company's common stock outstanding immediately after giving effect to such exercise; provided, however, that upon prior notice to the Company, the holder may increase or decrease the beneficial ownership limitation, provided further that in no event shall the beneficial ownership limitation exceed 9.99%.

Pre-Merger Financing

On June 17, 2020, Ocuphire, Rexahn and certain investors entered into a Securities Purchase Agreement, which was amended and restated in its entirety on June 29, 2020 (as amended and restated, the ''Securities Purchase Agreement''). Pursuant to the Securities Purchase Agreement, the investors invested a total of $21.15 million in cash,

including $300,000 invested by five directors of Ocuphire Pharma, Inc., prior to the Merger and one director of Rexahn upon closing of the Merger (the ''Pre-Merger Financing''). The Pre-Merger Financing also included the issuance of Series A Warrants and Series B Warrants discussed further below.

Series A Warrants

The Series A Warrants were issued on November 19, 2020 at an initial exercise price of $4.4795 per share, were immediately exercisable upon issuance and have a term of five years from the date of issuance. The Series A Warrants are exercisable for 5,665,838 shares of common stock in the aggregate (without giving effect to any limitation on exercise contained therein) and were outstanding as of December 31, 2023. The Series A Warrants were accounted for and classified as equity on the accompanying balance sheets.

Series B Warrants

The Series B Warrants had an exercise price of $0.0001, were exercisable upon issuance and would have expired on the day following the later to occur of (i) the Reservation Date (as defined therein) or (ii) the date on which the investor's Series B Warrants would have been exercised in full (without giving effect to any limitation on exercise contained therein). None of the Series B Warrants were outstanding as of December 31, 2023. During the year ended December 31, 2023 and 2022, 17,869 and 60,832 warrants were exercised for shares of common stock, respectively. The Series B Warrants were accounted for and classified as equity on the accompanying balance sheets while outstanding.

9. License and Collaboration Agreements

Viatris License Agreement

On November 6, 2022, the Company entered into the Viatris License Agreement, pursuant to which it granted Viatris (as successor to Famy) an exclusive, perpetual, sub-licensable license to develop, manufacture, import, export and commercialize (i) PS, for treating (a) reversal of mydriasis, (b) night vision disturbances or dim light vision, and (c) presbyopia, and (ii) PS and low dose pilocarpine for treating presbyopia (together, the ''PS Products'') worldwide except for certain countries and jurisdictions in Asia (the ''Viatris Territory''). The Company retains the exclusive right to develop, manufacture, have manufactured, import, export and commercialize the PS Products outside of the Viatris Territory.

Under the terms of the Viatris License Agreement, the Company in partnership with Viatris, will develop the PS Products in the United States. Viatris will reimburse the Company for budgeted costs related to the development of the PS Products through FDA approval. Viatris will be responsible for developing the PS Products in countries and jurisdictions in the Viatris Territory outside of the United States. The parties established a joint steering committee, which oversees and makes decisions regarding the development of the PS Products. The committee is composed of an equal number of representatives of Viatris and Ocuphire. Viatris will commercialize the PS Products in the Viatris Territory for each indication that receives regulatory approval.

Pursuant to the Viatris License Agreement, the Company received a one-time non-refundable cash payment of $35 million in November 2022 for the exclusive, perpetual, sub-licensable license to develop, manufacture, import, export and commercialize the PS Products in the Viatris Territory. In addition, with respect to the PS Products, the Company will be eligible to receive potential additional payments of up to $130 million in the aggregate upon achieving certain specified regulatory or net sales milestones, with the first milestone payment of $10 million to be made following approval by the FDA of PS, for reversal of mydriasis which occurred during the third quarter of 2023. The Company will also receive tiered royalties, starting at low double-digit royalties up to low 20% royalties, based on the aggregate annual net sales of all PS Products in the United States, and will receive low double-digit royalties based on all annual net sales in the Viatris Territory outside of the United States. The royalty payments will continue on a country-by-country basis from the date of the first commercial sale of the first PS Product in a country of the Viatris Territory until December 31, 2040.

Either party may terminate the Viatris License Agreement upon written notice in the case of the other party's material breach (subject to applicable cure periods) or if the other party becomes subject to an insolvency event. In addition, the Company may terminate the agreement in its entirety if Viatris or its affiliates commences an action

challenging the validity, enforceability or scope of any of Ocuphire's patents that are exclusively licensed under the Viatris License Agreement. Additionally, if Viatris determines not to pursue development or commercialization of a PS Product in a country or jurisdiction in the Viatris Territory, Viatris may terminate the license with respect to such PS Product in such country or jurisdiction.

Both Ocuphire and Viatris have agreed to indemnify the other party against certain losses and expenses relating to any breach of the indemnifying party's obligations, representations, warranties or covenants under the Viatris License Agreement.

The Viatris License Agreement was accounted for under the provisions of ASC 606. In accordance with the provisions under ASC 606, the Company identified two distinct performance obligations at the effective date: (1) the license to its intellectual property (''license transfer'') and (2) research and development services.

The aggregate transaction price associated with the Viatris License Agreement, as adjusted for variable consideration subsequent to December 31, 2022, was $40.0 million which comprised the initial license transfer fee of $35.0 million and the $5.0 million payment anticipated under the research and development services that were not subject to cancellation. The transaction price was allocated between performance obligations based on their relative standalone selling price (''SSP''). The performance obligations for research and development services through the non-cancellation period were fully met by the Company as of the first quarter of 2023.

The SSP for the license transfer and for the research and development services was determined to be $ 287.8 million and $5.0 million, respectively. The SSP for the license transfer was determined based on a discounted royalty cash flow approach, taking into consideration assumptions, including projected worldwide net profit for each of the respective programs based on probability assessments, projections based on internal forecasts, industry data, and information from other guideline companies within the same industry and other relevant factors. The SSP for the research and development services was determined using a cost-plus margin approach, based on anticipated expenditure outlays within the first 120-day non-cancellation window. On a relative SSP basis, $39.3 million and $0.7 million of the transaction price was allocated to the license transfer and to the research and development services obligations, respectively.

The Company determined that the licenses transferred represented functional intellectual property. As such, the revenue related to the licenses was recognized at the point in time in which the license/know-how was delivered to Viatris which occurred during the fourth quarter of 2022. The Company determined that revenue related to the research and development services constrained to the 120-day non-cancellation period was to be recognized over time as the services are rendered based on an estimated percentage of completion input model.

Recognition of Revenue

On September 25, 2023, the Company met the $10 million milestone payment requirements attributed to the FDA's approval of PS, for reversal of mydriasis and included the milestone in the revenue recognized during the year ended December 31, 2023. The $10 million milestone payment was previously constrained by the Company with regard to its inclusion in the initial aggregate transaction price associated with the Viatris License Agreement. During the year ended December 31, 2022, the licenses transferred to Viatris represented functional intellectual property. As such, the revenue related to the licenses was recognized at the point in time in which the license/know-how was delivered to Famy which occurred during the fourth quarter of 2022. The Company determined that revenue related to the research and development services was to be recognized over time as the services are rendered based on an estimated percentage of completion input model.

Revenue recognized under the Viatris License Agreement during the years ended December 31, 2023 and 2022 was $19.0 million and $39.8 million, respectively.

Regulatory Milestones under the Viatris License Agreement

The Company has evaluated the regulatory milestones that may be received in connection with the Viatris License Agreement. There is uncertainty that the events to obtain the remaining regulatory milestones (aside from the approval by the FDA of PS, for reversal of mydriasis) will be achieved given the nature of clinical development and the stage of the development of the PS Products. These remaining regulatory milestones will be constrained until it is probable that a significant revenue reversal will not occur.

Sales Milestone and Royalty Payments

Sales milestones and royalties relate predominantly to a license of intellectual property granted to Viatris and are determined by sales or usage-based thresholds. The sales milestones and royalties are accounted for under the royalty recognition constraint and will be accounted for as constrained variable consideration. The Company applies the royalty recognition constraint for each commercial milestone and will not recognize revenue for each until the subsequent sale of a licensed product (achievement of each) occurs.

Each of the remaining regulatory and sales milestone performance obligations (aside from the $10 million milestone payment related to the FDA's approval of PS, for reversal of mydriasis) and the royalty payments were fully constrained as of December 31, 2023 and no revenue was recognized.

A reconciliation of the closing balance of the contract assets and unbilled receivables associated with the Viatris License Agreement is as follows as of December 31, 2023 and 2022 (in thousands):

	2023	2022
Contract Assets and Unbilled Receivables		
Balance as of beginning of period	$ 3,552	$ —
License transfer	—	(35,000)
Revenue recognized	19,049	39,850
Reclassification to accounts receivable related to costs billed under the Viatris License Agreement	(21,194)	(1,298)
Balance as of end of period	$ 1,407	$ 3,552

The remaining amounts in contract assets and unbilled receivables as of December 31, 2023 attributed to the research and development services are expected to be settled during the first quarter of 2024.

BioSense License and Assignment Agreement

On March 10, 2020, prior to the Merger, Rexahn entered into an amendment to its collaboration and license agreement, (as amended, the ''BioSense License and Assignment Agreement'') with BioSense to advance the development and commercialization of RX-3117 for all human uses in the Republic of Singapore, China, Hong Kong, Macau, and Taiwan (the ''BioSense Territory''). Under the terms of the BioSense License and Assignment Agreement, the Company (i) granted BioSense an exclusive license to develop and commercialize pharmaceutical products containing RX-3117 as a single agent for all human uses in the BioSense Territory and (ii) assigned and transferred all of the former Rexahn patents and patent applications related to RX-3117 in the BioSense Territory. The upfront payment consisted of an aggregate of $1,650,000, of which $1,550,000 was paid to Rexahn prior to the Merger and the remaining $100,000 during calendar year 2021.

Under the BioSense License and Assignment Agreement, the Company is eligible to receive additional milestone payments in an aggregate of up to $84,500,000 upon the achievement of development, regulatory and commercial goals and will also be eligible to receive tiered royalties at low double-digit rates on annual net sales in the BioSense Territory. The Company determined that none of the milestone payments under the BioSense License and Assignment Agreement were probable of payment as of December 31, 2023, and as a result, no revenue related to the milestones was recognized as the achievement of events entitling the Company to any milestone payments were highly susceptible to factors outside of the Company's control. Future sales-based royalties related to the exclusive license to develop RX-3117 will be recognized in the period the underlying sales transaction occurs.

Payments received under the BioSense License and Assignment Agreement are subject to the CVR Agreement described in Note 2 – Merger.

Processa License Agreement

On June 16, 2021, the Company entered into a license agreement (the ''Processa License Agreement'') with Processa Pharmaceuticals, Inc. (''Processa''), pursuant to which the Company has agreed to grant Processa an exclusive license to develop, manufacture and commercialize RX-3117 globally, excluding the BioSense Territory.

Processa will make future payments to the Company upon the achievement of certain development and regulatory milestones, which primarily consist of dosing a patient in pivotal trials or having a drug indication approved by a regulatory authority in the United States or another country. In addition, Processa will pay the Company mid-single-digit percentage royalties based on annual sales under the license and will make one-time sales milestone payments based on the achievement during a calendar year of certain thresholds for annual sales. Processa is also required to give the Company 32% of any milestone payments received based on any sub-license agreement Processa may enter into with respect to the Processa License Agreement.The Company determined that none of the milestone payments under the Processa License Agreement were probable of payment as of December 31, 2023, and as a result, no revenue related to the milestones was recognized, as the achievement of events entitling the Company to any milestone payments were highly susceptible to factors outside of the Company's control.

Processa is required to use commercially reasonable efforts, at its sole cost and expense, to conduct development activities in one or more countries, including meeting specific diligence milestones that consist of: (i) first patient administered drug in a clinical trial of a licensed product prior to the three (3) year anniversary of the effective date; and (ii) first patient administered drug in a pivotal clinical trial of a licensed product or first patient administered drug in a clinical trial for a second indication of a licensed product prior to the five (5) year anniversary of the effective date. Either party may terminate the agreement in the event of a material breach of the agreement that has not been cured following written notice and a 120-day opportunity to cure such breach, and Processa may terminate the agreement for any reason upon 120 days prior written notice to Ocuphire.

Future payments received under the Processa License Agreement will be subject to the CVR Agreement described in Note 2 – Merger.

10. Net (loss) income per share

Basic (loss) income per share of common stock is computed by dividing net (loss) income by the weighted average number of shares of common stock outstanding during the period. Diluted earnings or loss per share of common stock is computed similarly to basic loss or earnings per share except the weighted average shares outstanding are increased to include additional shares from the assumed exercise of any common stock equivalents, if dilutive. The Company's warrants, stock options and RSUs, while outstanding, are considered common stock equivalents for this purpose. Diluted earnings is computed utilizing the treasury method for the warrants, stock options and RSUs. Incremental common stock equivalents that were antidilutive were excluded in calculating diluted income per share. For the year ended December 31, 2023, no common stock equivalents were included in the diluted loss per share because such inclusion would be anti-dilutive given the net loss reported for the prior year period.

The following table presents the computation of weighted average common shares considered in the computation of diluted net (loss) income per share:

	2023	2022
Denominator (weighted average shares)		
Basic common shares outstanding	21,589,821	19,931,080
Dilutive stock options	—	589,165
Dilutive warrants	—	76,967
Diluted common shares outstanding	21,589,821	20,597,212

The following potential common shares were not considered in the computation of diluted net (loss) income per share as their effect would have been anti-dilutive for the year end periods presented below:

	2023	2022
Series A, Series B and RDO warrants	7,204,299	7,145,201
Stock options	4,410,258	2,346,879
RSUs	801,700	—
Former Rexahn warrants	58,597	60,713

11. Income Taxes

The effective tax rate for the years ended December 31, 2023 and 2022 was 0.1 percent and 1.7 percent , respectively.

A reconciliation of income tax computed at the statutory federal income tax rate to the provision (benefit) for income taxes included in the accompanying statements of comprehensive (loss) income is as follows for the years ended December 31, 2023 and 2022:

	2023	2022
Income tax (benefit) provision at federal statutory rate	(21.0)%	21.0%
Valuation allowance	23.8	(21.4)
State income tax, net of federal benefit	(4.9)	4.9
Financing contracts	3.2	—
Stock options	1.0	0.4
Research and development	(3.9)	(3.1)
Other	1.9	(0.1)
Effective tax rate	0.1%	1.7%

The components of income tax provision (benefit) consisted of the following for the years ended December 31, 2023 and 2022 (in thousands):

	2023	2022
(Loss) income before income taxes:	$(9,974)	$18,203
Current:		
Federal	$ 2	$ 279
State	10	36
Total current tax provision (benefit)	12	$ 315
Deferred:		
Federal	—	—
State	—	—
Total tax provision (benefit)	$ 12	$ 315

Significant components of the Company's deferred tax assets and liabilities are summarized in the tables below as of December 31, 2023 and 2022 (in thousands):

	2023	2022
Deferred tax assets:		
Federal and state operating loss carryforwards	$ 12,780	$ 13,087
Acquired intangibles	547	547
Deferral of research and development costs	3,794	2,820
Organizational costs	6	7
Other	72	62
Stock-based compensation	1,835	1,152
Research and development credit carryforward	1,107	731
Subtotal	20,141	18,406
Valuation allowance	(20,141)	(17,770)
Total deferred tax assets, net of valuation allowance	—	636
Deferred tax liabilities:		
Deferred revenue	—	(636)
Total deferred tax liabilities	—	(636)
Net deferred tax assets	$ —	$ —

As of December 31, 2023 and 2022, the Company had gross deferred tax assets of approximately $20.1 million and $18.4 million, respectively. Realization of the deferred tax assets is primarily dependent upon future taxable income, if any, the amount and timing of which are uncertain. The Company has cumulative pre-tax losses and faces significant challenges to becoming profitable in the future. Accordingly, the net deferred tax assets have been fully offset by a valuation allowance of $20.1 million and $17.8 million as of December 31, 2023 and 2022, respectively. U.S. net deferred tax assets will continue to require a valuation allowance until the Company can demonstrate their realizability through sustained profitability or another source of income.

As of December 31, 2023 and 2022, the tax effect of the Company's federal net operating loss carryforwards was approximately $ 10.6 million and $10.9 million, respectively. The Company had federal research credit carryforwards as of December 31, 2023 and 2022 of approximately $ 1.1 million and $0.7 million, respectively. The federal net operating loss carryforwards will not expire and the tax credit carryforwards will begin to expire in 2041 if not utilized. As of December 31, 2023 and 2022, the Company had state net operating loss carryforwards with a tax effect of approximately $ 2.1 million and $2.2 million, respectively. The Company did not have any state research credit carryforwards as of December 31, 2023 and 2022. The state net operating loss carryforwards will begin to expire in 2028.

During the year ended December 31, 2023, the Company utilized federal and state net operating tax carryforwards with a tax effect in the amount of $0.2 million and $0.1 million, respectively, to offset taxable income. In addition, the Company also utilized its federal research credit carryforwards in the amount of $26,000 to partially offset its tax liability for the year ended December 31, 2023.

During the year ended December 31, 2022, the Company utilized federal and state net operating tax carryforwards with a tax effect in the amount of $4.8 million and $1.4 million, respectively, to offset taxable income. In addition, the Company also utilized its federal research credit carryforwards in the amount of $0.9 million to partially offset its tax liability for the year ended December 31, 2022.

Utilization of the net operating loss carryforwards and credits may be subject to a substantial annual limitation due to the ownership change limitations provided by Section 382 and Section 383 of the Internal Revenue Code of 1986, as amended, and similar state provisions. Generally, in addition to certain entity reorganizations, the limitation applies when one or more ''5-percent shareholders'' increase their ownership, in the aggregate, by more than 50 percentage points over a 3 year testing period, or beginning the day after the most recent ownership change, if shorter. The annual limitation may result in the expiration of net operating losses and credits before utilization. As a result of the Merger, the Company recorded deferred tax assets of $10.3 million relating to net operating loss carryforwards which were fully offset by a valuation allowance. The $10.3 million net deferred tax assets recorded in relation to the Merger did not include federal and state net operating loss carryforwards that were estimated to expire under Internal Revenue Code Sections 382 as a result of the Merger. The Company has not yet evaluated the impact of Section 382 and Section 383 on its remaining tax attributes that were generated by Ocuphire since the formation of the Company in 2018.

The Company recognizes interest and/or penalties related to uncertain tax positions in income tax expense. In accordance with ASC 740*, Income Taxes*, specifically related to uncertain tax positions, a Company is required to use a recognition threshold and a measurement attribute for the financial statement recognition and measurement of tax positions taken or expected to be taken in a tax return. For those benefits to be recognized, a tax position must be more likely than not to be sustained upon examination by taxing authorities. The Company believes its income tax filing positions and deductions will be sustained upon examination, and accordingly, no reserves or related accruals for interest and penalties have been recorded at December 31, 2023 and 2022.

The Company's corporate returns are subject to examination beginning with the 2019 tax year for federal income tax purposes and 2018 for state income tax purposes.

12. Deferred Compensation Plan

Effective October 1, 2021, the Company began offering a 401(k) plan (''401K Plan'') to its employees. All employees are eligible to participate in the 401K Plan. The Company makes matching contributions equal to 100% on the first 3% of compensation that is deferred as an elective deferral and an additional 50% on the next 2% of compensation. The Company's matching contributions are made on a monthly basis. During the years ended December 31, 2023 and 2022, the Company contributed $99,000 and $76,000 to the 401K Plan, respectively.

13. Subsequent Events

Under the 2020 Plan, the shares reserved automatically increase on January 1 of each year, for a period of not more than ten years from the date the 2020 Plan is approved by the stockholders of the Company, commencing on January 1, 2021 and ending on (and including) January 1, 2030, by an amount equal to 5% of the shares of common stock outstanding as of December 31 of the preceding calendar year. Notwithstanding the foregoing, the Board of Directors may act prior to January 1 of a given year to provide that there will be no January 1 increase in the share reserve for such year or that the increase in the share reserve for such year will be a lesser number of shares of common stock than would otherwise occur pursuant to the preceding sentence. On January 1, 2024, 1,198,875 shares were added to the 2020 Plan as a result of the evergreen provision.

On February 12, 2024, the Company issued a total of 435,000 stock options and 215,000 restricted stock units under the Inducement Plan to its newly appointed Chief Financial and Chief Scientific and Development Officers. The option awards have an exercise price of $2.66 per share. The options vest over a period of four years, with 25% vesting one year after the date of grant and the remaining 75% vesting in equal quarterly installments thereafter, and the RSUs vest in four equal installments on the first, second, third and fourth anniversary of the grant date of February 12, 2024

On January 10, 2024, the Company filed a Form S-3 shelf registration under the Securities Act which was declared effective by the SEC on January 23, 2024 under which the Company may offer and sell, from time to time in its sole discretion, securities having an aggregate offering price up to $175 million.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

OCUPHIRE PHARMA, INC.

Dated: March 8, 2024

By: /s/ George Magrath
George Magrath
Chief Executive Officer and Director

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

By /s/ George Magrath — Date: March 8, 2024
George Magrath
Chief Executive Officer and Director (Principal Executive Officer)

By /s/ Nirav Jhaveri — Date: March 8, 2024
Nirav Jhaveri
Chief Financial Officer (Principal Financial Officer)

By /s/ Amy Rabourn — Date: March 8, 2024
Amy Rabourn
Senior Vice President of Finance (Principal Accounting Officer)

By /s/ Sean Ainsworth — Date: March 8, 2024
Sean Ainsworth
Director

By /s/ James S. Manuso — Date: March 8, 2024
James S. Manuso
Director

By /s/ Cam Gallagher — Date: March 8, 2024
Cam Gallagher
Director

By /s/ Jay Pepose — Date: March 8, 2024
Jay Pepose
Director

By /s/ Richard J. Rodgers — Date: March 8, 2024
Richard J. Rodgers
Director

By /s/ Susan K. Benton — Date: March 8, 2024
Susan K. Benton
Director