Filed Pursuant to Rule 424(b)(5)
Registration No. 333-276462

PROSPECTUS SUPPLEMENT
(to Prospectus dated January 23, 2024)

12,219,736 Shares of Common Stock
Warrants to Purchase up to 21,052,631 Shares of Common Stock
Pre-Funded Warrants to Purchase 8,832,895 Shares of Common Stock
Up to 29,885,526 Shares of Common Stock underlying the Warrants and Pre-Funded Warrants

We are offering 12,219,736 shares of our common stock and warrants to purchase up to 21,052,631 shares of our common stock (the "Warrants") pursuant to this prospectus supplement and the accompanying prospectus. Each share of our common stock is being sold together with a Warrant to purchase one share of our common stock. The shares of our common stock and Warrants are immediately separable and will be issued separately, but will be purchased together in this offering. The public offering price for each share of our common stock and related Warrant is $0.9500. Each Warrant will be exercisable immediately at an exercise price of $0.9500 per share and will be exercisable immediately upon issuance and will expire on the five year anniversary of the date of issuance. The holder of the Warrant may, at their sole discretion, exercise each of their Warrants for one Pre-Funded Warrant at an exercise price of $0.9499 (which is the per share exercise price minus $0.0001).

We are also offering 8,832,895 Pre-Funded Warrants (as defined below) to certain purchasers, whose purchase of common stock and Warrants in this offering would otherwise result in the purchaser, together with its affiliates and related parties, beneficially owning more than 4.99% of our outstanding common stock immediately following the consummation of this offering, the opportunity to purchase, if they so choose pre-funded warrants ("Pre-Funded Warrants") in lieu of the common stock and Warrants that would otherwise result in ownership in excess of 4.99% (or, at the election of the purchaser, 9.99%) of our outstanding common stock. The public offering price for each Pre-Funded Warrant will equal the price per share minus $0.0001, and the exercise price of each Pre-Funded Warrant will be $0.0001 per share of our common stock. The Pre-Funded Warrants offered hereby will be immediately exercisable and may be exercised at any time until exercised in full.

For each Pre-Funded Warrant we sell, the number of shares of common stock we are offering will be decreased on a one-for-one basis. Because we will issue a Warrant with the issuance of each share of common stock or Pre-Funded Warrant, the number of Warrants sold in this offering will not change as a result of a change in the mix of the shares of common stock and Pre-Funded Warrants sold.

We are also offering the shares of our common stock that are issuable from time to time upon exercise of the Warrants and the Pre-Funded Warrants.

We refer to the shares of our common stock, the Warrants, the Pre-Funded Warrants and the shares of our common stock issued or issuable upon exercise of the Warrants and Pre-Funded Warrants, collectively, as the "Securities."

In a concurrent private placement, we are also selling to George Magrath, MD, MBA, MS, our Chief Executive Officer, a total of 392,157 shares of common stock and 392,157 warrants to purchase shares of common stock, at an offering price of $1.275, and to Cam Gallagher, MBA, the chairman of our board of directors, 784,314 shares of common stock and 784,314 warrants to purchase shares of common stock, at an offering price of $1.275. The warrants will be exercisable immediately upon issuance at an initial exercise price of $1.15, expire on the five-year anniversary of the original issuance date and may be called by the Company 30 days following the release of the Company's OPGx-BEST1 DUO-1001 Cohort 1 data upon achievement of a volume weighted average price of our common stock for 30 consecutive trading days of over $1.725 per share and the trading average daily volume for such 30 day period exceeds $150,000 per trading day. The shares of common stock and warrants, along with the shares underlying such warrants, being offered in the private placement are not being registered under the Securities Act of 1933, as amended (the "Securities Act") or applicable state securities laws, are not being offered pursuant to this prospectus supplement and the accompanying prospectus and are being offered pursuant to the exemption provided under Section 4(a)(2) of the Securities Act, and/or Regulation D promulgated thereunderin.

Our common stock is listed on the Nasdaq Capital Market ("Nasdaq") under the symbol "IRD". The last reported sale price of our common stock on Nasdaq on March 19, 2025 was $1.15 per share. There is no established trading market for the Warrants or the Pre-Funded Warrants, and we do not expect a market to develop. We do not intend to apply to list the Warrants or the Pre-Funded Warrants on any securities exchange or other nationally recognized trading system. Without an active trading market, the liquidity of the Warrants and the Pre-Funded Warrants will be limited.

We are a "smaller reporting company" as defined under federal securities laws and as such, have elected to comply with reduced public company reporting requirements. See "Prospectus Supplement Summary — Implications of Being a Smaller Reporting Company."

Investing in our common stock involves significant risks that are described in the "Risk Factors" section beginning on page S-53 of this prospectus supplement and page 7 of the accompanying prospectus, and in the other documents that are incorporated by reference herein. You should read the entire prospectus supplement and the accompanying prospectus, including any information incorporated by reference herein or therein, carefully before you make your investment decision.

	Per Share and Related Warrant	Per Share and Related Pre-Funded Warrant	Total
Public offering price	$0.9500	$0.9499	$19,999,999.45
Underwriting discounts and commissions(1)	$0.0570	$0.0570	$ 1,199,999.97
Proceeds, before expenses, to us(2)	$0.8930	$0.8929	$18,799,169.48

(1) Includes an underwriting discount of 6.0% on the public offering price. See the section titled "Underwriting" beginning on page S-107 of this prospectus supplement for a description of the compensation payable to the underwriter.

(2) The amount of offering proceeds to us presented in this table does not give effect to the exercise, if any, of the Warrants or the Pre-Funded Warrants being issued in connection with this offering.

Neither the Securities and Exchange Commission ("SEC") nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus supplement or the accompanying base prospectus. Any representation to the contrary is a criminal offense.

The underwriter expects to deliver the shares of common stock, Warrants and Pre-Funded Warrants against payment therefor on or about March 24, 2025.

Sole Managing Underwriter

Craig-Hallum

Prospectus supplement dated March 21, 2025

TABLE OF CONTENTS

PROSPECTUS SUPPLEMENT

PROSPECTUS

ABOUT THIS PROSPECTUS SUPPLEMENT

This document is part of a "shelf" registration statement on Form S-3 (File No. 333-276462) that we filed with the SEC on January 10, 2024 and was declared effective on January 23, 2024 and is in two parts. The first part is this prospectus supplement, which describes the specific terms of the offering being made pursuant to this prospectus supplement, and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part, the accompanying prospectus dated January 23, 2024, including the documents incorporated by reference therein, provides more general information, some of which may not apply to this offering. Generally, when we refer to this "prospectus," we are referring to both parts of this document combined.

Before you invest, you should carefully read this prospectus supplement, the accompanying prospectus, all information incorporated by reference herein and therein, and the additional information described under "*Where You Can Find More Information*" and "*Incorporation of Certain Information by Reference*." These documents contain information you should consider when making your investment decision. To the extent that any statement that we make in this prospectus supplement and/or the accompanying prospectus is inconsistent with statements made in the accompanying prospectus or in any documents incorporated by reference, the statements made in this prospectus supplement will be deemed to modify or supersede those made in the accompanying prospectus or such documents incorporated by reference, as applicable; however, if any statement in one of these documents is inconsistent with a statement in another document having a later date and that is incorporated by reference herein, the statement in the document having the later date modifies or supersedes the earlier statement.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to the registration statement to which the accompanying prospectus forms a part or to any document that is incorporated by reference in this prospectus supplement or the accompanying prospectus were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

You should rely only on the information contained or incorporated by reference in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference herein and in any free writing prospectus we provide you. Neither we nor the underwriter have authorized anyone to provide you with different or additional information. If anyone provides you with different or inconsistent information, you should not rely on it. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference herein and in any free writing prospectus we provide you is accurate only as of the date on those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement, the accompanying prospectus, including the documents incorporated by reference herein, when making your investment decision. You should also read and consider the information in the documents we have referred you to in the sections of this prospectus supplement and the accompanying prospectus entitled "*Where You Can Find More Information*" and "*Incorporation of Certain Information by Reference*."

The distribution of this prospectus supplement and the accompanying prospectus and the offering of the Securities in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement and the accompanying prospectus must inform themselves about, and observe any restrictions relating to, the offering of the Securities and the distribution of this prospectus supplement and the accompanying prospectus outside the United States. This prospectus supplement and the accompanying prospectus does not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any Securities offered by this prospectus supplement and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

Unless the context otherwise indicates references in this prospectus supplement to the "Company," "Opus," "we," "us," "our" and similar terms refer to Opus Genetics, Inc. (formerly known as Ocuphire Pharma, Inc.) and its subsidiaries.

This prospectus supplement and the information incorporated herein or therein by reference include trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included or incorporated by reference in this prospectus supplement are the property of their respective owners.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus, and the other documents we have filed with the SEC that are incorporated by reference herein contain "forward-looking statements" within the meaning of the U.S. Private Securities Litigation Reform Act of 1995 and releases issued by the SEC and within the meaning 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"), which statements involve risks and uncertainties. All statements, other than statements of historical facts, contained in this prospectus supplement, the accompanying prospectus and the other documents we have filed with the SEC that are incorporated by reference herein, including statements regarding our strategy, future operations, future financial position, projected costs, prospects, plans and objectives of management, may be deemed to be forward-looking statements.

Words such as, but not limited to, "anticipate," "aim," "believe," "contemplate," "continue," "could," "design," "estimate," "expect," "intend," "may," "might," "ongoing," "plan," "possible," "potential," "predict," "project," "seek," "should," "suggest," "strategy," "target," "will," "would," and similar expressions or phrases, or the negative of those expressions or phrases, are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. The forward-looking statements included herein represent management's current judgment and expectations, but our actual results, events and performance could differ materially from those in the forward- looking statements. We undertake no obligation to revise any forward-looking statements in order to reflect events or circumstances that might subsequently arise. You should not place undue reliance on forward looking statements. The cautionary statements set forth in this prospectus supplement, including in "Risk Factors" and elsewhere, identify important factors which you should consider in evaluating our forward-looking statements. These factors include, among other things:

- failure to successfully integrate our businesses with Former Opus (as defined below);
- the impact the Opus Acquisition (as defined below) has on the value of our common stock;
- the success and timing of regulatory submissions and pre-clinical and clinical trials, including enrollment and data readouts;
- regulatory requirements or developments, including potential changes to third-party reimbursement practices;
- changes to or unanticipated events in connection with clinical trial designs and regulatory pathways;
- delays or difficulties in the enrollment of patients in clinical trials;
- substantial competition, including from generic versions of our product candidates;
- rapid technological change;
- our development of sales, marketing and distribution infrastructure and drug research and discovery capabilities;
- future revenue losses and profitability;
- compliance with health and safety laws and regulations;
- changes in capital resource requirements;
- risks related to our inability to obtain sufficient additional capital to continue to advance our product candidates and preclinical programs;
- domestic and worldwide legislative, regulatory, political and economic developments;
- our dependency on key personnel;
- changes in market opportunities and acceptance;
- reliance on third parties to conduct our clinical trials and supply and manufacture drug supplies;
- future, potential product liability and securities litigation;
- our current focus on the cash-pay utilization for future sales of RYZUMVI;

- system failures, unplanned events, or cyber incidents;
- risks that our licensing or partnership arrangements may not facilitate the commercialization or market acceptance of our product candidates;
- establishing and maintaining licensing or partnership arrangements and/or strategic alliances;
- risks that our product candidates do not receive domestic and/or foreign marketing approval;
- future fluctuations in the market price of our common stock and dilutive risks associated with our common stock
- actions by activist stockholders;
- the success and timing of commercialization of any of our product candidates;
- obtaining and maintaining our intellectual property rights;
- potential lawsuits relating to our intellectual property rights;
- the success of mergers and acquisitions;
- other risks and uncertainties, including those listed under the captain "Risk Factors" in this prospectus supplement; and
- our expected use of the proceeds from this offering.

Although we believe that we have a reasonable basis for each forward-looking statement contained in this prospectus supplement, the accompanying prospectus, and the other documents we have filed with the SEC that are incorporated by reference herein, we caution you that these statements are based on our projections of the future that are subject to known and unknown risks and uncertainties and other factors that may cause our actual results, level of activity, performance or achievements expressed or implied by these forward-looking statements, to differ. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. All forward-looking statements are qualified in their entirety by this cautionary statement. Forward-looking statements should be regarded solely as our current plans, estimates and beliefs. We have included important factors in the cautionary statements included in this prospectus supplement, the accompanying prospectus, and the other document documents we have filed with the SEC that are incorporated by reference herein, particularly in the section entitled "Risk Factors," beginning on page S-53 of this prospectus supplement, which we believe could cause our actual results to be materially different from the plans, intentions and expectations disclosed in the forward-looking statements we make. Moreover, we operate in a very competitive and rapidly changing environment and new risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make.

Any forward-looking statement speaks only as of the date on which that statement is made. We assume no obligation to update any forward-looking statements to reflect events or circumstances after the date of this prospectus supplement, except as may otherwise be required by the federal securities laws.

You should read this prospectus supplement, the accompanying prospectus, documents we have filed with the SEC that are incorporated by reference herein and therein and any free writing prospectus we provide you completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in the foregoing documents by these cautionary statements.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights certain information about us, this offering and selected information contained elsewhere in or incorporated by reference into this prospectus supplement and the accompanying prospectus. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in our Securities. For a more complete understanding of our company and this offering, we encourage you to read and consider carefully the more detailed information in this prospectus supplement and the accompanying prospectus, including the information incorporated by reference into this prospectus supplement and the accompanying prospectus, and the information referred to under the heading "Risk Factors" in this prospectus supplement on page S-53 and in the documents incorporated by reference into this prospectus supplement and the accompanying prospectus.

Overview

Opus Genetics, Inc. (the "Company," "Opus," "we," "us," or "our") is a clinical-stage ophthalmic biotechnology company developing gene therapies for the treatment of inherited retinal diseases ("IRDs") and other types of therapies for additional ophthalmic disorders.

Opus was founded in February 2018 as Ocuphire Pharma, Inc. and has since undergone several transactions:

- In April 2018, Ocuphire Pharma, Inc. merged with Ocularis Pharma, LLC, the original innovator of phentolamine mesylate ophthalmic solution.
- In January 2020, Ocuphire Pharma, Inc. obtained from Apexian Pharmaceuticals, Inc. certain rights to its Ref-1 inhibitor program, including APX3330.
- In November 2020, Ocuphire Pharma, Inc. completed a reverse merger into Rexahn Pharmaceuticals, Inc. ("Rexahn"), a publicly traded company that had ceased its business of drug development activities, and simultaneously raised $21.2 million through an offering of common shares and warrants to purchase common shares. The combined company continued to operate under the name of Ocuphire Pharma, Inc.
- On October 22, 2024, Ocuphire Pharma, Inc. acquired a private corporation then operating under the name of "Opus Genetics Inc." ("Private Opus") pursuant to the terms of an Agreement and Plan of Merger, dated as of October 22, 2024 (such agreement, the "Merger Agreement" and the transaction consummated via the Merger Agreement, the "Opus Acquisition"), by and among the Company, Private Opus, and certain merger subsidiaries party thereto.

Our expanded pipeline in the wake of the Opus Acquisition includes assets from the adeno-associated virus ("AAV") based gene therapy portfolio of Private Opus that address mutations in genes that cause different forms of Leber congenital amaurosis ("LCA"), bestrophinopathy, and retinitis pigmentosa.

Our most advanced gene therapy program is designed to address mutations in the LCA5 gene ("LCA5"), which encodes the lebercilin protein. More specifically, we are developing OPGx-LCA5 to treat LCA5-associated IRD, an early-onset retinal degeneration, and an open-label, dose-escalation Phase 1/2 clinical trial is ongoing. The trial has shown clinical proof-of-concept—one-year data has provided evidence that the therapy supported visual improvement in three out of three adult patients participating in the trial, each of whom has late-stage disease. Enrollment of the first pediatric patient in the LCA5 Phase 1/2 trial occurred in the first quarter of 2025, with the first data anticipated in the third quarter of 2025. Successful completion of a registrational trial would position Opus to potentially submit a Biologic License Application (BLA) for OPGx-LCA5 as early as 2027.

OPGx-BEST1 is another gene therapy candidate in our portfolio, which Private Opus acquired from Iveric Bio, a biopharmaceutical company focused on the discovery and development of novel treatments for retinal diseases, in late 2022. This asset is being developed for the treatment of IRDs associated with mutations in the BEST1 gene ("Best Disease"), which can lead to legal blindness. In preclinical studies conducted in a naturally occurring canine model of Best Disease, OPGx-BEST1 provided evidence in support of a first-in-man clinical trial. We aim to obtain preliminary data for a Phase 1/2 clinical study by the first quarter of 2026.

Apart from gene therapies, our pipeline also includes Phentolamine Ophthalmic Solution 0.75%, a non-selective alpha-1 and alpha-2 adrenergic antagonist to reduce pupil size, which is currently being evaluated in two Phase 3 trials for the treatment of presbyopia and dim (mesopic) light vision disturbances, as well as APX3330, a novel small-molecule inhibitor of Ref-1 designed to slow the progression of non-proliferative diabetic retinopathy ("NPDR").

Recent Developments

Patent Infringement Lawsuit

On March 14, 2025, in collaboration with our commercialization partner FamyGen Life Sciences, Inc., we filed a complaint for patent infringement of certain RYZUMVI patents against Sandoz Inc. ("Sandoz") in the District of New Jersey in response to Sandoz's Abbreviated New Drug Application filing seeking approval to manufacture, use or sell a generic version of RYZUMVI in the U.S. prior to expiration of the RYZUMVI patents. The complaint seeks, among other relief, equitable relief enjoining Sandoz from infringing the RYZUMVI patents. The Company intends to vigorously enforce its intellectual property rights relating to RYZUMVI.

FDA Type D Meeting

On March 3, 2025, the Company held a constructive Type D meeting with the U.S. Food and Drug Administration (FDA) regarding OPGx LCA5. The FDA meeting was held to discuss the potential regulatory path for OPGx LCA5, including the design of a potential registrational study. Opus proposed a single arm, adaptive design Phase 1/2/3 study, to enroll approximately 19 patients, with a primary endpoint utilizing the multi-luminance orientation and mobility test (MLoMT), which is a functional vision and patient mobility test. The company also received constructive feedback on its proposed statistical analysis plan (SAP) as well as chemistry, manufacturing, and controls (CMC). The FDA requested additional information on these topics, and Opus plans to submit further materials in the second quarter of 2025.

Activist Stockholder Matter

On February 2, 2025, Mina Sooch, our former Chief Executive Officer, submitted a Notice of Stockholder Nomination of Individuals for Election as Directors at the 2025 Annual Meeting of Stockholders to the Company, indicating her intent to nominate a control slate of seven candidates for election to the Board at the 2025 annual meeting of stockholders (the "Annual Meeting"): Michael Burrows, Carolyn Cassin, Martin Dober, Mark H. Ravich, Ms. Sooch, Vitalie Stelea and John R. Weber (the "Sooch Nominees"). On March 3, 2025, Ms. Sooch sent a letter to the Company, notifying the Company of the withdrawal of the nomination of Vitalie Stelea. Additional information regarding the Annual Meeting can be found in our preliminary proxy statement for the Annual Meeting, which was filed on March 20, 2025 with the SEC (as may be subsequently amended by our definitive proxy statement for the Annual Meeting).

Preliminary Results for the Fiscal Year ended December 31, 2024

Preliminary unaudited consolidated operating results for the year ended December 31, 2024 and certain preliminary financial condition information as of December 31, 2024 are as follows:

- Net loss for the year ended December 31, 2024 is expected to be approximately $56.8 million.
- Net cash used in operating activities for the year ended December 31, 2024 was approximately $25.6 million.
- As of December 31, 2024 we had approximately $30.3 million in cash and cash equivalents.

The information above is based on preliminary unaudited information and estimates for the year ended December 31, 2024, is not a comprehensive statement of our financial results for this period, and is subject to change pending completion of our financial closing procedures, final adjustments, completion of the audit of our financial statements and other developments that may arise between now and the time the audit of our financial statements is completed. This preliminary estimate may change. Our expectation with respect to our cash and cash equivalents at December 31, 2024, is based upon management estimates and is the responsibility of management. In addition, Ernst & Young LLP, our independent registered public accounting firm, has not

completed its audit procedures with respect to this preliminary financial information and does not express an opinion or any other form of assurance with respect to this preliminary financial information. During the course of the preparation of our financial statements and related notes as of and for the year ended December 31, 2024, we may identify items that would require us to make material adjustments to this preliminary financial information. As a result, prospective investors should exercise caution in relying on this information and should not draw any inferences from this information. This preliminary financial information should not be viewed as a substitute for full financial statements prepared in accordance with United States generally accepted accounting principles and audited by our auditors.

Corporate Information

Our principal executive offices are located at 8 Davis Drive, Suite 220, Durham, NC 27709. Our telephone number is (248) 957-9024. Our website address is www.opusgtx.com. Additionally, our filings with the SEC are posted on our website at www.opusgtx.com. The information found on or accessible through our website is not part of this or any other report we file with or furnish to the SEC. The public can also obtain copies of these filings by accessing the SEC's website at http://www.sec.gov.

Implications of Being a Smaller Reporting Company

We are a "smaller reporting company" as defined in the Exchange Act. We may take advantage of certain of the scaled disclosures available to smaller reporting companies and will be able to take advantage of these scaled disclosures for so long as our voting and non-voting common stock held by non-affiliates is less than $250.0 million measured on the last business day of our second fiscal quarter, or our annual revenue is less than $100.0 million during the most recently completed fiscal year and our voting and non-voting common stock held by non-affiliates is less than $700.0 million measured on the last business day of our second fiscal quarter.

THE OFFERING

Common stock offered by us	12,219,736 shares of common stock. Each share of our common stock is being sold together with a Warrant to purchase one share of our common stock. The shares of our common stock and Warrants are immediately separable and will be issued separately, but will be purchased together in this offering.
Warrants offered by us	Warrants to purchase up to 21,052,631 shares of our common stock. Each Warrant will have an exercise price of $0.9500 per share of common stock and will be immediately exercisable upon issuance and expire on the fifth anniversary of the date of issuance. The holder of the Warrant may, at their sole discretion, exercise each of their Warrants for one Pre-Funded Warrant at an exercise price of $0.9499 (which is the per share exercise price minus $0.0001). We are also offering the shares of our common stock that are issuable from time to time upon exercise of the Warrants. The exercise price of the Warrants and the number of shares into which the Warrants may be exercised are subject to adjustment in certain circumstances. See "*Description of the Securities We Are Offering*" on page S-102 of this prospectus supplement.
Pre-Funded Warrants offered by us	We are also offering 8,832,895 Pre-Funded Warrants to purchase one share of our common stock to certain purchasers, whose purchase of common stock and the related Warrant in this offering would otherwise result in the purchaser, together with its affiliates and related parties, beneficially owning more than 4.99% of our outstanding common stock immediately following the consummation of this offering. Each Pre-Funded Warrant will be immediately exercisable upon issuance an exercise price of $0.0001 per share of our common stock and may be exercised at any time until exercised in full. We are also offering the shares of our common stock that are issuable from time to time upon exercise of the Pre-Funded Warrants. The exercise price of the Pre-Funded Warrants and the number of shares into which the Pre-Funded Warrants may be exercised are subject to adjustment in certain circumstances. See "*Description of the Securities We Are Offering*" on page S-102 of this prospectus supplement.
Concurrent Private Placement	In a concurrent private placement, we are also selling to George Magrath, MD, MBA, MS, our Chief Executive Officer, a total of 392,157 shares of common stock and 392,157 warrants to purchase shares of common stock, at an offering price of $1.275, and to Cam Gallagher, MBA, the chairman of our board of directors, 784,314 shares of common stock and 784,314 warrants to purchase shares of common stock, at an offering price of $1.275.

Common stock outstanding immediately prior to this offering and the concurrent private placement	31,568,457
Common stock to be outstanding immediately after this offering and the concurrent private placement	44,964,664 shares of common stock (assuming no exercise of any Warrants or Pre-Funded Warrants issued in this offering)
Use of proceeds	We estimate that the net proceeds to us from this offering, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, will be approximately $18,684,999.48 (excluding any proceeds that may be received upon the cash exercise of the Warrants and the Pre-Funded Warrants issued in this offering). We intend to use the net proceeds from this offering for general corporate purposes and working capital, including for preclinical studies and clinical trials and the advancement of our product candidates. See "*Use of Proceeds*" on page S-97 of this prospectus supplement.
Risk factors	Investing in our Securities involves significant risks. You should carefully read the section entitled "*Risk Factors*" in this prospectus supplement and the accompanying base prospectus, as well as the other information included or incorporated by reference in this prospectus supplement, before deciding to invest in any of our Securities.
Nasdaq symbol	Our common stock is listed on the Nasdaq Capital Market under the symbol "IRD". There is no established trading market for the Warrants or the Pre-Funded Warrants, and we do not expect a market to develop. We do not intend to apply to list the Warrants or the Pre-Funded Warrants on any securities exchange or other nationally recognized trading system. Without an active trading market, the liquidity of the Warrants and the Pre-Funded Warrants will be limited.

The number of shares of common stock to be outstanding after the offering is based on 32,047,266 shares of common stock outstanding as of March 17, 2025, and excludes:

- 7,204,299 shares of common stock issuable upon the exercise of warrants outstanding as of March 17, 2025, with a weighted-average exercise price of $4.82 per share;
- 7,035,253 shares of common stock issuable upon the exercise of outstanding stock options outstanding as of March 17, 2025 under our 2018 Equity Incentive Plan, 2020 Equity Incentive Plan and 2021 Inducement Plan;
- 1,019,418 shares of common stock reserved for future issuance under our 2020 Equity Incentive Plan and 2021 Inducement Plan outstanding as of March 17, 2025;
- 2,039,387 unvested restricted stock awards as of March 17, 2025; and
- up to 14,145,374 shares of common stock that are issuable upon conversion of the 14,145.374 shares of our Series A Preferred Stock.

Unless expressly indicated or the context requires otherwise, all information in this prospectus supplement is as of March 17, 2025 and assumes no conversion of Series A preferred stock, no exercise of outstanding stock options described above, no settlement of unvested restricted stock units described above and no exercise of the Warrants and Pre-Funded Warrants issued in connection with this offering.

BUSINESS

Opus Genetics, Inc. (the "Company," "Opus," "we," "us," or "our") is a clinical-stage ophthalmic biotechnology company developing gene therapies for the treatment of inherited retinal diseases ("IRDs") and other types of therapies for additional ophthalmic disorders.

Opus was founded in February 2018 as Ocuphire Pharma, Inc. and has since undergone several transactions:

- In April 2018, Ocuphire Pharma, Inc. merged with Ocularis Pharma, LLC, the original innovator of phentolamine mesylate ophthalmic solution.
- In January 2020, Ocuphire Pharma, Inc. obtained from Apexian Pharmaceuticals, Inc. certain rights to its Ref-1 inhibitor program, including APX3330.
- In November 2020, Ocuphire Pharma, Inc. completed a reverse merger into Rexahn Pharmaceuticals, Inc. ("Rexahn"), a publicly traded company that had ceased its business of drug development activities, and simultaneously raised $21.2 million through an offering of common shares and warrants to purchase common shares. The combined company continued to operate under the name of Ocuphire Pharma, Inc.
- On October 22, 2024, Ocuphire Pharma, Inc. acquired a private corporation then operating under the name of "Opus Genetics Inc." ("Private Opus") pursuant to the terms of an Agreement and Plan of Merger, dated as of October 22, 2024 (such agreement, the "Merger Agreement" and the transaction consummated via the Merger Agreement, the "Opus Acquisition"), by and among the Company, Private Opus, and certain merger subsidiaries party thereto.

Our expanded pipeline in the wake of the Opus Acquisition includes assets from the adeno-associated virus ("AAV") based gene therapy portfolio of Private Opus that address mutations in genes that cause different forms of Leber congenital amaurosis ("LCA"), bestrophinopathy, and retinitis pigmentosa.

Our most advanced gene therapy program is designed to address mutations in the LCA5 gene ("LCA5"), which encodes the lebercilin protein. More specifically, we are developing OPGx-LCA5 to treat LCA5-associated IRD, an early-onset retinal degeneration, and an open-label, dose-escalation Phase 1/2 clinical trial is ongoing. The trial has shown clinical proof-of-concept—one-year data has provided evidence that the therapy supported visual improvement in three out of three adult patients participating in the trial, each of whom has late-stage disease. Enrollment of the first pediatric patient in the LCA5 Phase 1/2 trial occurred in the first quarter of 2025, with the first data anticipated in the third quarter of 2025. Successful completion of a registrational trial would position Opus to potentially submit a Biologic License Application (BLA) for OPGx-LCA5 as early as 2027. The program has received Rare Pediatric Disease Designation and Orphan Drug Designation from the U.S. Food and Drug Administration ("FDA"). As with the other company IRD pipeline programs, we estimate that the direct cost of the program, through BLA submission, would be approximately $25-$35 million.

OPGx-BEST1 is another gene therapy candidate in our portfolio, which Private Opus acquired from Iveric Bio, a biopharmaceutical company focused on the discovery and development of novel treatments for retinal diseases, in late 2022. This asset is being developed for the treatment of IRDs associated with mutations in the BEST1 gene ("Best Disease"), which can lead to legal blindness. In preclinical studies conducted in a naturally occurring canine model of Best Disease, OPGx-BEST1 provided evidence in support of a first-in-man clinical trial. We aim to obtain preliminary data for a Phase 1/2 clinical study by the first quarter of 2026.

Apart from gene therapies, our pipeline also includes Phentolamine Ophthalmic Solution 0.75%, a non-selective alpha-1 and alpha-2 adrenergic antagonist to reduce pupil size, which is currently being evaluated in two Phase 3 trials for the treatment of presbyopia and dim (mesopic) light vision disturbances, as well as APX3330, a novel small-molecule inhibitor of Ref-1 designed to slow the progression of non-proliferative diabetic retinopathy ("NPDR").

In November 2022, we entered into a license and collaboration agreement (the "Viatris License Agreement") with a company now known as Viatris, Inc. ("Viatris"), pursuant to which we 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 produced by adrenergic agonists (e.g., phenylephrine) or parasympatholytic agents (e.g., tropicamide), or a combination thereof, under the brand

name RYZUMVI® in September 2023, and the product launched commercially in April 2024. The VEGA-3 Phase 3 clinical trial evaluating PS for the treatment of presbyopia (age-related blurry near vision) completed enrollment and topline results are expected in the first half of 2025. Additionally, for the treatment of decreased vision under mesopic (low) light conditions following keratorefractive surgery, we received FDA agreement under Special Protocol Assessment ("SPA") for LYNX-2, a Phase 3 Trial of PS. LYNX-2 completed enrollment and topline results are expected mid-year 2025. We expect that an additional Phase 3 study of LYNX-3 for the treatment of decreased vision under mesopic (low) light conditions following keratorefractive surgery will commence in the second half of 2025.

APX3330 has completed a Phase 2 clinical study in 103 patients and FDA agreement under SPA was reached for a Phase 3 program. However, due to the capital requirements and developmental timelines associated with APX3330, we are currently seeking a strategic partner to advance the clinical development of this diabetic retinopathy program and redirecting existing resources toward the acquired gene therapy programs.

Many of the Company's employees, directors, advisors and consultants have been involved in the development and commercialization of a variety of innovative ophthalmic drugs including approved products such as LUXTURNA marketed by Spark Therapeutics (a member of the Roche group) and Novartis, IZERVAY™ marketed by Astellas, VABYSMO® marketed by Roche, LUMIFY® marketed by Bausch & Lomb Incorporated, ZIRGAN® marketed by Bausch & Lomb Incorporated, DUREZOL® marketed by Novartis, 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., DIQUAS® marketed by Santen Company Limited, AzaSite® marketed by Inspire Pharmaceuticals and DEXTENZA® marketed by Ocular Therapeutix, Inc. The management team, led by Chief Executive Officer George Magrath, MD, collectively has significant experience in operating pharmaceutical companies and discovering, developing, and commercializing treatments in multiple therapeutic areas.

Strategy

The Company's goal is to develop leading gene therapies to treat IRDs. We will also continue developing or seeking partnerships to develop our product candidates that existed prior to the Opus Acquisition. The key elements of our strategy we aim to achieve are the following:

- **Advance the clinical development of our gene therapy products.** OPGx-LCA5 is designed to address a form of LCA due to biallelic mutations in the LCA5, which encodes the lebercilin protein. New six-month efficacy and safety data on OPGx-LCA5 was presented at a virtual KOL event on December 11, 2024 and showed improvement in visual function in the first three adult patients treated, each of whom has late-stage disease. A pediatric cohort to test the therapy in younger subjects is in progress.

  OPGx-BEST1 is being developed for the treatment of Best disease, a monogenic central maculopathy which can lead to legal blindness. Preclinical studies conducted in a naturally occurring genetic canine model of Best disease treated with OPGx-BEST1 provided evidence in support of a first in man clinical trial. We aim to obtain preliminary data for a Phase 1/2 clinical study by the first quarter of 2026.

- **Future IRD programs.** Beyond clinical development of OPGx-LCA5 and OPGx-BEST1, Opus has a preclinical portfolio of other AAV gene therapy candidates targeting different forms of vision threatening IRDs, including retinitis pigmentosa (e.g. adRP-RHO, CNGB1) and LCA (e.g., NMNAT1, RDH12). These programs can be potentially further developed for clinical applications, subject to capital availability.

- **Maximize the value of APX3330 through partnership.** In December 2024, we reached agreement with the FDA under SPA for a Phase 3 clinical trial evaluating oral APX3330 for the treatment of moderate to severe NPDR. The SPA agreement reflects that the proposed Phase 3 trial design, and planned analyses adequately address the objectives necessary to support a New Drug Application (NDA) submission for treatment of NPDR, subject to a successful outcome of the trial and review of all the data in the NDA, if submitted. The agreed primary endpoint for this clinical trial is a reduction

in 3-step or greater worsening on the binocular diabetic retinopathy severity scale (DRSS) score, compared to placebo. We are seeking a partner to advance the clinical development of APX3330, as we focus our resources on advancing our gene therapy candidates for IRDs.

- **Complete late-stage development of PS programs.** PS was approved by the FDA for the treatment for pharmacologically-induced mydriasis under the brand name RYZUMVI in September 2023 and was launched commercially in April 2024.

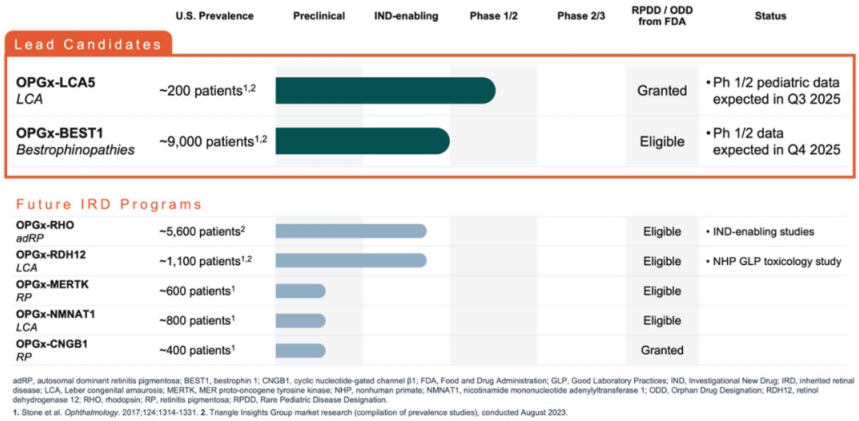
  We continue to develop PS in new indications. There are two ongoing Phase 3 studies encompassing the use of PS in two new indications: 1) the VEGA-3 Phase 3 clinical trial evaluating PS for the treatment of presbyopia (age-related blurry near vision) and 2) the LYNX-2 Phase 3 clinical trial for the treatment of mesopic (low) light conditions following keratorefractive surgery.

  The FDA has granted Fast Track designation for Phentolamine Ophthalmic Solution 0.75% as treatment for significant chronic night driving impairment with concomitant increased risk of motor vehicle accidents and debilitating loss of best spectacle corrected mesopic vision in keratorefractive patients with photic phenomena (i.e., glare, halos, starburst). Fast Track status has been designated to facilitate the development and expedite the review of drugs to treat serious conditions that fill an unmet medical need.

  We expect interim topline data in the first half of 2025 for presbyopia and mid-2025 for decreased vision under mesopic (low) light conditions following keratorefractive surgery. We expect that an additional Phase 3 study of LYNX-3 for the treatment of decreased vision under mesopic (low) light conditions following keratorefractive surgery will commence in the second half of 2025.

  If approved, the use of PS in these indications will also be commercialized by Viatris in the U.S. and major non-U.S. markets pursuant to the Viatris License Agreement.

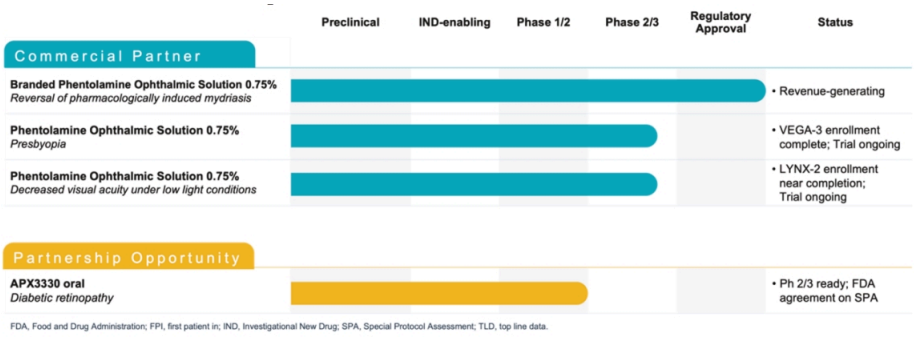
IRD Pipeline



adRP, autosomal dominant retinitis pigmentosa; BEST1, bestrophin 1; CNGB1, cyclic nucleotide-gated channel β1; FDA, Food and Drug Administration; GLP, Good Laboratory Practices; IND, Investigational New Drug; IRD, inherited retinal disease; LCA, Leber congenital amaurosis; MERTK, MER proto-oncogene tyrosine kinase; NHP, nonhuman primate; NMNAT1, nicotinamide mononucleotide adenylyltransferase 1; ODD, Orphan Drug Designation; RDH12, retinol dehydrogenase 12; RHO, rhodopsin; RP, retinitis pigmentosa; RPDD, Rare Pediatric Disease Designation.

1. Stone et al. *Ophthalmology*. 2017;124:1314-1331. 2. Triangle Insights Group market research (compilation of prevalence studies), conducted August 2023.

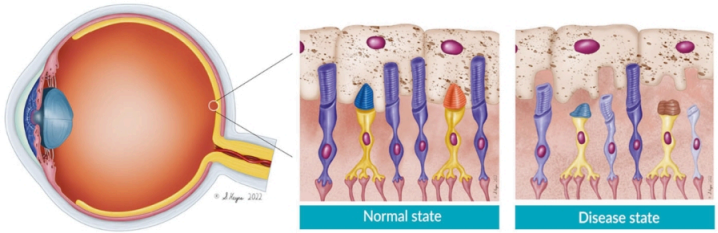
Phentolamine and APX3330 Pipeline:



OPGx-LCA5 Pipeline

OPGx-LCA5 is designed to address LCA5, which is a severe, early-onset form of IRD. The LCA5 gene encodes for the protein lebercilin, a ciliary protein which is critical for bidirectional protein trafficking in photoreceptor inner and outer segments. Photoreceptors are retinal cells that enable vision by absorbing light and transducing it into an electrochemical signal that is communicated to the visual centers of the brain. In LCA5, the outer segments do not properly develop and photoreceptor function is severely impaired. However, studies have reported evidence that these photoreceptors can survive through the third decade of life, suggesting a broad window of opportunity for therapeutic intervention through gene augmentation.

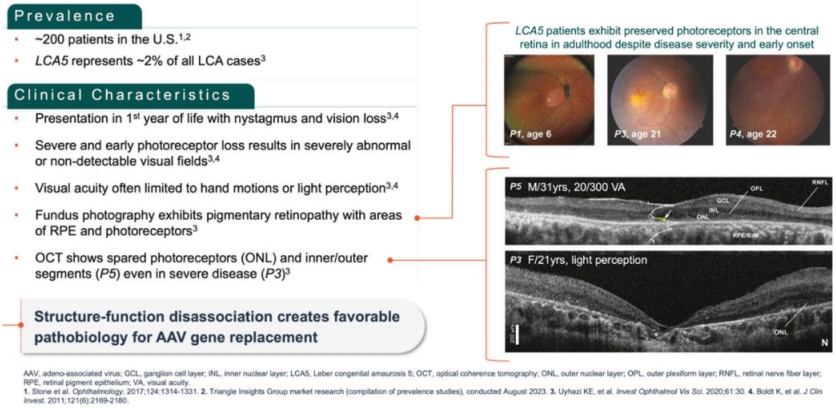
LCA5 Mechanism of Disease:



Mechanism of Action

OPGx-LCA5 uses an adeno-associated virus 8 ("AAV8") vector to deliver a functional LCA5 to the outer retina. OPGx-LCA5 is the same promoter technology as used with Luxturna. OPGx-LCA5 is administered through a validated surgical delivery method via subretinal injection. OPGx-LCA5's efficacy endpoints include measurement of functional vision using: 1) the Multi-Luminance orientation and Mobility Test (MLoMT); 2) Full-Field Stimulus Testing (FST), which measures the retina's sensitivity to light; and 3) microperimetry, which measures point-wise sensitivity to light.

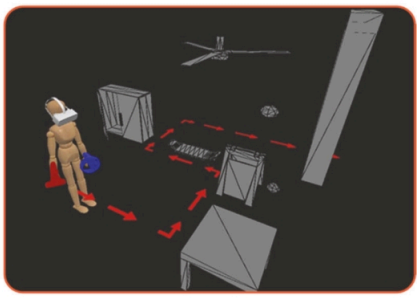
LCA5 Disease Overview:



AAV, adeno-associated virus; GCL, ganglion cell layer; INL, inner nuclear layer; LCA5, Leber congenital amaurosis 5; OCT, optical coherence tomography; ONL, outer nuclear layer; OPL, outer plexiform layer; RNFL, retinal nerve fiber layer; RPE, retinal pigment epithelium; VA, visual acuity.
1. Stone et al. *Ophthalmology*. 2017;124:1314-1331. 2. Triangle Insights Group market research (compilation of prevalence studies), conducted August 2023. 3. Uyhazi KE, et al. *Invest Ophthalmol Vis Sci*. 2020;61:30. 4. Boldt K, et al. *J Clin Invest*. 2011;121(6):2169-2180.

Functional Vision Assessment with a Multi-Luminance orientation and Mobility Test (MLoMT):

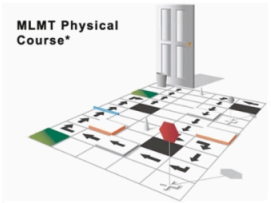
- MLoMT utilizes a readily available VR headset with body trackers to navigate a virtual course
- Household objects are presented at increasing illumination while the subject follows a path of red arrows
- Subject identifies and "touches" obstacles while following the path
- Establishes a threshold of functional vision that may be used to assess impact of disease and treatments
- Enormous amount of data automatically collected
- Relates well with clinical readouts (visual acuity, visual fields, and visual sensitivity)

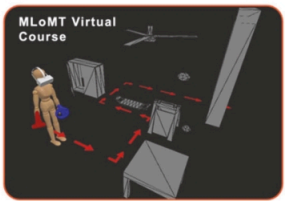


MLoMT, Multi-luminance orientation and mobility test; VR, virtual reality.
Bennett J, et al. *Transl Vis Sci Technol*. 2023;12:28.

MLoMT Builds Upon the Success of MLMT®:

- Ability to conduct numerous tests over a broader range of lighting levels and in a quicker timeframe
- Ability to duplicate test across sites
- Minimal equipment and room requirements
- No physical obstacles that could cause harm in a collision
- Ability to test one or both eyes
- Automated capture of quantitative parameters (no requirement of a reading center)





MLMT® and Multi-Luminance Mobility Test® are registered trademarks of Spark Therapeutics, Inc.
*MLMT physical course was utilized in the FDA registrational studies for Luxturna.
FDA, Food and Drug Administration; MLoMT, Multi-luminance orientation and Mobility Test; MLMT, Multi-Luminance Mobility Test.
1. Bennett J, et al. *Transl Vis Sci Technol*. 2023;12:28; 2. Aleman et al. *Clin Ophthalmol*. 2021;15:939

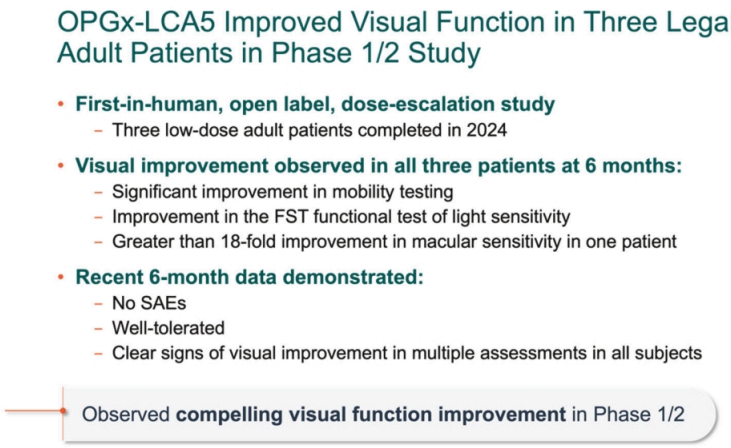
Clinical Development Process and Plan

OPGx-LCA5 is currently being evaluated in a Phase 1/2 clinical trial at the University of Pennsylvania designed to evaluate its safety and preliminary efficacy in patients with IRD due to biallelic mutations in LCA5. New six-month efficacy and safety data on OPGxLCA5 was presented at a virtual KOL event on December 11, 2024 and showed improvement in visual function in the first three adult patients treated, each of whom has late-stage disease.

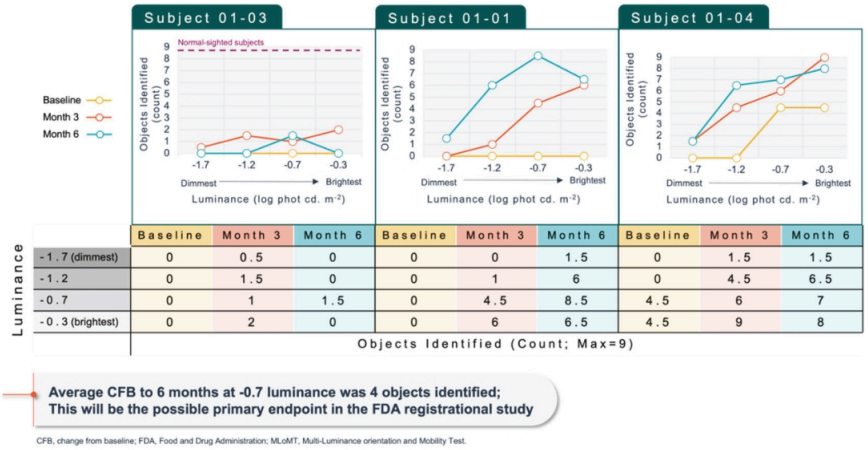
Treatment of three pediatric subjects (13-17 years of age) was initiated in February 2025 with all three pediatric patients expected to receive treatment by the end of April 2025. OPGx-LCA5's efficacy endpoints include measurement of functional vision using: 1) the Multi-Luminance orientation and Mobility Test (MLoMT); 2) Full-Field Stimulus Testing (FST), which measures the retina's sensitivity to light; and 3) microperimetry, which measures point-wise sensitivity to light.

Based on current estimates, the Company anticipates dosing the first patient for the OPGx-LCA5 in a pivotal study in November 2026, releasing top-line efficacy data in the first quarter of 2028, followed by BLA filing in the second quarter of 2028.

OPGx-LCA5 Phase 1/2 Study 6-Month Data Summary:

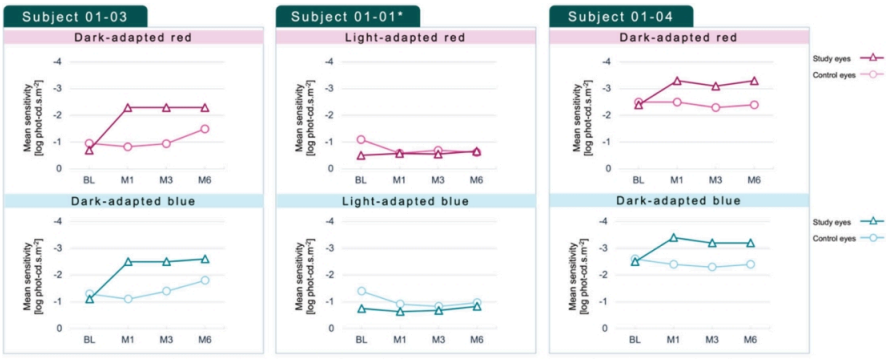


MLoMT: All Treated Subjects Identified More Objects at 3 and 6 Months Compared to Baseline:



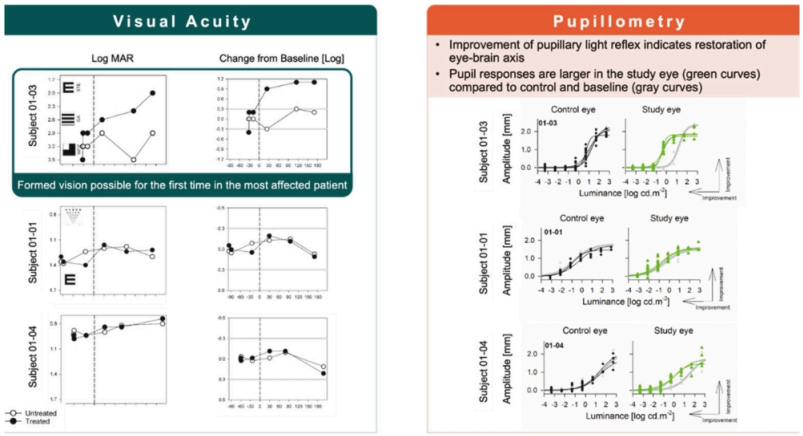
CFB, change from baseline; FDA, Food and Drug Administration; MLoMT, Multi-Luminance orientation and Mobility Test.

Full-field Stimulus Testing: Retinal Sensitivity Gains Comparable to Adult Patients Treated with Luxturna:

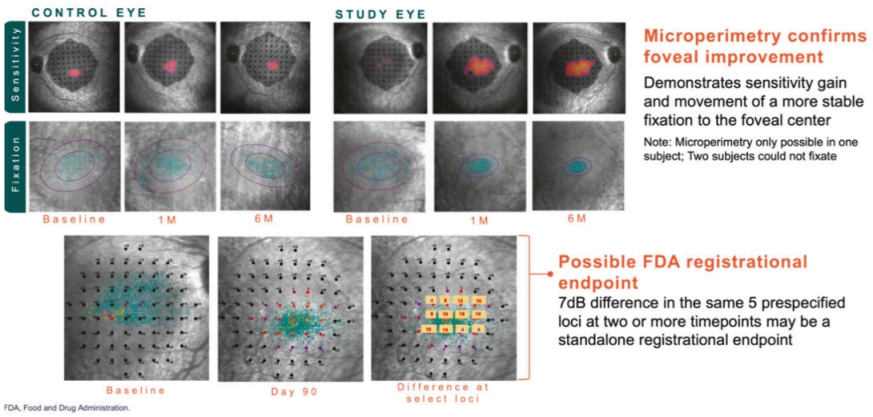


*Subject 01-01 was measured in light-adapted conditions; Remaining rod function was strong enough that it interfered with measuring cone function; to isolate and measure cone responses, rods had to be desensitized by adapting the eye to white light
Note: Subject 01-03 and 01-04 are cone-mediated disease and Subject 01-01 is rod-mediated disease.
BL, baseline; M, month.

Broad Clinical Efficacy in Visual Acuity and Pupillometry:



Greater than 18-Fold Improvement in Macular Sensitivity in Subject 01-04:



FDA, Food and Drug Administration.

OPGx-BEST1 Pipeline

OPGx-BEST1 is in development for the treatment of BEST1-associated retinal disease, an inherited retina disease that causes macular degeneration. The BEST1 gene encodes for bestrophin-1, a protein that functions as a retinal pigment epithelial ("RPE") cell membrane channel.

Mechanism of Action

The OPGx-BEST1 targets BEST1 using the AAV2 capsid employed in Luxturna and an RPE-specific promoter. This gene therapy approach aims to restore normal function of the RPE cells such that they can provide proper support to the photoreceptors, the cells that detect light.

OPGx-BEST1 Demonstrated Structural and Functional Improvement in an IND-enabling Toxicology Study:

Unilateral subretinal injection of OPGx-BEST1 at 3 doses over 13 weeks in canine model of *BEST1* disease:

Key Efficacy Findings

- Stage II/III lesions regressed or disappeared
- Focal reattachment of photoreceptor-RPE interface
- No disease in treated areas → Potential evidence of protection
- All dose groups exhibited significant improvement in ERG retinal function; dose-dependent increase observed in low and high groups

Key Safety Findings

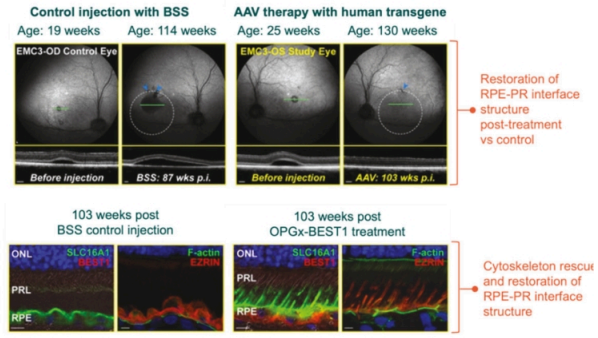
- No signs of ocular toxicity at low and mid doses
- Minor fundus discoloration at high dose with no histological findings
- NOAEL identified

BEST1, bestrophin 1; ERG, electroretinogram; NOAEL, no-observed-adverse-effect-level; RPE, retinal pigment epithelium.

BEST1 Proof of Concept: Restored Retinal Structure Observed in IND-Enabling Studies with OPGx-BEST1:

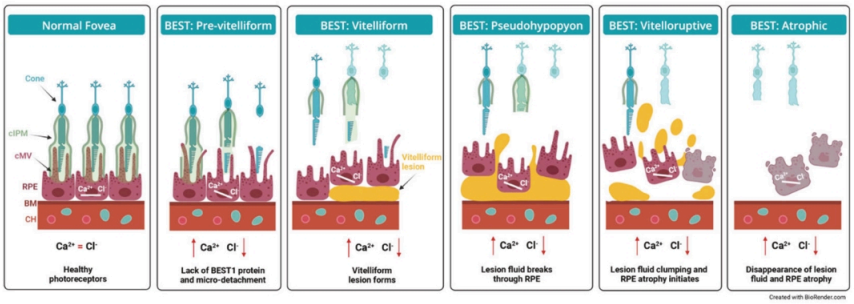
AAV-treated canine model of autosomal recessive *BEST1* disease demonstrated:

- Reversal of lesions and microdetachments
- Restoration of the RPE-photoreceptor interface architecture
- No safety signals observed



AAV, adeno-associated virus; BEST1, bestrophin 1; BSS, balanced salt solution; IND, Investigational New Drug; PR, photoreceptor; RPE, retinal pigment epithelium.
Guziewicz, et al. *PNAS*. 2018;115:E2839–E2848.

BEST1 Mechanism of Disease:



The BEST1 disease affects ~9000 patients in the U.S alone., and accounts for 3.5% of all IRDs. It is characterized by retinal lesions, with symptoms including dimness of vision, metamorphosphia (distorted vision), and areas of vision loss or scotoma (blind spot). The BEST1 gene encodes for bestrophin-1, a protein that functions as a RPE cell membrane channel. The BEST1 channel, when activated by calcium (Ca2+) ions, controls chloride (Cl-) ion transfer into and out of the RPE cell. This function is crucial to the maintenance of homeostasis between the photoreceptors (rods and cones) and RPE cells. Mutations in BEST1 disrupt this homeostasis and result in the breakdown of the interphotoreceptor matrix (IPM) and microvilli (MV) connections with the RPE. Retinal lesions form containing vitelliform material ("egg-yolk" like) between the RPE and Bruch's membrane (BM)/choroid (CH). These vitelliform lesions disrupt and cause atrophy of the RPE. Without support from the RPE, photoreceptor cells critical for normal vision die, resulting in progressive vision loss.

Clinical Development Process and Plan

OPGx-BEST1 which is designed for treatment of BEST1-associated retinal disease is ready for the clinic. As many of these subjects are found in Europe, a site (in addition to the inclusion of US sites that have a quicker regulatory start up) will be planned for inclusion as part of the clinical development plan for this asset. This plan is based on the IND-enabling studies, where we observed compelling proof-of-concept efficacy data in a naturally occurring genetic canine bestrophinopathy model with acceptable safety and tolerability to inform clinical trial implementation. We aim to obtain preliminary data for a Phase 1/2 clinical study by the first quarter of 2026.

Based on current estimates, the Company anticipates dosing the first patient for the OPGx-BEST1 in a pivotal study in the second quarter of 2027, releasing top-line efficacy data in the second quarter of 2028, followed by BLA filing in the third quarter of 2028.

Other Pre-Clinical IRD Programs Pipeline

	Age of Onset	U.S. Prevalence	Program Stage
OPGx-RHO *adRP*	Varies from late childhood to late adulthood[1]	~5,600 patients[2]	IND-enabling
OPGx-RDH12 *LCA*	As early as 1 year, with legal blindness before third decade of life[3]	1,100 patients[1,4]	IND-enabling
OPGx-MERTK *RP*	Second decade of life; generally before 18 years[5]	~600 patients[4]	Pre-IND
OPGx-NMNAT1 *LCA*	Early childhood; frequently within first year of life[6]	~800 patients[4]	Pre-IND
OPGx-CNGB1 *RP*	Young adult onset with slow progression & preserved visual acuity through late adulthood[7]	~400 patients[4]	Pre-IND; Collaboration with NIH-funded consortium of university researchers and Foundation of the NIH's Bespoke Gene Therapy Consortium through Phase 1

adRP, autosomal dominant retinitis pigmentosa; CNGB1, cyclic nucleotide-gated channel β1; IND, Investigational New Drug; LCA, Leber congenital amaurosis; MERTK, MER proto-oncogene tyrosine kinase; NMNAT1, nicotinamide mononucleotide adenylyltransferase 1; NIH, National Institutes of Health; RDH12, retinol dehydrogenase 12; RHO, rhodopsin; RP, retinitis pigmentosa; VA, visual acuity.
1. Sahel J, et al. *Cold Spring Harb Perspect Med*. 2015;5:a017111. 2. Triangle Insights Group market research (compilation of prevalence studies), conducted August 2023. 3. Daich Varela M, et al. *Ophthalmic Genet*. 2022;43:301-306. 4. Stone EM, et al. *Ophthalmology*. 2017;124:1314-1331. 5. Audo I, et al. *Hum Mutat*. 2018;39:887-913. 6. Yi Z, et al. *Eye (Lond)*. 2022;36:2279-2285. 7. Nassisi M, et al. *Hum Mutat*. 2021;42:641-666.

OPGx-RHO

OPGx-RHO is a gene therapy that targets autosomal dominant retinitis pigmentosa caused by RHO mutations (RHO-adRP). RHO-adRP affects approximately 5,600 people in the U.S., making it one of the most common IRDs, albeit not as common as BEST.

Encoded by the RHO gene, rhodopsin is an important component of the photopigment in rod photoreceptors that absorbs light and provides structure to the rod outer segments. Autosomal dominant mutations in rhodopsin cause RHO-adRP, which is characterized by progressive death of the rod photoreceptors that can lead to vision loss. OPGx-RHO is designed to preserve the rod photoreceptors by replacing a patient's RHO gene with a functional copy of the gene. We are continuing grant-supported preclinical IND-enabling studies for OPGx-RHO in 2025.

OPGx-RDH12

OPGx-RDH12 is designed to restore protein expression and halt functional deterioration in patients with retinal dystrophy caused by mutations in the retinal dehydrogenase (RDH12) gene.

Patients with RDH12 mutations, which affect approximately 1,100 people in the U.S., often have early visual acuity loss with retinal structural changes by two years of age, and longitudinal studies have reported a steep decline in visual acuity within the second decade of life. OPGx-RDH12 leverages AAVs to transport a functional gene to photoreceptors in the retina. In preclinical studies of OPGx-RDH12 in cellular and mouse models, we observed evidence of functional improvement of RDH12 activity.

OPGx-MERTK

Mutations in the MERTK gene cause a rod-cone dystrophy with early macular atrophy, with retinitis pigmentosa being the most common phenotype. Preclinical studies have shown proof of concept in rats and mice and an early clinical trial with an AAV vector was carried out several years ago with mixed results. We are developing OPGx-MERTK as a modern AAV vector for the treatment of MERTK IRD, which affects approximately 600 people in the U.S.

OPGx-NMNAT1

OPGx-NMNAT1 is a gene augmentation therapy designed to halt functional deterioration in pediatric patients with retinal degenerative disease caused by mutations in the nicotinamide mononucleotide adenylyltransferase 1 (NMNAT1) gene, which affects approximately 800 people in the U.S. NMNAT1 is an enzyme required for regenerating an essential metabolite, nicotinamide adenine dinucleotide (NAD+), in cell nuclei. Photoreceptors, in particular, are highly vulnerable to loss of NMNAT1 function. Preclinical data in a mouse model exhibiting key features of the human disease provided evidence of the potential for OPGx-NMNAT1 delivered via AAV to stabilize disease progression.

OPGx-CNGB1

OPGx-CNGB1 is an AAV gene therapy being developed for a late onset form of retinitis pigmentosa due to mutations in the CNGB1 gene, which affects approximately 400 people in the U.S. We are collaborating with a consortium of university researchers funded by the National Institute of Health ("NIH") and the Foundation of the NIH's Bespoke Gene Therapy Consortium to bring this therapy into and through a Phase 1 clinical trial.

RYZUMVI and Phentolamine Ophthalmic Solution 0.75% (PS) Pipeline

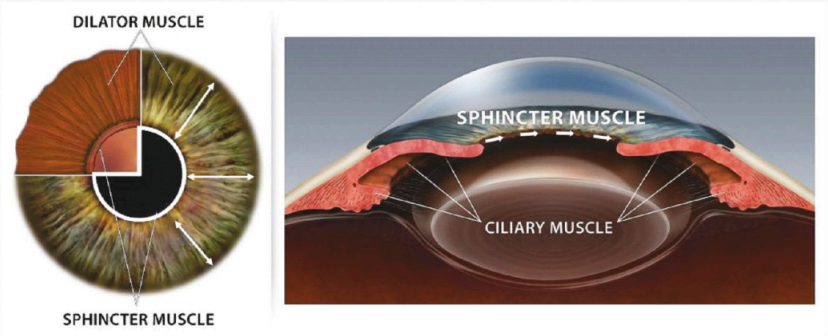
In November 2022, we entered into the Viatris License Agreement with Viatris, pursuant to which we granted Viatris an exclusive license to develop, manufacture, import, export and commercialize (i) our refractive product candidate PS, for treating (a) reversal of pharmacologically-induced mydriasis, (b) decreased vision under mesopic (low) light conditions after keratorefractive surgery, and (c) presbyopia; and (ii) PS with low dose pilocarpine for treating presbyopia worldwide except for certain countries and jurisdictions in Asia. PS was approved by the FDA for the treatment of pharmacologically-induced mydriasis under the brand name RYZUMVI in September 2023, which triggered a $10 million milestone payment under the Viatris License Agreement. RYZUMVI was commercialized by Viatris in April 2024.

Mechanism of Action

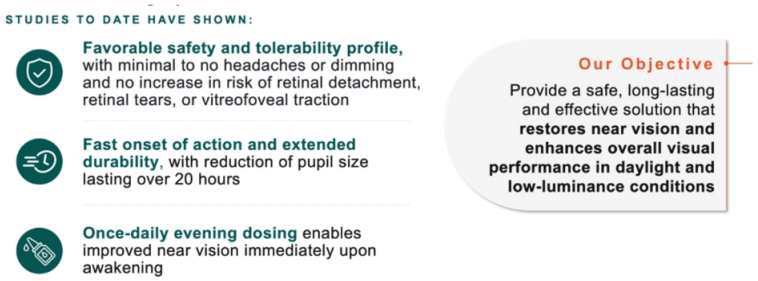
PS is a once-daily sterile eye drop formulation of phentolamine mesylate designed to reduce pupil diameter and improve visual acuity. The active pharmaceutical ingredient of PS, phentolamine mesylate, is a non-selective alpha-1 and alpha-2 adrenergic antagonist that inhibits activation of the smooth muscle of the iris, reducing pupil diameter (FIGURE 1).

For the treatment of pharmacologically-induced mydriasis indication, 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, we believe 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 low dose pilocarpine. 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 in the periphery of the cornea.

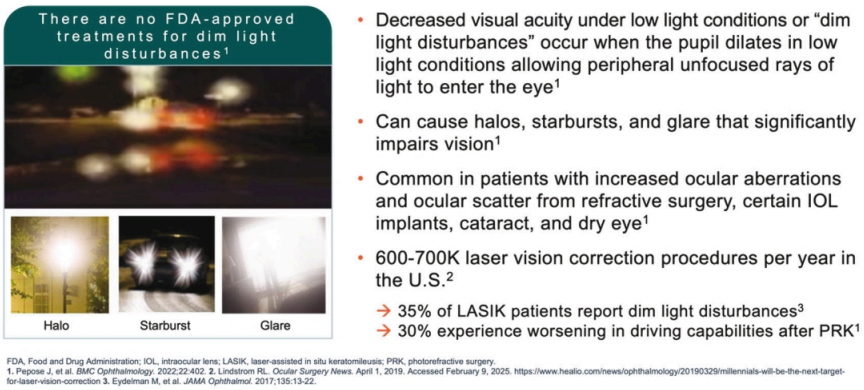
Figure 1



Overview of PS for Presbyopia and Decreased Vision Under Mesopic (Low) Light Conditions after Keratorefractive Surgery:



Decreased Vision Under Mesopic (Low) Light Conditions:



Clinical Development Process and Plan

PS has been assessed in 13 investigator-initiated and company-sponsored Phase 1, Phase 2, and Phase 3 clinical trials. Across all these trials, over 900 adult subjects 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 meetings of the American Academy of Ophthalmology (AAO), Association for Research in Vision and Ophthalmology (ARVO), and American Society of Cataract and Refractive Surgery (ASCRS), and may be presented at future medical conferences.

VEGA Program: Presbyopia Indication for PS

Phase 3 VEGA-2 Trial (Completed)

VEGA-2 (NYXP-301) is a double-masked, randomized, placebo-controlled multi-center trial of PS, placebo and with adjunctive LDP compared with vehicle (placebo) in presbyopic patients. 333 subjects were randomized 1:1:1:1 to one of four treatment groups in two stages. The primary efficacy endpoint was met.

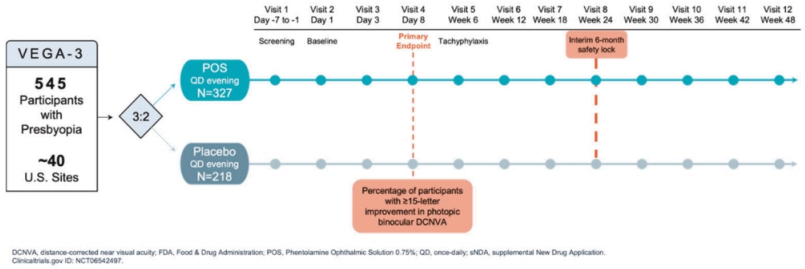
Phase 2 VEGA-1 Trial (Completed)

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 4:3:3:4 to one of four treatment groups. The primary efficacy endpoint for this study was met.

Phase 3 VEGA-3 Trial

We and Viatris are currently conducting the VEGA-3 (NYXP-302) trial as a double-masked, randomized, placebo-controlled, multicenter trial in approximately 545 patients with presbyopia. This second registration trial will evaluate the 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. Topline data is expected in the first half of 2025.

VEGA-3 Phase 3 Pivotal Study Design:



DCNVA, distance-corrected near visual acuity; FDA, Food & Drug Administration; POS, Phentolamine Ophthalmic Solution 0.75%; QD, once-daily; sNDA, supplemental New Drug Application.
Clinicaltrials.gov ID: NCT06542497.

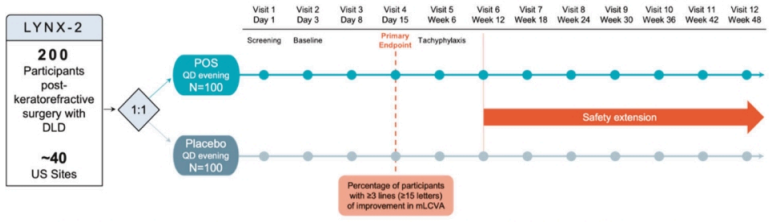
LYNX Program: Decreased Vision Under Dim (Mesopic or Low) Light Conditions After Keratorefractive Surgery Indication for PS

Phase 3 LYNX-1 Trial (Completed)

LYNX-1 (NYXDLD-301) was a Phase 3 double-masked, randomized, placebo-controlled, multi-center study comparing PS to placebo ophthalmic solution in 145 patients experiencing dim light vision disturbances at multiple sites across the U.S. Treatment was self-administered in each eye once daily at or near bedtime for 14 days. PS met the primary endpoint, showing a statistically significant higher percent of subjects with ≥ 15 Early Treatment Diabetic Retinopathy Study (ETDRS) letters (≥ 3 lines) of improvement compared to baseline in monocular mLCVA at Day 8). A total of 66 treatment-emergent adverse events ("TEAEs") were reported in 23 subjects (32%) treated with POS and 22 TEAEs were reported in 12 subjects (16%) treated with placebo. All TEAEs were mild or moderate in intensity, except for one severe TEAE (instillation site pain) experienced by a subject in the PS group. No subjects had any TEAEs leading to withdrawal from the study. One subject in each treatment group (POS and placebo) had TEAEs leading to study medication discontinuation.

We are developing PS in partnership with Viatris. In November 2022, we submitted an NDA for PS for the treatment of pharmacologically induced-mydriasis, which was approved in September 2023. In December 2023, we entered into agreement under SPA with the FDA for PS for decreased vision under dim (mesopic or low) light conditions following keratorefractive surgery.

LYNX-2 Phase 3 Pivotal Study Design:



DLD, dim light disturbances; FDA, Food and Drug Administration; mLCVA mesopic low contrast best-corrected distance visual acuity; POS, Phentolamine Ophthalmic Solution 0.75%; QD, once daily; SPA, Special Protocol Assessment.
Clinicaltrials.gov ID: NCT06349759

Based on the positive results observed in the first Phase 3 trial, LYNX-1, we and Viatris are continuing trials for the treatment of decreased vision under dim (mesopic or low) light conditions following keratorefractive surgery. LYNX-2 has completed enrollment and topline results are expected mid-year 2025. We expect that a clinical trial for LYNX-3 will commence in the second half of 2025.

APX3330 Pipeline

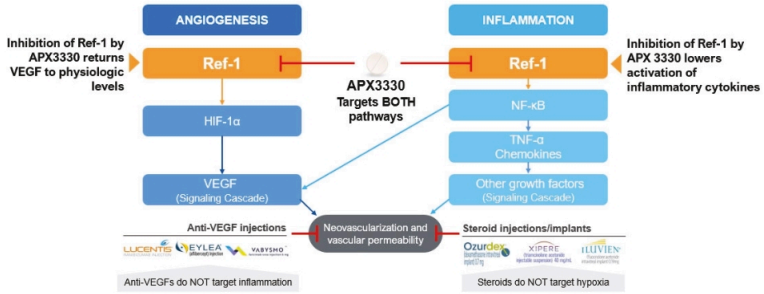
Mechanism of Action

APX3330 is a selective small molecule that is designed to act 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 signalling 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.

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 below for a visual description).

Figure 2



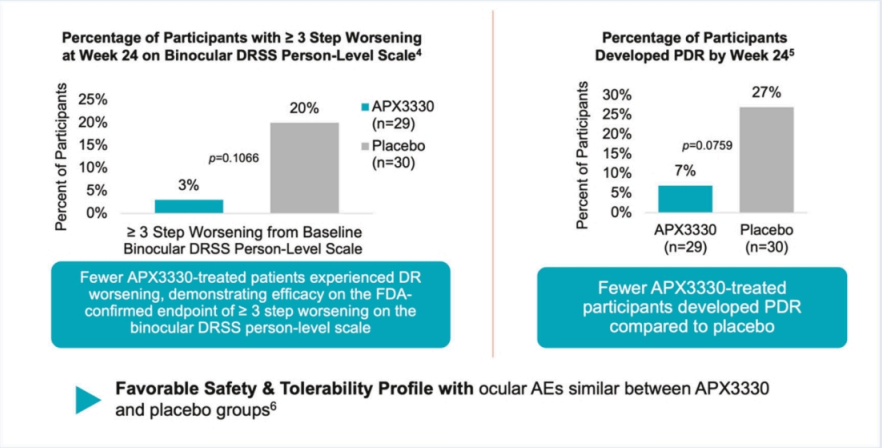
Note: Eylea® is registered trademark of Regeneron and Lucentis® is registered trademark of Roche/Genentech, VABYSMO™ is a registered trademark of the Roche Group, OZURDEX® is registered trademark of Allergan, XIPERE® is registered trademark of Clearside Biomedical, Inc., ILUVIEN® is registered trademark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

Clinical Development Process and Plan

APX3330 has been studied in over 375 healthy volunteers or patients with hepatitis or cancer or diabetic retinopathy.

In August 2022 we completed ZETA-1, a Phase 2b double-masked, randomized, placebo-controlled, multi-center trial in 103 patients with DR and DME. 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. The ZETA-1 trial did not meet the primary endpoint in the study eye; however, the trial provided evidence of the potential for clinically meaningful prevention of progression of diabetic retinopathy when evaluating both eyes. In the ZETA-1 trial, 13% of subjects within the placebo arm compared to 5% of subjects within the APX3330 arm worsened by ≥ 3 step on binocular person-level scale from baseline at week 24. Additional efficacy endpoints were directionally supportive of the biological effect of APX3330 in slowing the progression of DR and preserving vision.

ZETA-1 Phase 2 Subset Analysis Results:



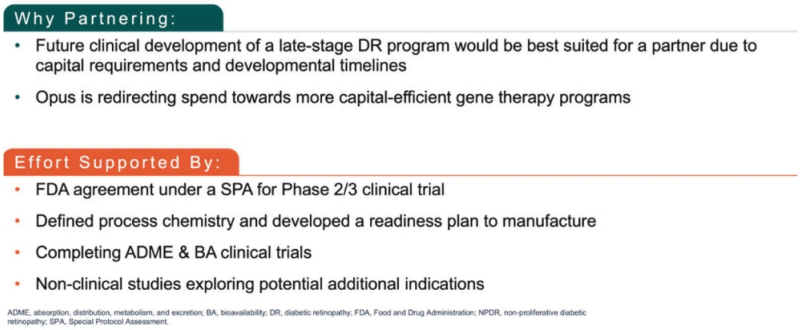
AEs, adverse events; DR, diabetic retinopathy; DRSS, Diabetic Retinopathy Severity Scale; NPDR, non-proliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy.

Sources: Data on file. 4. ZETA-1 Table 14.2.2.7.6.; ZETA-1 Table 14.2.6.7.5.; ZETA-1 Tables: 14.3.1.1, 14.3.1.7, 14.3.1.10, 16.2.7.

Overall, there were 211 adverse events ("AEs") in 64 subjects, with only 31 of these AEs 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.

For APX3330, we conducted an EOP2 meeting with the FDA and shared the outcome of the meeting in October 2023 which stated the agreement on the registrational program including confirmation of the primary endpoint for registration of a systemic agent for DR. In December 2024, the Company reached agreement with the FDA under SPA related to a Phase 3 clinical trial design. However, due to the capital requirements and developmental timelines of APX3330, which was recently approved for a Phase 3 clinical trial evaluating its oral treatment of moderate to severe NPDR, the Company is seeking a strategic partner to advance the clinical development of this late-stage diabetic retinopathy program and will redirect its existing resources towards the acquired gene therapy programs.

APX3330 is Primed for a Pivotal Study and Available for Partnering:



Overview of Eye Disease Market

Inherited Retinal Disease Market

Retinal degenerations are a devastating cause of severe vision loss beginning in childhood and progressing into adulthood. There are over 300 genetic mutations associated with IRDs. Only one of these, RPE65, has an

approved treatment, Luxturna. Many of the mutations attributable to IRDs may be amenable to gene augmentation therapy using an established, standardized subretinal delivery method. Our pipeline addresses seven of these mutations with variable prevalence as a potential one-time treatment. Precedent for one-time gene therapy treatments supports pricing consistent with the value delivered by the product.

Pricing for Approved Gene Therapies:

Product	Luxturna®*	Zolgensma®	Zynteglo™	Skysona™	Elevidys™
Indication	Biallelic *RPE65* Mutation-Associated Retinal Dystrophy	<2 years old with Spinal muscular atrophy (SMA)	β-thalassemia patients who require regular red blood cell transfusions	4-17-year-olds with Cerebral Adrenoleukodystrophy (CALD)	Ambulatory 4-5-year-olds with Duchenne Muscular Dystrophy (DMD)
Technology Type	AAV vector-based	AAV vector-based	Autologous hematopoietic stem cell-based	Autologous hematopoietic stem cell-based	AAV vector-based
Dosing Regimen	1.5 x 10^{11} vg per eye, on separate days, but no fewer than 6 days apart	1.1 × 10^{14} vg per kg of body weight, IV over 60 minutes	5.0 × 10^{6} CD34+ cells per kg of body weight, each bag via IV in <30 minutes	5.0 × 10^{6} CD34+ cells per kg of body weight minimum single dose	1.33 ×10^{14} vg per kg of body weight, IV over 1-2 hours (<10mL/kg/hr)
ROA	Subretinal	Intravenous	Intravenous	Intravenous	Intravenous
Approval Date	December 2017	May 2019	August 2022	September 2022	June 2023
Patent Expiry	June 2025	December 2029	December 2029	December 2032	N/A

*WAC for dosing both eyes; half for single eye.
AAV, adeno-associated virus; IV, intravenous; RPE, retinal pigment epithelium; ROA, route of administration; WAC, wholesaler acquisition cost.
Luxturna® is a registered trademark of Spark Therapeutics, Inc.; Zolgensma® is a registered trademark of Novartis Gene Therapies, Inc.; Zynteglo™ is a trademark of bluebird bio, Inc.; Skysona™ is a trademark of bluebird bio, Inc.; Elevidys™ is a trademark of Sarepta Therapeutics, Inc.
Sources: Company websites.

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 in addition to an age-related loss in accommodation known as presbyopia.

Presbyopia is common in patients over the age of 40 years, which results in decreased ability to see objects at near due to a loss of accommodative function. This condition affects nearly 133 million Americans and usually requires reading glasses, bifocals/varifocals, contact lenses or surgical refractive treatment to enable clear vision at near.

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. There are 600,000 to 700,000 laser vision correction procedures conducted every year, of these 35% of LASIK patients report dim light disturbances post treatment.

Our pipeline includes PS, which has been approved by the FDA to treat pharmacologically-induced mydriasis and which is currently the subject of the VEGA-3 Phase 3 clinical trial for treatment of presbyopia.

Diabetic Retinopathy Market

Diabetic Retinopathy ("DR") is an eye disease resulting from diabetes, affecting over 10 million patients in the U.S. alone, in which chronically elevated blood sugar levels result in damage to the microvascular blood vessels of 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 left untreated and if exposure to elevated blood sugar levels persist. Approximately 8 million patients in the U.S. have NPDR and are at risk of progressing to PDR (as defined below) if left untreated.
- ***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 to the retina that results in loss of vision.

Therapies for NPDR and PDR are distinct. For NPDR, treatment is usually directed at observation, lifestyle changes, and control of elevated blood sugars that all lead to the progression of NPDR. Additionally, the current treatment paradigm is for physicians to wait and monitor early-stage DR/NPDR patients, with anti-VEGF (as defined below), steroid injectable therapy or laser treatment reserved for patients who advance to the proliferative form of DR or Diabetic Macular Edema ("DME").

Sales and Marketing

In November 2022, we entered into the Viatris License Agreement for the development and commercialization of all PS indications in the U.S. and ex-U.S. markets (excluding certain countries in Asia). Viatris is responsible for any commercialization activities associated with any approved PS indications.

Currently, we do not have any employees dedicated to the sales and marketing of any of our pipeline products. We may look to build our own sales and marketing infrastructure or pursue a partnership to commercialize any future drugs upon approval.

Manufacturing

We contract with manufacturers to produce bulk drug substances and drug products for use in our preclinical studies and clinical trials, utilizing reliable and reproducible processes and common manufacturing techniques which are consistent with applicable regulations for the intended use. We do not have any long-term agreements but do intend to secure such arrangements for drug substances or drug products in the event any of our products being developed become commercialized. We do not currently own or operate, and we have no current plans to establish, any manufacturing facilities.

OPGx-LCA5

The manufacturing of current Good Manufacturing Practice ("cGMP") cGMP-grade OPGx-LCA5 drug substance and drug product for nonclinical toxicology and clinical studies was performed at an academic manufacturing partner, using an adherent process, with in-house and outsourced testing. The current batch size is 50 Liters.

We are developing plans for technical transfer and scale-up of the manufacturing process, including analytical support, for pivotal Phase 3 clinical and pre-commercial readiness, at a commercial scale CDMO.

OPGx-BEST1

Manufacturing of cGMP-grade OPGx-BEST1 drug substance and drug product for BEST nonclinical toxicology and clinical studies was performed at Catalent Incorporated, with in-house and outsourced testing. Process and analytical development work for OPGx-BEST1 were conducted at small scale. Following scale-up, replicate batches were produced at 200L scale, using the same process used for the Good Laboratory Practice (GLP) toxicology studies. Batches of drug product, drug substance, and diluent were placed on stability programs which remain ongoing.

The are no current or ongoing manufacturing agreements. We are developing plans for technical transfer and of the OPGx-BEST1 manufacturing process, including analytical support, for pivotal Phase 3 clinical and pre-commercial readiness.

Other Pre-clinical IRD Assets

The remaining IRD pipeline, including OPGx-RHO, OPGx-RDH12, OPGx-MERTK, OPGx-NMNAT1, and OPGx-GNGB1, are pre-clinical candidates in varying stages of phase appropriate development, based on the asset. Manufacturing completed to date has been conducted to support non-clinical toxicology programs, at a scale of 50L or less, with planning to support technical transfer and scale up ongoing. There are no current or ongoing manufacturing agreements in place. A request for proposal process, to include small scale process development, technical transfer, and analytical method development, to identify a manufacturing partner is being conducted. The overall corporate strategy is to advance each from the current manufacturing status, from pre-clinical into clinical Phase 1/2 readiness consolidated with a contract drug manufacturing organization (CDMO) meeting capability requirements under cGMP manufacturing conditions.

Phentolamine Solution (PS)

Pursuant to the Viatris License Agreement, we have transferred commercial manufacturing responsibilities for RYZUMVI to Viatris. Transfer of commercial manufacturing responsibilities for additional indications for which PS is in development is intended. Currently, we use purchase orders with multiple manufacturers for PS clinical supply manufacturing. We are qualifying our selected manufacturers to provide bulk drug substances and drug products in conjunction with the planned sNDA regulatory submissions to the FDA.

APX3330

APX3330 is a solid 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 in development, and plans for production scale up according to cGMP regulatory requirements are established. Previously, the APX3330 drug product manufacturer 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. We have reformulated the drug product and increased the dose strength to 300 mg for convenient once or twice a day dosing and completed one human bioavailability trial with the new formulation to demonstrate comparability with the prior investigational product. Planning to complete the remaining process development, scale up, and validation are established, pending execution following a partnership agreement.

License Agreements

Apexian Sublicense Agreement

On January 21, 2020, the Company entered into a sublicense agreement with Apexian Pharmaceuticals, Inc. pursuant to which it obtained an exclusive worldwide patent and other intellectual property rights relating to a Ref-1 Inhibitor program, including APX3330, for the treatment of ophthalmic or diabetic diseases. In exchange for the patent and other intellectual rights, the Company agreed to certain milestone payments and royalty payments on future sales. As of December 31, 2024, 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.

University of Pennsylvania LCA5/RDH12 License Agreement

On June 15, 2022, Opus entered into an amended and restated license agreement (the "LCA5/RDH12 Agreement") with the Trustees of the University of Pennsylvania ("Penn") pursuant to which it was granted an exclusive, royalty-bearing license to certain patents and a non-exclusive license to certain information relating to products directed towards treatment or correction of mutation of LCA5 or of RDH12 genes. In return for the patent and information rights, Opus agreed to certain milestone payments and royalty payments on future sales. As of December 31, 2024 there was sufficient uncertainty with regard to any future cash milestone payments under the LCA5/RDH12 Agreement that no liabilities were recorded related to the agreement.

Iveric Asset Purchase Agreement – BEST1 and RHO Programs

On December 23, 2022, Opus entered into an asset purchase agreement with Iveric (the "Iveric Agreement") pursuant to which the Company acquired intellectual property licenses relating to BEST1 and RHO products. In return for the patent and information rights, Opus agreed to certain development milestone payments and royalty payments on future sales and commercial milestones. As of December 31, 2024 there was sufficient uncertainty with regard to any future cash milestone payments under the Iveric Agreement that no liabilities were recorded related to the agreement.

Penn and University of Florida BEST1 License Agreement

On April 10, 2019, Iveric entered into an exclusive patent license agreement with knowhow (the "BEST1 License") by and between Penn and the University of Florida Research Foundation ("UF") pursuant to which the Company has exclusive patent rights and non-exclusive knowhow and data rights with regard to products to treat diseases associated with mutations in the BEST1 gene. In return for these rights, the Company is obligated

to make certain development milestone payments and royalty payments on future sales of such products. As of December 31, 2024 there was sufficient uncertainty with regard to any future cash milestone payments under the BEST1 License that no liabilities were recorded related to the agreement.

Penn and UF RHO License Agreement

On June 6, 2018, Iveric entered into an exclusive patent license agreement with knowhow (the "RHO License") by and between Penn and UF pursuant to which the Company has exclusive patent rights and non-exclusive knowhow and data rights with regard to products to treat rhodopsin-mediated diseases. In return for these rights, the Company is obligated to make certain development milestone payments and royalty payments on future sales of such products. As of December 31, 2024 there was sufficient uncertainty with regard to any future cash milestone payments under the RHO License that no liabilities were recorded related to the agreement.

Massachusetts Eye and Ear Infirmary License Agreement

On November 9, 2021, Opus entered into a license agreement (the "MEEI License") with the Massachusetts Eye and Ear Infirmary ("MEEI"), granting an exclusive worldwide license of MEEI patents for use in the NMNAT1 program for all products and processes including the treatment of retinal disease in humans, and a non-exclusive worldwide license to technological information. In return for these rights, the Company is obligated to make certain development milestone payments and royalty payments on future sales of such products. As of December 31, 2024 there was sufficient uncertainty with regard to any future cash milestone payments under the MEEI License that no liabilities were recorded related to the agreement.

Intellectual Property

Gene Therapy

We in-license multiple patents and patent applications directed to our gene therapy programs. We also own one patent family directed to our MERTK therapeutic program. Our patent estate for each gene therapy program, as of December 31, 2024, is described in more detail below.

For our LCA5 therapeutic program, we in-license one patent family directed to compositions of matter and therapeutic methods using such compositions of matter. The patent family contains patents in the U.S., Japan, Australia, and South Korea and pending patent applications in the U.S., Europe, and additional foreign countries. The foregoing U.S. patent expires in 2039, and the Japanese, Australian, and South Korean patents, including any patents that may be granted based on the foregoing pending patent applications, will expire in 2038, each not including any patent term extension.

For our BEST1 therapeutic program, we in-license four patent families. The first patent family is directed to compositions of matter and therapeutic methods using such compositions of matter and has patent applications pending in the U.S., Europe, Japan, and additional foreign countries. If the foregoing patent applications are granted, these patents would expire in 2039, not including any patent term extension. The second and third patent families are each directed to methods of treatment and have patent applications pending in the U.S., Europe, Japan, and additional foreign countries. These patents, if granted, would expire in 2041, not including any patent term extension. The fourth patent family is direct to methods of treatment and methods for assessing treatment and has patent applications pending in the U.S. and Europe. These patents, if granted, would expire in 2042, not including any patent term extension.

For our RHO therapeutic program, we in-license two patent families, each directed to compositions of matter and therapeutic methods using such compositions of matter. The first patent family has patents in the U.S., Europe, Japan, and additional foreign countries, while the second patent family has patents in Japan and China. Each patent family also has patent applications pending in the U.S., Europe, and additional foreign countries. The foregoing patents, including any patents granted based on the foregoing patent applications, will expire from 2037 to 2039, not including any patent term extension.

For our MERTK therapeutic program, we own one international patent application to compositions of matter and therapeutic methods using such compositions of matter. This patent, if granted based on the foregoing patent application to be filed based on the international patent application, would expire in 2044, not including any patent term extension.

For our RDH12 therapeutic program, we in-license one patent family directed to compositions of matter and therapeutic methods using such compositions of matter, consisting of patents in the U.S., Japan, Australia, and additional foreign countries and pending patent applications in the U.S., Europe, and additional foreign countries. The foregoing patents, including any patents granted based on the pending patent applications, will expire in 2037, not including any patent term extension.

For our NMNAT1 therapeutic program, we in-license one patent family directed to compositions of matter and therapeutic methods using such compositions of matter, consisting of pending patent applications in the U.S., Europe, Japan, and additional foreign countries. These patents, if granted based on the pending patent applications, would expire in 2041, not including any patent term extension.

For our CNGB1 therapeutic program, we in-license one patent family directed to compositions of matter and therapeutic methods using such compositions of matter. This patent family contains a patent in Japan and pending patent applications in the U.S., Europe, and additional foreign countries, whereby the Japanese patent and patent applications, if granted, based on the foregoing pending patent applications, expire in year 2038, not including any patent term extension.

PS

Our 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. We own all of the worldwide rights to PS for all indications, but out-license certain rights to PS pursuant to the Viatris License Agreement.

Our patent estate relating to PS contains over 12 U.S. patents, over seven pending U.S. non-provisional patent applications, a pending international patent application, as well as issued patents in Australia, Canada, Europe, Japan, and Mexico and pending patent applications in Europe, Japan, and other foreign countries. Multiple U.S. patents and counterpart Australian, Canadian, European, and Japanese patents are directed to aqueous phentolamine mesylate formulations and are scheduled to expire in 2034. Additional multiple U.S. patents and counterpart Australian, Canadian, European, and Japanese patents are directed to methods of improving visual performance using, for example, phentolamine mesylate and are scheduled to expire in 2034.

We also own two U.S. patents with claims to methods of treating presbyopia, and one U.S. patent with claims to methods of treating mydriasis—each of the foregoing U.S. patents are scheduled to expire in 2039. Additionally, we own one pending U.S. patent application with claims to treating presbyopia and two pending U.S. patent applications with claims to treating mydriasis. Counterpart patent applications are pending in Europe, Japan, and other foreign countries—if granted based on these pending applications, these patents would expire in 2039. Patent applications are also pending in the U.S., Europe, Japan, and other foreign countries directed to additional methods for treating mydriasis—if granted based on the foregoing patent applications, these patents would expire in 2042.

We also own two U.S. patents, one pending U.S. patent application, and pending foreign patent applications in Europe, Japan, and additional foreign countries directed to high-purity phentolamine mesylate and methods for making the same. We also have a pending international patent application, pending U.S. patent application, and pending European patent application directed to particular phentolamine mesylate crystal forms and their use—if granted based on the foregoing patent applications, these patents would expire in 2043.

We have obtained registration of the “RYZUMVI” trademark in the United States.

APX3330

As of December 31, 2024, the patent estate that we in-license 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, and additional foreign countries, and pending patent applications in Europe, Japan, and additional foreign countries. The license is for the use and commercialization of APX3330 and related compounds covered by the subject patents and patent applications in the field of human health uses for ophthalmic and diabetes mellitus indications.

One in-licensed U.S. patent is directed to methods of treating diabetic retinopathy and other diseases using, for example, APX3330, and is scheduled to expire in year 2030, not including any patent term extension.

Counterpart patents have issued in Europe, Japan, and additional foreign countries, which are scheduled to expire in year 2028. A separate in-licensed patent family directed to methods of treating wet Age-Related Macular Degeneration and other diseases using, for example, APX2009 or APX2014, contains one U.S. patent, one pending U.S. patent application, and patents in Europe, Japan, and additional foreign countries, as well as a pending patent application in Canada—these patents, including any patents granted based on the pending patent applications, will expire in 2039. Additional in-licensed patents and patent applications are directed to methods of treating certain retinal diseases, combination therapy, and/or derivatives of APX3330—these patents, including any patents granted based on the foregoing pending patent applications, will expire from 2028 to 2039, not including any patent term extension.

In addition, as of December 31, 2024, we own one U.S. provisional patent application, one U.S.non-provisional patent application, one international patent application, and patent applications in Europe, Japan, and additional foreign countries and directed to methods of treating diabetic retinal diseases using APX3330. Patents, if granted, based on the foregoing patent applications would expire from 2042 to 2045, not including any patent term extension. Additionally, we own one pending international patent application with counterpart patent applications pending in the U.S., Taiwan, and Argentina directed to APX3330 salts and esters—these patents, if granted based on the foregoing patent applications, would expire in 2043, not including any patent term extension.

Competition

We and our development partners 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 us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient enrollment for clinical trials, and acquiring products, product candidates or other technologies complementary to our programs. Smaller and other early-stage companies may also prove to be significant competitors if they choose to partner with large, established companies.

Inherited Retinal Diseases

While we are not currently aware of any direct competitors for our OPGx-LCA5 gene therapy program, there are various companies developing gene therapies for the treatment of IRDs, which may ultimately directly compete with us in the future. To our knowledge, there are no active IRD gene therapy programs in development for the treatment of LCA5, BEST1, NMNAT1, or MerTK genes. With respect to the RDH12 gene, there is an investigator-initiated trial in China and a program from MeiraGTX. For the Rho program, Octant Bio appears to have a preclinical program. Cell therapies and optogenetics are potential competition for late stages for our diseases from genes of interest at which point, gene augmentation may be less efficacious.

PS

Phentolamine Ophthalmic Solution 0.75% is in development for additional indications of presbyopia as well as decreased visual acuity under low light conditions following keratorefractive surgery. There are multiple potential competitors for the treatment of presbyopia including Lenz Therapeutics (LNZ100 - 1.75% Aceclidine) and AbbVie (VUITY® (pilocarpine hydrochloride ophthalmic solution) - 1.25%). We are not aware of direct competition for the treatment of DLD following keratorefractive surgery.

In January 2025, we received a Paragraph IV Certification Notice ("Notice Letter") that Sandoz, Inc., a provider of generic and biosimilar medicines ("Sandoz"), submitted an Abbreviated New Drug Application (ANDA) to the FDA seeking approval to manufacture, use or sell a generic version of RYZUMVI for the reversal of pharmacologically-induced mydriasis in the U.S. prior to the expiration of six of our patents listed in the FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations* publication (the "Orange Book"). The Notice Letter alleges that these patents are invalid or unenforceable or will not be infringed by the generic product described in Sandoz's ANDA. If the challenge by Sandoz is successful, it could result in the introduction of a generic competitor to the market before the expiration of our patents, thereby reducing our market share and potential future revenue from sales of RYZUMVI for reversal of pharmacologically-induced mydriasis. In March 2025, in collaboration with our commercialization partner for RYZYMVI®, we filed a complaint for patent infringement of certain RYZYMVI® patents against Sandoz in the District of New Jersey in response to Sandoz's ANDA filing. The complaint seeks, among other relief, equitable relief enjoining Sandoz from infringing the RYZUMVI patents.

APX3330

There are multiple products currently used to treat diabetic retinopathy and macular edema including anti-VEGF therapies, including faricimab-svoa (Vabysmo), ranibizumab (Lucentis) and aflibercept (Eylea). There are also multiple additional therapies in research and development stages for the treatment of diabetic retinopathy. Photocoagulation and vitrectomies may also be used to treat diabetic retinopathy.

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(the so-called "Brexit"). The Japanese Pharmaceuticals and Medical Devices Agency (PMDA) 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 and Biologics in the United States

In the United States, the FDA regulates drug and biological products under the Federal Food, Drug, and Cosmetic Act, or FDCA, and the Public Health Service Act, or PHSA, respectively, and implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. The failure to comply with applicable requirements under the FDCA, PHSA 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, untitled 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 or biological 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 human clinical trials, including adequate and well-controlled 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, or the safety, purity, and potency of the proposed biologic, for each proposed indication;
- manufacturing, packaging, labelling, and distribution of drug substances and drug products consistent with the FDA's cGMP regulations, as well as 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, BLA or supplements;
- review of the product by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with cGMP requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- satisfactory completion of FDA audits of clinical trial site(s) to assure compliance with GCPs and the integrity of the clinical data;
- FDA approval of application; 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 evaluations of product chemistry, toxicity and formulation, as well as *in vitro* and *in vivo* animal studies to assess the safety and activity of the product candidate 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 or biological 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 (or Independent Ethics Committee (IEC or EC), within Europe) 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 Opus 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 or BLA

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 or biological product 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 or biological product 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 or biological product 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 labelling 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 or biological product; 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 or biological product 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 an 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 or biological product 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 or biologic candidate and, among other things, must develop methods for testing the identity, strength, quality, purity, and potency of the final drug or biologic. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the drug or biological candidate does not undergo unacceptable deterioration over its shelf life.

Submission of an NDA or BLA 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 application requesting approval to market the drug or biological product for one or more indications. Under federal law, the submission of most NDAs and BLAs are subject to an application user fee. The sponsor of an approved NDA or BLA 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 or biologics with orphan designation and a waiver for certain small businesses. The FDA conducts a preliminary review of an NDA or BLA 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 or BLA 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 and BLAs. 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 or BLA, 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 or BLA submission, including drug or biologic component manufacturing (such as active pharmaceutical ingredients), finished drug or biological 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 or BLA, 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 or biologic 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 or BLA

On the basis of the FDA's evaluation of the NDA or BLA 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 or BLA, 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 safety of drugs or biologics 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 labelling claims, are subject to further testing requirements and FDA review and approval.

Post-Approval Requirements

Drugs and biologics 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 and biological product manufacturers and other entities involved in the manufacture and distribution of approved products 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 labelling 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 BLAs, or supplements to approved applications, 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 and biological products 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 an NCE, 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.

Biosimilars and Reference Product Exclusivity

The Patient Protection and Affordable Care Act, known as the Affordable Care Act, signed into law on March 23, 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009 ("BPCIA") which created an abbreviated approval pathway for biological products shown to be similar to, or interchangeable with, an FDA-licensed reference biological product. This amendment to the PHSA attempts to minimize duplicative testing. Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical study or studies. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product and, for products administered multiple times, the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law. In addition, recent legislative and regulatory proposals have sought to reduce or altogether eliminate the distinctions between interchangeable products and conventional biosimilar products, making the long-term status of these products unclear.

Pediatric Studies and Exclusivity

Under the Pediatric Research Equity Act of 2003, an NDA or BLA, or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the drug or biological 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 or BLA 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 or biological 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 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 or BLA. 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 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 or biological 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 or BLA, plus the time between the submission date of an application 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 or biological 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 or biologics 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. We cannot provide any assurance that any patent term extension with respect to any U.S. patent will be obtained or, 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 medicinal 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 we obtain FDA approval for a product, we would need to obtain the necessary approvals by the comparable foreign regulatory authorities before we 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 Clinical Trials Regulation (EU) No 536/2014, a system for the approval of clinical trials in the European Union has been implemented. Under the applicable 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 Regulation 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, mutual recognition or a national 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 simultaneous 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 labelling 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, as amended. 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 Regulation 536/2014, and the GCP Directive 2005/28/EC, as well as in the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Guideline for Good Clinical Practice, which have been adopted by the CHMP. Pursuant to the Clinical Trials Regulation and Directive 2005/28/EC, as amended, a system for the approval of clinical trials in the European Union has been implemented. 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. All ongoing clinical trials in the EU are subject to the provisions of the CTR as of January 31, 2025. In addition, on June 18, 2024, new CTIS transparency rules came into effect, requiring scheduled publication of certain key clinical trial information. 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 the Clinical Trials Regulation 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.

Under the Clinical Trials Regulation, it is also possible to submit a streamlined application procedure via a single entry point, the EU portal and a single set of documents to be prepared and submitted for the application. Other main characteristics of the Clinical Trials Regulation include: 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 (“NCE”) and gene therapy products, qualify for eight years of data exclusivity (also called “regulatory data protection”) 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 the generic product cannot enter the market 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 an NCE 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, which can be further extended by two years if pediatric studies have been conducted in accordance with an agreed pediatric investigational plan. 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 of the EMA, 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.

It is noted that a wholesale revision of the EU pharmaceutical legislation is currently underway, which will have a direct impact on the regulatory protections afforded to medicinal products such as data exclusivity, marketing protection, market exclusivity for orphan indications and pediatric extension. On April 26, 2023, the European Commission adopted a proposal for a new Directive and a new Regulation. The legislative proposals provide for reduced periods of regulatory protections across the categories listed above. The text is now being deliberated at the level of the Council of the EU and it is not expected that the law, when adopted, will become applicable until 2026 at the earliest.

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 and good manufacturing practice. 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 GMP 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 our 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 has been 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 was eliminated effective 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 United States Supreme Court dismissed a judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the law. In the future, there may be additional challenges and/or amendments to the ACA. It remains to be seen precisely what any new legislation will provide, when or if it will be enacted, and what impact it will have on the availability and cost of healthcare items and services, including drug and biological products. 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 our potential drug candidates include:

- A special, non-deductible 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;
- Expansion of manufacturers' rebate liability under the Medicaid Drug Rebate Program ("MDRP") by (i) increasing the minimum rebate for both branded and generic drugs; (ii) revising the definition of "average manufacturer price," or AMP, which must be reported to the government for purposes of calculating Medicaid drug rebates on outpatient prescription drugs; and (iii) creating a new methodology by which rebates owed by manufacturers under the MDRP are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- Expansion of the types of entities eligible for the 340B drug discount program;

- Provisions authorizing the creation of a new independent nonprofit organization called the Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and
- Establishment of 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 eight 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, P the American Rescue Plan Act of 2021 was signed 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. Additionally, federal agency priorities, leadership, policies, rulemaking, communications, spending, and staffing may be significantly impacted by election cycles, including, for example, the current presidential administration's commitment to significantly reduce government spending through cuts to federal healthcare programs and reductions in the workforces of key

government agencies, such as HHS, FDA, and CMS. Efforts by the current administration to limit federal agency budgets or personnel may lead to slower response times and longer review periods, potentially affecting our ability to continue development of our product candidates or obtain regulatory approval for our product candidates.

The pharmaceutical industry is also subject to regulatory changes as the result of judicial challenges. For example, on June 28, 2024, the U.S. Supreme Court issued an opinion holding that courts reviewing agency action pursuant to the Administrative Procedure Act ("APA") "must exercise their independent judgment" and "may not defer to an agency interpretation of the law simply because a statute is ambiguous." The decision will have a significant impact on how lower courts evaluate challenges to agency interpretations of law, including those by CMS and other agencies with significant oversight of the healthcare industry. The new framework is likely to increase both the frequency of such challenges and their odds of success by eliminating one way in which the government previously prevailed in such cases. As a result, significant regulatory policies may be subject to increased litigation and judicial scrutiny. Any resulting changes in regulation may result in unexpected delays, increased costs, or other negative impacts that are difficult to predict but could have a material adverse effect on our business and financial condition. For example, certain of these changes could impose additional limitations on the rates we will be able to charge for our future products or the amounts of reimbursement available for our future products from governmental agencies or third-party payors.

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 Opus, 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 ("AKS"), which is a criminal law that prohibits, among other things, persons and entities from knowingly and wilfully 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 or Medicaid. The AKS has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, pharmacies, purchasers, and formulary managers on the other, including, for example, consulting/speaking arrangements, discount and rebate offers, grants, charitable contributions, and patient support offerings, among others. 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. Further, courts have found that the AKS has been violated if any "one purpose" of an arrangement involving remuneration is to induce referrals of federal healthcare program business. Violations of the AKS can result in significant civil monetary penalties and criminal fines, per each violation, additional civil penalties and treble damages under the federal Civil False Claims Act ("FCA"), as described in detail further below, as well as imprisonment and mandatory exclusion from participation in government health care programs, meaning that federal healthcare programs would no longer reimburse (directly or indirectly) for products or services furnished by the excluded entity or individuals. Although there are a number of statutory exceptions and regulatory safe harbors to the AKS that protect certain common industry activities from prosecution, these exceptions and safe harbors are narrowly drawn. Arrangements that do not fully satisfy all elements of an available exception or safe harbor are evaluated based on the specific facts and circumstances and are typically subject to increased scrutiny;
- The FCA, 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 AKS can serve as a basis for liability under the FCA. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. Pharmaceutical manufacturers have been investigated and/or subject to government enforcement actions asserting liability under the FCA for a variety of alleged activities, including alleged off-label promotion of drugs, purportedly concealing price concessions in the pricing information submitted to the government for government price reporting purposes, and allegedly providing free product to customers with the expectation that the customers would bill federal healthcare programs for the product. Violations of the FCA may result in significant civil fines and penalties for each false claim, currently ranging from $14,308 - $28,619 per false claim or statement for penalties assessed after January 15, 2025, treble damages, and potential exclusion from participation in federal healthcare programs. There is also the federal Criminal False Claims Act, which is similar to the FCA 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 AKS; and (4) failing to report and return a known overpayment;
- The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal statutes that impose criminal liability for knowingly and wilfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, or to obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program; knowingly and wilfully embezzling or stealing from a healthcare benefit program; wilfully preventing, obstructing, misleading, or delaying a criminal investigation of a healthcare offense; and knowingly and wilfully falsifying, concealing or covering up a material fact or making any materially false statements in connection with the delivery of or payment for healthcare benefits, items, or services. Similar to the federal Anti-Kickback Statute, a person or entity need not have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- The federal Physician Payments Sunshine Act ("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 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. The Sunshine Act also requires certain manufacturers, among others, to track and report ownership and investment interests held by U.S.-licensed 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 wilfully embezzling or stealing from a healthcare benefit program, wilfully obstructing a criminal investigation of a healthcare offense, and knowingly and wilfully 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 AKS, 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;
- 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 may be broader in scope than their federal equivalents; and
- State laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; 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" in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures.
- Additionally, we expect certain of 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:
- We expect to be required to participate in the MDRP in order for federal payment to be available for our products under Medicaid. Medicaid is a government health insurance program for eligible low-income adults, children, families, pregnant women, and people with certain disabilities and it is jointly funded by the federal and state governments. The MDRP requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of the HHS 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.
- Under federal law, we further expect to be required to participate in the 340B drug pricing program, which 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. In addition, after multiple delays, the final rule implementing civil monetary penalties against manufacturers for instances of overcharging 340B covered entities became effective on January 1, 2019. Accordingly, if we have an approved product, we could be subject to such penalties if the government were to find that we knowingly and intentionally overcharged a 340B covered entity.

- Additionally, 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 products which may qualify as "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

In the U.S. and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients and healthcare providers are unlikely to use our products unless third-party payor coverage is provided and reimbursement by such payor is adequate to cover a significant portion of the cost of our products. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other comparable government authorities. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors, including government health programs in the U.S. such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, the product.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. Obtaining coverage and reimbursement approval of a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide to each payor supporting scientific, clinical and cost-effectiveness data for the use of our products on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement will be obtained. Nonetheless, product candidates may not be considered medically necessary or cost-effective. A decision by a third-party payor not to cover a product could reduce physician utilization once the product is approved and have a material adverse effect on sales, our operations and financial condition. Additionally, a third-party payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor. Third-party coverage and reimbursement may not be available to enable us to maintain price levels sufficient to cover our costs, including research, development, manufacture, sale and distribution.

The containment of healthcare costs also has become a priority of federal, state and foreign governments, and the prices of products have been a focus in this effort. 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.

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 AMP 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. Further, 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 taken steps to implement the IRA, including: releasing the first round of negotiated maximum prices, which will be effective in 2026, for the ten drugs that were subject to the IRA's negotiation process; releasing quarterly lists of Medicare Part B products that are subject to adjusted coinsurance rates based on the inflationary rebate provisions of the IRA; releasing guidance outlining the methodology for identifying certain manufacturers eligible to participate in the phase-in period where discounts on applicable products will be lower than those required by the Medicare Part D Manufacturer Discount Program; releasing final guidance on the implementation of the Medicare Part D Manufacturer Discount Program; and announcing a list of fifteen additional drugs that will be subject to price negotiations during 2025 with the negotiated prices becoming effective in 2027. It remains to be seen how these drug pricing initiatives will affect the broader pharmaceutical industry. Payment methodologies may also be subject to changes under regulatory initiatives. For example, on February 14, 2023, HHS issued a report, which, among other things, selected three potential drug affordability and accessibility models to be tested by the CMS Innovation Center. Specifically, the report addressed: (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.

Moreover, individual states in the United States have 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. It is likely 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 for a pharmaceutical manufacturer's products or additional pricing pressure.

Coverage policies and third-party payor reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future. It is difficult to predict how Medicare coverage and reimbursement policies will be applied to products for which the company receives marketing approval in the future and coverage and reimbursement under different federal healthcare programs is not always consistent. Further, private payors often follow the coverage and reimbursement policies established under Medicare. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our products for which we receive marketing approval.

Outside of the US, in the EU and the UK, the price of prescription only medicines is subject to governmental control, determined on a national level. Pricing negotiations with national payors can last up to years following the grant of a marketing authorization and are subject to proving clinical effectiveness, cost

effectiveness and an appropriate budget impact. In some jurisdictions, such as the UK and Germany, a further positive recommendation from health technology on cost-effectiveness is required for the products to be actually prescribed and reimbursed by the respective national health systems.

As of January 12, 2025, the new EU Health Technology Regulation No 2021/2282 has become applicable in respect of new advanced therapy medicinal products (which include gene therapy products) and oncology medicines. The Regulation imposes a new procedure, a joint clinical assessment at a centralized level, as a mandatory step for the assessment of the pricing and reimbursement of medicinal products by national authorities. It requires companies applying for products in scope to make relevant submissions for the joint clinical assessment, in line with a number of prespecified criteria. By 2030 it will apply to all medicinal products.

Human Capital Resources

As of December 31, 2024, we had 17 full-time employees, with the following assignments: four engaged in clinical research and development activities, one of whom holds a Ph.D. degree, four engaged in research and development activities and also business development, and nine engaged in finance, business development, human resources, and administrative support. We plan to continue to utilize expert consultants and contract organizations to support execution of the day-to-day operations. None of our employees are represented by labor unions or covered by collective bargaining agreements.

We believe that we maintain good relations with our employees We have expanded efforts to prioritize employee engagement by conducting employee surveys and offering increased professional development opportunities and education assistance benefits.

RISK FACTORS

Investing in our Securities involves risk. Before deciding whether to invest in our Securities, you should consider carefully the risks and uncertainties described below. You should also consider the risks, uncertainties and assumptions discussed under the heading "Risk Factors" included in our most recent Annual Report on Form 10-K as revised or supplemented by our most recent Quarterly Report on Form 10-Q, each of which are on file with the SEC and are incorporated herein by reference, and which may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future. There may be other unknown or unpredictable economic, business, competitive, regulatory or other factors that could have material adverse effects on our future results. If any of these risks actually occurs, our business, business prospects, financial condition or results of operations could be seriously harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment. Please also read carefully the section in this prospectus supplement entitled "Special Note Regarding Forward-Looking Statements."

Risks Related to This Offering

We have broad discretion in the use of the net proceeds from this offering.

Our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways with which you may not agree. Accordingly, you will be relying on the judgment of our management with regard to the use of the net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. It is possible that the net proceeds will be invested or otherwise used in a way that does not yield a favorable, or any, return for the Company.

Our stockholders may experience significant dilution as a result of future equity offerings and exercise of outstanding options.

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock. We cannot assure you that we will be able to sell shares or other securities in any other offering at a price per share that is equal to or greater than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock or other securities convertible into or exchangeable for our common stock in future transactions may be higher or lower than the price per share in this offering.

In addition, we have a number of securities allowing the purchase of our common stock. As of March 17, 2025, 1,019,418 shares of common stock were reserved for future issuance under our stock incentive plans. As of that date, there were also options to purchase 7,035,253 shares of our common stock outstanding. The exercise of outstanding options having an exercise price per share that is less than the offering price per share in this offering will increase dilution to investors in this offering.

You may experience immediate and substantial dilution in the net tangible book value per share of the common stock offered hereby or that may be issued upon the exercise of any Warrant or Pre-Funded Warrants.

If the price per share of our common stock being offered or that may be issued upon the exercise of any Warrant or Pre-Funded Warrants is higher than the net tangible book value per share of our common stock, you will suffer immediate and substantial dilution in the net tangible book value of the common stock you purchase in this offering or the common stock underlying the Warrants or Pre-Funded Warrants you purchase in this offering. In addition, we have a significant number of stock options, warrants, unvested restricted stock units and convertible Series A Preferred Stock outstanding. The exercise of any of these outstanding options and warrants, the vesting and settlement of these restricted stock units and the conversion of our Series A Preferred Stock will result in further dilution to investors. For a further description of the dilution that you will experience immediately after this offering, see the section of this prospectus supplement entitled "Dilution."

Our stock price and the trading volume of our stock may be volatile and investors may not be able to resell shares of our common stock at or above the price they paid.

The trading price of our common stock could be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. In particular, the market for biopharmaceutical companies has experienced extreme volatility that has often been unrelated to the operating performance or prospects of particular companies. The market price for our common stock may be influenced by many factors, including:

- the announcement of new products or product enhancements by us or our competitors;
- changes in our relationships with our licensors, licensees, or other strategic partners;
- developments concerning intellectual property rights and regulatory approvals;
- variations in our and our competitors' results of operations;
- 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;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- other factors described in the "Risk Factors" sections of our Annual Report on Form 10-K for the year ended December 31, 2023 and in subsequent filings, which are incorporated by reference into this prospectus supplement.

In addition, the stock markets in general, and the markets for biopharmaceutical stocks in particular, have experienced volatility that may have been unrelated to the operating performance of the issuer. These broad market fluctuations may adversely affect the trading price or liquidity of our common stock.

We do not intend to pay dividends on our common stock, so any returns will be limited to the value of our stock.

We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock.

There is no public market for the Warrants or the Pre-Funded Warrants being offered in this offering.

There is no established public trading market for the Warrants or the Pre-Funded Warrants being offered in this offering, and we do not expect a market to develop. In addition, we do not intend to apply to list the Warrants or the Pre-Funded Warrants on any securities exchange or nationally recognized trading system, including Nasdaq. Without an active market, the liquidity of the Warrants and the Pre-Funded Warrants will be limited.

Holders of Warrants and Pre-Funded Warrants purchased in this offering will have no rights as holders of common stock until such holders exercise such Warrants and Pre-Funded Warrants and acquire our common stock.

Until holders of Warrants and Pre-Funded Warrants acquire shares of our common stock upon exercise of such Warrants and Pre-Funded Warrants, such holders will have no rights with respect to the shares of our common stock underlying such Warrants and Pre-Funded Warrants. Upon exercise of the Warrants or the Pre-Funded Warrants, the holders will be entitled to exercise the rights of a holder of common stock only as to matters for which the record date occurs after the exercise date.

The Warrants being offered may not have value.

Each Warrant offered by us in this offering will be exercisable immediately at an exercise price of $0.95 per share and will expire on the fifth anniversary of the date of issuance, after which any unexercised Warrants will

expire and have no further value. In the event that the market price of our common stock does not exceed the exercise price of the Warrants during the period when they are exercisable, the Warrants may not have any value. If the Warrants expire with no value, we will not receive any proceeds from the exercise of the Warrants to fund our operations.

Risks Related to the Opus Acquisition

The integration with Former Opus presents challenges, and the failure to successfully integrate the businesses could have a material adverse effect on our business, financial condition and results of operations.

The Opus Acquisition combined two independent companies with different operations and focuses on drug development. We are devoting significant management attention and resources to integrating our business practices and portfolio of assets and reorienting our operations so that we may focus on developing gene therapy treatments. We may fail to realize some or all of the anticipated benefits of the Opus Acquisition if the integration process takes longer than expected or is more costly than expected. Potential difficulties we may encounter in the integration process include the following:

- the inability to successfully combine our assets in a manner that permits us to expand our product pipeline or achieve the anticipated benefits from the Opus Acquisition, which would result in the anticipated benefits of the Opus Acquisition not being realized partly or wholly in the time frame currently anticipated or at all;
- the creation of uniform standards, controls, procedures, policies and information systems;
- the addition of new personnel, including new management, which may be difficult to smoothly integrate; and
- potential unknown liabilities and unforeseen increased expenses, delays or regulatory conditions associated with the Opus Acquisition.

It is likely that the integration process could result in the diversion of our management's attention, the disruption or interruption of, or the loss of momentum in our ongoing businesses or potential partnerships which could adversely affect our ability to maintain our current business relationships or the ability to achieve the anticipated benefits of the Opus Acquisition, or could otherwise adversely affect our business and financial results.

After the Opus Acquisition, we significantly expanded our product pipeline and business operations and shifted our business strategies, and these changes may not result in an improvement in the value of our common stock.

Following the Opus Acquisition, we are now a biotech company focused on developing gene therapies to treat inherited retinal diseases ("IRDs"). We expanded our product pipeline by including gene therapy programs. We cannot guarantee that implementing the Opus Acquisition and related transactions will not impair stockholder value or otherwise adversely affect our business. The Opus Acquisition poses significant integration challenges between our businesses and management teams which could result in management and business disruptions, any of which could harm our results of operation, business prospects, and impair the value of the Opus Acquisition to our stockholders.

In the event we are unable to realize the strategic benefits currently anticipated from the Opus Acquisition, our stockholders will have experienced substantial dilution of their ownership interest without receiving any commensurate benefit. We have devoted and will continue to devote significant management attention and resources to integrate the two companies and we may not manage these processes successfully. Delays in this process could adversely affect the combined company's business, financial results, financial condition and stock price. Even if we are able to integrate the business operations successfully, there can be no assurance that this integration will result in the realization of the full benefits anticipated. It is also possible that undisclosed, contingent or other liabilities or problems in connection with the acquired company may arise in the future of which we were previously unaware. These undisclosed liabilities could have an adverse effect on our business, financial condition and prospects.

If our stockholders do not approve the conversion of our Series A Preferred Stock at the 2025 Annual Meeting of Stockholders, we may be required to divert funds from our business to pay dividends on outstanding shares of Series A Preferred Stock.

In connection with the Opus acquisition, we issued 14.1 thousand shares of convertible Series A Preferred Stock to existing stockholders of Former Opus. The shares of Series A Preferred Stock will be convertible into shares of common stock, subject to stockholder approval at the 2025 Annual Meeting of Stockholders, to be held in April 2025. If the conversion is not approved by stockholders, the holders of Series A Preferred Stock will be entitled to quarterly cash dividends commencing on October 15, 2025. The payment of such dividends could divert capital away from the development of our business to the detriment of our stockholders.

Risks Related to the Development of Our Gene Therapy Products and other Product Candidates

Our gene therapy product candidates are based on a novel technology, which makes it difficult to predict the time and cost of development and of subsequently obtaining regulatory approval.

We have focused our business on the development of gene therapy programs for the treatment of IRDs and plan to continue to expand our gene therapy portfolio. Our future success depends on our successful development of viable gene therapy products. There can be no assurance that we will not experience problems or delays in developing new products and that such problems or delays will not cause unanticipated costs, or that any such development problems can be solved. We may be unable to reduce development timelines and costs for our other gene therapy development programs. We also may experience unanticipated problems or delays in expanding our manufacturing capacity, which may prevent us from completing our clinical trials, meeting the obligations of our collaborations or successfully.

In addition, the clinical trial requirements of the FDA and other regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of such product candidates. The regulatory approval process for novel product candidates such as our products, including OPGx-BEST, can be more expensive and take longer than for other, better known or more extensively studied product candidates. Even if we are successful in developing additional product candidates, it is difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for these product candidates, or how long it will take to commercialize any other products for which we receive marketing approval.

Regulatory bodies and any new guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these product candidates or lead to significant post-approval limitations or restrictions. As we advance our product candidates, we will be required to consult with these regulatory and advisory groups and comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of certain of our product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient product revenue, and our business, financial condition, results of operations and prospects would be materially and adversely affected.

Our gene therapy approach utilizes vectors derived from viruses, which may be perceived as unsafe or may result in unforeseen adverse events. Negative public opinion and increased regulatory scrutiny of gene therapy may damage public perception of the safety of our product and product candidates and adversely affect our ability to conduct our business or obtain regulatory approvals for our product candidates.

Gene therapy remains a novel technology with few approved to date in the United States and EU. Public perception may be influenced by claims that gene therapy is unsafe, and gene therapy may not gain the acceptance of the public or the medical community. In particular, our success will depend upon physicians who specialize in the treatment of genetic diseases targeted by our product and product candidates, if approved, prescribing treatments that involve the use of our product and product candidates, if approved, in lieu of, or in addition to, existing treatments with which they are familiar and for which greater clinical data may be available. More restrictive government regulations or negative public opinion would have an adverse effect on our business, financial condition, results of operations and prospects and may delay or impair the development and commercialization of our product candidates or demand for any products we may develop. For example, earlier

gene therapy trials led to several well-publicized adverse events, including cases of leukemia and death seen in other trials using other vectors. Serious adverse events in our clinical trials, or other clinical trials involving gene therapy products or our competitors' products, even if not ultimately attributable to the relevant product candidates, and the resulting publicity, could result in increased government regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any products for which we obtain marketing approval.

Gene therapies are novel, complex and difficult to manufacture. We could experience production problems in our network of external facilities that result in delays in our development or commercialization programs or otherwise adversely affect our business.

Our gene therapy product and product candidates require processing steps that are more complex than those required for most chemical pharmaceuticals. Moreover, unlike chemical pharmaceuticals, the physical and chemical properties of a biologic such as ours generally cannot be fully characterized. As a result, assays of the finished product may not be sufficient to ensure that the product will perform in the intended manner. Accordingly, we employ multiple steps to control our manufacturing process to assure that the product or product candidate is made strictly and consistently in compliance with the process. Problems with the manufacturing process, even minor deviations from the normal process, could result in product defects or manufacturing failures that result in lot failures, product recalls, product liability claims or insufficient inventory. We may encounter problems achieving adequate quantities and quality of clinical-grade materials that meet FDA, EU or other applicable standards or specifications with consistent and acceptable production yields and costs.

In addition, the FDA, the EMA and other foreign regulatory authorities may require us to submit samples of any lot of any approved product together with the protocols showing the results of applicable tests at any time. Under some circumstances, the FDA, the EMA or other foreign regulatory authorities may require that we not distribute a lot until the agency authorizes its release. Slight deviations in the manufacturing process, including those affecting quality attributes and stability, may result in unacceptable changes in the product that could result in lot failures or product recalls. We have experienced lot failures in the past and there is no assurance we will not experience such failures in the future. Lot failures or product recalls could cause us to delay product launches or clinical trials, which could be costly to us and otherwise harm our business, financial condition, results of operations and prospects. We also may encounter problems hiring and retaining the experienced specialist scientific, quality control and manufacturing personnel needed to operate our manufacturing process, which could result in delays in our production or difficulties in maintaining compliance with applicable regulatory requirements.

Because we are developing product candidates for the treatment of IRDs in which there is less clinical experience for gene therapy products as compared to other diseases and, in some programs, using new endpoints or techniques, there is increased risk that certain regulatory authorities may not consider the endpoints of our clinical trials to provide clinically meaningful results.

There are no pharmacologic therapies approved to treat IRDs caused by LCA5-associated gene mutations in the United States or EU. In addition, there has been limited clinical trial experience for the development of pharmaceuticals to treat IRDs. Certain aspects of IRDs render efficacy endpoints historically used for vision clinical trials less applicable as clinical endpoints, which may require the use of novel clinical endpoints. As a result, the design and conduct of clinical trials for these disorders is subject to increased risk. In addition, the treatment of certain IRDs, such as BEST1 mutations, may require assessment of clinical endpoints that reflect a stabilization, as opposed to an improvement, of functional vision. Assessing these endpoints may require longer periods of observation and may delay the completion of any trials we may undertake.

Our gene therapy product candidates and the process for administering our gene therapy product candidates may cause undesirable and unforeseen side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial potential or result in significant negative consequences following any potential marketing approval.

There have been several significant adverse side effects in gene therapy treatments in the past, including reported cases of leukemia and death seen in other trials using other vectors. While new recombinant vectors have been developed to reduce these side effects, gene therapy is still a relatively new approach to disease

treatment and additional adverse side effects could develop. There also is the potential risk of delayed adverse events following exposure to gene therapy products due to persistent biologic activity of the genetic material or other components of products used to carry the genetic material.

Possible adverse side effects that could occur with treatment with gene therapy products include an immunologic reaction early after administration which, while not necessarily adverse to the patient's health, could substantially limit the effectiveness of the treatment. In previous clinical trials involving AAV vectors for gene therapy, some subjects experienced the development of a T-cell response, whereby after the vector is within the target cell, the cellular immune response system triggers the removal of transduced cells by activated T-cells. If our vectors demonstrate a similar effect, which we are unable to mitigate with immuno-suppressive regimens, we may decide or be required to halt or delay further clinical development of our product candidates and our commercial efforts could be materially and adversely affected.

In addition to any potential side effects caused by the product candidate, the administration process or related procedures also can cause adverse side effects. If any such adverse events occur, our marketing authorization or clinical trials could be suspended or terminated.

In addition, the FDA could impose a Risk Evaluation and Mitigation Strategy ("REMS"), and other non-US regulatory authorities could impose other specific obligations as a condition of approval to ensure that the benefits of our product candidates outweigh their risks, which could delay approval or commercial acceptance of our product candidates. A REMS may include, among other things, a communication plan to health care practitioners or patients, and elements to assure safe use, such as restricted distribution methods, patient registries, and other risk minimization tools. Similar risk management programs could be imposed by equivalent authorities in foreign jurisdictions, including by the European Commission. Furthermore, if we or others later identify undesirable side effects caused by our product candidate, several potentially significant negative consequences could result, including:

- regulatory authorities may suspend or withdraw approvals of such product candidate;
- regulatory authorities may require additional warnings or limitations of use in product labeling;
- we may be required to change the way a product candidate is administered or conduct additional clinical trials;
- we could be sued and held liable for harm caused by our products to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of any products for which we receive marketing approval and could significantly harm our business, financial condition, results of operations and prospects.

Orphan Drug Designation and Rare Pediatric Disease Designation, among other designations by the FDA, may not lead to a faster development, regulatory review or approval process and it does not increase the likelihood that any of our gene therapy product candidates will receive marketing approval in the United States. The potential award of a Priority Review Voucher may not result in a financial benefit to us.

We received Orphan Drug Designation in September 2024 and Rare Pediatric Disease Designation in August 2024 for OPGx-LCA5 to treat LCA5, an early-onset retinal degeneration that causes vision loss. We may, in the future, apply for such designations for our other gene therapy product candidates in the United States.

Under the Orphan Drug Act of 1983, the FDA may designate a product candidate as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as having a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. Orphan drug status provides incentives that include specialized guidance to help expedite development, exemption from user fees and potential for seven years of market exclusivity following approval. Qualification to maintain orphan drug status is generally monitored by the regulatory authorities during the orphan drug exclusivity period, currently seven years from the date of approval in the United States. It is possible that another company also holding orphan drug designation for the same product candidate will receive marketing approval for the same indication before we do. If that were to happen, our applications for that indication may not be approved until the competing company's period of exclusivity expires. Even if we are the

first to obtain marketing authorization for an orphan drug indication, there are circumstances under which a competing product may be approved for the same indication during the seven-year period of marketing exclusivity, such as if the later product is shown to be clinically superior to the orphan product, or if the later product is deemed a different product than ours. Further, the seven-year marketing exclusivity would not prevent competitors from obtaining approval of the same product candidate as ours for indications other than those in which we have been granted orphan drug designation, or for the use of other types of products in the same indications as our orphan products.

Under the Food and Drug Administration Safety and Innovation Act (FDASIA) of 2012 the FDA is authorized to award a priority review voucher ("PRV") to a drug sponsor upon approval of that sponsor's drug to treat a rare pediatric disease. A drug sponsor can later redeem the voucher when submitting another new drug application to treat any disease or condition in adults or children, or it may sell or transfer the voucher to another sponsor. A voucher entitles a sponsor to a 6-month priority review by the FDA rather than the 10-month standard review. In some instances, recipients of PRVs have transferred them to other drug developers in exchange for substantial financial consideration. Even if OPGx-LCA5 is approved, it is not certain that we will be awarded a PRV as it may no longer meet the conditions for such an award at that time. In addition, even if we receive a PRV, there can be no assurance that we will be able to apply it to review of one of our other drug candidates or to transfer it for substantial financial consideration, if at all. The FDA may also revoke any priority review voucher if the rare pediatric disease drug for which the voucher was awarded is not marketed in the U.S. within one year following the date of approval.

For the purposes of this program, a "rare pediatric disease" is a (a) serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years, including age groups often called neonates, infants, children, and adolescents; and (b) rare disease or conditions within the meaning of the Orphan Drug Act. The FDA may determine that an NDA or BLA for one or more of our product candidates does not meet the eligibility criteria for a priority review voucher upon approval. Moreover, due to the current statutory authority for the RPD and voucher program, the FDA may not award the voucher to sponsors of marketing applications unless either (i) the drug has received rare pediatric disease designation as of December 20, 2024, and is then approved by the FDA no later than September 30, 2026; or (ii) Congress reauthorizes the program. If Congress does not enact legislation reauthorizing the program, additional indications will not be eligible for an RPD designation or priority review voucher. Even if legislation is enacted that extends the date by which approval of the rare pediatric disease-designated drug must obtain approval to receive a priority review voucher, we may not obtain approval by that date, and even if we do, we may not obtain a priority review voucher.

If we request orphan drug designation or rare pediatric disease designation for our other current or future product candidates, there can be no assurances that the FDA will grant any of our product candidates such designation. Accordingly, even if we believe one of our product candidates meets the criteria for designations, the FDA may disagree. In any event, the receipt of a designation, or the redemption of a PRV for a product candidate, may not result in a faster development process, review or approval compared to products considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA, nor does it limit the ability of the FDA to grant orphan drug designation to product candidates of other companies that treat the same indications as our product candidates prior to our product candidates receiving exclusive marketing approval. Further, there may be changes to the regulatory scheme surrounding these designations, which render them obsolete.

We may encounter substantial delays in our planned clinical trials, or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidates. Clinical testing is expensive, time-consuming and uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. Events that may prevent successful or timely commencement and completion of preclinical and clinical development include:

- delays in reaching a consensus with regulatory authorities on trial design;
- delays in reaching agreement on acceptable terms with prospective CROs and clinical trial sites;

- delays in opening clinical trial sites or obtaining required institutional review board or independent Ethics Committee approval at each clinical trial site;
- delays in recruiting and enrolling suitable subjects to participate in our clinical trials, due to factors such as the size of the trial or subject population, process for identifying subjects, design or expansion of protocols, eligibility and exclusive criteria, perceived risks and benefits of the relevant product candidate or gene therapy generally, availability of competing therapies and trials, severity of the disease under investigation, need and length of time required to discontinue other potential therapies, availability of genetic testing, availability and proximity of trial sites for prospective subjects, ability to obtain subject consent and referral practices of physicians;
- imposition of a clinical hold by regulatory authorities, including as a result of a serious adverse event or after an inspection of our clinical trial operations or trial sites;
- failure by us, any CROs we engage or any other third parties to adhere to clinical trial requirements;
- failure to perform in accordance with GCP, or applicable regulatory guidelines in the European Union and other countries;
- delays in the testing, validation, manufacturing and delivery of our product candidates to the clinical sites, including delays by third parties with whom we have contracted to perform;
- delays in having subjects complete participation in a trial or return for post-treatment follow-up;
- clinical trial sites or subjects dropping out of a trial;
- selection of clinical endpoints that require prolonged periods of clinical observation or analysis of the resulting data;
- occurrence of serious adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- occurrence of serious adverse events in trials of the same class of agents conducted by other sponsors; or
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols.

Any inability to successfully complete research studies and preclinical and clinical development could result in additional costs to us or impair our ability to generate revenues from product sales, regulatory and commercialization milestones and royalties. In addition, if we make manufacturing or formulation changes to our product candidates, we may need to conduct additional studies to bridge our modified product candidates to earlier versions. Clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates, if approved, or allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates, if approved, and may harm our business, financial condition, results of operations and prospects.

We may be negatively impacted if the results of our planned clinical trials are inconclusive or if there are safety concerns or serious adverse events associated with our product candidates.

If the results of our planned clinical trials are inconclusive or if there are safety concerns or serious adverse events associated with our product candidates, we may:

- be delayed in obtaining marketing approval for our product candidates, if at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to changes in the way the product is administered;
- be required to perform additional clinical trials to support approval or be subject to additional post-marketing testing or other requirements;
- have regulatory authorities withdraw, vary or suspend their approval of the product or impose restrictions on its distribution in the form of a modified risk evaluation and mitigation;

- be subject to the addition of labeling statements, such as warnings or contraindications;
- be sued; or
- experience damage to our reputation.

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.

The results from the prior nonclinical studies and clinical trials for our product candidates 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. 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 the Company's business and financial prospects, would be adversely affected. Further, our product candidates may not be approved even if they achieve their respective primary endpoints in additional Phase 3 registration trials. The FDA 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 the FDA for a Phase 3 study for PS for decreased vision under dim (mesopic or low) light conditions after keratorefractive surgery, 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. 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 like if public health concerns emerge that were unrecognized at the time of the SPA agreement.

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. However, 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, 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:

- perceived risks and benefits of gene therapy-based approaches or our product candidate under study;
- availability of genetic testing for potential subjects;
- 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; and
- proximity and availability of clinical trial sites for prospective patients.

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.

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.

We may expend a substantial amount of our 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.

We are currently internally focusing on developing gene therapy development programs. As a result, we may forego or delay pursuit of opportunities for other indications from our non-gene therapy portfolio or with other potential product candidates that later prove to have greater clinical success or 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 the Commercialization of RYZUMVI and Product Candidates which Obtain Marketing Approval

We depend heavily on the success of our product pipeline. If we fail to find strategic partners or we (including our strategic partner) fail to adequately commercialize our pipeline products, our business will be materially harmed.

Our business depends largely on the successful clinical development, regulatory approval and commercialization of gene therapies 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. APX3300 is still in clinical development and we are seeking a strategic partner to continue its development. We (or any future our strategic partners) plan to invest a significant portion of our efforts and financial resources in the development of our products. Further, we have already spent significant efforts in developing our pipeline of products. Our ability to generate product revenues depends heavily on obtaining marketing approval for and commercializing our gene therapy products and PS for additional indications.

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/BLA 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, our commercial opportunity will be limited. The success of our product candidates could be impacted by several factors, including the following:

- 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, the Company has rights to certain compounds for use in ophthalmic and diabetic diseases. The Company does not control the development of these compounds in other non-ophthalmic and non-diabetic 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 the Company.

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.

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

We are focused on the development of our gene therapy candidates for IRDs and our other 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 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 our products have been tested in relatively small patient populations, at a limited range of daily doses, and for limited durations to date, it is possible that our clinical trials have or will indicate an apparent positive effect 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 product candidates lack 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:

- we may 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.

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, including in the gene therapy field, 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. While there are currently no direct competitors for our OPGx-LCA5 gene therapy program, there are various companies developing gene therapies for the treatment of IRDs, which may ultimately directly compete with us in the future. Further, other pharmaceutical companies may develop therapies for the same indications that would compete with 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, such as using artificial intelligence and machine learning, 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.

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 our products.

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 our 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.

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 our product candidates, if approved, among physicians, patients, third-party payors, and others in the medical community.

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, particularly in the gene therapy space, which is a growing industry. If 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 or our partners' sales and marketing strategies;
- our or our partners' 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 or our partners' 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.
- ability of physicians to identify patients with rare genetic diseases (IRDs).
- limited genetic testing conducted on potential patients.

Aside from RYZUMVI, which we launched through the Viatris partnership, we have not yet sold any of our products. Further, our gene therapy products, if approved, may have limited commercial opportunity due to the relatively uncommon genetic conditions targeted by such 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 conducted limited 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 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.

In January 2025, we received notice from Sandoz Inc., a provider of generic and biosimilar medicines ("Sandoz"), that it has filed an ANDA for a generic version of RYZUMVI and submitted a Paragraph IV certification asserting that certain patents for RYZUMVI are invalid or unenforceable or will not be infringed by their generic product. This certification could lead to protracted and costly litigation to defend our patent rights. The potential litigation could divert management's attention and resources away from our core business operations and strategic initiatives, including the development and commercialization of our gene therapy products. Further, the uncertainty surrounding the outcome of the patent challenge could negatively impact investor confidence and our stock price. If Sandoz is successful in their challenge, it could result in the introduction of a generic competitor to the market before the expiration of our patents, thereby reducing our market share and potential future revenue from sales of RYZUMVI. Such result may also undermine the value of our intellectual property portfolio, which could affect our ability to secure partnerships or financing in the future.

If approved, our investigational products regulated as biologics may face competition from biosimilars approved through an abbreviated regulatory pathway.

In March 2010, the U.S. Congress enacted the Patient Protection and Affordable Care Act ("ACA"), including a subtitle called the Biologics Price Competition and Innovation Act of 2009 ("BPCIA") which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until twelve years from the date on which the reference product was first licensed. During this twelve-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of its product. The law is complex and

is still being interpreted and implemented by the FDA. Any processes adopted by the FDA to implement the BPCIA could have a material adverse effect on the future commercial prospects for our biological products.

We believe that our gene therapy product candidates, if approved as a biological product under a BLA, should qualify for the twelve-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to Congressional action or otherwise, or that the FDA will not consider our product candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. Jurisdictions in addition to the United States have established abbreviated pathways for regulatory approval of biological products that are biosimilar to earlier approved reference products. For example, the EU has had an established regulatory pathway for biosimilars since 2006. Moreover, the extent to which a biosimilar, once approved, could be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products will depend on a number of marketplace and regulatory factors that are still developing.

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 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 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.

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.

Risks Related to Our Financial Position and Need for Additional Capital

We have not generated significant 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 launched in April 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 our gene therapy candidates and other product candidates;
- obtain approvals on late-stage drugs in development and the receipt of associated financial payments from our partner.
- 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 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 our product candidates that we develop; and

achieve market acceptance of our product candidates.

Furthermore, as of December 31, 2024, we had an accumulated deficit of $138 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 products currently in our pipeline are 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 as a combined company 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. 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 ability to secure grant funding from government and nongovernment foundations;
- 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 capital.

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 financings, structured financings such as royalty monetization, and 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.

Our forecasts and projections rely in large part upon assumptions and analyses developed by us. If these assumptions or analyses prove to be incorrect, our actual operating results, revenues and expenses may be materially different from our forecasted results.

Our forecasts and projections, including projected budgets, results, revenues and expenses based on assumptions, analyses and estimates developed by our management and are subject to substantial uncertainty. These projections are not prepared with a view toward compliance with published guidelines of the American Institute of Certified Public Accountants, and neither our registered public accountants nor any other independent expert or outside party compiles or examines our projections. Accordingly, no such person expresses any opinion or any other form of assurance with respect to our projections.

Even though these forecasts and projections are presented with numerical specificity, they are inherently subject to significant business, regulatory, clinical trial result, economic, competitive and global risks, uncertainties and contingencies, many of which are beyond our control, and are based upon specific assumptions with respect to future business decisions, some of which will change. Global or macroeconomic trends may also affect our business and may necessitate changes in our forecasts or projections. Accordingly, you should not rely on our forecasts or projections as a guarantee of our actual budgets, operating results, revenues or expenses in the future.

Our forecasts and projections also include assumptions about risks and uncertainties that include, but are not limited to, risks discussed elsewhere in this prospectus supplement.

As a result, all or some of our forecasts and projections may prove to be incorrect, inaccurate and/or vary from quarter to quarter and thus our actual budgets, operating results, revenues and expenses may differ materially from those forecasted or projected. If that were to occur, you could lose your entire investment. Investors are urged to consider our prospects in light of the risks and uncertainties life sciences companies encounter when developing new biotechnology products and not to rely upon our forecasts or projections in making an investment decision regarding 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 federal statutes, including the False Claims Act and the Anti-Kickback Statute, along with analogous state and foreign laws and regulations, 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 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, former President Biden signed the American Rescue Plan Act of 2021 into law, which eliminated 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 2025, 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, former 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.

Moreover, there is significant uncertainty regarding the legislative and regulatory changes that will be implemented or proposed by the administration of President Trump and the current U.S. Congress. The development of our product candidates may be delayed by other events beyond our control. For example, action by the new Trump Administration to limit federal agency budgets or personnel may result in reductions to the FDA's budget, employees, and operations, which may lead to slower response times and longer review periods, potentially affecting our ability to progress development of our product candidates or obtain regulatory approval for our product candidates.

The biopharmaceutical and medical device industries are subject to extensive regulatory obligations and policies that may be subject to significant and abrupt change, including due to judicial challenges, election cycles, and resulting regulatory updates and changes in policy priorities.

On June 28, 2024, the U.S. Supreme Court issued an opinion holding that courts reviewing agency action pursuant to the Administrative Procedure Act (APA) "must exercise their independent judgment" and "may not defer to an agency interpretation of the law simply because a statute is ambiguous." The decision may have a significant impact on how lower courts evaluate challenges to agency interpretations of law, including those by the HHS, CMS, FDA and other agencies with significant oversight of the biopharmaceutical and medical device industries. The new framework is likely to increase both the frequency of such challenges and their odds of success by eliminating one way in which the government previously prevailed in such cases. As a result, significant regulatory policies will be subject to increased litigation and judicial scrutiny.

In addition, federal agency priorities, leadership, policies, rulemaking, communications, spending, and staffing may be significantly impacted by election cycles. For example, the current presidential administration's commitment to significantly reduce government spending through cuts to federal healthcare programs and reductions in the workforces of key government agencies, such as the HHS, FDA, and CMS. Efforts by the current administration to limit federal agency budgets or personnel may result in reductions to agency budgets, employees, and operations, which may lead to slower response times and longer review periods, potentially affecting our ability to progress development of our product candidates or obtain regulatory approval for our product candidates.

Any resulting changes in regulation may result in unexpected delays, increased costs, or other negative impacts on our business that are difficult to predict.

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. 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 the Health Insurance Portability and Accountability Act of 1996, 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 or our partners 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 or our partners are found to have promoted such off-label uses, we or they 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 or our partners cannot successfully manage the promotion of our product candidates, if approved, we or they 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 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, the FDA published guidance documents related to informed consent and GCPs that may present additional requirements to CROs.

In August 2023, the 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, the 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, the 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 the 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 BLA 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, the 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") (21 CFR parts 210 and 211) for manufacture 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 and could potentially lead to a recall of commercial product or a shortage of clinical supplies. Additionally, 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 our product candidates for nonclinical and clinical testing purposes and intend to continue to do so in the future, 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, one supplier in India for raw materials for the drug substance for APPX330, and one manufacturer in the United States 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 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 purity) 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 other potential problems related to transfers, we have established additional sources of supply for the registered starting materials, with U.S. manufacturers, for the active pharmaceutical ingredient APX3330 and are working towards t a second suppler of the active pharmaceutical ingredient for PS located in India. 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. Any future transfers of manufacturing to a different third party will 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;
- collaborators may determine, as a part of product life-cycle management, that changes to the product are necessary or required, that could include the formulation, container closure system, packaging, etc. which could affect the development or commercialization of the applicable product candidate.

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 a new collaboration for APX3330 on commercially reasonable terms, we may have to alter or halt our development, manufacturing, and commercialization plans related to the APX3330 program.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. Following the Opus Acquisition, we have discontinued our internal development of APX3330 and are pursuing a potential partnership to further advance this exciting program to allow us to focus on our gene therapy programs while extending our cash runway. 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.

If we engage in additional 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 continue to 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.

Our strategy of focusing on the cash-pay utilization for future sales of RYZUMVI may limit our ability to increase sales or achieve profitability with this product.

With regard to the commercialization of RYZUMVI, our strategy is to focus on cash-pay utilization. This focus may limit the potential pricing and profitability of this product. We believe pursuing a non-insurance reimbursed product strategy in connection with RYZUMVI allows for meaningful strategic advantages in the United States, including pricing and marketing flexibility. However, companies offering products competitive to RYZUMVI may nonetheless try to compete on price, both directly through rebates, promotional programs, and coupons, as well as indirectly through product bundling and customer loyalty programs. In addition, we cannot predict how the market, including customers, doctors, patients, and governmental agencies, will react to this strategy. If RYZUMVI does not achieve sufficient success and market acceptance, if we face retaliation from third parties as a result of this arrangement and program (for example, in the form of non-coverage determinations, limitations on coverage, or unfavorable reimbursement with respect to our other products) or if any part of this arrangement is found to be non-compliant with applicable law or regulations, this could have a material adverse effect on our business, financial condition, cash flows, and results of operations and could cause the market value of our common shares to decline. Our business, financial results, and future prospects will be materially harmed if we cannot generate sufficient consumer demand for RYZUMVI with this strategy.

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. Under certain conditions, 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 patents related to our 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 are involved in a patent litigation lawsuit with a competitor on RYZUMVI® and we may become involved in additional 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. For example, we received notice that Sandoz Inc. ("Sandoz") filed an abbreviated new drug application with the U.S. FDA seeking permission to market a generic version of RYZYMVI® for the mydriasis indication recited on our RYZUMVI® product label. The notice received from Sandoz alleges that certain of our U.S. patents to RYZYMVI® are invalid. Additionally, the notice received from the competitor alleges that certain of our U.S. patents would not be infringed by the competitor's generic version of RYZYMVI®. In March 2025, in collaboration with our commercialization partner for RYZYMVI®, we filed a complaint for patent infringement of certain RYZYMVI® patents against Sandoz in the District of New Jersey in response to Sandoz's ANDA filing. The complaint seeks, among other relief, equitable relief enjoining Sandoz from infringing the RYZUMVI patents.

To counter infringement or unauthorized use of our patents and other intellectual property rights, we may be required to file additional infringement claims against Sandoz and/or infringement claims against other parties, which can be expensive and time consuming. In addition, in an infringement proceeding, a court may decide that one of more of our patents 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 licensed from third parties (such as Apexian Pharmaceuticals, Inc. for product candidates ("Apexian") for our APX3330 product candidate under development, and the University of Pennsylvania and/or University of Florida and other entities for multiple product candidates under development in our gene therapy program) and our additional pipeline candidates, and the termination of, or reduction or loss of rights under, these licenses 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.

We exclusively license, for example, from the University of Pennsylvania and/or University of Florida certain patents and patent applications for products under development for our gene therapy program. Rights granted under the agreements are subject to various milestone payment, royalty, and other obligations on us, and may be revocable under certain circumstances including if we 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 a license 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 one or more of the products under development in our gene therapy program. Also, 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 these agreements.

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,, 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.

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, particularly changes that may occur as a result of the recent U.S. presidential election;
- 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 could 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. We have experienced cyber attacks in the past. While these attacks did not have a significant impact to the Company, we may continue to experience such attacks. 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. Moreover, the rapid evolution and increased adoption of artificial intelligence technologies may intensify our cybersecurity risks. 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

The market price of our common stock is expected to be volatile.

The market price of our common stock has been, and may continue to be, subject to significant fluctuations. Some of the factors that may cause the market price of our common stock to fluctuate include:

- 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; and
- the results of clinical trials of our gene therapy products, 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 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 our 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.

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. It is also possible that potential plaintiffs may file lawsuits relating to the Opus Acquisition, as litigation and related claims frequently follow the announcement and completion of business transactions, including mergers like the one we consummated. Litigation often is expensive and diverts management's attention and resources, which could seriously harm our business. The outcome of any future litigation is uncertain and, if not resolved we may incur significant costs and damages to our reputation.

Actions of activist stockholders could adversely affect our business and stock price and cause us to incur significant expenses.

We strive to maintain constructive, ongoing communications with all of our stockholders, and welcome their views and opinions with the goal of enhancing value for all our stockholders. Nonetheless, certain activist stockholders may from time to time engage in proxy solicitations, advance stockholder proposals, or otherwise attempt to effect changes or acquire control over the Company. We are currently the target of a proxy contest initiated by Mina Sooch, our former Chief Executive Officer, who has nominated six candidates for election to the Board. Responding to proxy contests, proposals, and other actions by activist stockholders requires, and may in the future require, us to incur significant legal and consulting costs, proxy solicitation expenses, and administrative and associated costs. In addition, responding to proxy contests, proposals, and other actions by activist stockholders may divert the attention of our Board, management team and employees and disrupt our business and operations.

Perceived uncertainties as to our future direction, our ability to execute on our strategy, or changes to the composition of our Board or management team could arise from proposals by activist stockholders (including Ms. Sooch) or a proxy contest. Such perceived uncertainties could interfere with our ability to execute our strategic plans, be exploited by our competitors and/or other activist stockholders, result in the loss of potential business opportunities, make it more difficult to attract and retain financial professionals and qualified employees, and adversely impact our relationship with existing and potential business partners, any of which could have a material adverse effect on our business. Further, actual or perceived actions of activist stockholders may cause significant fluctuations in our stock price based upon temporary or speculative market perceptions or other factors that do not necessarily reflect the Company's underlying fundamentals and prospects. Additionally, we may in the future become party to litigation as a result of matters arising in connection with a proxy contest or other activist stockholder actions, which could serve as a distraction to our Board and management and could require us to incur significant additional costs.

USE OF PROCEEDS

We estimate that the net proceeds to us from this offering will be approximately $18,684,999.48 after deducting underwriting discounts and commissions and estimated offering expenses payable by us and excluding proceeds, if any, from the exercise of Warrants or Pre-Funded Warrants issued in this offering.

We intend to use the net proceeds from this offering for general corporate purposes and working capital, including for preclinical studies and clinical trials and the advancement of our product candidates.

This expected use of net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual use of net proceeds may vary significantly depending on numerous factors, including the actual net proceeds from this offering, the progress of our development efforts, the timing and costs associated with the manufacture and supply of any of our product candidates and any unforeseen cash needs. As a result, our management will have broad discretion over the use of the net proceeds from this offering.

We may temporarily invest the net proceeds in a variety of capital preservation instruments, including investment grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government, or may hold such proceeds as cash until they are used for their stated purpose. We have not determined the amount of net proceeds to be used specifically for such purposes.

DESCRIPTION OF CAPITAL STOCK

General

As of the date of this prospectus supplement, our certificate of incorporation authorizes us to issue up to 135,000,000 shares of capital stock, all with a par value of $0.0001 per share, of which: 125,000,000 shares are designated as common stock and 10,000,000 shares are designated as preferred stock.

The following summary describes the material terms of our capital stock. The description of capital stock is qualified by reference to our certificate of incorporation and our bylaws.

Common Stock

As of December 31, 2024, 31,574,657 shares of common stock were outstanding. All outstanding shares of common stock are duly authorized, validly issued, fully paid, and nonassessable. All authorized but unissued shares of our common stock are available for issuance by our board of directors without any further stockholder action, except as required by the listing standards of Nasdaq.

Voting Rights

Generally, holders of Common Stock are entitled to cast one vote for each share held of record on all matters submitted to a vote of the stockholders, including the election of directors. Accordingly, the holders of a majority of the outstanding shares of Common Stock entitled to vote in any election of directors can elect all of the directors standing for election, if they so choose, other than any directors that holders of any Preferred Stock we may issue may be entitled to elect. Except as may be provided in the Certificate of Incorporation or by our board of directors (the "Board"), holders of Common Stock have the exclusive right to vote for the election of directors and for all other purposes.

Dividend Rights

Holders of our Common Stock have equitable rights to receive dividends, as may be lawfully declared from time to time by our Board, subject to any preferential rights of holders of any outstanding shares of Preferred Stock, as described below.

Liquidation

In the event of our liquidation, dissolution, or winding up, the holders of common stock will be entitled to share ratably in the assets legally available for distribution to stockholders after the payment of or provision for all of our debts and other liabilities, subject to the prior rights of any preferred stock then-outstanding.

Rights and Preferences

Holders of common stock have no preemptive or conversion rights or other subscription rights and there are no redemption or sinking fund provisions applicable to the common stock. The rights, preferences, and privileges of holders of common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Preferred Stock

Our board of directors may, without further action by our stockholders, fix the rights, preferences, privileges and restrictions of up to an aggregate of 10,000,000 shares of preferred stock in one or more series and authorize their issuance. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of such series, any or all of which may be greater than the rights of our common stock. The issuance of our preferred stock could adversely affect the voting power of holders of our common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation. In addition, the issuance of preferred stock could have the effect of decreasing the market price of our common stock and could also have the effect of delaying, deferring or preventing a change of control or other corporate action.

Series A Preferred Stock

On October 22, 2024, the Company filed a Certificate of Designation of Preferences, Rights and Limitations of the Series A Non-Voting Convertible Preferred Stock with the Secretary of State of the State of Delaware (the "Certificate of Designation"), designating 14,146 shares of authorized preferred stock of the Company as the Series A Preferred Stock. As of December 31, 2024, 14,145.374 shares of Series A Preferred Stock were outstanding.

Voting Rights

Holders of Series A Preferred Stock generally do not have voting rights, except with respect to certain protective matters such as amendments to our Certificate of Incorporation or the Certificate of Designation that alter or change adversely the powers, preferences or rights given to the Series A Preferred Stock.

Dividends

Holders of Series A Preferred Stock are entitled to receive dividends on shares of Series A Preferred Stock (on an as-if-converted-to-common-stock basis) equal to and in the same form, and in the same manner, as dividends (other than dividends on shares of our Common Stock payable in the form of Common Stock) actually paid on shares of our Common Stock when, as and if such dividends (other than dividends payable in the form of Common Stock) are paid on shares of our Common Stock. Additionally, commencing on October 15, 2025, holders of Series A Preferred Stock will be entitled to receive, as and if declared by the Board, cumulative quarterly cash dividends equal to $15.26 per share of Series A Preferred Stock on October 15, 2025 and $26.00 per share of Series A Preferred Stock for quarterly dividends thereafter. The Company cannot pay any dividends (other than dividends payable in the form of Common Stock) on shares of Common Stock unless the full dividends payable to holders of Series A Preferred Stock are paid at the same time.

Liquidation

The Series A Preferred Stock ranks on parity with our Common Stock with respect to the payment of dividends and distributions of assets upon liquidation, dissolution or winding up of the Corporation, whether voluntarily or involuntarily.

Conversion

Upon approval by the Company's stockholders, each share of Series A Preferred Stock will be automatically converted into 1,000 shares of Common Stock, effective as of 5:00 p.m. Eastern Time on the third business day following such approval. No fractional shares of Common Stock will be issued upon conversion of the Series A Preferred Stock; rather, in lieu of any fractional shares to which a holder of Series A Preferred Stock would otherwise be entitled, the Company will pay such holder cash equal to such fraction multiplied by the closing price of a share of Common Stock on the Nasdaq Stock Market on such date. In the event that the Company (i) pays a stock dividend or otherwise makes a distribution or distributions payable in shares of Common Stock, (ii) subdivides outstanding shares of Common Stock into a larger number of shares, or (iii) combines (including by way of a reverse stock split) outstanding shares of Common Stock into a smaller number of shares, then the conversion ratio described above will be adjusted by the multiple of a fraction in which the numerator is the number of shares of Common Stock outstanding immediately after such event and the denominator is the number of shares of Common Stock outstanding immediately prior to such event.

Other Rights and Preferences

The shares of Series A Preferred Stock are not redeemable. A holder of Series A Preferred Stock may transfer his, her or its shares of Series A Preferred Stock in whole, or in part, together with all accompanying rights, without the consent of the Company so long as such transfer is in compliance with applicable securities laws and with the terms of any lock-up agreement that such shares of Series A Preferred Stock are subject to. In the event that the Company engages in a certain type of business combination, holders of Series A Preferred Stock are entitled to receive the same kind and amount of securities, cash, or property as they would have received if they had converted their shares into Common Stock immediately before the transaction.

Options and Restricted Stock

As of December 31, 2024, (i) 1,420,288 shares of common stock remain available for issuance under our 2020 Equity Incentive Plan and the 2021 Inducement Plan, stock options to purchase an aggregate of 2,564,766 shares of common stock were outstanding under our 2020 Equity Incentive Plan and stock options to purchase an aggregate of 1,782,800 shares of common stock were outstanding under our 2021 Inducement Plan, and (ii) 1,130,430 unvested shares of restricted stock were outstanding.

Warrants

As of December 31, 2024, 7,204,299 warrants to purchase shares of our capital stock were outstanding, with a weighted average exercise price of $4.82 (subject to adjustment).

Anti-Takeover Effects of Delaware Law and Our Certificate of Incorporation and Bylaws

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could make it more difficult to complete an acquisition of us by means of a tender offer, a proxy contest or otherwise or the removal and replacement of our incumbent officers and directors.

Removal of Directors; Board Vacancies; Board Size. Our amended and restated certificate of incorporation provides for the removal of any of our directors with or without cause and requires a stockholder vote of at least sixty-six and two-thirds percent (66 2/3%) of the voting power of all then outstanding shares of stock. In addition, our amended and restated certificate of incorporation provides that any vacancy occurring on our board of directors may be filled by a majority of directors then in office, even if less than a quorum, unless the board of directors determines that such vacancy shall be filled by the stockholders. Finally, the authorized number of directors may be changed only by a resolution of the board of directors. This system of removing directors, filling vacancies and fixing the size of the board makes it more difficult for stockholders to replace a majority of the directors.

Special Stockholder Meetings. Our amended and restated certificate of incorporation and our amended and restated bylaws provide that a special meeting of stockholders may be called only by a resolution adopted by a majority of our board of directors or by the chairman of the board.

Stockholder Advance Notice Procedure. Our amended and restated bylaws establish an advance notice procedure for stockholders to make nominations of candidates for election as directors or to bring other business before an annual meeting of our stockholders. The amended and restated bylaws provide that any stockholder wishing to nominate persons for election as directors at, or bring other business before, an annual meeting must deliver to our secretary a written notice of the stockholder's intention to do so. To be timely, the stockholder's notice must be delivered to or mailed and received by us not more than 120 days, and not less than 90 days before the anniversary date of the preceding annual meeting, except that if the annual meeting is set for a date that is not within 30 days before or 60 days after such anniversary date, we must receive the notice not earlier than the close of business on the 120th day prior to the annual meeting and not later than the close of business on the later of (i) the 90th day prior to the annual meeting or (ii) the tenth day following the day on which we first made public announcement of the date of meeting. The notice must include the following information:

- as to director nominations, all information relating to each director nominee that is required by the rules of the Securities and Exchange Commission to be disclosed in solicitations of proxies, or is otherwise required by Regulation 14A of the Exchange Act;
- as to any other business that the stockholder proposes to bring before the meeting, a brief description of the business to be proposed, the reasons for conducting such business at the meeting and, if any, the stockholder's material interest in the proposed business; and
- the name and address of the stockholder who intends to make the nomination and the class and number of our shares beneficially owned of record;

Undesignated Preferred Stock. The ability to authorize undesignated preferred stock makes it possible for our board of directors to issue preferred stock with voting or other rights or preferences that could have the effect of delaying, deferring, preventing or otherwise impeding any attempt to change control of us.

Delaware Anti-Takeover Statute. We are subject to Section 203 of the Delaware General Corporation Law, which prohibits persons deemed "interested stockholders" from engaging in a "business combination" with a

publicly traded Delaware corporation for three years following the date these persons become interested stockholders unless the business combination is, or the transaction in which the person became an interested stockholder was, approved in a prescribed manner or another prescribed exception applies. Generally, an "interested stockholder" is a person who, together with affiliates and associates, owns, or within three years prior to the determination of interested stockholder status did own, 15% or more of a corporation's voting stock. Generally, a "business combination" includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. The existence of this provision may have an anti-takeover effect with respect to transactions not approved in advance by the board of directors, such as discouraging takeover attempts that might result in a premium over the market price of our common stock.

Business Combinations with Interested Stockholders. Our amended and restated certificate of incorporation provides that certain "business combinations" with "interested stockholders" require approval by the holders of at least a majority of the voting power of our then outstanding shares of voting stock not beneficially owned by any interested stockholder or an affiliate or associate thereof. The foregoing restriction does not apply, however, if the transaction is either approved by a majority of our "continuing directors" or certain minimum price and procedural and other requirements are met. Generally, a "business combination" includes a merger, consolidation, liquidation, recapitalization or other similar transaction or a sale, lease, transfer or other disposition of assets or securities having an aggregate fair market value of $15 million or more. An "interested stockholder" generally means a beneficial owner of 20% or more of our voting stock, certain assignees of such beneficial owners and certain of our affiliates that within the preceding two years were the beneficial owner of 20% or more of our voting stock. A "continuing director" is defined as any member of our board who is not an affiliate or associate or representative of the interested stockholder and was a member of the board prior to the time the interested stockholder became such, and any successor of a continuing director who is unaffiliated with the interested stockholder and is recommended or elected by at least two-thirds of the continuing directors then on the board.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Equiniti Trust Company, LLC. The transfer agent and registrar's address is 55 Challenger Road, Floor 2, Ridgefield Park, NJ 07660.

Listing on the Nasdaq Capital Market

Our common stock is listed on the Nasdaq Capital Market under the symbol "IRD."

DESCRIPTION OF THE SECURITIES WE ARE OFFERING

We are offering 12,219,736 shares of our common stock, Warrants to purchase up to 21,052,631 shares of our common stock and 8,832,895 Pre-Funded Warrants. We are also registering the shares of our common stock issuable from time to time upon exercise of the Warrants and Pre-Funded Warrants offered hereby. The following description of our Securities summarizes the material terms and provisions of the common stock, Warrants and Pre-Funded Warrants we are offering under this prospectus supplement and the accompanying prospectus.

Common Stock

We are offering 12,219,736 shares of our common stock. Each share of our common stock is being sold together with a Warrant to purchase one share of our common stock. The shares of our common stock and Warrants are immediately separable and will be issued separately, but will be purchased together in this offering. The public offering price for each share of our common stock and related Warrant is $0.95. Each Warrant will be exercisable immediately at an exercise price of $0.95 per share and will be exercisable during the period commencing on March 25, 2025 and ending on the fifth anniversary of the date of issuance.

The material terms of our common stock are described under "Description of Capital Stock" on page S-98 of this prospectus supplement.

Warrants

The following summary of certain terms and provisions of the Warrants that are being offered hereby is not complete and is subject to, and qualified in its entirety by, the provisions of the Warrant, the form of which will be filed as an exhibit to a Current Report on Form 8-K in connection with this offering and incorporated by reference into the registration statement of which this prospectus supplement forms a part. Prospective investors should carefully review the terms and provisions of the form of Warrant for a complete description of the terms and conditions of the Warrant.

Pursuant to a warrant agency agreement (the "Warrant Agreement") by and among us and Equiniti Trust Company, together as warrant agent (the "Warrant Agent"), the Warrants will be issued in book-entry form and shall initially be represented only by one or more global warrants deposited with the Warrant Agent.

Duration and Exercise Price. Each Warrant offered hereby will have an initial exercise price per share equal to $0.95. The holder of the Warrant may, at their sole discretion, exercise each of their Warrants for one Pre-Funded Warrant at an exercise price of $0.9499 (which is the per share exercise price minus $0.0001). The Warrants are exercisable at any time after their original issuance and at any time up to the date that is five years after their original issuance. The exercise price is subject to appropriate adjustment in the event of certain stock dividends and distributions, stock splits, stock combinations, reclassifications or similar events affecting our common stock and also upon any distributions of assets, including cash, stock or other property to our stockholders.

Exercisability. The Warrants will be exercisable, at the option of each holder, in whole or in part, by delivering to us a duly executed exercise notice accompanied by payment in full for the number of shares of our common stock purchased upon such exercise (except in the case of a cashless exercise as discussed below). A holder (together with its affiliates) may not exercise any portion of the Warrant to the extent that the holder would own more than 4.99% of the outstanding common stock immediately after exercise, except that upon at least 61 days' prior notice from the holder to us, the holder may increase the amount of ownership of outstanding stock after exercising the holder's Warrants up to 9.99% of the number of shares of our common stock outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of the Warrants. Purchasers of Warrants in this offering may also elect prior to the issuance of the Warrants to have the initial exercise limitation set at 9.99% of our outstanding common stock. No fractional shares of common stock will be issued in connection with the exercise of a Warrant. In lieu of fractional shares, we will either pay the holder an amount in cash equal to the fractional amount multiplied by the exercise price or round up to the next whole share.

Cashless Exercise. If, at the time a holder exercises its Warrants, a registration statement registering the issuance of the shares of common stock underlying the Warrants under the Securities Act is not then effective or available and an exemption from registration under the Securities Act is not available for the issuance of such shares, then in lieu of making the cash payment otherwise contemplated to be made to us upon such exercise in

payment of the aggregate exercise price, the holder may elect instead to receive upon such exercise (either in whole or in part) the net number of shares of common stock determined according to a formula set forth in the Warrants.

Transferability. Subject to applicable laws, a Warrant may be transferred at the option of the holder upon surrender of the Warrant to us together with the appropriate instruments of transfer.

Fractional Shares. No fractional shares of common stock will be issued upon the exercise of the Warrants. Rather, the number of shares of common stock to be issued will, at our election, either be rounded up to the nearest whole number or we will pay a cash adjustment in respect of such final fraction in an amount equal to such fraction multiplied by the exercise price.

Call Feature. The warrants are callable by us in certain circumstances. Subject to certain exceptions, in the event that the warrants are outstanding, if, after the closing date, (i) the Company has announced OPGx-BEST1 DUO-1001 Cohort 1 data, (ii) the volume weighted average price of our common stock for 30 consecutive trading days (the "Measurement Period" which 30 consecutive trading day period shall not have commenced until after the initial exercise date) exceeds $1.43, which is equal to 150% of the initial exercise price of the Warrant (subject to adjustment for forward and reverse stock splits, recapitalizations, stock dividends and similar transactions after the initial exercise date), (iii) the trading average daily volume for such Measurement Period exceeds $150,000 per trading day and (iv) the warrant holder is not in possession of any information that constitutes or might constitute, material non-public information which was provided by the Company, any of our subsidiaries, or any of our officers, directors, employees, agents or affiliates, then we may, within one trading day of the end of such Measurement Period, upon notice (a "Call Notice"), call for cancellation of all or any portion of the warrants for which a notice of exercise has not yet been delivered (a "Call") for consideration equal to $0.001 per warrant share. Any portion of a warrant subject to such Call Notice for which a notice of exercise shall not have been received by the Call Date (as hereinafter defined) will be canceled at 6:30 p.m. (New York City time) on the 30th trading day after the date the Call Notice is sent by the Company (such date and time, the "Call Date"). Our right to call the warrants shall be exercised ratably among the holders based on the then outstanding warrants.

Trading Market. There is no established trading market for any of the Warrants, and we do not expect a market to develop. We do not intend to apply for a listing for any of the Warrants on any securities exchange or other nationally recognized trading system. Without an active trading market, the liquidity of the Warrants will be limited.

Right as a Stockholder. Except as otherwise provided in the Warrants or by virtue of the holders' ownership of shares of our common stock, the holders of Warrants do not have the rights or privileges of holders of our common stock, including any voting rights, until such Warrant holders exercise their Warrants.

Fundamental Transaction. In the event of a fundamental transaction, as described in the Warrants and generally including any reorganization, recapitalization or reclassification of our common stock, the sale, transfer or other disposition of all or substantially all of our properties or assets, our consolidation or merger with or into another person, the acquisition of more than 50% of our outstanding common stock, or any person or group becoming the beneficial owner of 50% of the voting power represented by our outstanding common stock, the holders of the Warrants will be entitled to receive upon exercise of the Warrants the kind and amount of securities, cash or other property that the holders would have received had they exercised the Warrants immediately prior to such fundamental transaction. Additionally, as more fully described in the Warrants, in the event of certain fundamental transactions, the holders of the Warrants will be entitled to receive consideration in an amount equal to the Black Scholes Value of the remaining unexercised portion of the Warrants on the date of consummation of such fundamental transaction.

Waivers and Amendments. No term of the Warrants may be amended or waived without the written consent of the Company and the holder or the beneficial owner of such Warrant.

Pre-Funded Warrants

The following summary of certain terms and provisions of the Pre-Funded Warrants offered hereby is not complete and is subject to, and qualified in its entirety by, the provisions of the Pre-Funded Warrant, the form of which will be filed as an exhibit to a Current Report on Form 8-K in connection with this offering and incorporated by reference into the registration statement of which this prospectus supplement forms a part.

Prospective investors should carefully review the terms and provisions set forth in the form of Pre-Funded Warrant. The Pre-Funded Warrant will be issued in certificate form.

The term "pre-funded" refers to the fact that the purchase price of our common stock in this offering includes almost the entire exercise price that will be paid under the Pre-Funded Warrants, except for a nominal remaining exercise price of $0.0001. The purpose of the Pre-Funded Warrants is to enable investors that may have restrictions on their ability to beneficially own more than 4.99% (or, upon election of the holder, 9.99%) of our outstanding common stock following the consummation of this offering the opportunity to make an investment in the Company without triggering their ownership restrictions, by receiving Pre-Funded Warrants in lieu of our common stock which would result in such ownership of more than 4.99% (or 9.99%), and receive the ability to exercise their option to purchase the shares underlying the Pre-Funded Warrants at such nominal price at a later date. The holder of a Pre-Funded Warrant will not be deemed a holder of our underlying common stock until the Pre-Funded Warrant is exercised.

Duration and Exercise Price. The Pre-Funded Warrants offered hereby will have an exercise price of $0.0001 per share. The Pre-Funded Warrants will be immediately exercisable and may be exercised at any time until exercised in full. The exercise prices and numbers of shares of common stock issuable upon exercise are subject to appropriate adjustment in the event of stock dividends, stock splits, reorganizations or similar events affecting our common stock.

Exercise Limitation. A holder (together with its affiliates) may not exercise any portion of such holder's Pre-Funded Warrants to the extent that the holder would own more than 4.99% (or, upon the election of the holder prior to the issuance of any Pre-Funded Warrants, 9.99%) of the common stock then outstanding after giving effect to such exercise.

Transferability. Subject to applicable laws, a Pre-Funded Warrant may be transferred at the option of the holder upon surrender of the Pre-Funded Warrant to us together with the appropriate instruments of transfer.

Fractional Shares. No fractional shares or scrip representing fractional shares of common stock will be issued upon the exercise of the Pre-Funded Warrants. Rather, the number of shares of common stock to be issued will, at our election, either be rounded up to the nearest whole number or we will pay a cash adjustment in respect of such final fraction in an amount equal to such fraction multiplied by the exercise price.

Trading Market. There is no established trading market for any of the Pre-Funded Warrants, and we do not expect a market to develop. We do not intend to apply for a listing for any of the Pre-Funded Warrants on any securities exchange or other nationally recognized trading system. Without an active trading market, the liquidity of the Pre-Funded Warrants will be limited.

Rights as a Shareholder. Except as otherwise provided in the Pre-Funded Warrants or by virtue of the holders' ownership of shares of our common stock, the holders of Pre-Funded Warrants do not have the rights or privileges of holders of our common stock, including any voting rights, until such Pre-Funded Warrant holders exercise their Pre-Funded Warrants.

Fundamental Transaction. In the event of a fundamental transaction, as described in the Pre-Funded Warrants and generally including any reorganization, recapitalization or reclassification of our common stock, the sale, transfer or other disposition of all or substantially all of our properties or assets, our consolidation or merger with or into another person, the acquisition of more than 50% of our outstanding common stock, or any person or group becoming the beneficial owner of 50% of the voting power represented by our outstanding common stock, the holders of the Pre-Funded Warrants will be entitled to receive upon exercise of the Pre-Funded Warrants the kind and amount of securities, cash or other property that the holders would have received had they exercised the Pre-Funded Warrants immediately prior to such fundamental transaction.

Waivers and Amendments. No term of the Pre-Funded Warrants may be amended or waived without the written consent of the holder of such Pre-Funded Warrant.

DILUTION

If you purchase Securities in this offering, your ownership interest will be diluted to the extent of the difference between the public offering price per share of our common stock or that may be issued upon exercise of any Pre-Funded Warrants offered hereby and our net tangible book value per share immediately after the offering and the as-adjusted net tangible book value per share of our common stock immediately after this offering. We calculate net tangible book value per share by dividing the net tangible book value (our tangible assets less our total liabilities) by the number of outstanding shares of our common stock.

The historical net tangible book value of our common stock as of December 31, 2024 was $26,283,000, or $0.83 per share, based on 31,574,657 shares of common stock outstanding as of December 31, 2024.

After giving effect to our sale of 22,229,103 shares of our common stock in this offering and the concurrent private placement, assuming the exercise of any Pre-Funded Warrants that are sold in this offering and no exercise of any of the Warrants, and after deducting underwriting discounts and commissions and estimated offering expenses, our as-adjusted net tangible book value as of December 31, 2024 would have been $46,198,000, or $0.86 per share of common stock. This represents an immediate increase in net tangible book value of $0.03 per share to existing stockholders and an immediate dilution in net tangible book value of $0.09 per share to purchasers of common stock in this offering.

The following table illustrates this dilution on a per-share basis (unaudited):

Combined public offering price per share of common stock		$0.95
Historical net tangible book value per share as of December 31, 2024	$0.83	
Increase in net tangible book value per share attributable to this offering	$0.03	
As adjusted net tangible book value per share after giving effect to this offering		$0.86
Dilution per share to new investors purchasing shares in this offering		$0.09

The table and discussion above are based on 31,574,657 shares of common stock outstanding as of December 31, 2024, and excludes:

- 7,204,299 shares of common stock issuable upon the exercise of warrants outstanding as of December 31, 2025, with a weighted-average exercise price of $4.82 per share;
- 5,073,736 shares of common stock issuable upon the exercise of outstanding stock options outstanding as of December 31, 2024 under our 2018 Equity Incentive Plan, 2020 Equity Incentive Plan and 2021 Inducement Plan;
- 1,420,289 shares of common stock reserved for future issuance under our 2020 Equity Incentive Plan and 2021 Inducement Plan outstanding as of December 31, 2024;
- 1,393,230 unvested restricted stock awards as of December 31, 2024; and
- up to 14,145,374 shares of common stock that are issuable upon conversion of the 14,145.374 shares of our Series A Preferred Stock.

To the extent that outstanding stock options and/or warrants are exercised, new stock options are issued, Series A Preferred Stock is converted, restricted stock units are settled or we issue additional shares of common stock in the future, there will be further dilution to investors purchasing shares of common stock in this offering.

DIVIDEND POLICY

We have never declared or paid cash dividends on our common stock. We currently intend to retain all available funds and any future earnings use in the operation of our business and do not anticipate paying any cash dividends on our common stock in the foreseeable future. Any future determination to declare cash dividends will be made at the discretion of our Board, subject to compliance with applicable laws and covenants under current or future credit facilities, which may restrict or limit our ability to pay dividends, and will depend on our financial condition, operating results, capital requirements, general business conditions and other factors that our Board may deem relevant.

UNDERWRITING

Craig-Hallum Capital Group LLC ("Craig-Hallum" or the "underwriter") is acting as sole underwriter for the offering. Subject to the terms and conditions set forth in an underwriting agreement between us and the underwriter, we have agreed to sell to the underwriter, and the underwriter has agreed to purchase from us, at the public offering price less the underwriting discounts and commissions, the following number of shares of common stock, Warrants and Pre-Funded Warrants.

Underwriter	Number of Shares of Common Stock	Number of Warrants	Number of Pre-Funded Warrants
Craig Hallum Capital Group LLC	12,219,736	21,052,631	8,832,895

We have agreed to indemnify the underwriter against certain liabilities, including liabilities under the Securities Act of 1933, as amended (the "Securities Act"), relating to losses or claims resulting from material misstatements in or omissions from this prospectus supplement, the registration statement of which this prospectus supplement is a part, certain free writing prospectuses that may be used in the offering and in any marketing materials used in connection with this offering and to contribute to payments the underwriter may be required to make in respect of those liabilities.

Commissions and Discounts

The following table shows the combined public offering price, underwriting discounts and commissions and proceeds, before expenses, to us.

	Per Share and Related Warrant	Per Share and Related Pre-Funded Warrant	Total
Public offering price	$0.9500	$0.9499	$19,999,999.45
Underwriting discounts and commissions(1)	$0.0570	$0.0570	$ 1,199,999.97
Proceeds, before expenses, to us(2)	$0.8930	$0.8929	$18,799,169.48

(1) Includes an underwriting discount of 6.0% on the public offering price.

(2) The amount of offering proceeds to us presented in this table does not give effect to the exercise, if any, of the Warrants or the Pre-Funded Warrants being issued in connection with this offering.

The underwriting agreement provides that the obligation of the underwriter to pay for and accept delivery of the securities offered by this prospectus supplement is subject to the approval of certain legal matters by its counsel and to certain other conditions. The underwriter is obligated to take and pay for all of the shares, Warrants and Pre-Funded Warrants offered by this prospectus supplement if any such securities are taken. The underwriter reserves the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

The estimated total expenses of the offering payable by us, exclusive of the underwriting discounts and commissions, are approximately $300,000, which includes legal, accounting and printing costs and various other fees associated with the registration and listing of our common stock and common stock underlying our Warrants, as applicable. We have agreed to reimburse the underwriter for certain of its expenses incurred in connection with this offering in an amount up to $115,000.

We have also agreed to pay the underwriter a tail fee equal to three percent (3.0%) of the total gross proceeds received by us from any investor, if during the period ending one (1) month following the term of the underwriters engagement, we consummate a transaction led by an underwriter or placement agent other than Craig-Hallum, is consummated or a definitive agreement or letter of intent or other evidence of commitment is entered into which subsequently results in a transaction being consummated.

Lock-Up Agreements

We have agreed to not sell any shares of our common stock, or any securities convertible into or exercisable or exchangeable into shares of common stock, subject to certain exceptions, for a period of ninety (90) days after the closing of this offering unless we obtain prior written consent of the underwriter. Consent may be given at any time without public notice, and the underwriter may consent in its sole discretion. In addition, each of our directors and executive officers has entered into a lock-up agreement with the underwriter. Under the lock-up

agreements, subject to certain limited circumstances, our directors and officers may not sell or transfer any common stock or securities convertible into or exchangeable or exercisable for common stock during the period from the date of this prospectus continuing through the date ninety (90) days after the date of this prospectus without first obtaining the written consent of the underwriter. This consent may be given at any time without public notice, and the underwriter may consent in its sole discretion. We have also agreed, subject to certain exceptions, not to enter into a Variable Rate Transaction (as defined in the underwriting agreement) for ninety (90) days after the closing of this offering.

Listing

Our common stock is listed on the Nasdaq Capital Market under the symbol "IRD." There is no established trading market for the Warrants or the Pre-Funded Warrants, and we do not expect a trading market to develop. We do not intend to list the Warrants or the Pre-Funded Warrants on any securities exchange or nationally recognized trading system. Without a trading market, the liquidity of the Warrants and the Pre-Funded Warrants will be extremely limited.

Price Stabilization, Short Positions and Penalty Bids

To facilitate this offering, the underwriter may engage in transactions that stabilize, maintain or otherwise affect the price of our common stock during and after the offering. Specifically, the underwriter may over-allot or otherwise create a short position in our common stock for its own account by selling more shares of common stock than we have sold to the underwriter. The underwriter may close out any short position by either exercising its option to purchase additional shares or purchasing shares in the open market.

In addition, the underwriter may stabilize or maintain the price of our common stock by bidding for or purchasing shares in the open market and may impose penalty bids. If penalty bids are imposed, selling concessions allowed to broker-dealers participating in this offering are reclaimed if shares previously distributed in this offering are repurchased, whether in connection with stabilization transactions or otherwise. The effect of these transactions may be to stabilize or maintain the market price of our common stock at a level above that which might otherwise prevail in the open market. The imposition of a penalty bid may also affect the price of our common stock to the extent that it discourages resales of our common stock. The magnitude or effect of any stabilization or other transactions is uncertain. These transactions may be effected on the Nasdaq or otherwise and, if commenced, may be discontinued at any time.

In connection with this offering, the underwriter may also engage in passive market making transactions in our common stock on the Nasdaq. Passive market making consists of displaying bids on the Nasdaq by the prices of independent market makers and effecting purchases limited by those prices in response to order flow. Rule 103 of Regulation M promulgated by the SEC limits the amount of net purchases that each passive market maker may make and the displayed size of each bid. Passive market making may stabilize the market price of our common stock at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

Neither we nor the underwriter make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. In addition, neither we nor the underwriter make any representation that the underwriter will engage in these transactions or that any transaction, if commenced, will not be discontinued without notice.

Affiliations

The underwriter and its affiliates are full-service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. The underwriter may in the future engage in investment banking and other commercial dealings in the ordinary course of business with us or our affiliates. The underwriter may in the future receive customary fees and commissions for these transactions.

In the ordinary course of its various business activities, the underwriter and its affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers, and

such investment and securities activities may involve securities and/or instruments of the issuer. The underwriter and its affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Electronic Offer, Sale and Distribution

In connection with this offering, the underwriter or certain of the securities dealers may distribute prospectuses by electronic means, such as e-mail. In addition, the underwriter may facilitate Internet distribution for this offering to certain of its Internet subscription customers. The underwriter may allocate a limited number of shares for sale to its online brokerage customers. An electronic prospectus is available on the Internet websites maintained by any such underwriter. Other than the prospectus in electronic format, the information on the websites of the underwriter is not part of this prospectus supplement or the accompanying prospectus.

Selling Restrictions

General

Other than in the United States, no action has been taken by us or the underwriter that would permit a public offering of the securities offered by this prospectus supplement in any jurisdiction where action for that purpose is required. The securities offered by this prospectus supplement may not be offered or sold, directly or indirectly, nor may this prospectus supplement or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus supplement comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus supplement. This prospectus supplement does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus supplement in any jurisdiction in which such an offer or a solicitation is unlawful.

European Economic Area.

In relation to each Member State of the European Economic Area (each, a "Relevant State"), no securities have been offered or will be offered pursuant to the offering to the public in that Relevant State prior to the publication of a prospectus in relation to the securities which has been approved by the competent authority in that Relevant State or, where appropriate, approved in another Relevant State and notified to the competent authority in that Relevant State, all in accordance with the Prospectus Regulation, except that securities may be offered to the public in that Relevant State at any time:

- to any legal entity which is a qualified investor as defined under Article 2 of the Prospectus Regulation;
- to fewer than 150 natural or legal persons (other than qualified investors as defined under Article 2 of the Prospectus Regulation), subject to obtaining the prior consent of the representative for any such offer; or
- in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of securities shall require us or any of the representative to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation.

For the purposes of this provision, the expression an "offer to the public" in relation to any securities in any Relevant State means the communication in any form and by any means of sufficient information on the terms of the offer and any securities to be offered so as to enable an investor to decide to purchase or subscribe for any securities, and the expression "Prospectus Regulation" means Regulation (EU) 2017/1129, as amended.

United Kingdom.

No securities have been offered or will be offered pursuant to the offering to the public in the United Kingdom prior to the publication of a prospectus in relation to the securities which has been approved by the Financial Conduct Authority, except that the securities may be offered to the public in the United Kingdom at any time:

- to any legal entity which is a qualified investor as defined under Article 2 of the UK Prospectus Regulation;
- to fewer than 150 natural or legal persons (other than qualified investors as defined under Article 2 of the UK Prospectus Regulation), subject to obtaining the prior consent of the representative for any such offer; or
- in any other circumstances falling within Section 86 of the Financial Services and Markets Act 2000 (the "FMSA"),

provided that no such offer of the securities shall require us or any representative to publish a prospectus pursuant to Section 85 of the FSMA or supplement a prospectus pursuant to Article 23 of the UK Prospectus Regulation. For the purposes of this provision, the expression an "offer to the public" in relation to the securities in the United Kingdom means the communication in any form and by any means of sufficient information on the terms of the offer and any securities to be offered so as to enable an investor to decide to purchase or subscribe for any securities and the expression "UK Prospectus Regulation" means Regulation (EU) 2017/1129 as it forms part of domestic law by virtue of the European Union (Withdrawal) Act 2018.

Canada.

The securities may be sold in Canada only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the securities must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus supplement (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriter is not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Switzerland.

The shares may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange (the "SIX") or on any other stock exchange or regulated trading facility in Switzerland. This document has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the shares or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, or the shares have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, and the offer of shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes ("CISA"). Accordingly, no public distribution, offering or advertising, as defined in CISA, its implementing ordinances and notices, and no distribution to any non-qualified investor, as

defined in CISA, its implementing ordinances and notices, shall be undertaken in or from Switzerland, and the investor protection afforded to acquirers of interests in collective investment schemes under CISA does not extend to acquirers of shares.

Australia.

No placement document, prospectus, product disclosure statement or other disclosure document has been lodged with the Australian Securities and Investments Commission ("ASIC"), in relation to the offering.

This prospectus supplement does not constitute a prospectus, product disclosure statement or other disclosure document under the Corporations Act 2001 (the "Corporations Act"), and does not purport to include the information required for a prospectus, product disclosure statement or other disclosure document under the Corporations Act.

Any offer in Australia of the shares may only be made to persons (the "Exempt Investors") who are "sophisticated investors" (within the meaning of section 708(8) of the Corporations Act), "professional investors" (within the meaning of section 708(11) of the Corporations Act) or otherwise pursuant to one or more exemptions contained in section 708 of the Corporations Act so that it is lawful to offer the shares without disclosure to investors under Chapter 6D of the Corporations Act.

The shares applied for by Exempt Investors in Australia must not be offered for sale in Australia in the period of 12 months after the date of allotment under the offering, except in circumstances where disclosure to investors under Chapter 6D of the Corporations Act would not be required pursuant to an exemption under section 708 of the Corporations Act or otherwise or where the offer is pursuant to a disclosure document which complies with Chapter 6D of the Corporations Act. Any person acquiring shares must observe such Australian on-sale restrictions.

This prospectus supplement contains general information only and does not take account of the investment objectives, financial situation or particular needs of any particular person. It does not contain any securities recommendations or financial product advice. Before making an investment decision, investors need to consider whether the information in this prospectus supplement is appropriate to their needs, objectives and circumstances, and, if necessary, seek expert advice on those matters.

LEGAL MATTERS

Certain legal matters in connection with this offering and the validity of the securities offered by this prospectus supplement will be passed upon for us by Sidley Austin LLP. The underwriter is being represented in connection with this offering by Ellenoff Grossman & Schole LLP.

EXPERTS

The financial statements of Opus Genetics, Inc. (formerly known as Ocuphire Pharma, Inc.) appearing in Opus Genetics, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2023, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon, included therein, and incorporated herein by reference. The financial statements of the Former Opus appearing in Opus Genetics, Inc.'s Current Report on Form 8-K/A dated January 7, 2025 have been audited by Ernst & Young LLP, as set forth in their report included therein and incorporated herein by reference. Such financial statements are incorporated herein by reference in reliance upon such reports given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of a registration statement that we have filed with the SEC. Certain information in the registration statement has been omitted from this prospectus in accordance with the rules of the SEC. For further information, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. Statements contained in this prospectus supplement or incorporated by reference concerning the contents of any contract or any other document are not necessarily complete. If a contract or document has been filed or incorporated by reference as an exhibit to the registration statement, we refer you to the copy of the contract or document that has been filed. Each statement in this prospectus supplement or incorporated by reference relating to a contract or document filed as an exhibit is qualified in all respects by the filed exhibit. The SEC maintains a web site (http://www.sec.gov) that contains reports, proxy and information statements and other information regarding issuers like us that file electronically with the SEC.

We are subject to the reporting and information requirements of the Exchange Act of 1934, as amended, and, as a result, we file periodic reports, proxy statements and other information with the SEC. These periodic reports, proxy statements and other information will be available for access at the web site of the SEC referred to above.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference the information and reports we file with it, which means that we can disclose important information to you by referring you to these documents. The information incorporated by reference is an important part of this prospectus supplement, and information that we file later with the SEC will automatically update and supersede the information already incorporated by reference. This prospectus supplement incorporates by reference the documents set forth below that we have previously filed with the SEC, other than information in such documents that is deemed to be furnished and not filed:

- our Annual Report on Form 10-K for the year ended December 31, 2023, filed with the SEC on March 8, 2024;
- the information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2023 from our definitive proxy statement on Schedule 14A (other than information furnished rather than filed), which was filed with the SEC on April 29, 2024;
- our Preliminary Proxy Statement on Schedule 14A, filed with the SEC on March 20, 2025, as amended by Amendment No. 1 to the Preliminary Proxy Statement on Schedule 14A, filed with the SEC on March 21, 2025;
- our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2024 filed with the SEC on May 10, 2024, June 30, 2024 filed with the SEC on August 13, 2024 and September 30, 2024 filed with the SEC on November 12, 2024;
- our Current Reports on Form 8-K and Form 8-K/A filed with the SEC on February 16, 2024, April 17, 2024, June 13, 2024, October 22, 2024, January 7, 2025, January 14, 2025, January 23, 2025, January 24, 2025, March 4, 2025 and March 20, 2025; and
- the description of our common stock contained in our Registration Statement on Form 8-A, dated June 7, 2019, including any amendments or reports filed for the purpose of updating such description, including Exhibit 4.11 to the Annual Report on Form 10-K for the year ended December 31, 2021.

All documents that we file (but not those that we furnish) pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act on or after the date of this prospectus supplement and prior to the termination of the offering of any of the securities covered under this prospectus supplement shall be deemed to be incorporated herein by reference into this prospectus and will automatically update and supersede the information in this prospectus supplement and any previously filed documents.

Any statement contained herein or in a document incorporated or deemed to be incorporated by reference in this prospectus supplement shall be deemed to be modified, superseded or replaced for purposes of this prospectus supplement to the extent that a statement contained in this prospectus supplement, or in any other subsequently filed document which also is or is deemed to be incorporated by reference in this prospectus supplement, modifies, supersedes or replaces such earlier statement. Any statement so modified, superseded or replaced shall not be deemed, except as so modified, superseded or replaced, to constitute a part of this prospectus supplement. Nothing in this prospectus shall be deemed to incorporate information furnished but not filed with the SEC pursuant to Item 2.02 or Item 7.01 of Form 8-K.

You can obtain any of the filings incorporated by reference into this prospectus supplement through us or from the SEC through the SEC's website at http://www.sec.gov. Upon request, we will provide, without charge, a copy of any or all of the reports and documents referred to above which have been incorporated by reference into this prospectus. Prospective investors may obtain documents incorporated by reference in this prospectus supplement by requesting them in writing or by telephone from us at our executive offices at:

Opus Genetics, Inc.
8 Davis Drive, Suite 220
Durham, NC 27709
(248) 957-9024
Attn: Dr. George Magrath, Chief Executive Officer

Exhibits to the filings will not be sent, however, unless those exhibits have specifically been incorporated by reference in this prospectus supplement.

PROSPECTUS

$175,000,000

Common Stock
Preferred Stock
Debt Securities
Warrants

We may, from time to time, offer and sell up to $175,000,000 of any combination of the securities described in this prospectus, either individually or in combination, at prices and on terms described in one or more supplements to this prospectus. We may also offer common stock or preferred stock upon conversion of debt securities, or common stock upon conversion of preferred stock, or common stock, preferred stock or debt securities upon exercise of warrants.

This prospectus describes some of the general terms that may apply to an offering of our securities. We will provide the specific terms of these offerings and securities in one or more supplements to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. The prospectus supplement and any related free writing prospectus may also add, update or change information contained in this prospectus. You should carefully read this prospectus, the applicable prospectus supplement and any related free writing prospectus, as well as the documents incorporated by reference, before buying any of the securities being offered.

This prospectus may not be used to consummate a sale of securities unless accompanied by a prospectus supplement.

We will sell these securities directly to investors, through agents designated from time to time or to or through underwriters or dealers, on a continuous or delayed basis. For additional information on the methods of sale, you should refer to the section entitled "Plan of Distribution" in this prospectus on page 27 and in the applicable prospectus supplement. If any underwriters are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such underwriters and any applicable discounts or commissions and over-allotment options will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement.

Our common stock is listed on the Nasdaq Capital Market under the symbol "OCUP." On January 9, 2024, the last reported sale price of our common stock on the Nasdaq Capital Market was $3.25 per share. The applicable prospectus supplement will contain information, where applicable, as to other listings, if any, on the Nasdaq Capital Market or other securities exchange of the securities covered by the prospectus supplement.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading "Risk Factors" contained in this prospectus on page 7, in our most recent Annual Report on Form 10-K and Quarterly Report on Form 10-Q incorporated by reference into this prospectus, in the applicable prospectus supplement and in any free writing prospectuses we have authorized for use in connection with a specific offering, and under similar headings in the other documents that are incorporated by reference into this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is January 23, 2024.

TABLE OF CONTENTS

You should rely only on the information contained in, or incorporated by reference into, this prospectus and the applicable prospectus supplement, along with the information contained in any free writing prospectuses we have authorized for use in connection with a specific offering. We have not authorized anyone to provide you with different information. We are not making an offer to sell or seeking an offer to buy securities under this prospectus or the applicable prospectus supplement and any related free writing prospectus in any jurisdiction where the offer or sale is not permitted. The information contained in this prospectus, the applicable prospectus supplement or any related free writing prospectus, and the documents incorporated by reference herein and therein, are accurate only as of their respective dates, regardless of the time of delivery of this prospectus, the applicable prospectus supplement or any related free writing prospectus, or any sale of a security.

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or SEC, using a "shelf" registration process under the Securities Act of 1933, as amended, or the Securities Act. Under this shelf registration statement, we may sell from time to time in one or more offerings up to a total dollar amount of $175,000,000 of common stock and preferred stock, various series of debt securities and/or warrants to purchase any of such securities, either individually or in combination with other securities as described in this prospectus. This prospectus provides you with a general description of the securities we may offer.

Each time we sell any type or series of securities under this prospectus, we will provide a prospectus supplement that will contain more specific information about the terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. We may also add, update or change in a prospectus supplement or free writing prospectus any of the information contained in this prospectus or in the documents we have incorporated by reference into this prospectus. This prospectus, together with the applicable prospectus supplement, any related free writing prospectus and the documents incorporated by reference into this prospectus and the applicable prospectus supplement, will include all material information relating to the applicable offering. You should carefully read both this prospectus and the applicable prospectus supplement and any related free writing prospectus, together with the additional information described under "Where You Can Find More Information," before buying any of the securities being offered.

This prospectus may not be used to consummate a sale of securities unless accompanied by a prospectus supplement.

Neither we, nor any agent, underwriter or dealer has authorized anyone to provide you with any information other than contained in, or incorporated by reference into, this prospectus and the applicable prospectus supplement, along with the information contained in any free writing prospectuses we have authorized for use in connection with a specific offering. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should not assume that the information contained in or incorporated by reference in this prospectus or any prospectus supplement or in any such free writing prospectus is accurate as of any date other than their respective dates. Our business, financial condition, results of operations and prospects may have changed since those dates.

This prospectus contains and incorporates by reference market data and industry statistics and forecasts that are based on independent industry publications and other publicly available information. Although we believe that these sources are reliable, we do not guarantee the accuracy or completeness of this information and we have not independently verified this information. Although we are not aware of any misstatements regarding the market and industry data presented in this prospectus and the documents incorporated herein by reference, these estimates involve risks and uncertainties and are subject to change based on various factors, including those discussed under the heading "Risk Factors" contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus. Accordingly, investors should not place undue reliance on this information.

This prospectus contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described below under the section entitled "Where You Can Find More Information."

Except as otherwise indicated herein or as the context otherwise requires, references in this prospectus to "Ocuphire," "the company," "we," "us," "our" and similar references refer to Ocuphire Pharma, Inc., a corporation under the laws of the State of Delaware.

This prospectus and the information incorporated herein by reference include trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included or incorporated by reference into this prospectus, any applicable prospectus supplement or any related free writing prospectus are the property of their respective owners.

PROSPECTUS SUMMARY

This summary highlights selected information contained elsewhere in this prospectus or incorporated by reference herein and does not contain all of the information that you need to consider in making your investment decision. You should carefully read the entire prospectus, the applicable prospectus supplement and any related free writing prospectus, including the risks of investing in our securities discussed under the heading "Risk Factors" contained in this prospectus, the applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus. You should also carefully read the information incorporated by reference into this prospectus, including our financial statements and related notes, and the exhibits to the registration statement of which this prospectus is a part, before making your investment decision.

Ocuphire Pharma, Inc.

Overview

We are a clinical-stage ophthalmic 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 first-in-class 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. Through inhibition of Ref-1, APX3330 normalizes the levels of VEGF to physiologic levels, unlike biologics that deplete VEGF below the levels required for normal function. APX3330 is an oral tablet administered twice per day for the treatment of diabetic retinopathy ("DR").

DR affects approximately 10 million people with diabetes and is projected to impact over 14 million Americans by 2050. DR is classified as Non-Proliferative Diabetic Retinopathy ("NPDR"), the early stage of the disease in which symptoms may be mild or nonexistent 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 80% of the DR patients have NPDR that will 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 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 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 FDA agreed upon registration endpoint of ≥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. A successful 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 Phase 3 registration endpoint supporting the advancement of APX3330 into Phase 3. Ocuphire plans to submit a Special Protocol Assessment ("SPA") to agree on the clinical trial protocol and statistical analysis plan for the Phase 3 trials.

Prior to Ocuphire in-licensing the APX3330 product candidate, it had been studied by other sponsors in a total of 11 clinical trials (6 Phase 1 and 5 Phase 2) in a total of over 420 healthy volunteers or patients (with over 340 APX3330-treated) for inflammatory (hepatic) and oncology indications, and had demonstrated evidence of target engagement, consistent pharmacokinetics, durability, and favorable safety and tolerability. Treatment-related

adverse events were uncommon, and most were mild in severity. No clinically significant changes were observed in liver, kidney, or heart function. There were no treatment-related effects on hematologic or blood chemistry evaluations. APX3330 demonstrated favorable safety and tolerability in the ZETA-1 trial, consistent with the safety data from the prior 11 clinical trials.

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

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

Phentolamine Ophthalmic Solution 0.75% (POS)

In November 2022, we entered into a license and collaboration agreement (the "Nyxol 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 our refractive product candidate Phentolamine Ophthalmic Solution 0.75%, formerly known as Nyxol ("POS") for treating (a) reversal of pharmacologically-induced mydriasis, (b) night vision disturbances or dim light vision ("DLD"), and (c) presbyopia, and (ii) POS and low dose pilocarpine for treating presbyopia (together, the "Nyxol Products") worldwide except for certain countries and jurisdictions in Asia (the "Viatris Territory").

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

POS is a once-daily eye drop formulation of phentolamine mesylate designed to reduce pupil diameter and improve visual acuity. POS 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 DLD (halos, glares and starbursts). Our management believes these multiple indications potentially represent a significant market opportunity. POS 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 patients (with over 650 POS-treated) and has demonstrated promising clinical data across the three targeted refractive indications.

We submitted a new drug application ("NDA") to the U.S. Food and Drug Administration ("FDA") in November 2022 under the 505(b)(2) pathway for POS for RM; the FDA approved the NDA in September 2023 under the brand name RYZUMVI™, which triggered a $10 million milestone payment under the Nyxol License Agreement.

We reported positive top-line data from multiple late-stage clinical trials for POS in RM, presbyopia and DLD. We reported positive top-line data from Phase 3 trials in RM: MIRA-2 in March 2021, MIRA-3 in March 2022 and MIRA-4 in April 2022. We also reported positive top-line data from a Phase 2 trial of POS for treatment of presbyopia, both as monotherapy and with low-dose pilocarpine (pilocarpine hydrochloride ophthalmic solution 0.4%, "LDP") as adjunctive therapy (VEGA-1). We reported top-line data from a Phase 3 trial in DLD in May 2022 (LYNX-1). 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 DLD, a SPA has been submitted and Viatris is also expected to continue Phase 3 development in the first half of 2024 following FDA 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.

Phentolamine Ophthalmic Solution 0.75% (POS)

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 POS alone and POS 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 POS under the brand name RYZUMVI™ for the treatment of RM; for this approval we received a $10 million milestone payment under the Nyxol License Agreement.

In October 2023, a SPA was submitted to the FDA for DLD and Viatris, our development and commercial partner, is expected to continue Phase 3 development in the first half of 2024 following FDA agreement.

In November 2023, we announced the successful outcome of the EOP2 meeting with the FDA, at which we obtained agreement on the registration endpoint supporting the advancement of APX3330 into Phase 3. Ocuphire plans to submit a SPA to agree on the clinical trial protocol and statistical analysis plan for the Phase 3 trials and will share specifics on the study design parameters and anticipated timing once agreed with the FDA.

Management Transitions

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 position and remains on the Board.

On November 27, 2023, the Company announced the appointment of Joseph K. Schachle, as Chief Operating Officer.

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.

Global Economic Conditions

Generally, worldwide economic conditions remain uncertain, particularly due to the effects of the conflict between Russia and Ukraine and potentially between Israel and Hamas, disruptions in the banking system and financial markets, lingering COVID-19 pandemic, increased inflation and increased interest rates. The general economic and capital market conditions, both in the U.S. and worldwide, have been volatile in the past and at times have adversely affected our access to capital and increased the cost of capital. The capital and credit markets may not be available to support future capital raising activity on favorable terms. If economic conditions decline, our future cost of equity or debt capital and access to the capital markets could be adversely affected.

Additionally, our operating results could be materially impacted by changes in the overall macroeconomic environment and other economic factors. Changes in economic conditions, supply chain constraints, logistics challenges, labor shortages, the conflicts in Ukraine and the Middle East, disruptions in the banking system and financial markets, and steps taken by governments and central banks, particularly in response to the COVID-19 pandemic as well as other stimulus and spending programs, have led to higher inflation, which has led to an increase in costs and has caused changes in fiscal and monetary policy, including increased interest rates.

Risks Associated with our Business

Our business is subject to numerous risks, as described under the heading "Risk Factors" contained in the applicable prospectus supplement and in any free writing prospectuses we have authorized for use in connection with a specific offering, and under similar headings in the documents that are incorporated by reference into this prospectus.

Description of Securities We May Offer

We may offer shares of our common stock and preferred stock, various series of debt securities and/or warrants to purchase any of such securities, either individually or in combination, with a total dollar amount up to $175,000,000 from time to time under this prospectus, together with the applicable prospectus supplement and any related free writing prospectus, at prices and on terms to be determined at the time of any offering. We may also offer common stock, preferred stock and/or debt securities upon the exercise of warrants. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

- designation or classification;
- aggregate principal amount or aggregate offering price;
- maturity;
- original issue discount;
- rates and times of payment of interest or dividends;
- redemption, conversion, exercise, exchange or sinking fund terms;
- ranking;
- restrictive covenants;
- voting or other rights;
- conversion or exchange prices or rates and, if applicable, any provisions for changes to or adjustments in the conversion or exchange prices or rates and in the securities or other property receivable upon conversion or exchange; and
- a discussion of material United States federal income tax considerations, if any.

The applicable prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change any of the information contained in this prospectus or in the documents we have incorporated by reference. However, no prospectus supplement or free writing prospectus will offer a security that is not registered and described in this prospectus at the time of the effectiveness of the registration statement of which this prospectus is a part.

This prospectus may not be used to consummate a sale of securities unless it is accompanied by a prospectus supplement.

We may sell the securities directly to investors or to or through agents, underwriters or dealers. We, and our or their agents, underwriters or dealers reserve the right to accept or reject all or part of any proposed purchase of securities. If we do offer securities to or through agents, underwriters or dealers, we will include in the applicable prospectus supplement:

- the names of those agents, underwriters or dealers;
- applicable fees, discounts and commissions to be paid to them;
- details regarding over-allotment options, if any; and
- the net proceeds to us, if any.

Common Stock

We may issue shares of our common stock from time to time. Each holder of our common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders, including the election of directors. Under our amended and restated certificate of incorporation, as amended, or certificate of incorporation, and second amended and restated bylaws, or bylaws, our stockholders do not have cumulative voting rights. Because of this, the holders of a majority of the shares of common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they should so choose. Subject to preferences that may be applicable to any then-outstanding preferred stock, holders of common stock are entitled to receive ratably those dividends, if any, as may be declared from time to time by our board of directors out of legally available funds. In the event of our liquidation, dissolution or winding up, holders of common stock are entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any then-outstanding shares of preferred stock. Holders of common stock have no preemptive, conversion or subscription rights and there are no redemption or sinking fund provisions applicable to the common stock. The rights, preferences and privileges of the holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate in the future. In this prospectus, we have summarized certain general features of the common stock under "Description of Capital Stock—Common Stock." We urge you, however, to read the applicable prospectus supplement (and any related free writing prospectus that we may authorize to be provided to you) related to any common stock being offered.

Preferred Stock

We may issue shares of our preferred stock from time to time, in one or more series. Our board of directors will determine the designations, voting powers, preferences and rights of the preferred stock, as well as the qualifications, limitations or restrictions thereof, including dividend rights, conversion rights, preemptive rights, terms of redemption or repurchase, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of any series, or the designation of such series, any or all of which may be greater than the rights of our common stock. Convertible preferred stock will be convertible into our common stock or exchangeable for other securities. Conversion may be mandatory or at your option and would be at prescribed conversion rates.

If we sell any series of preferred stock under this prospectus, we will fix the designations, voting powers, preferences and rights of such series of preferred stock, as well as the qualifications, limitations or restrictions thereof, in the certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that describes the terms of the series of preferred stock that we are offering before the issuance of the related series of preferred stock. In this prospectus, we have summarized certain general features of the preferred stock under "Description of Capital Stock—Preferred Stock." We urge you to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the series of preferred stock being offered, as well as the complete certificate of designation that contains the terms of the applicable series of preferred stock.

Debt Securities

We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. The senior debt securities will rank equally with any other unsecured and unsubordinated debt. The subordinated debt securities will be subordinate and junior in right of payment, to the extent and in the manner described in the instrument governing the debt, to all of our senior indebtedness. Convertible or exchangeable debt securities will be convertible into or exchangeable for our common stock or our other securities. Conversion or exchange may be mandatory or optional (at our option or the holders' option) and would be at prescribed conversion or exchange rates.

Any debt securities issued under this prospectus will be issued under one or more documents called indentures, which are contracts between us and a national banking association or other eligible party, as trustee. In this prospectus, we have summarized certain general features of the debt securities under "Description of Debt Securities." We urge you, however, to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the series of debt securities being offered, as

well as the complete indenture and any supplemental indentures that contain the terms of the debt securities. A form of indenture has been filed as an exhibit to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

Warrants

We may issue warrants for the purchase of common stock, preferred stock and/or debt securities in one or more series. We may issue warrants independently or in combination with common stock, preferred stock and/or debt securities offered by any prospectus supplement. In this prospectus, we have summarized certain general features of the warrants under "Description of Warrants." We urge you, however, to read the applicable prospectus supplement (and any related free writing prospectus that we may authorize to be provided to you) related to the particular series of warrants being offered, as well as any warrant agreements and warrant certificates, as applicable, that contain the terms of the warrants. We have filed forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants that may be offered as exhibits to the registration statement of which this prospectus is a part. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of warrant and/or the warrant agreement and warrant certificate, as applicable, that contain the terms of the particular series of warrants we are offering, and any supplemental agreements, before the issuance of such warrants.

Any warrants issued under this prospectus may be evidenced by warrant certificates. Warrants also may be issued under an applicable warrant agreement that we enter into with a warrant agent. We will indicate the name and address of the warrant agent, if applicable, in the prospectus supplement relating to the particular series of warrants being offered.

Use of Proceeds

Except as described in any applicable prospectus supplement or in any free writing prospectuses we have authorized for use in connection with a specific offering, we currently intend to use the net proceeds from this offering for working capital and general corporate purposes, which may include, among other things, funding research and development programs, vendor payables, hiring additional personnel, and capital expenditures.

Company Information

Our principal executive offices are located at 37000 Grand River Avenue, Suite 120, Farmington Hills, MI 48335. Our telephone number is (248) 957-9024. Our website address is www.ocuphire.com. The information contained in, or accessible through, our website does not constitute part of this prospectus, should not be relied on in determining whether to make an investment decision, and the inclusion of our website address in this prospectus is an inactive textual reference only.

Implications of Being a Smaller Reporting Company

We are a "smaller reporting company" under federal securities laws. For as long as we continue to be a smaller reporting company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies, including, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We may continue to be a smaller reporting company if either (i) the market value of our stock held by non-affiliates is less than $250 million or (ii) our annual revenue was less than $100 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than $700 million. As long as we remain a smaller reporting company and non-accelerated filer, we are exempt from the attestation requirement in the assessment of our internal control over financial reporting by our independent auditors pursuant to section 404(b) of the Sarbanes-Oxley Act of 2002 (the "Sarbanes-Oxley Act") but are required to make our own internal assessment of the effectiveness of our internal controls over financial reporting.

RISK FACTORS

Investing in our securities involves a high degree of risk. Before deciding whether to invest in our securities, you should carefully read the entire prospectus, the applicable prospectus supplement and any related free writing prospectus, including the risks of investing in our securities discussed under the heading "Risk Factors" contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus. You should also carefully read the information incorporated by reference into this prospectus, including our financial statements, and the exhibits to the registration statement of which this prospectus is a part, and which may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future.

The risks described in these documents are not the only ones we face, but those that we consider to be material. There may be other unknown or unpredictable economic, business, competitive, regulatory or other factors that could have material adverse effects on our future results. Past financial performance may not be a reliable indicator of future performance, and historical trends should not be used to anticipate results or trends in future periods. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow could be seriously harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment. Please also read carefully the section below entitled "Forward-Looking Statements."

FORWARD-LOOKING STATEMENTS

This prospectus and the documents we have filed with the SEC that are incorporated by reference contain "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. These statements relate to future events or to our future operating or financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. All statements other than statements of historical facts contained in this prospectus, including statements regarding our future results of operations and financial condition, business strategy and plans and objectives of management for future operations, are forward-looking statements. In some cases, forward-looking statements may be identified by words such as "anticipate," "believe," "continue," "could," "design," "estimate," "expect," "intend," "may," "plan," "potentially," "predict," "project," "should," "will" or the negative of these terms or other similar expressions.

We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. You should refer to the "Risk Factors" section contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus, for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. Given these risks, uncertainties and other factors, many of which are beyond our control, we cannot assure you that the forward-looking statements in this prospectus will prove to be accurate, and you should not place undue reliance on these forward-looking statements. These risks include, among other things, that:

- we currently depend entirely on the success of Phentolamine Ophthalmic Solution 0.75% (POS) and APX3330, our only product candidates, and we may never complete clinical development of, receive marketing approval for, or successfully commercialize, POS alone or as adjunctive therapy with low dose pilocarpine (LDP), APX3330, or other product candidates we may pursue in the future for any indication;
- Viatris has exclusive rights to commercialize our POS products in key global markets and Viatris' failure to timely develop or commercialize these products would have a material adverse effect on our business and operating results;
- 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;
- 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 our development timelines;
- we expect to incur losses for the foreseeable future and may never achieve or maintain profitability;
- adverse global economic conditions could have a negative effect on our business results of operations and financial condition and liquidity;
- adverse developments affecting the financial services industry could negatively affect our current and projected business operations, financial condition and results of 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;
- 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;
- our employees or our representatives may engage in misconduct or other improper activities, including violating applicable regulatory standards and requirements or engaging in insider trading, which could significantly harm our business;

- we face substantial competition, which may result in others discovering, developing, or commercializing products before or more successfully than we do;
- we lack experience in commercializing products, which may have an adverse effect on our business;
- if we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell, market, and distribute APX3330, if approved, we may not be successful in commercializing APX3330 if and when it is approved;
- 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 are unable to control all aspects of our clinical trials due to our reliance on clinical research organizations, contract development and manufacturing organizations and other third parties that assist us in conducting clinical trials;
- we are unable to control the supply, manufacture and testing of bulk drug substances and the formulation, testing and packaging of preclinical and clinical drug supplies of our product candidates, and will be unable to control these elements at the commercial stage, due to our reliance on third-party manufacturers and analytical facilities;
- 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;
- 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 ours, 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 depend on intellectual property sublicensed from Apexian Pharmaceuticals, Inc. (“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 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 will need to develop and expand our company and may encounter difficulties in managing this development and expansion, which could disrupt our operations;
- our insurance policies are expensive and protect only from some business risk, which leaves us exposed to significant uninsured liabilities;
- environmental, social, and governance matters and any related reporting obligations may impact our business;
- 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 price 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; and
- there is uncertainty regarding the use of proceeds, if any, from this offering.

These risks are not exhaustive. Other sections of this prospectus may include additional factors that could harm our business and financial performance. Moreover, we operate in a very competitive and rapidly changing environment.

New risks and uncertainties emerge from time to time, and it is not possible for our management to predict all risks and uncertainties nor can we assess the impact of all such factors on our business or the extent to which any such factor, or combination of such factors, may cause actual results to differ from those contained in, or implied by, any forward-looking statements.

You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. Except as required by law, we undertake no obligation to update publicly any forward-looking statements for any reason after the date of this prospectus or to conform these statements to actual results or to changes in our expectations.

In addition, “we believe” and “we expect” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this prospectus, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

You should read this prospectus and the documents that we reference in this prospectus and have filed as exhibits to the registration statement of which this prospectus is a part with the understanding that our actual future results, levels of activity, performance and achievements may be different from what we expect. We qualify all of our forward-looking statements by these cautionary statements.

USE OF PROCEEDS

Except as described in any applicable prospectus supplement or in any free writing prospectuses we have authorized for use in connection with a specific offering, we currently intend to use the net proceeds from this offering for working capital and general corporate purposes, which may include, among other things, funding research and development programs, vendor payables, hiring additional personnel, and capital expenditures.

DESCRIPTION OF CAPITAL STOCK

General

As of the date of this prospectus, our certificate of incorporation authorizes us to issue up to 85,000,000 shares of capital stock, all with a par value of $0.0001 per share, of which: 75,000,000 shares are designated as common stock and 10,000,000 shares are designated as preferred stock.

The following summary describes the material terms of our capital stock. The description of capital stock is qualified by reference to our certificate of incorporation and our bylaws.

Common Stock

As of September 30, 2023, 22,610,131 shares of common stock were outstanding. All outstanding shares of common stock are duly authorized, validly issued, fully paid, and nonassessable. All authorized but unissued shares of our common stock are available for issuance by our board of directors without any further stockholder action, except as required by the listing standards of Nasdaq.

Voting Rights

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders, including the election of directors, and do not have cumulative voting rights. Accordingly, the holders of a majority of the outstanding shares of common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they so choose, other than any directors that holders of any preferred stock we may issue may be entitled to elect.

Dividend Rights

Subject to preferences that may be applicable to any then-outstanding preferred stock, holders of common stock are entitled to receive ratably those dividends, if any, as may be declared by the board of directors out of legally available funds.

Liquidation

In the event of our liquidation, dissolution, or winding up, the holders of common stock will be entitled to share ratably in the assets legally available for distribution to stockholders after the payment of or provision for all of our debts and other liabilities, subject to the prior rights of any preferred stock then-outstanding.

Rights and Preferences

Holders of common stock have no preemptive or conversion rights or other subscription rights and there are no redemption or sinking fund provisions applicable to the common stock. The rights, preferences, and privileges of holders of common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Preferred Stock

As of September 30, 2023, no shares of preferred stock were outstanding. Our board of directors may, without further action by our stockholders, fix the rights, preferences, privileges and restrictions of up to an aggregate of 10,000,000 shares of preferred stock in one or more series and authorize their issuance. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of such series, any or all of which may be greater than the rights of our common stock. The issuance of our preferred stock could adversely affect the voting power of holders of our common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation. In addition, the issuance of preferred stock could have the effect of decreasing the market price of our common stock and could also have the effect of delaying, deferring or preventing a change of control or other corporate action.

We will fix the designations, voting powers, preferences and rights of the preferred stock of each series we issue under this prospectus, as well as the qualifications, limitations or restrictions thereof, in the certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus

is a part, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that describes the terms of the series of preferred stock we are offering. We will describe in the applicable prospectus supplement the terms of the series of preferred stock being offered, including, to the extent applicable:

- the title and stated value;
- the number of shares we are offering;
- the liquidation preference per share;
- the purchase price;
- the dividend rate, period and payment date and method of calculation for dividends;
- whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- the procedures for any auction and remarketing;
- the provisions for a sinking fund;
- the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;
- any listing of the preferred stock on any securities exchange or market;
- whether the preferred stock will be convertible into our common stock, and, if applicable, the conversion price, or how it will be calculated, and the conversion period;
- whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price, or how it will be calculated, and the exchange period;
- voting rights of the preferred stock;
- preemptive rights;
- restrictions on transfer, sale or other assignment;
- whether interests in the preferred stock will be represented by depositary shares;
- a discussion of material United States federal income tax considerations applicable to the preferred stock;
- the relative ranking and preferences of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;
- any limitations on the issuance of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the preferred stock.

If we issue shares of preferred stock under this prospectus, the shares will be fully paid and non-assessable.

Options and Restricted Stock

As of September 30, 2023, (i) 1,016,033 shares of common stock remain available for issuance under our 2020 Plan and 2021 Inducement Plan, stock options to purchase an aggregate of 2,249,950 shares of common stock were outstanding under our 2020 Equity Incentive Plan, or 2020 Plan, stock options to purchase an aggregate of 133,000 shares of common stock were outstanding under our 2021 Inducement Plan, and stock options to purchase an aggregate of 1,086,439 shares of common stock were outstanding under our 2018 Equity Incentive Plan, or 2018 Plan, and (ii) 282,008 unvested shares of restricted stock were outstanding.

Warrants

As of September 30, 2023, 7,262,896 warrants to purchase shares of our capital stock were outstanding, with a weighted average exercise price of $5.09 (subject to adjustment).

Anti-Takeover Effects of Delaware Law and Our Certificate of Incorporation and Bylaws

Our amended and restated certificate of incorporation and second amended and restated bylaws contain provisions that could make it more difficult to complete an acquisition of us by means of a tender offer, a proxy contest or otherwise or the removal and replacement of our incumbent officers and directors.

Removal of Directors; Board Vacancies; Board Size. Our amended and restated certificate of incorporation provides for the removal of any of our directors only for cause and requires a stockholder vote of at least a majority of the voting power of the then outstanding voting stock. In addition, our amended and restated certificate of incorporation provides that any vacancy occurring on our board of directors may be filled by a majority of directors then in office, even if less than a quorum, unless the board of directors determines that such vacancy shall be filled by the stockholders. Finally, the authorized number of directors may be changed only by a resolution of the board of directors. This system of removing directors, filling vacancies and fixing the size of the board makes it more difficult for stockholders to replace a majority of the directors.

Special Stockholder Meetings. Our amended and restated certificate of incorporation and our second amended and restated bylaws provide that a special meeting of stockholders may be called only by a resolution adopted by a majority of our board of directors or by the chairman of the board.

Stockholder Advance Notice Procedure. Our second amended and restated bylaws establish an advance notice procedure for stockholders to make nominations of candidates for election as directors or to bring other business before an annual meeting of our stockholders. The second amended and restated bylaws provide that any stockholder wishing to nominate persons for election as directors at, or bring other business before, an annual meeting must deliver to our secretary a written notice of the stockholder's intention to do so. To be timely, the stockholder's notice must be delivered to or mailed and received by us not more than 120 days, and not less than 90 days before the anniversary date of the preceding annual meeting, except that if the annual meeting is set for a date that is not within 30 days before or 60 days after such anniversary date, we must receive the notice not earlier than the close of business on the 120th day prior to the annual meeting and not later than the close of business on the later of (i) the 90th day prior to the annual meeting or (ii) the tenth day following the day on which we first made public announcement of the date of meeting. The notice must include the following information:

- as to director nominations, all information relating to each director nominee that is required by the rules of the Securities and Exchange Commission to be disclosed in solicitations of proxies, or is otherwise required by Regulation 14A of the Exchange Act;
- as to any other business that the stockholder proposes to bring before the meeting, a brief description of the business to be proposed, the reasons for conducting such business at the meeting and, if any, the stockholder's material interest in the proposed business; and
- the name and address of the stockholder who intends to make the nomination and the class and number of our shares beneficially owned of record;

Undesignated Preferred Stock. The ability to authorize undesignated preferred stock makes it possible for our board of directors to issue preferred stock with voting or other rights or preferences that could have the effect of delaying, deferring, preventing or otherwise impeding any attempt to change control of us.

Delaware Anti-Takeover Statute. We are subject to Section 203 of the Delaware General Corporation Law, which prohibits persons deemed "interested stockholders" from engaging in a "business combination" with a publicly traded Delaware corporation for three years following the date these persons become interested stockholders unless the business combination is, or the transaction in which the person became an interested stockholder was, approved in a prescribed manner or another prescribed exception applies. Generally, an "interested stockholder" is a person who, together with affiliates and associates, owns, or within three years prior to the determination of interested stockholder status did own, 15% or more of a corporation's voting stock. Generally, a "business combination" includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. The existence of this provision may have an anti-takeover effect with respect to transactions not approved in advance by the board of directors, such as discouraging takeover attempts that might result in a premium over the market price of our common stock.

Business Combinations with Interested Stockholders. Our amended and restated certificate of incorporation provides that certain "business combinations" with "interested stockholders" require approval by the holders of

at least a majority of the voting power of our then outstanding shares of voting stock not beneficially owned by any interested stockholder or an affiliate or associate thereof. The foregoing restriction does not apply, however, if the transaction is either approved by a majority of our "continuing directors" or certain minimum price and procedural and other requirements are met. Generally, a "business combination" includes a merger, consolidation, liquidation, recapitalization or other similar transaction or a sale, lease, transfer or other disposition of assets or securities having an aggregate fair market value of $15 million or more. An "interested stockholder" generally means a beneficial owner of 20% or more of our voting stock, certain assignees of such beneficial owners and certain of our affiliates that within the preceding two years were the beneficial owner of 20% or more of our voting stock. A "continuing director" is defined as any member of our board who is not an affiliate or associate or representative of the interested stockholder and was a member of the board prior to the time the interested stockholder became such, and any successor of a continuing director who is unaffiliated with the interested stockholder and is recommended or elected by at least two-thirds of the continuing directors then on the board.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Equiniti Trust Company.

Listing on the Nasdaq Capital Market

Our common stock is listed on the Nasdaq Capital Market under the symbol "OCUP."

DESCRIPTION OF DEBT SECURITIES

We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. While the terms we have summarized below will apply generally to any debt securities that we may offer under this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement. The terms of any debt securities offered under a prospectus supplement may differ from the terms described below. Unless the context requires otherwise, whenever we refer to the indenture, we also are referring to any supplemental indentures that specify the terms of a particular series of debt securities.

We will issue the debt securities under the indenture that we will enter into with the trustee named in the indenture. The indenture will be qualified under the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act. We have filed the form of indenture as an exhibit to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

The following summary of material provisions of the debt securities and the indenture is subject to, and qualified in its entirety by reference to, all of the provisions of the indenture applicable to a particular series of debt securities. We urge you to read the applicable prospectus supplements and any related free writing prospectuses related to the debt securities that we may offer under this prospectus, as well as the complete indenture that contains the terms of the debt securities.

General

The indenture does not limit the amount of debt securities that we may issue. It provides that we may issue debt securities up to the principal amount that we may authorize and may be in any currency or currency unit that we may designate. Except for the limitations on consolidation, merger and sale of all or substantially all of our assets contained in the indenture, the terms of the indenture do not contain any covenants or other provisions designed to give holders of any debt securities protection against changes in our operations, financial condition or transactions involving us.

We may issue the debt securities issued under the indenture as “discount securities,” which means they may be sold at a discount below their stated principal amount. These debt securities, as well as other debt securities that are not issued at a discount, may be issued with “original issue discount,” or OID, for U.S. federal income tax purposes because of interest payment and other characteristics or terms of the debt securities. Material U.S. federal income tax considerations applicable to debt securities issued with OID will be described in more detail in any applicable prospectus supplement.

We will describe in the applicable prospectus supplement the terms of the series of debt securities being offered, including:

- the title of the series of debt securities;
- any limit upon the aggregate principal amount that may be issued;
- the maturity date or dates;
- the form of the debt securities of the series;
- the applicability of any guarantees;
- whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;
- whether the debt securities rank as senior debt, senior subordinated debt, subordinated debt or any combination thereof, and the terms of any subordination;
- if the price (expressed as a percentage of the aggregate principal amount thereof) at which such debt securities will be issued is a price other than the principal amount thereof, the portion of the principal amount thereof payable upon declaration of acceleration of the maturity thereof, or if applicable, the portion of the principal amount of such debt securities that is convertible into another security or the method by which any such portion shall be determined;

- the interest rate or rates, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;
- our right, if any, to defer payment of interest and the maximum length of any such deferral period;
- if applicable, the date or dates after which, or the period or periods during which, and the price or prices at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemption provisions;
- the date or dates, if any, on which, and the price or prices at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder's option to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;
- the denominations in which we will issue the series of debt securities, if other than denominations of $1,000 and any integral multiple thereof;
- any and all terms, if applicable, relating to any auction or remarketing of the debt securities of that series and any security for our obligations with respect to such debt securities and any other terms which may be advisable in connection with the marketing of debt securities of that series;
- whether the debt securities of the series shall be issued in whole or in part in the form of a global security or securities; the terms and conditions, if any, upon which such global security or securities may be exchanged in whole or in part for other individual securities; and the depositary for such global security or securities;
- if applicable, the provisions relating to conversion or exchange of any debt securities of the series and the terms and conditions upon which such debt securities will be so convertible or exchangeable, including the conversion or exchange price, as applicable, or how it will be calculated and may be adjusted, any mandatory or optional (at our option or the holders' option) conversion or exchange features, the applicable conversion or exchange period and the manner of settlement for any conversion or exchange;
- if other than the full principal amount thereof, the portion of the principal amount of debt securities of the series which shall be payable upon declaration of acceleration of the maturity thereof;
- additions to or changes in the covenants applicable to the particular debt securities being issued, including, among others, the consolidation, merger or sale covenant;
- additions to or changes in the events of default with respect to the securities and any change in the right of the trustee or the holders to declare the principal, premium, if any, and interest, if any, with respect to such securities to be due and payable;
- additions to or changes in or deletions of the provisions relating to covenant defeasance and legal defeasance;
- additions to or changes in the provisions relating to satisfaction and discharge of the indenture;
- additions to or changes in the provisions relating to the modification of the indenture both with and without the consent of holders of debt securities issued under the indenture;
- the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars;
- whether interest will be payable in cash or additional debt securities at our or the holders' option and the terms and conditions upon which the election may be made;
- the terms and conditions, if any, upon which we will pay amounts in addition to the stated interest, premium, if any and principal amounts of the debt securities of the series to any holder that is not a "United States person" for federal tax purposes;
- any restrictions on transfer, sale or assignment of the debt securities of the series; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, any other additions or changes in the provisions of the indenture, and any terms that may be required by us or advisable under applicable laws or regulations.

Conversion or Exchange Rights

We will set forth in the applicable prospectus supplement the terms on which a series of debt securities may be convertible into or exchangeable for our common stock or our other securities. We will include provisions as to settlement upon conversion or exchange and whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock or our other securities that the holders of the series of debt securities receive would be subject to adjustment.

Consolidation, Merger or Sale

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the indenture will not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of our assets as an entirety or substantially as an entirety. However, any successor to or acquirer of such assets (other than a subsidiary of ours) must assume all of our obligations under the indenture or the debt securities, as appropriate.

Events of Default under the Indenture

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the following are events of default under the indenture with respect to any series of debt securities that we may issue:

- if we fail to pay any installment of interest on any series of debt securities, as and when the same shall become due and payable, and such default continues for a period of 90 days; provided, however, that a valid extension of an interest payment period by us in accordance with the terms of any indenture supplemental thereto shall not constitute a default in the payment of interest for this purpose;
- if we fail to pay the principal of, or premium, if any, on any series of debt securities as and when the same shall become due and payable whether at maturity, upon redemption, by declaration or otherwise, or in any payment required by any sinking or analogous fund established with respect to such series; provided, however, that a valid extension of the maturity of such debt securities in accordance with the terms of any indenture supplemental thereto shall not constitute a default in the payment of principal or premium, if any;
- if we fail to observe or perform any other covenant or agreement contained in the debt securities or the indenture, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive written notice of such failure, requiring the same to be remedied and stating that such is a notice of default thereunder, from the trustee or holders of at least 25% in aggregate principal amount of the outstanding debt securities of the applicable series; and
- if specified events of bankruptcy, insolvency or reorganization occur.

If an event of default with respect to debt securities of any series occurs and is continuing, other than an event of default specified in the last bullet point above, the trustee or the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series, by notice to us in writing, and to the trustee if notice is given by such holders, may declare the unpaid principal of, premium, if any, and accrued interest, if any, due and payable immediately. If an event of default specified in the last bullet point above occurs with respect to us, the principal amount of and accrued interest, if any, of each issue of debt securities then outstanding shall be due and payable without any notice or other action on the part of the trustee or any holder.

The holders of a majority in principal amount of the outstanding debt securities of an affected series may waive any default or event of default with respect to the series and its consequences, except defaults or events of default regarding payment of principal, premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Subject to the terms of the indenture, if an event of default under an indenture shall occur and be continuing, the trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the trustee reasonable indemnity. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee, or exercising any trust or power conferred on the trustee, with respect to the debt securities of that series, provided that:

- the direction so given by the holder is not in conflict with any law or the applicable indenture; and
- subject to its duties under the Trust Indenture Act, the trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

A holder of the debt securities of any series will have the right to institute a proceeding under the indenture or to appoint a receiver or trustee, or to seek other remedies only if:

- the holder has given written notice to the trustee of a continuing event of default with respect to that series;
- the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made written request;
- such holders have offered to the trustee indemnity satisfactory to it against the costs, expenses and liabilities to be incurred by the trustee in compliance with the request; and
- the trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 90 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities.

We will periodically file statements with the trustee regarding our compliance with specified covenants in the indenture.

Modification of Indenture; Waiver

We and the trustee may change an indenture without the consent of any holders with respect to specific matters:

- to cure any ambiguity, defect or inconsistency in the indenture or in the debt securities of any series;
- to comply with the provisions described above under “Description of Debt Securities—Consolidation, Merger or Sale;”
- to provide for uncertificated debt securities in addition to or in place of certificated debt securities;
- to add to our covenants, restrictions, conditions or provisions such new covenants, restrictions, conditions or provisions for the benefit of the holders of all or any series of debt securities, to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default or to surrender any right or power conferred upon us in the indenture;
- to add to, delete from or revise the conditions, limitations, and restrictions on the authorized amount, terms, or purposes of issue, authentication and delivery of debt securities, as set forth in the indenture;
- to make any change that does not adversely affect the interests of any holder of debt securities of any series in any material respect;
- to provide for the issuance of and establish the form and terms and conditions of the debt securities of any series as provided above under “Description of Debt Securities—General” to establish the form of any certifications required to be furnished pursuant to the terms of the indenture or any series of debt securities, or to add to the rights of the holders of any series of debt securities;

- to evidence and provide for the acceptance of appointment under any indenture by a successor trustee; or
- to comply with any requirements of the SEC in connection with the qualification of any indenture under the Trust Indenture Act.

In addition, under the indenture, the rights of holders of a series of debt securities may be changed by us and the trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series that is affected. However, unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, we and the trustee may make the following changes only with the consent of each holder of any outstanding debt securities affected:

- extending the fixed maturity of any debt securities of any series;
- reducing the principal amount, reducing the rate of or extending the time of payment of interest, or reducing any premium payable upon the redemption of any series of any debt securities; or
- reducing the percentage of debt securities, the holders of which are required to consent to any amendment, supplement, modification or waiver.

Discharge

Each indenture provides that we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for specified obligations, including obligations to:

- provide for payment;
- register the transfer or exchange of debt securities of the series;
- replace stolen, lost or mutilated debt securities of the series;
- pay principal of and premium and interest on any debt securities of the series;
- maintain paying agencies;
- hold monies for payment in trust;
- recover excess money held by the trustee;
- compensate and indemnify the trustee; and
- appoint any successor trustee.

In order to exercise our rights to be discharged, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, any premium, if any, and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we provide otherwise in the applicable prospectus supplement, in denominations of $1,000 and any integral multiple thereof. The indenture provides that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company, or DTC, or another depositary named by us and identified in the applicable prospectus supplement with respect to that series. To the extent the debt securities of a series are issued in global form and as book-entry, a description of terms relating to any book-entry securities will be set forth in the applicable prospectus supplement.

At the option of the holder, subject to the terms of the indenture and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indenture and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required

by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange, we will impose no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

If we elect to redeem the debt securities of any series, we will not be required to:

- issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or
- register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Trustee

The trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs. Subject to this provision, the trustee is under no obligation to exercise any of the powers given it by the indenture at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, we will make interest payments by check that we will mail to the holder or by wire transfer to certain holders. Unless we otherwise indicate in the applicable prospectus supplement, we will designate the corporate trust office of the trustee as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the trustee for the payment of the principal of or any premium or interest on any debt securities that remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the debt security thereafter may look only to us for payment thereof.

Governing Law

The indenture and the debt securities will be governed by and construed in accordance with the internal laws of the State of New York, except to the extent that the Trust Indenture Act of 1939 is applicable.

DESCRIPTION OF WARRANTS

The following description, together with the additional information we may include in any applicable prospectus supplement and free writing prospectus, summarizes the material terms and provisions of the warrants that we may offer under this prospectus, which may consist of warrants to purchase common stock, preferred stock or debt securities and may be issued in one or more series. Warrants may be offered independently or in combination with common stock, preferred stock or debt securities offered by any prospectus supplement. While the terms we have summarized below will apply generally to any warrants that we may offer under this prospectus, we will describe the particular terms of any series of warrants in more detail in the applicable prospectus supplement. The following description of warrants will apply to the warrants offered by this prospectus unless we provide otherwise in the applicable prospectus supplement. The applicable prospectus supplement for a particular series of warrants may specify different or additional terms.

We have filed forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants that may be offered as exhibits to the registration statement of which this prospectus is a part. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of warrant and/or the warrant agreement and warrant certificate, as applicable, that contain the terms of the particular series of warrants we are offering, and any supplemental agreements, before the issuance of such warrants. The following summaries of material terms and provisions of the warrants are subject to, and qualified in their entirety by reference to, all the provisions of the form of warrant and/or the warrant agreement and warrant certificate, as applicable, and any supplemental agreements applicable to a particular series of warrants that we may offer under this prospectus. We urge you to read the applicable prospectus supplement related to the particular series of warrants that we may offer under this prospectus, as well as any related free writing prospectus, and the complete form of warrant and/or the warrant agreement and warrant certificate, as applicable, and any supplemental agreements, that contain the terms of the warrants.

General

We will describe in the applicable prospectus supplement the terms of the series of warrants being offered, including:

- the offering price and aggregate number of warrants offered;
- the currency for which the warrants may be purchased;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;
- in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at, and currency in which, this principal amount of debt securities may be purchased upon such exercise;
- in the case of warrants to purchase common stock or preferred stock, the number of shares of common stock or preferred stock, as the case may be, purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;
- the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreements and the warrants;
- the terms of any rights to redeem or call the warrants;
- any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;
- the dates on which the right to exercise the warrants will commence and expire;
- the manner in which the warrant agreements and warrants may be modified;
- a discussion of any material or special U.S. federal income tax considerations of holding or exercising the warrants;
- the terms of the securities issuable upon exercise of the warrants; and
- any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

Before exercising their warrants, holders of warrants will not have any of the rights of holders of the securities purchasable upon such exercise, including:

- in the case of warrants to purchase debt securities, the right to receive payments of principal of, or premium, if any, or interest on, the debt securities purchasable upon exercise or to enforce covenants in the applicable indenture; or
- in the case of warrants to purchase common stock or preferred stock, the right to receive dividends, if any, or, payments upon our liquidation, dissolution or winding up or to exercise voting rights, if any.

Exercise of Warrants

Each warrant will entitle the holder to purchase the securities that we specify in the applicable prospectus supplement at the exercise price that we describe in the applicable prospectus supplement. The warrants may be exercised as set forth in the prospectus supplement relating to the warrants offered. Unless we otherwise specify in the applicable prospectus supplement, warrants may be exercised at any time up to the close of business on the expiration date set forth in the prospectus supplement relating to the warrants offered thereby. After the close of business on the expiration date, unexercised warrants will become void.

Upon receipt of payment and the warrant or warrant certificate, as applicable, properly completed and duly executed at the corporate trust office of the warrant agent, if any, or any other office, including ours, indicated in the prospectus supplement, we will, as soon as practicable, issue and deliver the securities purchasable upon such exercise. If less than all of the warrants (or the warrants represented by such warrant certificate) are exercised, a new warrant or a new warrant certificate, as applicable, will be issued for the remaining warrants.

Governing Law

Unless we otherwise specify in the applicable prospectus supplement, the warrants and any warrant agreements will be governed by and construed in accordance with the laws of the State of New York.

Enforceability of Rights by Holders of Warrants

Each warrant agent, if any, will act solely as our agent under the applicable warrant agreement and will not assume any obligation or relationship of agency or trust with any holder of any warrant. A single bank or trust company may act as warrant agent for more than one issue of warrants. A warrant agent will have no duty or responsibility in case of any default by us under the applicable warrant agreement or warrant, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a warrant may, without the consent of the related warrant agent or the holder of any other warrant, enforce by appropriate legal action its right to exercise, and receive the securities purchasable upon exercise of, its warrants.

LEGAL OWNERSHIP OF SECURITIES

We can issue securities in registered form or in the form of one or more global securities. We describe global securities in greater detail below. We refer to those persons who have securities registered in their own names on the books that we or any applicable trustee, depositary or warrant agent maintain for this purpose as the "holders" of those securities. These persons are the legal holders of the securities. We refer to those persons who, indirectly through others, own beneficial interests in securities that are not registered in their own names, as "indirect holders" of those securities. As we discuss below, indirect holders are not legal holders, and investors in securities issued in book-entry form or in street name will be indirect holders.

Book-Entry Holders

We may issue securities in book-entry form only, as we will specify in the applicable prospectus supplement. This means securities may be represented by one or more global securities registered in the name of a financial institution that holds them as depositary on behalf of other financial institutions that participate in the depositary's book-entry system. These participating institutions, which are referred to as participants, in turn, hold beneficial interests in the securities on behalf of themselves or their customers.

Only the person in whose name a security is registered is recognized as the holder of that security. Securities issued in global form will be registered in the name of the depositary or its participants. Consequently, for securities issued in global form, we will recognize only the depositary as the holder of the securities, and we will make all payments on the securities to the depositary. The depositary passes along the payments it receives to its participants, which in turn pass the payments along to their customers who are the beneficial owners. The depositary and its participants do so under agreements they have made with one another or with their customers; they are not obligated to do so under the terms of the securities.

As a result, investors in a global security will not own securities directly. Instead, they will own beneficial interests in a global security, through a bank, broker or other financial institution that participates in the depositary's book-entry system or holds an interest through a participant. As long as the securities are issued in global form, investors will be indirect holders, and not legal holders, of the securities.

Street Name Holders

We may terminate a global security or issue securities in non-global form. In these cases, investors may choose to hold their securities in their own names or in "street name." Securities held by an investor in street name would be registered in the name of a bank, broker or other financial institution that the investor chooses, and the investor would hold only a beneficial interest in those securities through an account he or she maintains at that institution.

For securities held in street name, we or any applicable trustee or depositary will recognize only the intermediary banks, brokers and other financial institutions in whose names the securities are registered as the holders of those securities, and we or any applicable trustee or depositary will make all payments on those securities to them. These institutions pass along the payments they receive to their customers who are the beneficial owners, but only because they agree to do so in their customer agreements or because they are legally required to do so. Investors who hold securities in street name will be indirect holders, not holders, of those securities.

Legal Holders

Our obligations, as well as the obligations of any applicable trustee and of any third parties employed by us or a trustee, run only to the legal holders of the securities. We do not have obligations to investors who hold beneficial interests in global securities, in street name or by any other indirect means. This will be the case whether an investor chooses to be an indirect holder of a security or has no choice because we are issuing the securities only in global form.

For example, once we make a payment or give a notice to the legal holder, we have no further responsibility for the payment or notice even if that legal holder is required, under agreements with its participants or customers or by law, to pass it along to the indirect holders but does not do so. Similarly, we may want to obtain the approval of the legal holders to amend an indenture, to relieve us of the consequences of a default or of our obligation to comply with a particular provision of the indenture or for other purposes. In such an event, we would seek approval only from the holders, and not the indirect holders, of the securities. Whether and how the legal holders contact the indirect holders is up to the legal holders.

Special Considerations For Indirect Holders

If you hold securities through a bank, broker or other financial institution, either in book-entry form because the securities are represented by one or more global securities or in street name, you should check with your own institution to find out:

- how it handles securities payments and notices;
- whether it imposes fees or charges;
- how it would handle a request for the holders' consent, if ever required;
- whether and how you can instruct it to send you securities registered in your own name so you can be a holder, if that is permitted in the future;
- how it would exercise rights under the securities if there were a default or other event triggering the need for holders to act to protect their interests; and
- if the securities are in book-entry form, how the depositary's rules and procedures will affect these matters.

Global Securities

A global security is a security that represents one or any other number of individual securities held by a depositary. Generally, all securities represented by the same global securities will have the same terms.

Each security issued in book-entry form will be represented by a global security that we issue to, deposit with and register in the name of a financial institution or its nominee that we select. The financial institution that we select for this purpose is called the depositary. Unless we specify otherwise in the applicable prospectus supplement, DTC will be the depositary for all securities issued in book-entry form.

A global security may not be transferred to or registered in the name of anyone other than the depositary, its nominee or a successor depositary, unless special termination situations arise. We describe those situations below under "Special Situations When a Global Security Will Be Terminated." As a result of these arrangements, the depositary, or its nominee, will be the sole registered owner and legal holder of all securities represented by a global security, and investors will be permitted to own only beneficial interests in a global security. Beneficial interests must be held by means of an account with a broker, bank or other financial institution that in turn has an account with the depositary or with another institution that does. Thus, an investor whose security is represented by a global security will not be a legal holder of the security, but only an indirect holder of a beneficial interest in the global security.

If the prospectus supplement for a particular security indicates that the security will be issued in global form only, then the security will be represented by a global security at all times unless and until the global security is terminated. If termination occurs, we may issue the securities through another book-entry clearing system or decide that the securities may no longer be held through any book-entry clearing system.

Special Considerations for Global Securities

The rights of an indirect holder relating to a global security will be governed by the account rules of the investor's financial institution and of the depositary, as well as general laws relating to securities transfers. We do not recognize an indirect holder as a holder of securities and instead deal only with the depositary that holds the global security.

If securities are issued only in the form of a global security, an investor should be aware of the following:

- an investor cannot cause the securities to be registered in his or her name, and cannot obtain non-global certificates for his or her interest in the securities, except in the special situations we describe below;
- an investor will be an indirect holder and must look to his or her own bank, broker or other financial institution for payments on the securities and protection of his or her legal rights relating to the securities, as we describe above;
- an investor may not be able to sell interests in the securities to some insurance companies and to other institutions that are required by law to own their securities in non-book-entry form;

- an investor may not be able to pledge his or her interest in a global security in circumstances where certificates representing the securities must be delivered to the lender or other beneficiary of the pledge in order for the pledge to be effective;
- the depositary's policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor's interest in a global security;
- we and any applicable trustee have no responsibility for any aspect of the depositary's actions or for its records of ownership interests in a global security, nor do we or any applicable trustee supervise the depositary in any way;
- the depositary may, and we understand that DTC will, require that those who purchase and sell interests in a global security within its book-entry system use immediately available funds, and your bank, broker or other financial institution may require you to do so as well; and
- financial institutions that participate in the depositary's book-entry system, and through which an investor holds its interest in a global security, may also have their own policies affecting payments, notices and other matters relating to the securities.

There may be more than one financial intermediary in the chain of ownership for an investor. We do not monitor and are not responsible for the actions of any of those intermediaries.

Special Situations when a Global Security will be Terminated

In a few special situations described below, the global security will terminate and interests in it will be exchanged for physical certificates representing those interests. After that exchange, the choice of whether to hold securities directly or in street name will be up to the investor. Investors must consult their own banks, brokers or other financial institutions to find out how to have their interests in securities transferred to their own name, so that they will be direct holders. We have described the rights of holders and street name investors above.

Unless we provide otherwise in the applicable prospectus supplement, the global security will terminate when the following special situations occur:

- if the depositary notifies us that it is unwilling, unable or no longer qualified to continue as depositary for that global security and we do not appoint another institution to act as depositary within 90 days;
- if we notify any applicable trustee that we wish to terminate that global security; or
- if an event of default has occurred with regard to securities represented by that global security and has not been cured or waived.

The applicable prospectus supplement may also list additional situations for terminating a global security that would apply only to the particular series of securities covered by the applicable prospectus supplement. When a global security terminates, the depositary, and not we or any applicable trustee, is responsible for deciding the names of the institutions that will be the initial direct holders.

PLAN OF DISTRIBUTION

We may sell our securities covered by this prospectus in any of three ways (or in any combination):

- to or through underwriters or dealers;
- directly to one or more purchasers; or
- through agents.

We may distribute the securities:

- from time to time in one or more transactions at a fixed price or prices, which may be changed from time to time;
- at market prices prevailing at the time of sale;
- at prices related to the prevailing market prices; or
- at negotiated prices.

Each time we offer and sell securities covered by this prospectus, we will provide a prospectus supplement or supplements, if necessary, that will describe the method of distribution and set forth the terms of the offering, including:

- the name or names of any underwriters, dealers or agents;
- the amounts of securities underwritten or purchased by each of them;
- the purchase price of securities and the proceeds, if any, we will receive from the sale;
- any over-allotment options under which underwriters may purchase additional securities from us;
- any underwriting discounts or commissions or agency fees and other items constituting underwriters' or agents' compensation;
- the public offering price of the securities;
- any discounts, commissions or concessions allowed or reallowed or paid to dealers; and
- any securities exchange or market on which the securities may be listed.

Any public offering price and any discounts or concessions allowed or reallowed or paid to dealers may be changed from time to time. We may determine the price or other terms of the securities offered under this prospectus by use of an electronic auction. We will describe how any auction will determine the price or any other terms, how potential investors may participate in the auction and the nature of the obligations of the underwriter, dealer or agent in the applicable prospectus supplement.

Underwriters or dealers may offer and sell the offered securities from time to time in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale. If underwriters or dealers are used in the sale of any securities, the securities will be acquired by the underwriters or dealers for their own account and may be resold from time to time in one or more transactions described above. The securities may be either offered to the public through underwriting syndicates represented by managing underwriters, or directly by underwriters or dealers. Generally, the underwriters' or dealers' obligations to purchase the securities will be subject to certain conditions precedent. The underwriters or dealers will be obligated to purchase all of the securities if they purchase any of the securities, unless otherwise specified in the prospectus supplement. We may use underwriters with whom we have a material relationship. We will describe the nature of any such relationship in the prospectus supplement, naming the underwriter.

We may sell the securities through agents from time to time. The prospectus supplement will name any agent involved in the offer or sale of the securities and any commissions we pay to them. Generally, any agent will be acting on a best efforts basis for the period of its appointment. We may authorize underwriters, dealers or agents to solicit offers by certain purchasers to purchase the securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. The contracts will be subject only to those conditions set forth in the prospectus supplement, and the prospectus supplement will set forth any commissions we pay for solicitation of these contracts.

Agents, dealers and underwriters may be entitled to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, or to contribution with respect to payments which the agents, dealers or underwriters may be required to make in respect thereof. Agents, dealers and underwriters may be customers of, engage in transactions with, or perform services for us in the ordinary course of business.

All securities we may offer, other than common stock, will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities.

Any underwriter may engage in overallotment, stabilizing transactions, short covering transactions and penalty bids in accordance with Regulation M under the Securities Exchange Act of 1934, as amended. Overallotment involves sales in excess of the offering size, which create a short position. This short sales position may involve either "covered" short sales or "naked" short sales. Covered short sales are short sales made in an amount not greater than the underwriters' over-allotment option to purchase additional securities in this offering described above. The underwriters may close out any covered short position either by exercising their over-allotment option or by purchasing securities in the open market. To determine how they will close the covered short position, the underwriters will consider, among other things, the price of securities available for purchase in the open market, as compared to the price at which they may purchase securities through the over-allotment option. Naked short sales are short sales in excess of the over-allotment option. The underwriters must close out any naked short position by purchasing securities in the open market. A naked short position is more likely to be created if the underwriters are concerned that, in the open market after pricing, there may be downward pressure on the price of the securities that could adversely affect investors who purchase securities in this offering. Stabilizing transactions permit bids to purchase the underlying security for the purpose of fixing the price of the security so long as the stabilizing bids do not exceed a specified maximum. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a covering transaction to cover short positions.

Any underwriters who are qualified market makers on the Nasdaq Capital Market may engage in passive market making transactions in our common stock, preferred stock, warrants and debt securities, as applicable, on the Nasdaq Capital Market in accordance with Rule 103 of Regulation M, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded.

Any broker-dealer participating in the distribution of the shares of common stock may be deemed to be "underwriters" within the meaning of the Securities Act, and any commission paid, or any discounts or concessions allowed to, any such broker-dealer may be deemed to be underwriting commissions or discounts under the Securities Act. At the time a particular offering of the shares of common stock is made, a prospectus supplement, if required, will be distributed which will set forth the aggregate amount of shares of common stock being offered and the terms of the offering, including the name or names of any broker-dealers or agents, any discounts, commissions and other terms and any discounts, commissions or concessions allowed or reallowed or paid to broker-dealers.

Under the securities laws of some states, the shares of common stock may be sold in such states only through registered or licensed brokers or dealers. In addition, in some states the shares of common stock may not be sold unless such shares have been registered or qualified for sale in such state or an exemption from registration or qualification is available and is complied with.

In compliance with guidelines of the Financial Industry Regulatory Authority, or FINRA, the maximum consideration or discount to be received by any FINRA member or independent broker dealer may not exceed 8% of the aggregate amount of the securities offered pursuant to this prospectus and any applicable prospectus supplement.

Similar to other purchase transactions, an underwriter's purchase to cover the syndicate short sales or to stabilize the market price of our securities may have the effect of raising or maintaining the market price of our securities

or preventing or mitigating a decline in the market price of our securities. As a result, the price of our securities may be higher than the price that might otherwise exist in the open market. The imposition of a penalty bid might also have an effect on the price of the securities if it discourages resales of the securities.

Neither we nor the underwriters make any representation or prediction as to the effect that the transactions described above may have on the price of the securities. If such transactions are commenced, they may be discontinued without notice at any time.

We will pay all expenses of the registration of the shares of common stock pursuant to the waiver agreements, including, without limitation, Securities and Exchange Commission filing fees and expenses of compliance with state securities or “blue sky” laws.

Once sold under the registration statement, of which this prospectus forms a part, the shares of common stock will be freely tradable in the hands of persons other than our affiliates.

LEGAL MATTERS

Unless otherwise indicated in the applicable prospectus supplement, the validity of the securities offered by this prospectus, and any supplement thereto, will be passed upon for us by Honigman LLP.

EXPERTS

The consolidated financial statements of Ocuphire Pharma, Inc. appearing in Ocuphire Pharma, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2022 have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon included therein, and incorporated herein by reference. Such consolidated financial statements are, and audited financial statements to be included in subsequently filed documents will be, incorporated herein in reliance upon such report of Ernst & Young LLP pertaining to such financial statements (to the extent covered by consents filed with the Securities and Exchange Commission) given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of a registration statement we filed with the SEC. This prospectus does not contain all of the information set forth in the registration statement and the exhibits to the registration statement. For further information with respect to us and the securities we are offering under this prospectus, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. Neither we nor any agent, underwriter or dealer has authorized any person to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus is accurate as of any date other than the date on the front page of this prospectus, regardless of the time of delivery of this prospectus or any sale of the securities offered by this prospectus.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. The SEC maintains a website that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC, including Ocuphire. The address of the SEC website is www.sec.gov.

We maintain a website at www.ocuphire.com. Information contained in or accessible through our website does not constitute a part of this prospectus.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" the information we file with it, which means that we can disclose important information to you by referring you to those documents instead of having to repeat the information in this prospectus. The information incorporated by reference is considered to be part of this prospectus, and later information that we file with the SEC will automatically update and supersede this information. We incorporate by reference the documents listed below and any future filings (including those made after the date of the initial filing of the registration statement of which this prospectus is a part and prior to the effectiveness of such registration statement) we will make with the SEC under Sections 13(a), 13(c), 14, or 15(d) of the Exchange Act until the termination of the offering of the shares covered by this prospectus (other than information furnished under Item 2.02 or Item 7.01 of Form 8-K):

- our Annual Report on Form 10-K for the year ended December 31, 2022, filed with the SEC on March 30, 2023, and the information specifically incorporated by reference into our Definitive Proxy Statement on Schedule 14A, filed with the SEC on May 1, 2023;
- our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2023, June 30, 2023, and September 30, 2023 filed with the SEC on May 15, 2023, August 11, 2023, and November 13, 2023 respectively;
- our Current Reports on Form 8-K filed with the SEC on January 25, 2023, April 21, 2023, June 2, 2023, June 9, 2023, June 14, 2023, August 11, 2023; September 27, 2023; November 1, 2023; November 2, 2023; November 27, 2023; and December 6, 2023; and
- the description of common stock set forth in the Registration Statement on Form 8-A, filed with the SEC on June 7, 2019, including any amendments thereto or reports filed for the purposes of updating this description, as updated by Exhibit 4.6 to our Annual Report on Form 10-K for the year ended December 31, 2022, filed with the SEC on March 30, 2023, including any amendments or reports filed for the purposes of updating this description.

We will furnish without charge to each person, including any beneficial owner, to whom this prospectus is delivered, upon written or oral request, a copy of any or all of the documents incorporated by reference, including exhibits to these documents. You may request a copy of these documents by writing or telephoning us at the following address:

Ocuphire Pharma, Inc.
37000 Grand River Avenue, Suite 120
Farmington Hills, MI 48335
(248) 957-9024
Attn: Dr. George Magrath, Chief Executive Officer

12,219,736 Shares of Common Stock
Warrants to Purchase up to 21,052,631 Shares of Common Stock
Pre-Funded Warrants to Purchase 8,832,895 Shares of Common Stock
Up to 21,052,631 Shares of Common Stock underlying the Warrants and Pre-Funded Warrants

PROSPECTUS SUPPLEMENT

Craig-Hallum

March 21, 2025