PROSPECTUS SUPPLEMENT (To Prospectus dated August 17, 2023)



31,800,000 Shares of Common Stock Pre-Funded Warrants to Purchase 23,700,000 Shares of Common Stock

Pursuant to this prospectus supplement and the accompanying prospectus, we are offering in a registered direct offering to certain purchasers (i) 31,800,000 shares of our common stock, par value \$0.001 per share, and, in lieu of shares of common stock to certain investors that so choose, (ii) pre-funded warrants to purchase 23,700,000 shares of our common stock, or the pre-funded warrants. The purchase price of each pre-funded warrant will equal the price per share at which shares of our common stock are being sold to the purchasers in this offering, minus \$0.001, and the exercise price of each pre-funded warrant will equal \$0.001 per share. This prospectus supplement also relates to the offering of the shares of our common stock issuable upon the exercise of such pre-funded warrants.

Our common stock is listed on the Nasdaq Global Select Market under the trading symbol "OPTN." On May 8, 2024, the last reported sale price of our common stock on the Nasdaq Global Select Market was \$1.04 per share. There is no established public trading market for the pre-funded warrants, and we do not expect a market to develop. We do not intend to list the pre-funded warrants on the Nasdaq Global Select Market or any other national securities exchange or nationally recognized trading system.

As a result of this offering, the exercise price of 30,268,000 warrants issued by us on November 23, 2022, or the 2022 Warrants, will be automatically adjusted from \$2.565 per share to the offering price of each share of common stock sold in this offering. In addition, the exercise price of 2,500,000 warrants issued to the holders of our senior secured notes, or the Pharmakon Senior Secured Notes, is being reduced from \$1.60 to the offering price of each share sold in this offering and the expiration date of such warrants issued to the holders of the Pharmakon Senior Secured Notes is being extended from November 18, 2024 to November 18, 2026. In addition, in a separate private placement transaction, we are issuing an aggregate of 4,680,000 shares of our common stock to the holders of the Pharmakon Senior Secured Notes in satisfaction of the \$4,680,000 of outstanding amendment and waiver fees owed under the Amended and Restated Note Purchase Agreement (as defined herein), which shares are being calculated based on the offering price of each share of common stock sold in this offering.

Investing in our securities involves a high degree of risk. Please read the "Risk Factors" beginning on page S-7 of this prospectus supplement, on page 6 of the accompanying prospectus and under similar headings in the documents incorporated by reference into this prospectus supplement and the accompanying prospectus, for a discussion of the factors you should carefully consider before deciding to purchase our securities.

	PER SHARE	PER PRE-FUNDED WARRANT	TOTAL ⁽¹⁾
Offering price	\$ 1.00	\$0.999	\$55,476,300

⁽¹⁾ The amount of the offering proceeds to us presented in this table does not give effect to any exercise of the warrants being issued in the offering.

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

We expect to deliver the securities to investors on or about May 10, 2024.

The date of this prospectus supplement is May 8, 2024.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus are part of a shelf registration statement on Form S-3 (File No. 333-273873) that we filed with the Securities and Exchange Commission, or SEC, on August 10, 2023 and was declared effective by the SEC on August 17, 2023, pursuant to which we may from time to time offer various securities in one or more offerings.

This document is in two parts. The first part is this prospectus supplement, which describes the terms of this offering of our securities and also adds to and updates the 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, including the documents incorporated by reference into the accompanying prospectus, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined.

To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying prospectus or in any document incorporated by reference into this prospectus supplement or the accompanying prospectus before the date of this prospectus supplement, on the other hand, or the information contained in any free writing prospectus prepared by us or on our behalf that we have authorized for use in connection with this offering, you should rely on the information in this prospectus supplement. If any statement in one of these documents is inconsistent with a statement in another document having a later date - for example, a document incorporated by reference into this prospectus supplement or into the accompanying prospectus - the statement in the document having the later date modifies or supersedes the earlier statement unless otherwise specified.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference into this 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 agreement, 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.

We have not authorized anyone to provide you with information different from, or in addition to, that contained in this prospectus supplement, the accompanying prospectus or any free writing prospectus prepared by or on behalf of us or to which we may have referred you in connection with this offering. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. The information in this prospectus supplement and the accompanying prospectus is accurate only as of their respective dates, regardless of the time of delivery of this prospectus supplement and accompanying prospectus or of any sale of our securities. Our business, financial condition, results of operations and prospects may have changed since those dates.

This prospectus supplement does not contain all of the information that is important to you. You should also read and consider the information in the documents we have referred you to in the sections of this prospectus supplement entitled "Where You Can Find More Information" and "Incorporation by Reference" and the sections of the accompanying prospectus entitled "Where You Can Find More Information" and "Incorporation by Reference". You should rely only on the information contained or incorporated by reference in this prospectus supplement.

OPTINOSE®, XHANCE® EDS®, and EXHALATION DELIVERY SYSTEMTM are trademarks of ours in the United States. Solely for convenience, trademarks and trade names referred to in this prospectus supplement, the accompanying prospectus, including logos, artwork and other visual displays, may appear without the ® or TM symbols, but such references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights to these trademarks and trade names. All other trademarks, trade names and service marks appearing in this prospectus supplement, the accompanying prospectus and in the documents incorporated by reference into this prospectus supplement or the accompanying prospectus are the property of their respective owners. We do not intend our use or display of other companies' trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

We are offering to sell, and seeking offers to buy, these securities only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the accompanying prospectus and the offering of the securities in certain jurisdictions may be restricted by law. For investors outside of the United States: we have not done anything that would permit this offering or possession or distribution of this prospectus supplement and accompanying prospectus in any jurisdiction where action for that purpose is required, other than in the United States. You are required to inform yourselves about and to observe any restrictions relating to this offering and the distribution of this prospectus supplement and the accompanying prospectus. This prospectus supplement and the accompanying prospectus do 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.

MARKET, INDUSTRY AND OTHER DATA

This prospectus supplement, the accompanying prospectus and the documents incorporated by reference into this prospectus supplement or the accompanying prospectus contain estimates, projections, market research and other information concerning our industry, our business, markets for XHANCE and the size of those markets, the prevalence of certain medical conditions, XHANCE market access, prescription data, inventory data and other physician, patient and payor data. Unless otherwise expressly stated, we obtain this information from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources as well as from our own internal estimates and research and from publications, research, surveys and studies conducted by third parties on our behalf. Information that is based on estimates, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are reflected in this information. As a result, you are cautioned not to give undue weight to such information.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights information contained in greater detail elsewhere in this prospectus supplement, the accompanying prospectus and in the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. This summary does not contain all of the information that you should consider in making your investment decision. You should read the entire prospectus supplement, the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus carefully before making an investment in our securities. You should carefully consider, among other things, our consolidated financial statements and related notes incorporated by reference in this prospectus supplement from our Annual Report on Form 10-K for the year ended December 31, 2023, or our 2023 Annual Report, and the sections titled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" included in our 2023 Annual Report and other documents incorporated by reference in this prospectus supplement and the accompanying prospectus.

Unless the context otherwise requires, we use the terms "Optinose," "Company," "we," "us," "our" and similar designations in this prospectus supplement to refer to OptiNose, Inc. and, where appropriate, our subsidiaries.

Company Overview

We are a specialty pharmaceutical company focused on the development and commercialization of products for patients treated by ear, nose and throat (ENT) and allergy specialists. Our first commercial product, XHANCE® (fluticasone propionate) nasal spray, 93 micrograms (mcg), is a therapeutic utilizing our proprietary Exhalation Delivery SystemTM (EDS®) that delivers a topically-acting corticosteroid for the treatment of chronic rhinosinusitis with and without nasal polyps. Chronic rhinosinusitis is a serious nasal inflammatory disease that is treated using therapies, such as intranasal steroids (INS), which have significant limitations. We believe XHANCE has a differentiated clinical profile with the potential to become part of the standard of care for this disease because it is able to deliver medication to the primary site of inflammation high and deep in the nasal passages in regions not adequately reached by conventional INS. Additionally, we believe the current practice of postoperative INS use could support XHANCE's adoption as a maintenance therapy to improve outcomes following sinus surgery.

XHANCE was approved by the United States (US) Food and Drug Administration (FDA) in September 2017 for the treatment of chronic rhinosinusitis with nasal polyps in patients 18 years of age or older. We made XHANCE widely available through commercial channels in April 2018. On March 15, 2024, the FDA approved XHANCE for the treatment of chronic rhinosinusitis without nasal polyps in patients 18 years of age and older.

We are relaunching XHANCE to focus on the comparatively larger market opportunity that we believe is created by the new indication. We plan to continue to focus our commercial efforts primarily to the ENT and allergy specialist audience while seeking partnerships to extend the commercialization of XHANCE into primary care.

For more information about our company, please refer to other documents that we have filed with the SEC and that are incorporated by reference into this prospectus supplement and the accompanying prospectus, as listed under the heading "Incorporation by Reference."

Recent Developments

Third Amendment to Amended and Restated Note Purchase Agreement

Concurrently with the pricing of this offering, we entered into a Third Amendment of that certain Amended and Restated Note Purchase Agreement, dated November 21, 2022, and amended on March 5, 2024 and March 8, 2024, among us and our subsidiary, OptiNose US, Inc., BioPharma Credit PLC, as collateral agent, and the purchasers party thereto from time to time

We have issued \$130.0 million of senior secured notes, which we refer to as the Pharmakon Senior Secured Notes, to date under the Amended and Restated Note Purchase Agreement, and there are no outstanding commitments for the purchasers to purchase any additional senior secured notes under the Amended and Restated Note Purchase Agreement. An aggregate amount of \$6.0 million is owed under the Amended and Restated Note Purchase Agreement for prior amendments and waivers, which

amount shall be reduced by \$1.3 million if the Pharmakon Senior Secured Notes are paid in full on or prior to November 21, 2024.

Effective upon our receipt of at least \$35 million in net proceeds from this offering, the Third Amendment provides for:

- a waiver of the requirement under the Amended and Restated Note Purchase Agreement that our audited financial statements not be subject to any qualification or statement as to "going concern". The requirement that the Company's audited and unaudited financial statements not be subject to any qualification or statement as to "going concern" will continue to apply to the Company's financial statements for the fiscal year ending December 31, 2025 and each fiscal quarter and fiscal year thereafter,
- the reduction of the minimum amount of cash and cash equivalents that we are required to maintain at all times under the Amended and Restated Note Purchase Agreement from \$30 million to \$20 million following the date of the first quarterly payment of principal due on September 30, 2025,
- our issuance of an aggregate of 4,680,000 shares of our common stock to the holders of the Pharmakon Senior Secured Notes in satisfaction of the \$4,680,000 of outstanding
 amendment and waiver fees owed under the Amended and Restated Note Purchase Agreement, which shares are being calculated based on the offering price of each share of
 common stock sold in this offering; and
- an amendment to that certain common stock warrant, dated November 18, 2021, issued to the holders of the Pharmakon Senior Secured Notes for the purchase of 2,500,000 shares of our common stock (such warrant is referred to herein as, the "Pharmakon Warrants") to (i) reduce the exercise price of the Pharmakon Warrants from \$1.60 per share to the offering price of each share sold in this offering, and (ii) extend the expiration date of the Pharmakon Warrants from November 18, 2024 to November 18, 2026.

Certain Preliminary Financial Information

For the three-month period ended March 31, 2024, we expect to report:

- approximately \$14.9 million in net revenue from sales of XHANCE,
- approximately \$21.7 of operating expenses, consisting of approximately \$1.2 million of research and development expenses and approximately \$20.5 million of selling, general and administrative expenses,
- · a loss from operations of approximately \$8.1 million; and
- · a net loss of approximately \$14.1 million.

As of March 31, 2024, we had approximately \$51.6 million of cash and cash equivalents.

These estimates of our net revenue from sales of XHANCE, operating expenses (including research and development expenses and selling, general and administrative expenses), loss from operations, net loss and cash and cash equivalents are preliminary and subject to completion. As a result, this unaudited preliminary financial information reflects our preliminary estimates with respect to such information, based on information currently available to management, and may vary from our actual financial results and position as of March 31, 2024. Further, these preliminary estimates are not a comprehensive statement or estimate of our financial results or financial condition as of and for the quarter ended March 31, 2024. The unaudited preliminary net revenue from sales of XHANCE, operating expenses (including research and development expenses and selling, general and administrative expenses), loss from operations, net loss and cash and cash equivalents included herein has been prepared by, and is the responsibility of, management. Our independent registered public accounting firm, Ernst & Young LLP, has not audited, reviewed, compiled or completed its procedures with respect to such unaudited financial information and, accordingly, Ernst & Young LLP does not express an opinion or any other form of assurance with respect thereto. It is possible that we or our independent registered public accounting firm may identify items that require us to make adjustments to the financial information set forth above. These estimates should not be viewed as a substitute for financial statements prepared in

accordance with accounting principles generally accepted in the United States and they are not necessarily indicative of the results to be achieved in any future period. Accordingly, you should not draw any conclusions based on the foregoing estimates and should not place undue reliance on these preliminary estimates. We assume no duty to update these preliminary estimates except as required by law.

2024 Financial Guidance

For full year 2024, we expect:

- our consolidated XHANCE net product revenues will be between \$85 million and \$95 million;
- our average net product revenues per prescription will exceed \$230, which is an increase from our previously announced guidance of greater than \$220; and
- our total GAAP operating expenses (selling, general and administrative expenses and research and development expenses) will be between \$95 million and \$101 million, of which we expect approximately \$6 million will be stock-based compensation.

Corporate Information

We were incorporated under the laws of the State of Delaware in May 2010. Our corporate office is located at 1020 Stony Hill Road, Suite 300, Yardley, PA 19067. Our telephone number is (267) 364-3500.

Our primary executive offices are located at 1020 Stony Hill Road, Suite 300, Yardley, Pennsylvania 19067 and our telephone number is (267) 364-3500. Our website address is www.optinose.com. We make available free of charge on our website our annual, quarterly and current reports, including amendments to such reports, as soon as reasonably practicable after we electronically file such material with, or furnish such material to, the SEC. The information contained in, or that can be accessed through, our website is not part of this prospectus supplement, the accompanying prospectus or any other report or document that we file with or furnish to the SEC. We have included our website address in this prospectus supplement as an inactive textual reference and do not intend it to be an active link to our website.

Implications of Being a Smaller Reporting Company

We are a "smaller reporting company," meaning that the market value of our shares held by non-affiliates is less than \$700 million and our annual revenue was less than \$100 million during the most recently completed fiscal year. We have elected to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company, we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and have reduced disclosure obligations regarding executive compensation.

THE OFFERING

Common stock offered by us

31,800,000 shares.

Pre-Funded Warrants offered by us

We are also offering, in lieu of common stock to certain investors, pre-funded warrants to purchase 23,700,000 shares of our common stock. The purchase price of each pre-funded warrant will equal the price per share at which shares of our common stock are being sold to the public in this offering, minus \$0.001, and the exercise price of each pre-funded warrant will equal \$0.001 per share. Each pre-funded warrant will be exercisable from the date of issuance until the date the warrant is exercised in full, subject to an ownership limitation. See the section entitled "Description of the Securities we are Offering." This prospectus supplement also relates to the offering of the shares of our common stock issuable upon the exercise of such pre-funded warrants.

Common stock to be outstanding immediately after this offering

144,838,726 shares (assuming no exercise of the pre-funded warrants offered hereby).

We estimate that the net proceeds to us from this offering will be approximately \$55.0 million (assuming no exercise of the prefunded warrants offered hereby), after deducting estimated offering expenses payable by us. We intend to use the net proceeds from this offering for working capital and general corporate purposes, including the commercialization of XHANCE. See "Use of Proceeds" on page S-13 of this prospectus supplement for a more complete description.

Use of Proceeds

Risk Factors

You should read the "Risk Factors" section beginning on page S-7 of this prospectus supplement and in the documents incorporated by reference herein for a discussion of certain of the factors to consider carefully before deciding to purchase any of our securities. "OPTN."

Nasdaq Global Select Market Symbol

> There is no established public trading market for the pre-funded warrants, and we do not expect a market to develop. We do not intend to list the pre-funded warrants on the Nasdaq Global Select Market or any other national securities exchange or nationally recognized trading system. Without an active trading market, the liquidity of the pre-funded warrants will be limited. See the section entitled "Description of the Securities we are Offering."

Outstanding Shares

The number of shares of our common stock to be outstanding immediately after this offering is based on 113,038,726 shares of our common stock outstanding as of March 31, 2024. Unless specifically stated otherwise, the information in this prospectus supplement is as of March 31, 2024, and excludes:

- 9,294,484 shares of our common stock issuable upon the exercise of stock options outstanding as of March 31, 2024 at a weighted-average exercise price of \$4.64 per share;
- 11,000 shares of our common stock issuable upon the exercise of stock options granted subsequent to March 31, 2024, at a weighted-average exercise price of \$1.14 per share;
- 4,927,069 shares of our common stock underlying our restricted stock units outstanding as of March 31, 2024;
- 8,047,882 shares of our common stock reserved for future issuance under our Amended and Restated 2010 Stock Incentive Plan, or the 2010 Plan, as of March 31, 2024;

- 2,500,000 shares of our common stock issuable upon the exercise of warrants outstanding as of March 31, 2024 at an exercise price of \$1.60 per share (these warrants are referred to herein as the Pharmakon Warrants and are subject to adjustment as described below);
- 30,268,000 shares of our common stock issuable upon the exercise of warrants outstanding as of March 31, 2024 at an exercise price of \$2.565 per share (these warrants are referred to herein as the 2022 Warrants and are subject to adjustment as described below);
- up to \$50.0 million of shares of our common stock that may be issued and sold from time to time under an "at-the-market" equity offering program pursuant to that certain Open Market Sale AgreementSM, dated as of August 11, 2021 with Jefferies LLC, of which no shares have been sold to date;
- 1,248,161 shares of our common stock reserved for future issuance under our 2017 Employee Stock Purchase Plan, or the 2017 ESPP, as of March 31, 2024;
- 4,680,000 shares of our common stock to the holders of the Pharmakon Senior Secured Notes in satisfaction of \$4,680,000 of outstanding amendment and waiver fees owed under
 the Amended and Restated Note Purchase Agreement, which shares are being calculated based on the offering price of each share of common stock sold in this offering; and
- 23,700,000 shares of our common stock issuable upon the exercise of pre-funded warrants offered hereby.

The 30,268,000 outstanding 2022 Warrants have anti-dilution price protection and this offering will result in the exercise price of such warrants being reduced from \$2.565 to the offering price of each share sold in this offering. In addition, the exercise price of the 2,500,000 Pharmakon Warrants is expected to be reduced from \$1.60 to the offering price of each share sold in this offering and the expiration date of the Pharmakon Warrants is expected to be extended from November 18, 2024 to November 18, 2026 in connection with the closing of this offering.

Unless otherwise indicated, all information in this prospectus supplement assumes no exercise or settlement of the outstanding stock options, warrants and restricted stock units described above.

RISK FACTORS

An investment in our securities involves a high degree of risk. You should carefully consider the risks and uncertainties described below, as well as those set forth under the heading "Risk Factors" in our 2023 Annual Report, which is incorporated by reference in this prospectus supplement. Our business, operating results, financial condition or prospects could be materially and adversely affected by any of these risks and uncertainties. In that case, the trading price of our common stock could decline and you might lose all or part of your investment. In addition, the risks and uncertainties discussed below are not the only ones we face. Our business, operating results, financial condition or prospects could also be harmed by risks and uncertainties not currently known to us or that we currently do not believe are material, and these risks and uncertainties could result in a loss of all or part of your investment. In assessing the risks and uncertainties described below, you should also refer to the other information contained in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus, including our consolidated financial statements and the related notes thereto, before making a decision to invest in our securities.

Risks Related to Our Financial Position and Capital Resources

We have a significant amount of warrants with anti-dilution price protection and this offering will result in the exercise price on such warrants being reduced to the offering price of each share sold in this offering.

We have 30,268,000 outstanding 2022 Warrants with anti-dilution price protection. This offering will result in the exercise price on such warrants being reduced from \$2.565 to the offering price of each share sold in this offering. In addition, in the event of a fundamental transaction, as defined in the 2022 Warrants, in certain circumstances each holder of a 2022 Warrant will have the right to require us to repurchase its 2022 Warrant for cash at the Black Scholes Value (as defined in the 2022 Warrants). The reduction of the exercise price of the 2022 Warrants as a result of this offering has the effect of increasing the Black Scholes Value in the event of a fundamental transaction. In addition, the exercise price of the 2022 Warrants will be further reduced in the event of certain other future offerings of securities at a lower price to the then current exercise price of the 2022 Warrants (subject to limited exceptions). Such warrants may deter future investors and can result in further dilution to our investors

In addition, the exercise price of the 2,500,000 Pharmakon Warrants is expected to be reduced from \$1.60 to the offering price of each share sold in this offering and the expiration date of the Pharmakon Warrants is expected to be extended from November 18, 2024 to November 18, 2026 in connection with the closing of this offering.

Risks Related to This Offering and Ownership of Our Securities

You will experience immediate and substantial dilution if you purchase our securities in this offering.

Since the price per share of our common stock and the price per pre-funded warrant being offered is substantially higher than the net tangible book deficit per share of our common stock, you will suffer substantial dilution with respect to the securities you purchase in this offering. Our net tangible book deficit as of December 31, 2023 was approximately \$86.6 million, or \$(0.77) per share of our common stock, based on 112,399,495 shares of our common stock outstanding on December 31, 2023.

Based on the offering price of \$1.00 per share of our common stock and \$0.999 per pre-funded warrant (which equals the public offering price per share of common stock less the \$0.001 per share exercise price of each such pre-funded warrant) (and including shares of common stock issued and any proceeds received upon exercise of the pre-funded warrants, but excluding any resulting accounting associated with the pre-funded warrants), and after deducting estimated offering expenses payable by us, our as adjusted net tangible book deficit as of December 31, 2023, would have been approximately \$31.6 million, or approximately \$(0.19) per share of our common stock. As a result, investors purchasing securities in this offering will incur immediate dilution of \$1.19 per share. See "Dilution" for a more detailed discussion of the dilution you will incur if you purchase securities in this offering, if anything, in the event of our liquidation. See "Dilution" on page S-14 of this prospectus supplement for a more detailed discussion of the dilution you will incur if you purchase shares of our common stock or pre-funded warrants in this offering.

In addition, as of March 31, 2024, we had outstanding stock options to purchase an aggregate of 9,294,484 shares of our common stock subject to outstanding stock options at a weighted-average exercise price of \$4.64 per share, 4,927,069 shares of our common stock underlying outstanding restricted stock units, warrants to purchase an aggregate of 2,500,000 shares of our common stock at an

exercise price of \$1.60 per share (referred to herein as the Pharmakon Warrants), and warrants to purchase an aggregate of 30,268,000 shares of our common stock at an exercise price of \$2.565 per share (referred to herein as the 2022 Warrants) (provided that the exercise price of the 2022 Warrants will be reduced, and the exercise price of the Pharmakon Warrants is expected to be reduced, to the offering price of each share sold in this offering). To the extent these outstanding stock options or warrants are exercised or these outstanding restricted stock units vest and settle into shares, there will be further dilution to investors in this offering. In addition, in a private placement, we are issuing an aggregate of 4,680,000 shares of our common stock to the holders of the Pharmakon Senior Secured Notes in satisfaction of \$4,680,000 of outstanding amendment and waiver fees owed under the Amended and Restated Note Purchase Agreement, which shares are being calculated based on the offering price of each share of common stock sold in this offering.

Substantial future sales of shares of our common stock could cause the market price of our common stock to decline,

The market price of our common stock could decline as a result of substantial sales of our common stock, particularly sales by our directors, executive officers and significant stockholders, a large number of shares of our common stock becoming available for sale or the perception in the market that holders of a large number of shares intend to sell their shares.

As of March 31, 2024, there were 9,294,484 shares of our common stock subject to outstanding stock options at a weighted-average exercise price of \$4.64 per share, 4,927,069 shares of our common stock underlying outstanding restricted stock units, warrants to purchase an aggregate of 2,500,000 shares of our common stock at an exercise price of \$1.60 per share (referred to herein as the Pharmakon Warrants), and warrants to purchase an aggregate of 30,268,000 shares of our common stock at an exercise price of \$2.565 per share (referred to herein as the 2022 Warrants) (provided that the exercise price of the 2022 Warrants will be reduced, and the exercise price of the Pharmakon Warrants is expected to be reduced, to the offering price of each share sold in this offering). As of March 31, 2024, we had also reserved (i) 8,047,882 shares of our common stock for future issuance under the 2010 Plan and (ii) 1,248,161 shares of our common stock for future issuance under the 2017 ESPP, each of which also includes an evergreen provision that automatically increases the number of shares reserved for future issuance under the applicable plan each year. In addition, we are also offering pre-funded warrants to purchase up to an aggregate of 23,700,000 shares of our common stock, which will be exercisable on the initial grant date. Accordingly, these shares of our common stock may be freely sold in the public market upon issuance as permitted by any applicable vesting requirements, subject to compliance with applicable securities laws. In addition, in a private placement, we are issuing an aggregate of 4,680,000 shares of our common stock to the holders of the Pharmakon Senior Secured Notes in satisfaction of \$4,680,000 of outstanding amendment and waiver fees owed under the Amended and Restated Note Purchase Agreement, which shares are being calculated based on the offering price of each share of common stock sold in this offering.

We have previously entered into the Open Market Sale AgreementSM, dated as of August 11, 2021 with Jefferies LLC, pursuant to which, from time to time, we may offer and sell shares of our common stock with an aggregate offering price of up to \$50,000,000 under an "at-the-market" offering program. As of the date of this prospectus supplement, we have common stock that we may issue and sell for gross proceeds of up to \$50.0 million that remain available under our at-the-market offering program. To the extent that we sell shares of our common stock pursuant to our at-the-market offering program, investors purchasing shares of common stock in this offering could experience further dilution.

Moreover, if we issue stock options, performance stock units, restricted stock units, warrants or other securities to purchase or acquire our common stock in the future and those stock options, performance stock units, restricted stock units, warrants or other securities are exercised, converted or settled you may experience further dilution. Holders of shares of our common stock have no preemptive rights that entitle them to purchase their pro rata share of any offering of shares of any class or series.

Further, we may issue shares of our common stock or securities convertible into our common stock from time to time in connection with a financing, acquisition, investment or otherwise. Any such issuance could result in substantial dilution to our existing stockholders and cause the trading price of our common stock to decline.

We have broad discretion in the use of the net proceeds to us from this offering and may invest or spend the proceeds in ways with which you do not agree and in ways that may not increase the value of your investment.

We will have broad discretion in the application of the net proceeds to us from this offering, and you will be relying on the judgment of our management regarding the application of these proceeds. You may not agree with our decisions, and our management may not apply the net proceeds to us from this offering in ways that ultimately increase the value of your investment. We expect to use the net proceeds to us from this offering in the manner described in the "Use of Proceeds" section of this prospectus supplement. Our failure to apply these net proceeds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and negatively impact the commercialization of XHANCE. Pending their use, we intend to

invest the net proceeds to us from this offering in short- and intermediate-term, interest bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government. These investments may not yield a favorable return to our stockholders. If we do not invest or apply the net proceeds to us from this offering in ways that enhance stockholder value, we may fail to achieve expected financial results and it could compromise our ability to commercialize XHANCE or develop and commercialize other product candidates, any of which could cause the price of our common stock to decline.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain and you may never receive a return on your investment.

We have never declared or paid cash dividends on our capital stock, and you should not rely on an investment in our securities to provide dividend income. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. In addition, our Amended and Restated Note Purchase Agreement prohibits us, and the terms of any future debt agreements may also preclude us, from paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

The trading price of the shares of our common stock could be highly volatile, and purchasers of our common stock could incur substantial losses.

The price of our common stock is highly volatile and may be affected by developments directly affecting our business, as well as by developments out of our control or not specific to us. The pharmaceutical and biotechnology industries, in particular, and the stock market generally, are vulnerable to abrupt changes in investor sentiment. Prices of securities and trading volumes of companies in the pharmaceutical and biotechnology industries, including ours, can swing dramatically in ways unrelated to, or that bear a disproportionate relationship to, our performance. This volatility may affect the price at which you could sell the shares of our common stock, and the sale of substantial amounts of our common stock could adversely affect the price of our common stock. Our stock price is likely to continue to be volatile and subject to significant price and volume fluctuations in response to market and other factors, including those described in the sections entitled "Risk Factors" in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein.

As a result, you may not be able to sell your shares of common stock at or above the price at which you purchase them. In addition, the stock market in general, the Nasdaq Stock Market and the stock of pharmaceutical and bio pharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance.

There is no public market for the pre-funded warrants being offered in this offering.

There is no public trading market for 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 list the pre-funded warrants on the Nasdaq Global Select Market or any other national securities exchange or nationally recognized trading system. Without an active trading market, the liquidity of the pre-funded warrants will be limited.

Holders of the pre-funded warrants will have no rights as common stockholders until such holders exercise their pre-funded warrants and acquire our common stock.

Until holders of the pre-funded warrants exercise their pre-funded warrants and acquire shares of our common stock, such holders will have no rights with respect to the shares of our common stock underlying such pre-funded warrants.

We may not receive any additional funds upon the exercise of the pre-funded warrants.

Each pre-funded warrant may be exercised by way of a cashless exercise, meaning that the holder may not pay a cash purchase price upon exercise, but instead would receive upon such exercise the net number of shares of our common stock determined according to the formula set forth in the pre-funded warrant. Accordingly, we may not receive any additional funds upon the exercise of the pre-funded warrants.

Significant holders or beneficial holders of our common stock may not be permitted to exercise pre-funded warrants that they hold.

A holder of a pre-funded warrant will not be entitled to exercise any portion of any pre-funded warrant which, upon giving effect to such exercise, would cause (i) the aggregate number of shares of our common stock beneficially owned by the holder (together with its affiliates) to exceed 4.99 or 9.99% (at the initial election of the holder) of the number of shares of our common stock outstanding immediately after giving effect to the exercise, or (ii) the combined voting power of our securities beneficially owned by the holder (together with its affiliates) to exceed 4.99% or 9.99% (at the initial election of the holder) of the combined voting power of all of our securities then outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of the pre-funded warrants. Such percentage may be increased by the holder of the pre-funded warrant to any other percentage not in excess of 19.99% upon at least 61 days' prior notice from the holder to us. As a result, you may not be able to exercise your pre-funded warrants for shares of our common stock at a time when it would be financially beneficial for you to do so. In such circumstance you could seek to sell your pre-funded warrants to realize value, but you may be unable to do so in the absence of an established trading market for the pre-funded warrants.

NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus, particularly in the sections titled "Prospectus Summary" and "Risk Factors" in this prospectus supplement and the sections titled "Risk Factors," "Management's Discussion and Analysis of Financial Conditions and Results of Operations" and "Business" in our 2023 Annual Report, contain forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, included in this prospectus supplement, the accompanying prospectus or the documents incorporated by reference into this prospectus supplement and the accompanying prospectus, including statements regarding our future financial condition, results of operations, business strategy and plans and objectives of management for future operations, industry trends and other future events, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "believe," "will," "may," "estimate," "continue," "intend," "should," "plan," "expect," "predict," "project," "could," "potentially," "continue," "ongoing," "scheduled" or the negative of these terms or other similar expressions, although not all forward-looking statements contain these identifying terms. The forward-looking statements in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus include, among other things, statements about:

- the potential uses for and advantages of XHANCE®, the Exhalation Delivery System[™] (also referred to as, the EDS®) and related technologies;
- the potential to expand promotion of XHANCE into the primary care segment and our plans to seek a partner for such expansion;
- our belief that the current practice of postoperative intranasal steroid (INS) use could support XHANCE's adoption as a maintenance therapy to improve outcomes following sinus surgery;
- the potential for XHANCE to be the standard of care for the treatment of chronic rhinosinusitis with and without nasal polyps;
- the potential for direct-to-consumer (DTC) advertising to be a future driver of XHANCE prescription growth;
- the potential benefits of our patient affordability programs (including recent changes we made to the XHANCE co-pay assistance program) and their potential effect on XHANCE demand and financial results;
- our expectation for XHANCE prescriptions to be impacted by the seasonality observed in the INS market and the seasonal variation in patient visits with their doctor;
- our expectation for XHANCE prescriptions and average net revenue per prescription to be adversely impacted by the annual resetting of patient healthcare insurance plan deductibles and changes in individual patients' healthcare insurance coverage, both of which often occur in January;
- our expectation that research and development expenses in 2024 will be less than 2023;
- XHANCE prescription, net revenue, prescriber and other business trends;
- the potential for payor utilization management criteria to negatively impact XHANCE prescription volumes;
- the rate and degree of market acceptance and market opportunity of XHANCE;
- the potential for us to decrease our reliance on sole-source suppliers and increase the third party manufacturing capacity that is available to us;

- the financial results we expect to report for the quarter ended March 31, 2024;
- our expectation that for full year 2024 our consolidated XHANCE net product revenues will be between \$85 million and \$95 million;
- our expectation that for full year 2024 our average net product revenues per prescription will exceed \$230;
- our expectation that for full year 2024 our total GAAP operating expenses (selling, general and administrative expenses and research and development expenses) will be between \$95 million and \$101 million, of which we expect approximately \$6 million will be stock-based compensation;
- our expectation that we will produce positive income from operations (GAAP) for full year 2025;
- · our expectation that our base planned efforts focused on a specialty prescriber audience can grow XHANCE peak year net revenues to more than \$300 million;
- our belief that our existing cash and cash equivalents plus the net proceeds from this offering will be sufficient to fund our operations and debt service obligations through 2025;
- our expectations and the accuracy of our estimates regarding our future expenses, revenue, capital requirements, potential sources of capital and consequences of failing to obtain additional capital;
- legal and regulatory developments in the United States and foreign countries;
- the scope and duration of patent protection and other barriers to entry that we expect to benefit XHANCE;
- the performance of our third-party suppliers, manufacturers, wholesalers, distributors, HUB and preferred pharmacy network (PPN) partners; and
- our expected use of proceeds from this offering.

Forward-looking statements also include statements related to any expectations of revenues, expenses, cash flows, earnings or losses from operations, cash required to maintain current and planned operations, capital or other financial items; any statements of the plans, strategies and objectives of management for future operations; any plans or expectations with respect to product research, development and commercialization, including regulatory approvals; any other statements of expectations, plans, intentions or beliefs; and any statements of assumptions underlying any of the foregoing.

We cannot guarantee that the results and other expectations expressed, anticipated or implied in any forward-looking statement will be realized. Forward-looking statements are based upon our current expectations and assumptions and are subject to a number of known and unknown risks, uncertainties and other factors that could cause our actual results and other expectations to differ materially from the anticipated results or other expectations expressed, anticipated or implied in our forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in this prospectus supplement, our 2023 Annual Report, and in particular, the risks and uncertainties discussed therein under the caption "Risk Factors" and other documents we file with the SEC. You should read and interpret any forward-looking statements together with these risks. Moreover, we operate in a very competitive and rapidly changing environment. 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. As a result, you should not place undue reliance on forward-looking statements. Should known or unknown risks materialize, or should underlying assumptions prove inaccurate, actual results could differ materially from past results and those anticipated, estimated or projected in the forward-looking statements. You should bear this in mind as you consider any forward-looking statements. Our forward-looking statements speak only as of the dates on which they are made. We do not undertake any obligation to publicly update or revise our forward-looking statements even if experience or future changes makes it clear that any projected results expressed or implied in such statements will not be realized.

Before deciding to purchase our securities, you should carefully consider the risk factors discussed and incorporated by reference in this prospectus supplement and in the accompanying prospectus and in the registration statement of which this prospectus supplement and the accompanying prospectus form a part.

USE OF PROCEEDS

We estimate that the net proceeds from this offering, including proceeds from the sale of pre-funded warrants, after deducting estimated offering expenses payable by us, will be approximately \$55.0 million. We will receive nominal proceeds, if any, upon exercise of the pre-funded warrants.

We intend to use the net proceeds from this offering for working capital and general corporate purposes, including the commercialization of XHANCE.

Based on our current plans, we believe our existing cash and cash equivalents, together with the net proceeds from this offering, will be sufficient to fund our operations and debt service obligations through 2025. We have based these estimates on assumptions that may prove to be incorrect, and we could use our available capital resources sooner than we currently expect. In any event, we may require additional funding to be able to continue to support our commercialization activities or conduct additional research and development or business development activities. We may satisfy our future cash needs through the sale of equity securities, debt financings, working capital lines of credit, corporate collaborations or license agreements, grant funding, interest income earned on invested cash balances or a combination of one or more of these sources.

The amounts and timing of our use of the net proceeds from this offering will depend on a number of factors, such as the timing and progress of our commercialization efforts, research and development efforts, the timing and progress of any partnering efforts, technological advances and the competitive environment for our product candidates. As of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses for the net proceeds to us from the sale of the shares of our common stock and accompanying warrants offered by us under this prospectus supplement. Accordingly, our management will have broad discretion in the timing and application of these proceeds. Pending application of the net proceeds as described above, we intend to temporarily invest the proceeds in short-term, interest-bearing instruments.

Although we may use a portion of the net proceeds to us from this offering for the acquisition or licensing, as the case may be, of products, product candidates, technologies, compounds, other assets or complementary businesses, we have no current understandings, agreements or commitments to do so. Pending these uses, we plan to invest the net proceeds to us from this offering in short- and intermediate-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government.

DILUTION

Purchasers of our common stock or pre-funded warrants in this offering will experience immediate dilution to the extent of the difference between the offering price per share of our common stock or pre-funded warrants, as applicable, and the as adjusted net tangible book deficit per share of our common stock immediately after this offering.

As of December 31, 2023, our net tangible book deficit was \$86.6 million, or \$(0.77) per share of our common stock. Net tangible book deficit is the amount of our total tangible assets less our total liabilities. Net tangible book deficit per share is determined by dividing our net tangible book deficit by the aggregate number of shares of our common stock outstanding as of December 31, 2023.

Dilution per share to new investors represents the difference between the amount per share paid by purchasers of our common stock or pre-funded warrants in this offering and the as adjusted net tangible book deficit per share of our common stock immediately following the completion of this offering.

After giving effect to the sale of (i) 31,800,000 shares of our common stock in this offering at an offering price of \$1.00 and (ii) pre-funded warrants to purchase 23,700,000 shares of our common stock in this offering at the offering price of \$0.999 per pre-funded warrant (which equals the price per share at which shares of our common stock are being sold to the public in this offering, minus the \$0.001 per share exercise price of each such pre-funded warrant), including shares of common stock issuable upon exercise of the pre-funded warrants but excluding any resulting accounting associated therewith, and after deducting the estimated offering expenses payable by us, our as adjusted net tangible book deficit as of December 31, 2023 would have been approximately \$31.6 million, or approximately \$(0.19) per share of our common stock. This represents an immediate decrease in net tangible book deficit of \$0.58 per share of our common stock to our existing stockholders and an immediate dilution in net tangible book deficit of \$1.19 per share of our common stock to purchasers of our common stock and pre-funded warrants in this offering.

The following table illustrates this dilution on a per share basis:

Offering price per share	\$1.00
	• 111
Net tangible book deficit per share as of December 31, 2023	\$ (0.77)
Decrease in net tangible book deficit per share attributable to investors participating in this offering	\$0.58
As adjusted net tangible book deficit per share after this offering	\$(0.19)
Dilution per share to investors participating in this offering	\$1.19

The above table excludes

- 9,294,484 shares of our common stock issuable upon the exercise of stock options outstanding as of March 31, 2024 at a weighted-average exercise price of \$4.64 per share;
- 11,000 shares of our common stock issuable upon the exercise of stock options granted subsequent to March 31, 2024, at a weighted-average exercise price of \$1.14 per share;
- 4,927,069 shares of our common stock underlying our restricted stock units outstanding as of March 31, 2024;
- 8,047,882 shares of our common stock reserved for future issuance under our 2010 Plan as of March 31, 2024;
- 2,500,000 shares of our common stock issuable upon the exercise of warrants outstanding as of March 31, 2024 at an exercise price of \$1.60 per share (these warrants are referred to herein as the Pharmakon Warrants and are subject to adjustment as described below);

- 30,268,000 shares of our common stock issuable upon the exercise of warrants outstanding as of March 31, 2024 at an exercise price of \$2.565 per share (these warrants are referred to herein as the 2022 Warrants and are subject to adjustment as described below);
- up to \$50.0 million of shares of our common stock that may be issued and sold from time to time under an "at-the-market" equity offering program pursuant to that certain Open Market Sale AgreementSM, dated as of August 11, 2021 with Jefferies LLC, of which no shares have been sold to date;
- 1,248,161 shares of our common stock reserved for future issuance under our 2017 ESPP as of March 31, 2024; and
- 4,680,000 shares of our common stock to the holders of the Pharmakon Senior Secured Notes in satisfaction of \$4,680,000 of outstanding amendment and waiver fees owed under the Amended and Restated Note Purchase Agreement, which shares are being calculated based on the offering price of each share of common stock sold in this offering.

The 30,268,000 outstanding 2022 Warrants have anti-dilution price protection and this offering will result in the exercise price on such warrants being reduced from \$2.565 to the offering price of each share sold in this offering. In addition, the

exercise price of the 2,500,000 Pharmakon Warrants is expected to be reduced from \$1.60 to the offering price of each share sold in this offering and the expiration date of the Pharmakon Warrants is expected to be extended from November 18, 2024 to November 18, 2026 in connection with the closing of this offering.

To the extent that outstanding stock options or warrants are exercised, outstanding restricted stock units are settled or additional shares of our common stock are issued in the future, including pursuant to additional grants under our stock incentive plans, there will be further dilution to investors participating in this offering. In addition, we may choose to raise additional capital because of market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. If we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

DESCRIPTION OF THE SECURITIES WE ARE OFFERING

The following description of our common stock and pre-funded warrants summarizes the material terms and provisions thereof, including the material terms of the common stock and pre-funded warrants we are offering under this prospectus supplement and the accompanying prospectus.

Common Stock

The material terms and provisions of our common stock are described under the caption "General Description of Our Securities—Description of Our Common Stock" starting on page 12 of the accompanying prospectus.

Our common stock is listed on The Nasdaq Global Select Market under the symbol "OPTN."

Our transfer agent for our common stock is Broadridge Corporate Issuer Solutions, Inc.

Pre-Funded Warrants

The following is a summary of certain terms and conditions of the pre-funded warrants being offered in this offering. The following description is subject in all respects to the provisions contained in the pre-funded warrants.

Form

The pre-funded warrants will be issued as individual warrant agreements to the purchasers. The form of pre-funded warrant will be filed as an exhibit to a Current Report on Form 8-K that we expect to file with the SEC.

Term

The pre-funded warrants will expire on the date the warrant is exercised in full

Exercisability

The pre-funded warrants are exercisable at any time after their original issuance. The pre-funded warrants will be exercisable, at the option of each holder, in whole or in part by delivering to us a duly executed exercise notice and by payment in full of the exercise price in immediately available funds for the number of shares of common stock purchased upon such exercise. As an alternative to payment in immediately available funds, the holder may, in its sole discretion, elect to exercise the pre-funded warrant through a cashless exercise, in which the holder would receive upon such exercise the net number of shares of our common stock determined according to the formula set forth in the pre-funded warrant. No fractional shares of our common stock will be issued in connection with the exercise of a pre-funded warrant. In lieu of fractional shares, we will pay the holder an amount in cash equal to the fractional amount multiplied by the last closing trading price of our common stock on the exercise date.

Exercise Limitations

We may not effect the exercise of any pre-funded warrant, and a holder will not be entitled to exercise any portion of any pre-funded warrant that, upon giving effect to such exercise, would cause: (i) the aggregate number of shares of our common stock beneficially owned by such holder (together with its affiliates) to exceed 4.99% or 9.99% (at the initial election of the holder) of the number of shares of our common stock outstanding immediately after giving effect to the exercise; or (ii) the combined voting power of our securities beneficially owned by such holder (together with its affiliates) to exceed 4.99% or 9.99% (at the

initial election of the holder) of the combined voting power of all of our securities outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of the pre-funded warrants. However, any holder of a pre-funded warrant may increase or decrease such percentage to any other percentage not in excess of 19.99% upon at least 61 days' prior notice from the holder to us.

Exercise Price

The exercise price per whole share of our common stock purchasable upon the exercise of the pre-funded warrants is \$0.001 per share of common stock. The exercise price of the pre-funded warrants and the number of shares of our common stock issuable upon exercise of the pre-funded warrants 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, as well as upon any distribution of assets, including cash, stock or other property, to our stockholders.

Transferability

Subject to applicable laws, the pre-funded warrants may be offered for sale, sold, transferred or assigned without our consent.

Exchange Listing

There is no established trading market for the pre-funded warrants, and we do not expect a market to develop. We do not intend to apply for the listing of the pre-funded warrants on the Nasdaq Global Select Market, any other national securities exchange or any other nationally recognized trading system.

Fundamental Transactions

Upon the consummation 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 of 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 such holders would have received had they exercised the pre-funded warrants immediately prior to such fundamental transaction, without regard to any limitations on exercise contained in the pre-funded warrant. In the event the holder of a pre-funded warrant does not exercise the pre-funded warrant as contemplated by the fundamental transaction provisions in the pre-funded warrant upon the effective date of the consummation of such fundamental transaction.

No Rights as a Stockholder

Except by virtue of such holder's ownership of shares of our common stock, the holder of a prefunded warrant does not have the rights or privileges of a holder of our common stock, including any voting rights, until such holder exercises the pre-funded warrant.

CERTAIN MATERIAL UNITED STATES FEDERAL INCOME TAX CONSEQUENCES

The following discussion is a summary of the material U.S. federal income tax consequences of the purchase, ownership and disposition of shares of our common stock and pre-funded warrants issued pursuant to this offering, but does not purport to be a complete analysis of all potential tax effects. The effects of other U.S. federal tax laws, such as estate and gift tax laws, and any applicable state, local or non-U.S. tax laws are not discussed. This discussion is based on the Internal Revenue Code of 1986, as amended (the "Code"), Treasury Regulations promulgated thereunder, judicial decisions, and published rulings and administrative pronouncements of the U.S. Internal Revenue Service (the "IRS") in effect as of the date of this offering. These authorities may change or be subject to differing interpretations. Any such change or differing interpretation may be applied retroactively in a manner that could adversely affect a holder of our common stock or pre-funded warrants. We have not sought and do not intend to seek any rulings from the IRS regarding the matters discussed below. There can be no assurance the IRS or a court will not take a contrary position regarding the tax consequences of the purchase, ownership and disposition of our common stock or pre-funded warrants.

This discussion is limited to holders that hold our common stock or pre-funded warrants as a "capital asset" within the meaning of Section 1221 of the Code (generally, property held for investment). This discussion does not address all U.S. federal income tax consequences relevant to a holder's particular circumstances, including the impact of the alternative minimum tax or the unearned income Medicare contribution tax. In addition, it does not address consequences relevant to holders subject to particular rules, including, without limitation:

- · U.S. expatriates and certain former citizens or long-term residents of the U.S.;
- persons holding our common stock or pre-funded warrants as part of a hedge, straddle or other risk reduction strategy or as part of a conversion transaction or other integrated investment;
- banks, insurance companies, mutual funds, and other financial institutions;
- · brokers, dealers or traders in securities;
- · controlled foreign corporations, "passive foreign investment companies," and corporations that accumulate earnings to avoid U.S. federal income tax;
- "S corporations," partnerships or other entities or arrangements treated as partnerships for U.S. federal income tax purposes, or other pass-through entities (and, in each case, investors therein);
- · tax-exempt organizations or governmental organizations;
- · persons deemed to sell our common stock or pre-funded warrants under the constructive sale provisions of the Code;
- · persons for whom our stock constitutes "qualified small business stock" within the meaning of Section 1202 of the Code;
- · persons who hold or receive our common stock or pre-funded warrants pursuant to the exercise of any employee stock option or otherwise as compensation;
- U.S. persons whose functional currency is not the U.S. dollar;
- persons subject to special tax accounting rules as a result of any item of gross income with respect to our common stock or pre-funded warrants being taken into account in a financial statement;
- · tax-qualified retirement plans; and
- "qualified foreign pension funds" as defined in Section 897(1)(2) of the Code and "withholding qualified holders" as defined in Treasury Regulation Section 1.1445-1(g)(11).

If a partnership (or other entity treated as a partnership for U.S. federal income tax purposes) holds our common stock or pre-funded warrants, the tax treatment of a partner in the partnership will depend on the status of the partner, the activities of the partnership and certain determinations made at the partner level. Accordingly, partnerships holding our common stock or pre-funded warrants and the partners in such partnerships should consult their tax advisors regarding the U.S. federal income tax consequences to them.

THIS DISCUSSION IS FOR INFORMATION PURPOSES ONLY AND IS NOT INTENDED AS TAX ADVICE. INVESTORS SHOULD CONSULT THEIR TAX ADVISORS WITH RESPECT TO THE APPLICATION OF THE U.S. FEDERAL INCOME TAX LAWS TO THEIR PARTICULAR SITUATIONS AS WELL AS ANY TAX CONSEQUENCES OF THE PURCHASE, OWNERSHIP AND DISPOSITION OF OUR COMMON STOCK OR PRE-FUNDED WARRANTS ARISING UNDER THE U.S. FEDERAL ESTATE OR GIFT TAX LAWS OR UNDER THE LAWS OF ANY STATE, LOCAL OR NON-U.S. TAXING JURISDICTION OR UNDER ANY APPLICABLE INCOME TAX TREATY.

For purposes of this discussion, a "U.S. holder" is any beneficial owner of our common stock or pre-funded warrants that, for U.S. federal income tax purposes, is:

- an individual who is a citizen or resident of the U.S.;
- a corporation (or other entity treated as a corporation for U.S. federal income tax purposes) created or organized under the laws of the U.S., any state thereof, or the District of Columbia;
- · an estate, the income of which is subject to U.S. federal income tax regardless of its source; or
- a trust that (1) is subject to the primary supervision of a U.S. court and the control of one or more U.S. persons (within the meaning of Section 7701(a)(30) of the Code), or (2) has made a valid election under applicable Treasury Regulations to continue to be treated as a U.S. person.

For purposes of this discussion, a "non-U.S. holder" is a beneficial owner of our common stock or pre-funded warrants that is neither a U.S. holder nor an entity treated as a partnership for U.S. federal income tax purposes.

General Treatment of Pre-Funded Warrants

Although the law in this area is not completely settled, the pre-funded warrants are generally expected to be treated as shares of our common stock for U.S. federal income tax purposes and a holder of pre-funded warrants should generally be taxed in the same manner as a holder of common stock as described below. You should discuss with your tax advisor the consequences of the purchase, ownership and disposition of the pre-funded warrants, as well as the exercise of, certain adjustments to, and any payments in respect of the pre-funded warrants (including potential alternative characterizations). The balance of this discussion generally assumes that the characterization described above is respected for U.S. federal income tax purposes.

Tax Considerations Applicable to U.S. Holders

Distributions

We do not anticipate declaring or paying distributions to holders of our common stock in the foreseeable future. However, if we do make distributions on our common stock, those payments will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. To the extent those distributions exceed both our current and our accumulated earnings and profits, the excess will constitute a return of capital and will first reduce a U.S. holder's basis in our common stock, but not below zero, and then will be treated as gain from the sale of stock as described below under the section entitled "Tax Considerations Applicable to U.S. Holders—Gain on Disposition of Common Stock or Pre-Funded Warrants." A preferential U.S. federal income tax rate may apply to any dividends paid to noncorporate U.S. holders meeting certain holding period requirements.

The taxation of property received with respect to a pre-funded warrant on exercise other than common shares is unclear. It is possible such a receipt of property would be treated as a distribution on common stock as described in this section, although other treatments may also be possible. Investors should consult their tax advisors regarding the proper treatment of any such receipt of property in respect of the pre-funded warrants on exercise.

Gain on Disposition of Our Common Stock or Pre-Funded Warrants

Upon a sale or other taxable disposition of our common stock or pre-funded warrants, a U.S. holder generally will recognize capital gain or loss in an amount equal to the difference between the amount realized and the U.S. holder's adjusted tax basis in the common stock or pre-funded warrant. Capital gain or loss will constitute long-term capital gain or loss if such U.S. holder's holding period for the common stock or pre-funded warrant exceeds one year. Long-term capital gains derived by certain non-corporate U.S. holders, including individuals, are generally subject to taxation at preferential rates. The deductibility of capital losses is subject to certain limitations. U.S. holders who recognize losses with respect to a disposition of our common stock or pre-funded warrants should consult their own tax advisors regarding the tax treatment of such losses.

Exercise of Pre-Funded Warrants

As discussed above under the section entitled "Description of Pre-Funded Warrants—Exercisability," a U.S. holder may exercise the pre-funded warrant by payment of exercise price or through a cashless exercise. The U.S. federal income tax treatment of a cashless exercise of pre-funded warrants into our common stock is unclear, and a U.S. holder should consult their own tax advisors regarding the U.S. federal income tax consequences of a cashless exercise of pre-funded warrants. In general, however, a U.S. holder should not recognize gain or loss for U.S. federal income tax purposes upon exercise of a pre-funded warrant pursuant to either method, except to the extent such U.S. holder receives a cash payment for a fractional share that would otherwise have been issuable upon exercise of the pre-funded warrant, which will be treated as a sale subject to the rules described above under the section entitled "Tax Considerations Applicable to U.S. Holders—Gain on Disposition of Our Common Stock or Pre-Funded Warrants." A U.S. holder's initial tax basis in the share of common stock received upon exercise of the pre-funded warrant generally should be equal to the sum of (i) such U.S. holder's tax basis in the pre-funded warrant and (ii) the exercise price paid or treated as paid by such U.S. holder on the exercise of the pre-funded warrant. A U.S. holder's holding period in the common stock received upon exercise generally should include such U.S. holder's holding period in the pre-funded warrants exchanged therefor.

Certain Adjustments to the Pre-Funded Warrants

Under Section 305 of the Code, an adjustment to the number of shares of common stock that will be issued on the exercise of the pre-funded warrants, or an adjustment to the exercise price of the pre-funded warrants, may be treated as a constructive distribution to a U.S. holder of pre-funded warrants if, and to the extent that, such adjustment has the effect of increasing such U.S. holder's proportionate interest in our "earnings and profits" or assets, depending on the circumstances of such adjustment (for example, if such adjustment is to compensate for a distribution of cash or other property to our shareholders).

U.S. holders are encouraged to consult their own tax advisors regarding the application of Section of the Code to the pre-funded warrants.

Information Reporting and Backup Withholding

Information reporting requirements generally will apply to payments of dividends (including constructive dividends) on the common stock or pre-funded warrants and to the proceeds of a sale or other disposition of common stock or pre-funded warrants paid by us to you unless you are an exempt recipient, such as certain corporations. Backup withholding will apply to those payments if a U.S. holder fails to provide their taxpayer identification number, or certification of exempt status, or if a U.S. holder otherwise fails to comply with applicable requirements to establish an exemption.

Backup withholding is not an additional tax. Rather, any amounts withheld under the backup withholding rules may be allowed as a refund or a credit against a U.S. holder's U.S. federal income tax liability, if any, provided the required information is timely furnished to the IRS. Investors should consult their own tax advisors regarding their qualification for exemption from information reporting and backup withholding and the procedure for obtaining such exemption.

Tax Considerations Applicable to Non-U.S. Holders

Distributions

We do not anticipate declaring or paying distributions to holders of our common stock in the foreseeable future. However, if we do make distributions on our common stock, such distributions of cash or property will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Amounts not treated as dividends for U.S. federal income tax purposes will constitute a return of capital and first be applied against and reduce a non-U.S. holder's adjusted tax basis in its common stock, but not below zero. Any excess will be treated as capital gain and will be treated as described below under the section entitled "Sale or Other Disposition of Common Stock or Pre-Funded Warrants". Because we may not know the extent to which a distribution is a dividend for U.S. federal income tax purposes at the time it is made, for purposes of the withholding rules discussed below we or the applicable withholding agent may treat the entire distribution as a dividend.

Subject to the discussion below on backup withholding and the Foreign Account Tax Compliance Act (the "FATCA"), dividends paid to a non-U.S. holder of our common stock that are not effectively connected with the non-U.S. holder's conduct of a trade or business within the U.S. will be subject to U.S. federal withholding tax at a rate of 30% of the gross amount of the dividends (or such lower rate specified by an applicable income tax treaty).

Non-U.S. holders may be entitled to a reduction in or an exemption from withholding on dividends as a result of either (a) an applicable income tax treaty or (b) the non-U.S. holder holding our common stock in connection with the conduct of a trade or business within the U.S. and dividends being effectively connected with that trade or business. To claim such a reduction in or exemption from withholding, the non-U.S. holder must provide the applicable withholding agent with a properly executed (a) IRS Form W-8BEN or W-8BEN-E (or other applicable documentation) claiming an exemption from or reduction of the withholding tax under the benefit of an income tax treaty between the U.S. and the country in which the non-U.S. holder resides or is established, or (b) IRS Form W-8ECI stating that the dividends are not subject to withholding tax because they are effectively connected with the conduct by the non-U.S. holder of a trade or business within the U.S., as may be applicable. These certifications must be provided to the applicable withholding agent prior to the payment of dividends and must be updated periodically. Non-U.S. holders that do not timely provide the applicable withholding agent with the required certification, but that qualify for a reduced rate under an applicable income tax treaty, may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS.

If dividends paid to a non-U.S. holder are effectively connected with the non-U.S. holder's conduct of a trade or business within the U.S. (and, if required by an applicable income tax treaty, the non-U.S. holder maintains a permanent establishment in the U.S. to which such dividends are attributable), then, although exempt from U.S. federal withholding tax (provided the non-U.S. holder provides appropriate certification, as described above), the non-U.S. holder will be subject to U.S. federal income tax on such dividends on a net income basis at the regular graduated U.S. federal income tax rates. In addition, a non-U.S. holder that is a corporation may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on its effectively connected earnings and profits for the taxable year that are attributable to such dividends, as adjusted for certain items. Non-U.S. holders should consult their tax advisors regarding their entitlement to benefits under any applicable income tax treaty.

The taxation of property received with respect to a pre-funded warrant on exercise other than common shares is unclear. It is possible such a receipt of property would be treated as a distribution as described in this section, although other treatments may also be possible. Investors should consult their tax advisors regarding the proper treatment of any such receipt of property in respect of the pre-funded warrants on exercise.

Sale or Other Disposition of Common Stock or Pre-Funded Warrants

Subject to the discussions below on backup withholding and FATCA, a non-U.S. holder will not be subject to U.S. federal income tax on any gain realized upon the sale or other disposition of our common stock or pre-funded warrants unless:

- the gain is effectively connected with the non-U.S. holder's conduct of a trade or business within the U.S. (and, if required by an applicable income tax treaty, the non-U.S. holder maintains a permanent establishment in the U.S. to which such gain is attributable);
- the non-U.S. holder is a nonresident alien individual present in the U.S. for 183 days or more during the taxable year of the disposition and certain other requirements are met; or
- our common stock or pre-funded warrants constitute U.S. real property interests ("USRPIs") by reason of our status as a U.S. real property holding corporation ("USRPHC") for U.S. federal income tax purposes.

Gain described in the first bullet point above will generally be subject to U.S. federal income tax on a net income basis at the regular graduated U.S. federal income tax rates. A non-U.S. holder that is a foreign corporation also may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on such effectively connected gain, as adjusted for certain items.

A non-U.S. holder described in the second bullet point above will be subject to U.S. federal income tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on any gain derived from the disposition, which may be offset by certain U.S. source capital losses of the non-U.S. holder (even though the individual is not considered a resident of the U.S.) provided the non-U.S. holder has timely filed U.S. federal income tax returns with respect to such losses.

With respect to the third bullet point above, we believe we are not currently and do not anticipate becoming a USRPHC. Because the determination of whether we are a USRPHC depends on the fair market value of our USRPIs relative to the fair market value of our other business assets and our non-U.S. real property interests, however, there can be no assurance we are not a USRPHC or will not become one in the future. Even if we are or were to become a USRPHC, gain arising from the sale or other taxable disposition by a non-U.S. holder of our common stock will not be subject to U.S. federal income tax if our common stock is "regularly traded," as defined by applicable Treasury Regulations, on an established securities market such as the NYSE American, and such non-U.S. holder owned, actually and constructively, 5% or less of our common stock throughout the shorter of the five-year period ending on the date of the sale or other taxable disposition or the non-U.S. Holder's holding period. Special rules may apply to non-U.S. holders of pre-funded warrants, who should consult their tax advisors.

Non-U.S. holders should consult their tax advisors regarding potentially applicable income tax treaties that may provide for different rules than those described above.

Exercise of Pre-Funded Warrants

As discussed above under the section entitled "Description of Pre-Funded Warrants—Exercisability," a non-U.S. holder may exercise the pre-funded warrant by payment of the exercise price or through a cashless exercise. The U.S. federal income tax treatment of a cashless exercise of pre-funded warrants into our common stock is unclear, and non-U.S. holders should consult their own tax advisors regarding the U.S. federal income tax consequences of a cashless exercise of pre-funded warrants. In general, however, a non-U.S. holder should not recognize gain or loss for U.S. federal income tax purposes upon exercise of a pre-funded warrant pursuant to either method, except to the extent such non-U.S. holder receives a cash payment for a fractional share that would otherwise have been issuable upon exercise of the pre-funded warrant, which will be treated as a sale subject to the rules described above under the section entitled "Tax Considerations Applicable to Non-U.S. Holders—Gain on Disposition of Our Common Stock or Pre-Funded Warrants."

Certain Adjustments to the Pre-Funded Warrants

Under Section 305 of the Code, an adjustment to the number of shares of common stock that will be issued on the exercise of the pre-funded warrants, or an adjustment to the exercise price of the pre-funded warrants, may be treated as a constructive distribution to a non-U.S. holder of the pre-funded warrants if, and to the extent that, such adjustment has the effect of increasing such non-U.S. holder's proportionate interest in our "earnings and profits" or assets, depending on the circumstances of such adjustment (for example, if such adjustment is to compensate for a distribution of cash or other property to our shareholders).

In addition, regulations governing "dividend equivalents" under Section 871(m) of the Code may apply to the pre-funded warrants. Under those regulations, an implicit or explicit payment under the pre-funded warrants that references a dividend distribution on our common stock would generally be taxable to a non-U.S. holder as described under "Distributions" above. Such dividend equivalent amount would be taxable and subject to withholding whether or not there is actual payment of cash or other property, and we may satisfy any withholding obligations we have in respect of the pre-funded warrants by withholding from other amounts due to a non-U.S. holder.

Non-U.S. holders are encouraged to consult their own tax advisors regarding the application of Sections 305 and 871(m) of the Code to the pre-funded warrants.

Information Reporting and Backup Withholding

Subject to the discussion below on foreign accounts, a non-U.S. holder will not be subject to backup withholding with respect to distributions we make on our common stock or pre-funded warrants to the non-U.S. holder, provided the applicable withholding agent does not have actual knowledge or reason to know such holder is a U.S. person and the holder certifies its non-U.S. status, such as by providing a valid IRS Form W-8BEN, W-8BEN-E or W-8ECI, or other applicable certification. However, information returns generally will be filed with the IRS in connection with any distributions (including deemed distributions) made on our common stock or pre-funded warrants to a non-U.S. holder, regardless of whether any tax was actually withheld. Copies of these information returns may also be made available under the provisions of a specific treaty or agreement to the tax authorities of the country in which the non-U.S. holder resides or is established.

Information reporting and backup withholding may apply to the proceeds of a sale or other taxable disposition of our common stock or pre-funded warrants within the U.S., and information reporting may (although backup withholding generally will not) apply to the proceeds of a sale or other taxable disposition of our common stock or pre-funded warrants outside the U.S. conducted through certain U.S.-related financial intermediaries, in each case, unless the beneficial owner certifies under penalty of perjury that it is a non-U.S. holder on IRS Form W-8BEN or W-8BEN-E, or other applicable form (and the payor does not have actual knowledge or reason to know that the beneficial owner is a U.S. person) or such owner otherwise establishes an exemption. Proceeds of a disposition of our common stock or pre-funded warrants conducted through a non-U.S. broker generally will not be subject to backup withholding or information reporting. Non-U.S. holders should consult their tax advisors regarding the application of the information reporting and backup withholding rules to them.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules may be allowed as a refund or a credit against a non-U.S. holder's U.S. federal income tax liability, provided the required information is timely furnished to the IRS.

Additional Withholding Tax on Payments Made to Foreign Accounts

Withholding taxes may be imposed under Sections 1471 to 1474 of the Code ("FATCA") on certain types of payments made to non-U.S. financial institutions and certain other non-U.S. entities. Specifically, a 30% withholding tax may be imposed on dividends (including deemed dividends) paid on our common stock or pre-funded warrants, to a "foreign financial institution" or a "non-financial foreign entity" (each as defined in the Code), unless (1) the foreign financial institution undertakes certain diligence and reporting obligations, (2) the non-financial foreign entity either certifies it does not have any "substantial United States owners" (as defined in the Code) or furnishes identifying information regarding each substantial U.S. owner, or (3) the

foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from these rules. Because we may not know the extent to which a distribution is a dividend for U.S. federal income tax purposes at the time it is made, for purposes of these withholding rules we or the applicable withholding agent may treat the entire distribution as a dividend. While withholding under FATCA would have applied also to payments of gross proceeds from the sale or other disposition of stock on or after January 1, 2019, proposed Treasury Regulations eliminate FATCA withholding on payments of gross proceeds entirely. Taxpayers generally may rely on these proposed Treasury Regulations until final Treasury Regulations are issued. Prospective investors should consult their tax advisors regarding the potential application of these withholding provisions, including the proposed Treasury Regulations. Foreign financial institutions located in jurisdictions that have an intergovernmental agreement with the U.S. governing FATCA may be subject to different rules.

LEGAL MATTERS

The validity of the securities being offered hereby will be passed upon for us by Hogan Lovells US LLP.

EXPERTS

The consolidated financial statements of OptiNose, Inc. appearing in OptiNose, 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 (which contains an explanatory paragraph describing conditions that raise substantial doubt about the Company's ability to continue as a going concern as described in Note 2 to the consolidated financial statements), included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-3 under the Securities Act, of which this prospectus supplement forms a part. The rules and regulations of the SEC allow us to omit from this prospectus supplement certain information included in the registration statement. For further information about us and the securities we are offering under this prospectus supplement, you should refer to the registration statement and the exhibits and schedules filed with the registration statement. With respect to the statements contained in this prospectus supplement regarding the contents of any agreement or any other document, in each instance, the statement is qualified in all respects by the complete text of the agreement or document, a copy of which has been filed as an exhibit to the registration statement.

Because we are subject to the information and reporting requirements of the Exchange Act, we file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at http://www.sec.gov.

We make available free of charge on our website our annual, quarterly and current reports, including amendments to such reports, as soon as reasonably practicable after we electronically file such material with, or furnish such material to, the SEC. Please note, however, that we have not incorporated any other information by reference from our website, other than the documents listed under the heading "Incorporation by Reference" on page S-25 of this prospectus supplement. In addition, you may request copies of these filings at no cost by writing or telephoning us at the following address or telephone number:

OptiNose, Inc. 1020 Stony Hill Road, Suite 300 Yardley, Pennsylvania 19067 Telephone: (267) 364-3500

INCORPORATION BY REFERENCE

The SEC allows us to "incorporate by reference" information from other documents that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus supplement, and information in documents that we file later with the SEC will automatically update and supersede information contained in documents filed earlier with the SEC or contained in this prospectus supplement. We incorporate by reference into this prospectus supplement the documents listed below and any future filings that we may make with the SEC under Sections 13(a), 13(c), 14, or 15(d) of the Exchange Act prior to the termination of the offering under this prospectus supplement; provided, however, that we are not incorporating, in each case, any documents or information deemed to have been furnished and not filed, including any information that we disclose under Items 2.02 or 7.01 of any Current Report on Form 8-K, in accordance with SEC rules, unless otherwise specified below:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2023, filed with the SEC on March 7, 2024;
- our Current Reports on Form 8-K, filed with the SEC on February 23, 2024, March 7, 2024, March 8, 2024, March 14, 2024, March 15, 2024 and April 25, 2024 (including, with respect to our Current Report on Form 8-K filed on April 25, 2024, the information disclosed under Item 7.01 and in Exhibit 99.2 under Item 9.01);
- · our Definitive Proxy Statement on Schedule 14A, filed with the SEC on April 26, 2024 (other than the portions thereof that are furnished and not filed); and
- the description of our common stock contained in our Registration Statement on Form 8-A (File No. 001-38241) filed with the SEC on October 10, 2017, as updated by Exhibit 4.5 to our Annual Report on Form 10-K for the year ended December 31, 2023, including any further amendment or report filed for the purpose of updating such description.

Information in such future filings updates and supplements the information provided in this prospectus supplement and the accompanying prospectus. Any statements in any such future filings will automatically be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

To obtain copies of these filings, see "Where You Can Find More Information" on page S-25 of this prospectus supplement.



\$200,000,000

Common Stock Preferred Stock Warrants Debt Securities Units

We may offer to the public from time to time in one or more series or issuances:

- · shares of our common stock;
- shares of our preferred stock;
- warrants to purchase shares of our common stock, preferred stock and/or debt securities;
- · debt securities consisting of debentures, notes or other evidences of indebtedness;
- · units consisting of a combination of the foregoing securities; or
- any combination of these securities.

The aggregate initial offering price of all securities sold by us pursuant to this prospectus will not exceed \$200,000,000.

This prospectus provides a general description of the securities that we may offer. Each time that we offer securities under this prospectus, we will provide the specific terms of the securities offered, including the public offering price, in a supplement to this prospectus. Any prospectus supplement may add to, update or change information contained in this prospectus.

The securities may be sold by us to or through underwriters or dealers, directly to purchasers or through agents designated from time to time. For additional information on the methods of sale, you should refer to the section entitled "Plan of Distribution" in this prospectus and the comparable section of any applicable prospectus supplement. If any underwriters are involved in the sale of the securities with respect to which this prospectus is being delivered, the names of such underwriters and any applicable discounts or commissions and underwriter options will be set forth in the applicable prospectus supplement.

Our common stock is traded on the Nasdaq Global Select Market under the symbol "OPTN." On August 9, 2023, the closing price of our common stock was \$1.16. We have not yet determined whether the other securities that may be offered by this prospectus will be listed on any exchange, interdealer quotation system or over-the-counter market. If we decide to seek the listing of any such securities upon issuance, the prospectus supplement relating to those securities will disclose the exchange, quotation system or market on which those securities will be listed.

INVESTING IN OUR SECURITIES INVOLVES A HIGH DEGREE OF RISK. RISKS ASSOCIATED WITH AN INVESTMENT IN OUR SECURITIES WILL BE DESCRIBED IN THE APPLICABLE PROSPECTUS SUPPLEMENT AND CERTAIN OF OUR FILINGS WITH THE SECURITIES AND EXCHANGE COMMISSION INCORPORATED BY REFERENCE INTO THIS PROSPECTUS, AS DESCRIBED UNDER "RISK FACTORS" ON PAGE 6.

You should read this prospectus and any applicable prospectus supplement together with additional information described under the heading "Where You Can Find More Information" before you make your investment decision.

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 August 17, 2023.

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ABOUT THIS PROSPECTUS

This prospectus is a part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or the Commission, using a "shelf" registration process. Under this shelf registration process, we may offer to sell any of the securities, or any combination of the securities, described in this prospectus, in each case in one or more offerings, up to a total dollar amount of \$200,000,000.

This prospectus provides you only with a general description of the securities that we may offer. Each time securities are sold under the shelf registration statement, we will provide a prospectus supplement that will contain specific information about the terms of those securities and the terms of that offering. The prospectus supplement may also add, update or change information contained in this prospectus. If there is any inconsistency between the information in this prospectus and any prospectus supplement, you should rely on the information in the prospectus supplement. You should read both this prospectus and any prospectus supplement, including all documents incorporated by reference herein and therein, together with the additional information described under "Where You Can Find More Information" below.

The information contained in this prospectus is not complete and may be changed. You should rely only on the information provided in or incorporated by reference in this prospectus or in any prospectus supplement, or documents to which we otherwise refer you. We have not authorized anyone else to provide you with different information.

We have not authorized any dealer, agent or other person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus and any accompanying prospectus supplement. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus or an accompanying prospectus supplement. This prospectus and the accompanying prospectus supplement, if any, do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor do this prospectus and the accompanying prospectus supplement, if any, constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction. You should not assume that the information contained in this prospectus and the accompanying prospectus supplement, if any, is accurate on any date subsequent to the date set forth on the front of such document or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus and any accompanying prospectus supplement is delivered or securities are sold on a later date.

References in this prospectus to the terms "the Company," "OptiNose," "we," "our" and "us" or other similar terms mean OptiNose, Inc. and our wholly-owned subsidiaries, unless we state otherwise or the context indicates otherwise.

OPTINOSE®, XHANCE®, EDS® and EXHALATION DELIVERY SYSTEMTM are trademarks of ours in the United States. All other trademarks, trade names and service marks appearing in this prospectus are the property of their respective owners. We do not intend our use or display of other companies' trademarks, trade names or service marks to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference herein contain, and any prospectus supplement and the documents incorporated therein, may contain forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, included in this prospectus, any prospectus supplement or the documents incorporated herein and therein by reference, including statements regarding our future financial condition, results of operations, business strategy and plans and objectives of management for future operations, industry trends and other future events, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "believe," "will," "may," "estimate," "continue," "anticipate," "intend," "should," "plan," "expect," "predict," "project," "could," "potentially," "continue," "ongoing," "scheduled" or the negative of these terms or other similar expressions, although not all forward-looking statements contain these identifying terms. The forward-looking statements in this prospectus and the documents incorporated herein by reference include, among other things, statements about:

- · the potential uses for and advantages of XHANCE®, our product candidates and the Exhalation Delivery System (EDS) and related technologies;
- our planned activities in pursuit of a follow-on indication for chronic sinusitis;
- · the potential for XHANCE to be the first product approved by the U.S. Food and Drug Administration (FDA) for the treatment of chronic sinusitis;
- · the potential to expand into the primary care segment and our plans to seek a partner for such expansion;
- · our belief that the current practice of postoperative intranasal steroid (INS) use could support XHANCE's adoption as a maintenance therapy to improve outcomes following sinus surgery;
- · the potential for XHANCE to be the standard of care for the treatment of chronic rhinosinusitis with and without nasal polyps;
- · the potential benefits of our patient affordability programs and their potential effect on XHANCE demand and financial results;
- · our expectation for XHANCE prescriptions to be impacted by the seasonality observed in the INS market and the seasonal variation in patient visits with their doctor;
- our expectation for XHANCE prescriptions and average net revenue per prescription to be adversely impacted by the annual resetting of patient healthcare insurance plan deductibles and changes in individual patients' healthcare insurance coverage, both of which often occur in January;
- XHANCE prescription, net revenue, prescriber and other business trends;
- · the potential for increasing rates of enforcement of payor utilization management criteria to negatively impact XHANCE prescription volumes;
- our expectation that our research and development costs will significantly decrease in 2023 as compared to 2022;
- our expectation that our operating expenses (consisting of selling, general and administrative expenses and research and development expenses) in 2023 will be between \$88.0 million and \$93.0 million and that our non-cash stock-based compensation expense will be approximately \$6.0 million;

- · our expectation that XHANCE net product revenues for the full year of 2023 will be between \$64.0 million and \$70.0 million;
- our expectation that the average net product revenue per prescription for XHANCE for the full year of 2023 will be approximately \$200;
- our potential non-compliance with certain covenants of the A&R Note Purchase Agreement, and the consequences of failing to achieve compliance with such covenants or obtain a waiver or modification of such covenants;
- our belief that our existing cash and cash equivalents will be sufficient to fund our operations and debt service obligations for approximately the next 12 months if we are able to maintain compliance with the financial and other covenants and terms of the A&R Note Purchase Agreement or obtain a waiver to or modification of such covenants;
- our expectations and the accuracy of our estimates regarding our future expenses, revenue, capital requirements, potential sources of capital and consequences of failing to obtain additional capital;
- · our ability to continue as a going concern;
- · our plans to liquidate and dissolve our wholly-owned subsidiaries OptiNose AS and OptiNose UK in 2023;
- the potential for us to decrease our reliance on sole-source suppliers and increase the third party manufacturing capacity that is available to us;
- · our belief that our facilities meet our needs and that we could obtain alternative space on commercially reasonable terms;
- · our expectations regarding our ability to obtain and adequately maintain sufficient intellectual property protection for XHANCE; and
- · other statements relating to our future operations, financial performance and financial condition, prospects, strategies, objectives or other future events.

Forward-looking statements also include statements other than statements of current or historical fact, including, without limitation, all statements related to any expectations of revenues, expenses, cash flows, earnings or losses from operations, cash required to maintain current and planned operations, capital or other financial items; any statements of the plans, strategies and objectives of management for future operations; any plans or expectations with respect to product research, development and commercialization, including regulatory approvals; any other statements of expectations, plans, intentions or beliefs; and any statements of assumptions underlying any of the foregoing. We often, although not always, identify forward-looking statements by using words or phrases such as "likely", "expect", "intend", "anticipate", "estimate", "plan", "project", "forecast" and "outlook".

We cannot guarantee that the results and other expectations expressed, anticipated or implied in any forward-looking statement will be realized. The risks set forth under Item 1A of our Annual Report on Form 10-K for the fiscal year ended December 31, 2022, as revised or supplemented by our Quarterly Reports on Form 10-Q and other documents we file with the Commission, describe major risks to our business, and you should read and interpret any forward-looking statements together with these risks. A variety of factors, including these risks, could cause our actual results and other expectations to differ materially from the anticipated results or other expectations expressed, anticipated or implied in our forward-looking statements. Should known or unknown risks materialize, or should underlying assumptions prove inaccurate, actual results could differ materially from past results and those

anticipated, estimated or projected in the forward-looking statements. You should bear this in mind as you consider any forward-looking statements.

You should read this prospectus, any prospectus supplement and the documents that we incorporate by reference herein and therein completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements contained in this prospectus are made as of the date of this prospectus and we do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by applicable law.

MARKET, INDUSTRY AND OTHER DATA

This prospectus and any applicable prospectus supplement and the documents incorporated by reference herein and therein contain estimates, projections, market research and other information concerning our industry, our business, markets for XHANCE and the size of those markets, the prevalence of certain medical conditions, XHANCE market access, prescription data, inventory data and other physician, patient and payor data. Unless otherwise expressly stated, we obtain this information from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources as well as from our own internal estimates and research and from publications, research, surveys and studies conducted by third parties on our behalf. Information that is based on estimates, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are reflected in this information. As a result, you are cautioned not to give undue weight to such information.

THE COMPANY

Company Overview

We are a specialty pharmaceutical company focused on the development and commercialization of products for patients treated by ear, nose and throat (ENT) and allergy specialists. Our first commercial product, XHANCE® (fluticasone propionate) nasal spray, 93 micrograms (mcg), is a therapeutic utilizing our proprietary Exhalation Delivery System (EDS) that delivers a topically-acting corticosteroid for the treatment of chronic rhinosinusitis with nasal polyps and, if approved, chronic rhinosinusitis without nasal polyps (also commonly referred to as chronic sinusitis). Chronic rhinosinusitis is a serious nasal inflammatory disease that is treated using therapies, such as intranasal steroids (INS), which have significant limitations. We believe XHANCE has a differentiated clinical profile with the potential to become part of the standard of care for this disease because it is able to deliver medication to the primary site of inflammation high and deep in the nasal passages in regions not adequately reached by conventional INS.

In September 2017, the U.S. Food and Drug Administration (FDA) approved XHANCE for the treatment of nasal polyps in patients 18 years of age or older. XHANCE was made widely available through commercial channels in April 2018. In January 2023, the indication statement for XHANCE was changed from "for the treatment of nasal polyps" to "for the treatment of chronic rhinosinusitis with nasal polyps" to reflect current FDA labeling terminology. The change was not based on new XHANCE clinical trial data.

In March and June 2022, we announced positive top line results from our two Phase 3b clinical trials (ReOpen1 and ReOpen2) of XHANCE for a follow-on indication for the treatment of chronic sinusitis. The results of ReOpen1 and ReOpen2 are summarized in our Form 10-K for the year ended December 31, 2022, filed with the Commission on March 7, 2023. In February 2023, we submitted a prior approval efficacy supplement (sNDA) to support the approval of a new indication for XHANCE for the treatment of chronic rhinosinusitis. The FDA accepted the sNDA for review and assigned a Prescription Drug User Fee Act (PDUFA) target goal date of December 16, 2023. If the sNDA is approved, XHANCE has the potential to be the first drug therapy approved by the FDA for the treatment of chronic rhinosinusitis without nasal polyps.

For more information about our company, please refer to other documents that we have filed with the Commission and that are incorporated by reference into this prospectus, as listed under the heading "Incorporation by Reference."

Corporate Information

We were incorporated in Delaware in May 2010. Our predecessor entity OptiNose AS was formed under the laws of Norway in September 2000. In 2010, OptiNose AS became our whollyowned subsidiary as part of an internal reorganization. We are in the process of liquidating and dissolving OptiNose AS and another wholly-owned subsidiary, Optinose UK, both of which dissolutions are expected to be completed in 2023, in order to simplify our corporate structure.

Our primary executive offices are located at 1020 Stony Hill Road, Suite 300, Yardley, Pennsylvania 19067 and our telephone number is (267) 364-3500. Our website address is www.optinose.com. The information contained in, or that can be accessed through, our website is not part of this prospectus or any prospectus supplement that we may file or any other report or document that we file with or furnish to the Commission. We have included our website address in this prospectus as an inactive textual reference and do not intend it to be an active link to our website

RISK FACTORS

Investing in our securities involves a high degree of risk. The prospectus supplement applicable to each offering of our securities will contain a discussion of the risks applicable to an investment in our securities. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed under the heading "Risk Factors" in the applicable prospectus supplement, together with all of the other information contained or incorporated by reference in the prospectus supplement or appearing or incorporated by reference in this prospectus. You should also consider the risks, uncertainties and assumptions discussed under the heading "Risk Factors" in our most recent Annual Report on Form 10-K and our Quarterly Reports on Form 10-Q and other documents that we file with the Commission, which are incorporated herein by reference as described in this prospectus under the heading "Where You Can Find More Information". The risks and uncertainties we have described in such documents are not the only risks that we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our operations.

USE OF PROCEEDS

Except as otherwise provided in the applicable prospectus supplement relating to a specific offering, we intend to use the net proceeds from the sale of securities by us under this prospectus for general corporate purposes, which may include working capital, capital expenditures, research and development expenditures, clinical trial expenditures, commercial expenditures, debt service costs and repayment, acquisitions of new technologies, products or businesses, and investments. Additional information on the use of net proceeds from the sale of securities by us under this prospectus may be set forth in the prospectus supplement relating to the specific offering.

PLAN OF DISTRIBUTION

Our Plan of Distribution

We may sell the securities, from time to time pursuant to public offerings, negotiated transactions, block trades, "At the Market Offerings," within the meaning of Rule 415(a)(4) of the Securities Act, into an existing trading market, at prevailing market prices, or a combination of these methods.

We may sell the securities to or through underwriters or dealers, through agents or remarketing firms, or directly to one or more purchasers. We may distribute securities from time to time in one or more transactions:

- · at a fixed price or prices, which may be changed;
- at market prices prevailing at the time of sale;
- · at prices related to such prevailing market prices; or
- at negotiated prices.
- A prospectus supplement or supplements (and any related free writing prospectus that we may authorize to be provided to you) will describe the terms of the offering of the securities, including, to the extent applicable:
- · the name or names of the underwriters, dealers or agents, if any;
- if the securities are to be offered through the selling efforts of brokers or dealers, the plan of distribution and the terms of any agreement, arrangement, or understanding entered into with broker(s) or dealer(s) prior to the effective date of the registration statement, and, if known, the identity of any broker(s) or dealer(s) who will participate in the offering and the amount to be offered through each;
- · the purchase price of the securities or other consideration therefor, and the proceeds, if any, we will receive from the sale;
- if any of the securities being registered are to be offered otherwise than for cash, the general purposes of the distribution, the basis upon which the securities are to be offered, the amount of compensation and other expenses of distribution, and by whom they are to be borne;
- · any delayed delivery arrangements;
- any options under which underwriters may purchase additional securities from us;
- any agency fees or underwriting discounts and other items constituting agents' or underwriters' compensation;
- any public offering price;
- · any discounts, commissions or concessions allowed or reallowed or paid to dealers;
- · the identity and relationships of any finders, if applicable; and
- any securities exchange or market on which the securities may be listed.

Only underwriters named in the prospectus supplement will be underwriters of the securities offered by the prospectus supplement.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Unless otherwise indicated in the prospectus supplement, subject to certain conditions, the underwriters will be obligated to purchase all of the securities offered by the prospectus supplement, other than securities covered by any over-allotment or other option. Any public offering price and any discounts or concessions allowed or reallowed or paid to dealers may change from time to time. We may use underwriters, dealers or agents with whom we have a material relationship. We will describe in the prospectus supplement, naming the underwriter, dealer or agent, the nature of any such relationship.

We may use a remarketing firm to offer the securities in connection with a remarketing arrangement upon their purchase. Remarketing firms will act as principals for their own account or as agents for us. These remarketing firms will offer or sell the securities pursuant to the terms of the securities. A prospectus supplement will identify any remarketing firm and the terms of its agreement, if any, with us and will describe the remarketing firm's compensation. Remarketing firms may be deemed to be underwriters in connection with the securities they remarket.

If we offer and sell securities through a dealer, we or an underwriter will sell the securities to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale. The name of the dealer and the terms of the transaction will be set forth in the applicable prospectus supplement.

We may sell securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities and we will describe any commissions we will pay to the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, our agent will act on a best-efforts basis for the period of its appointment.

Dealers and agents participating in the distribution of the securities may be deemed to be underwriters, and compensation received by them on resale of the securities may be deemed to be underwriting discounts. If such dealers or agents were deemed to be underwriters, they may be subject to statutory liabilities under the Securities Act.

We may sell securities directly to one or more purchasers without using underwriters or agents. Underwriters, dealers and agents that participate in the distribution of the securities may be underwriters as defined in the Securities Act, and any discounts or commissions they receive from us and any profit on their resale of the securities may be treated as underwriting discounts and commissions under the Securities Act.

We may authorize agents or underwriters to solicit offers by certain types of institutional investors to purchase 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. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in the prospectus supplement.

We may provide agents, underwriters and dealers with indemnification against civil liabilities, including liabilities under the Securities Act, or contribution with respect to payments that the agents, underwriters or dealers may make with respect to these liabilities. Agents, underwriters and dealers, or their respective affiliates, may 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 underwriter 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 over-allotment, stabilizing transactions, short-covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Over-allotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum price. Syndicate-covering or other short-covering transactions involve purchases of the securities, either through exercise of the over-allotment option or in the open market after the distribution is completed, to cover short positions. 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 stabilizing or covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

Any underwriters that are qualified market makers on the Nasdaq Global Select Market may engage in passive market making transactions in the common stock on the Nasdaq Global Select Market in accordance with Regulation M under the Exchange Act, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the common stock. 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. Passive market making may stabilize the market price of the securities at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

GENERAL DESCRIPTION OF OUR SECURITIES

We may offer and sell, at any time and from time to time:

- · shares of our common stock;
- · shares of our preferred stock;
- warrants to purchase shares of our common stock, preferred stock and/or debt securities;
- debt securities consisting of debentures, notes or other evidences of indebtedness;
- · units consisting of a combination of the foregoing securities; or
- any combination of these securities.

The terms of any securities we offer will be determined at the time of sale. We may issue debt securities that are exchangeable for and/or convertible into common stock or any of the other securities that may be sold under this prospectus. When particular securities are offered, a supplement to this prospectus will be filed with the Commission, which will describe the terms of the offering and sale of the offered securities.

DESCRIPTION OF OUR COMMON STOCK

The following summary of the terms of our common stock is subject to and qualified in its entirety by reference to our fourth amended and restated certificate of incorporation and our amended and restated bylaws, copies of which are on file with the Commission as exhibits to previous filings with the Commission. Please refer to "Where You Can Find More Information" below for directions on obtaining these documents.

Outstanding Shares

Our fourth amended and restated certificate of incorporation, as amended, authorizes us to issue up to 355,000,000 shares, 350,000,000 of which are designated as common stock with a par value of \$0.001 per share. As of June 30, 2023, there were 112,091,735 shares of common stock outstanding, held by approximately 14 stockholders of record. This figure does not reflect the number of beneficial owners of shares of our common stock as a single stockholder of record often holds shares in nominee name (also referred to as, "street name") on behalf of multiple beneficial owners.

Voting Rights

Each holder of our common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders, other than election of directors, which is determined by a plurality of the votes cast by the stockholders entitled to vote on the election of such director. In addition, the affirmative vote of the holders of at least 66 2/3% of the voting power of all of the then outstanding voting stock is required to take certain actions, including amending certain provisions of our fourth amended and restated certificate of incorporation, such as the provisions relating to director liability, amending our bylaws or changing the Court of Chancery of the State of Delaware and United States District Court for the District of Delaware and any appellate courts thereof from being the sole and exclusive forums for certain actions brought by our stockholders against us or our directors, officers or employees.

Under our fourth amended and restated certificate of incorporation, as amended, and our amended and restated 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.

Dividends

Subject to the preferences that may be applicable to any outstanding preferred stock, holders of our common stock are entitled to receive ratably any dividends that may be declared by our board of directors out of funds legally available for that purpose.

Liquidation

In the event of our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preference of any outstanding preferred stock.

No Preemptive or Similar Rights

Our common stock is not entitled to preemptive rights and is not subject to conversion, redemption or sinking fund provisions. 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.

Outstanding Stock Options

As of June 30, 2023, we had outstanding options to purchase 10,634,934 shares of our common stock at a weighted-average exercise price of \$7.03 per share, pursuant to our Amended and Restated 2010 Stock Incentive Plan. As of June 30, 2023, there were 5,849,650 shares of our common stock reserved for future issuance under our Amended and Restated 2010 Stock Incentive Plan.

As of June 30, 2023, we had outstanding options to purchase 711,500 shares of our common stock at a weighted-average exercise price of \$1.70 per share, which options were issued outside of our equity compensation plan as an inducement material to certain individuals entering into employment with us in accordance with Nasdaq Listing Rule 5635(c)(4).

Outstanding Restricted Stock Units

As of June 30, 2023, we had 2,429,266 shares of our common stock underlying outstanding restricted stock units granted pursuant to our Amended and Restated 2010 Stock Incentive Plan.

Outstanding Warrants

2021 Warrants

In November 2021, we issued equity-classified common stock warrants (the 2021 Warrants) in connection with the Pharmakon Senior Secured Notes (as defined below) which warrants are exercisable for an aggregate of 2,500,000 shares of our common stock at an exercise price of \$1.60 per share (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 expire on November 14, 2024. As of June 30, 2023, all of the 2021 Warrants remained outstanding.

2022 Warrants

In November 2022, we issued liability-classified common stock warrants (the 2022 Warrants) in connection with an underwritten public offering which warrants are exercisable for an aggregate of 30,268,000 shares of our common stock at an exercise price of \$2.565 per share (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 expire on November 23, 2027.

If we issue or sell, or are deemed pursuant to the terms of the 2022 Warrants to have issued or sold, any shares of our common stock (excluding certain issuances defined in the 2022 Warrants as excluded issuances) for a price per share less than the exercise price of the 2022 Warrants in effect immediately prior to such issuance or sale or deemed issuance or sale (such event, a "dilutive issuance"), then immediately after such dilutive issuance the exercise price then in effect of the 2022 Warrants would be reduced to be equal to the price of the shares of our common stock issued in the dilutive issuance

In the event of a fundamental transaction, as defined in the 2022 Warrants, a holder of the 2022 Warrants would be entitled to receive upon exercise of such 2022 Warrants the kind and amount of securities, cash or other property that such holder would have received had it exercised such 2022 Warrants immediately prior to such fundamental transaction. In addition, in certain circumstances, upon a fundamental transaction, a holder of the 2022 Warrants would have the right to require us to repurchase such 2022 Warrants for cash at the Black Scholes Value (as defined in the 2022 Warrants).

As of June 30, 2023, all of the 2022 Warrants remained outstanding.

2017 Employee Stock Purchase Plan

As of June 30, 2023, there were 1,408,871 shares of our common stock reserved for future issuance under our 2017 Employee Stock Purchase Plan.

Registration Rights

In connection with our initial public offering in October 2017, we entered into that certain First Amendment to the Second Amended and Restated Registration Rights Agreement, dated October 2, 2017, with certain of our stockholders, or the Registration Rights Agreement.

As of the date of this prospectus, one stockholder still has registration rights pursuant to the Registration Rights Agreement with respect to 2,622,088 shares of common stock. After registration of these shares of common stock pursuant to these rights, these shares will become freely tradable without restriction under the Securities Act. The registration rights will terminate with respect to this stockholder on the date on which such stockholder ceases to beneficially own more than one percent of our shares of common stock then outstanding or can sell all of its registrable shares without limitation during a three-month period without registration pursuant to Rule 144 of the Securities Act or another similar exemption under the Securities Act. The stockholder has waived its piggyback registration rights in connection with the filing of this Registration Statement on Form S-3.

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

Delaware Anti-Takeover Law

Our fourth amended and restated certificate of incorporation, as amended, provides that we are subject to the provisions of Section 203 of the Delaware General Corporation Law, or Section 203. Section 203 generally prohibits a public Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a period of three years after the date of the transaction in which the person became an interested stockholder, unless:

- prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder.
- the interested stockholder owned at least 85% of the voting stock of the corporation outstanding upon consummation of the transaction, excluding for purposes of determining the number of shares outstanding (1) shares owned by persons who are directors and also officers and (2) shares owned by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or
- on or subsequent to the consummation of the transaction, the business combination is approved by the board of directors and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66 2/3% of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, pledge or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;

- subject to exceptions, any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder;
- · subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder; and
- · the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

Certificate of Incorporation and Bylaws

Provisions of our fourth amended and restated certificate of incorporation, as amended, and our amended and restated bylaws may delay or discourage transactions involving an actual or potential change of control or change in our management, including transactions in which stockholders might otherwise receive a premium for their shares, or transactions that our stockholders might otherwise deem to be in their best interests. Therefore, these provisions could adversely affect the price of our common stock. Among other things, our fourth amended and restated certificate of incorporation and our amended and restated bylaws:

- permit our board of directors to issue up to 5,000,000 shares of preferred stock, with any rights, preferences and privileges as it may designate, which issuance could result in the loss of voting control by other stockholders;
- provide that our board of directors is classified into three classes with staggered, three-year terms and that directors may only be removed for cause by the affirmative vote of the holders of at least a majority of the voting power of outstanding shares of our capital stock;
- provide that all vacancies on our board of directors, including as a result of newly created directorships, may, except as otherwise required by law, be filled only by the affirmative vote of a majority of directors then in office, even if less than a quorum;
- require that any action to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and not be taken by written consent;
- provide that stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide advance notice in writing, and also specify requirements as to the form and content of a stockholder's notice;
- require that the amendment of certain provisions of our certificate of incorporation relating to several anti-takeover measures and other provisions may only be approved by a vote of 66 2/3 % of our outstanding common stock;
- require that the amendment of our bylaws be approved by the affirmative vote of a majority of directors then in office or 66 2/3% of our outstanding common stock entitled to vote thereon;

- do not provide for cumulative voting rights, thereby allowing the holders of a majority of the shares of common stock entitled to vote in any election of directors to elect all of the directors standing for election; and
- provide that special meetings of our stockholders may be called only by the chairman or vice chairman of our board of directors, our chief executive officer, or a majority of our board of directors.

Choice of Forum

Our fourth amended and restated certificate of incorporation, as amended, provides that the Court of Chancery of the State of Delaware, or the United States District Court for the District of Delaware and any appellate courts thereof where subject matter jurisdiction is vested exclusively in the federal courts of the United States of America, will be the exclusive forum for:

- any derivative action or proceeding brought on our behalf;
- any action asserting a breach of fiduciary duty;
- any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our fourth amended and restated certificate of incorporation or our amended and restated bylaws; or
- · any action asserting a claim against us that is governed by the internal affairs doctrine.

The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with any action, a court could find the choice of forum provisions contained in our fourth amended and restated certificate of incorporation to be inapplicable or unenforceable in such action.

The Nasdaq Global Select Market

Our common stock is listed on the Nasdaq Global Select Market under the symbol "OPTN."

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Broadridge Corporate Issuer Solutions, Inc. The transfer agent's address is 1717 Arch St., Suite 1300, Philadelphia, Pennsylvania 19103.

DESCRIPTION OF OUR PREFERRED STOCK

We are authorized to issue up to 5,000,000 shares of preferred stock with a par value of \$0.001 per share. As of June 30, 2023, there were no shares of our preferred stock outstanding.

Our board of directors may, without further action by our stockholders, from time to time, direct the issuance of shares of preferred stock in series and may, at the time of issuance, determine and fix the number of shares of such series and the designation of such series, the voting powers, if any, of the shares of such series, the preferences and relative, participating, optional or other special rights, if any, and the qualifications, limitations or restrictions thereof, including without limitation thereof, dividend rights, conversion rights, redemption privileges and liquidation preferences, of the shares of such series. Satisfaction of any dividend preferences of outstanding shares of our preferred stock would reduce the amount of funds available for the payment of dividends on shares of our common stock. Holders of shares of our preferred stock may be entitled to receive a preference payment in the event of any liquidation, dissolution or winding-up of our Company before any payment is made to the holders of shares of our common stock. In some circumstances, the issuance of shares of preferred stock may render more difficult or tend to discourage a merger, tender offer or proxy contest, the assumption of control by a holder of a large block of our securities or the removal of incumbent management. Upon the affirmative vote of our board of directors, without stockholder approval, we may issue shares of preferred stock with voting and conversion rights which could adversely affect the holders of shares of our common stock. It is not possible to state the actual effect of the issuance of any shares of preferred stock on the rights of holders of common stock until the board of directors determines the specific rights attached to that preferred stock. We have no current plan to issue any shares of preferred stock.

If we offer a specific series of preferred stock under this prospectus, we will describe the terms of the preferred stock in the prospectus supplement for such offering and will file a copy of the certificate establishing the terms of the preferred stock with the Commission. To the extent required, this description will include:

- the title and stated value:
- · the number of shares offered, the liquidation preference per share and the purchase price;
- the dividend rate(s), period(s) and/or payment date(s), or method(s) of calculation for such 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, if any;
- · the provisions for a sinking fund, if any;
- · the provisions for redemption, if applicable;
- · any listing of the preferred stock on any securities exchange or market;
- whether the preferred stock will be convertible into our common stock or our other securities and, if applicable, the conversion price (or how it will be calculated), the conversion period and any other terms of conversion (including any anti-dilution provisions, if any);
- whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price (or how it will be calculated), the exchange period and any other terms of exchange (including any anti-dilution provisions, if any);

- · voting rights, if any, of the preferred stock;
- a discussion of any material and/or special U.S. federal income tax considerations applicable to the preferred stock;
- · the relative ranking and preferences of the preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of our affairs;
- any material limitations on 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 upon our liquidation, dissolution, or winding up; and
- · any other affirmative, negative or other covenants or contractual rights which might be attendant with the specific series of preferred stock.

The preferred stock offered by this prospectus, when issued, will not have, or be subject to, any preemptive or similar rights.

Transfer Agent and Registrar

The transfer agent and registrar for any series of preferred stock will be set forth in each applicable prospectus supplement.

DESCRIPTION OF OUR WARRANTS

We may issue warrants to purchase shares of our common stock, preferred stock and/or debt securities in one or more series together with other securities or separately, as described in each applicable prospectus supplement. Below is a description of certain general terms and provisions of the warrants that we may offer. Particular terms of the warrants will be described in the applicable warrant agreements and the applicable prospectus supplement for the warrants.

The applicable prospectus supplement will contain, where applicable, the following terms of and other information relating to the warrants:

- · the specific designation and aggregate number of, and the price at which we will issue, the warrants;
- the currency or currency units in which the offering price, if any, and the exercise price are payable;
- the designation, amount and terms of the securities purchasable upon exercise of the warrants;
- · if applicable, the exercise price for shares of our common stock and the number of shares of common stock to be received upon exercise of the warrants;
- if applicable, the exercise price for shares of our preferred stock, the number of shares of preferred stock to be received upon exercise of the warrants, and a description of that series of our preferred stock;
- if applicable, the exercise price for our debt securities, the amount of our debt securities to be received upon exercise of the warrants, and a description of that series of debt securities;
- the date on which the right to exercise the warrants will begin and the date on which that right will expire or, if the warrants may not be continuously exercised throughout that period, the specific date or dates on which the warrants may be exercised;
- whether the warrants will be issued in fully registered form or bearer form, in definitive or global form or in any combination of these forms, although, in any case, the form of a warrant included in a unit will correspond to the form of the unit and of any security included in that unit;
- · any applicable material U.S. federal income tax or foreign tax consequences;
- the identity of the warrant agent for the warrants, if any, and of any other depositaries, execution or paying agents, transfer agents, registrars or other agents;
- · the proposed listing, if any, of the warrants or any securities purchasable upon exercise of the warrants on any securities exchange or market;
- if applicable, the date from and after which the warrants and the common stock, preferred stock and/or debt securities will be separately transferable;
- · if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;
- · information with respect to book-entry procedures, if any;
- the anti-dilution provisions of the warrants, if any;
- · any redemption, put or call provisions;

- whether the warrants are to be sold separately or with other securities as parts of units; and
- any additional terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants.

Transfer Agent and Registrar

The transfer agent and registrar for any warrants will be set forth in the applicable prospectus supplement.

Description of Outstanding Warrants

See "Description of Our Capital Stock—Description of Our Common Stock—Outstanding Warrants."

DESCRIPTION OF OUR DEBT SECURITIES

This section describes the general terms and provisions of the debt securities that we may offer under this prospectus, any of which may be issued as convertible or exchangeable debt securities. We will set forth the particular terms of the debt securities we offer in a prospectus supplement. The extent, if any, to which the following general provisions apply to particular debt securities will be described in the applicable prospectus supplement. The following description of general terms relating to the debt securities and the indenture under which the debt securities will be issued are summaries only and therefore are not complete. You should read the indenture and the prospectus supplement regarding any particular issuance of debt securities.

We will issue the debt securities offered by this prospectus and any accompanying prospectus supplement under an indenture to be entered into between us and the trustee identified in the applicable prospectus supplement. The terms of the debt securities will include those stated in the indenture and those made part of the indenture by reference to the Trust Indenture Act of 1939, as in effect on the date of the indenture. We have filed or will file a copy of the form of indenture as an exhibit to the registration statement in which this prospectus is included. The indenture will be subject to and governed by the terms of the Trust Indenture Act of 1939.

We may offer under this prospectus up to an aggregate principal amount of \$200,000,000 in debt securities, or if debt securities are issued at a discount, or in a foreign currency, foreign currency units or composite currency, the principal amount as may be sold for an aggregate initial public offering price of up to \$200,000,000. Unless otherwise specified in the applicable prospectus supplement, the debt securities will represent direct, unsecured obligations of ours and will rank equally with all of our other unsecured indebtedness.

The following statements relating to the debt securities and the indenture are summaries, qualified in their entirety by reference to the detailed provisions of the indenture and the final form indenture as may be filed with a future prospectus supplement.

General

We may issue the debt securities in one or more series with the same or various maturities, at par, at a premium, or at a discount. We will describe the particular terms of each series of debt securities in a prospectus supplement relating to that series, which we will file with the Commission.

The prospectus supplement will set forth, to the extent required, the following terms of the debt securities in respect of which the prospectus supplement is delivered:

- · the title of the series;
- · the aggregate principal amount;
- the issue price or prices, expressed as a percentage of the aggregate principal amount of the debt securities;
- any limit on the aggregate principal amount;
- · the date or dates on which principal is payable;
- · the interest rate or rates (which may be fixed or variable) or, if applicable, the method used to determine such rate or rates;
- the date or dates from which interest, if any, will be payable and any regular record date for the interest payable;

- the place or places where principal and, if applicable, premium and interest, is payable;
- the terms and conditions upon which we may, or the holders may require us to, redeem or repurchase the debt securities;
- the denominations in which such debt securities may be issuable, if other than denominations of \$1,000 or any integral multiple of that number;
- · whether the debt securities are to be issuable in the form of certificated securities (as described below) or global debt securities (as described below);
- · the portion of principal amount that will be payable upon declaration of acceleration of the maturity date if other than the principal amount of the debt securities;
- · the currency of denomination;
- · the designation of the currency, currencies or currency units in which payment of principal and, if applicable, premium and interest, will be made;
- if payments of principal and, if applicable, premium or interest, on the debt securities are to be made in one or more currency units other than the currency of denomination, the manner in which the exchange rate with respect to such payments will be determined;
- if amounts of principal and, if applicable, premium and interest may be determined by reference to an index based on a currency or currencies or by reference to a commodity, commodity index, stock exchange index or financial index, then the manner in which such amounts will be determined;
- the provisions, if any, relating to any collateral provided for such debt securities;
- · any addition to or change in the covenants and/or the acceleration provisions described in this prospectus or in the indenture;
- any events of default, if not otherwise described below under "Events of Default";
- · the terms and conditions, if any, for conversion into or exchange for shares of our common stock or preferred stock;
- · any depositaries, interest rate calculation agents, exchange rate calculation agents or other agents; and
- · the terms and conditions, if any, upon which the debt securities shall be subordinated in right of payment to other indebtedness of OptiNose.

We may issue discount debt securities that provide for an amount less than the stated principal amount to be due and payable upon acceleration of the maturity of such debt securities in accordance with the terms of the indenture. We may also issue debt securities in bearer form, with or without coupons. If we issue discount debt securities or debt securities in bearer form, we will describe material U.S. federal income tax considerations and other material special considerations that apply to these debt securities in the applicable prospectus supplement. We may issue debt securities denominated in or payable in a foreign currency or currencies or a foreign currency unit or units. If we do, we will describe the restrictions, elections, and general tax considerations relating to the debt securities and the foreign currency or currencies or foreign currency unit or units in the applicable prospectus supplement.

Exchange and/or Conversion Rights

We may issue debt securities which can be exchanged for or converted into shares of our common stock or preferred stock. If we do, we will describe the terms of exchange or conversion in the prospectus supplement relating to these debt securities.

Transfer and Exchange

We may issue debt securities that will be represented by either:

- · "book-entry securities," which means that there will be one or more global securities registered in the name of a depositary or a nominee of a depositary; or
- · "certificated securities," which means that they will be represented by a certificate issued in definitive registered form.

We will specify in the prospectus supplement applicable to a particular offering whether the debt securities offered will be book-entry or certificated securities.

Certificated Debt Securities

If you hold certificated debt securities issued under an indenture, you may transfer or exchange such debt securities in accordance with the terms of the indenture. You will not be charged a service charge for any transfer or exchange of certificated debt securities but may be required to pay an amount sufficient to cover any tax or other governmental charge payable in connection with such transfer or exchange.

Global Securities

The debt securities of a series may be issued in the form of one or more global securities that will be deposited with a depositary or its nominees identified in the prospectus supplement relating to the debt securities. In such a case, one or more global securities will be issued in a denomination or aggregate denominations equal to the portion of the aggregate principal amount of outstanding debt securities of the series to be represented by such global security or securities.

Unless and until it is exchanged in whole or in part for debt securities in definitive registered form, a global security may not be registered for transfer or exchange except as a whole by the depositary for such global security to a nominee of the depositary and except in the circumstances described in the prospectus supplement relating to the debt securities. The specific terms of the depositary arrangement with respect to a series of debt securities will be described in the prospectus supplement relating to such series.

Protection in the Event of Change of Control

Any provision in an indenture that governs our debt securities covered by this prospectus that includes any covenant or other provision providing for a put or increased interest or otherwise that would afford holders of our debt securities additional protection in the event of a recapitalization transaction, a change of control of the Company, or a highly leveraged transaction will be described in the applicable prospectus supplement.

Covenants

Unless otherwise indicated in this prospectus or the applicable prospectus supplement, our debt securities may not have the benefit of any covenant that limits or restricts our business or operations, the pledging of our assets or

the incurrence by us of indebtedness. We will describe in the applicable prospectus supplement any material covenants in respect of a series of debt securities.

Consolidation, Merger and Sale of Assets

We may agree in any indenture that governs the debt securities of any series covered by this prospectus that we will not consolidate with or merge into any other person or convey, transfer, sell or lease our properties and assets substantially as an entirety to any person, unless such person and such proposed transaction meets various criteria, which we will describe in detail in the applicable prospectus supplement.

Defaults and Notice

The debt securities of any series will contain events of default to be specified in the applicable prospectus supplement, which may include, without limitation:

- failure to pay the principal of, or premium or make-whole amount, if any, on any debt security of such series when due and payable (whether at maturity, by call for redemption, through any mandatory sinking fund, by redemption at the option of the holder, by declaration or acceleration or otherwise);
- · failure to make a payment of any interest on any debt security of such series when due;
- · failure to perform or observe any other covenants or agreements in the indenture with respect to the debt securities of such series;
- · certain events relating to our bankruptcy, insolvency or reorganization; and
- · certain cross defaults, if and as applicable.

If an event of default with respect to debt securities of any series shall occur and be continuing, we may agree that the trustee or the holders of at least 25% in aggregate principal amount of the then outstanding debt securities of such series may declare the principal amount (or, if the debt securities of such series are issued at an original issue discount, such portion of the principal amount as may be specified in the terms of the debt securities of such series) of all debt securities of such series or such other amount or amounts as the debt securities or supplemental indenture with respect to such series may provide, to be due and payable immediately. Any provisions pertaining to events of default and any remedies associated therewith will be described in the applicable prospectus supplement.

Any indenture that governs our debt securities covered by this prospectus may require that the trustee under such indenture shall, within 90 days after the occurrence of a default, give to holders of debt securities of any series notice of all uncured defaults with respect to such series known to it. However, in the case of a default that results from the failure to make any payment of the principal of, premium or make-whole amount, if any, or interest on the debt securities of any series, or in the payment of any mandatory sinking fund installment with respect to debt securities of such series, if any, the trustee may withhold such notice if it in good faith determines that the withholding of such notice is in the interest of the holders of debt securities of such series. Any terms and provisions relating to the foregoing types of provisions will be described in further detail in the applicable prospectus supplement.

Any indenture that governs our debt securities covered by this prospectus will contain a provision entitling the trustee to be indemnified by holders of debt securities before proceeding to exercise any trust or power under the indenture at the request of such holders. Any such indenture may provide that the holders of at least a majority in aggregate principal amount of the then outstanding debt securities of any series may direct the time, method and place of conducting any proceedings for any remedy available to the trustee, or of exercising any trust or power

conferred upon the trustee with respect to the debt securities of such series. However, the trustee under any such indenture may decline to follow any such direction if, among other reasons, the trustee determines in good faith that the actions or proceedings as directed may not lawfully be taken, would involve the trustee in personal liability or would be unduly prejudicial to the holders of the debt securities of such series not joining in such direction.

Any indenture that governs our debt securities covered by this prospectus may endow the holders of such debt securities to institute a proceeding with respect to such indenture, subject to certain conditions, which will be specified in the applicable prospectus supplement and which may include, that the holders of at least a majority in aggregate principal amount of the debt securities of such series then outstanding make a written request upon the trustee to exercise its power under the indenture, indemnify the trustee and afford the trustee reasonable opportunity to act. Even so, such holders may have an absolute right to receipt of the principal of, premium or make-whole amount, if any, and interest when due, to require conversion or exchange of debt securities if such indenture provides for convertibility or exchangeability at the option of the holder and to institute suit for the enforcement of such rights. Any terms and provisions relating to the foregoing types of provisions will be described in further detail in the applicable prospectus supplement.

Modification of the Indenture

We and the trustee may modify any indenture that governs our debt securities of any series covered by this prospectus with or without the consent of the holders of such debt securities, under certain circumstances to be described in a prospectus supplement.

Defeasance; Satisfaction and Discharge

The prospectus supplement will outline the conditions under which we may elect to have certain of our obligations under the indenture discharged and under which the indenture obligations will be deemed to be satisfied.

Regarding the Trustee

We will identify the trustee and any relationship that we may have with such trustee, with respect to any series of debt securities, in the prospectus supplement relating to the applicable debt securities. You should note that if the trustee becomes a creditor of OptiNose, the indenture and the Trust Indenture Act of 1939 limit the rights of the trustee to obtain payment of claims in certain cases, or to realize on certain property received in respect of any such claim, as security or otherwise. The trustee and its affiliates may engage in, and will be permitted to continue to engage in, other transactions with us and our affiliates. If, however, the trustee acquires any "conflicting interest" within the meaning of the Trust Indenture Act of 1939, it must eliminate such conflict or resign.

Governing Law

The law governing the indenture and the debt securities will be identified in the prospectus supplement relating to the applicable indenture and debt securities.

Outstanding Senior Secured Notes

On September 12, 2019 (the Closing Date), we entered into a Note Purchase Agreement with funds managed by Pharmakon Advisors, LP (Pharmakon), the investment manager of BioPharma Credit Funds (BioPharma). The Note Purchase Agreement provided us with \$130.0 million in debt financing, of which \$80.0 million of Pharmakon Senior Secured Notes was issued on the Closing Date, \$30.0 million was issued on February 13, 2020, and \$20.0 million was issued on December 1, 2020.

On November 23, 2022, we amended and restated the Note Purchase Agreement (as so amended and restated, the A&R Note Purchase Agreement), among us, certain of our subsidiaries.and BioPharma Credit PLC, as collateral agent, and the purchasers party thereto from time to time. The A&R Note Purchase Agreement provides for an extension of the maturity date of the Pharmakon Senior Secured Notes from September 12, 2024 to June 30, 2027 (the New Maturity Date), and an extension of the interest-only period from September 2023 to September 2025, after which principal repayments will be made in eight equal quarterly installments of principal and interest through the New Maturity Date. As of June 30, 2023, the outstanding principal and back end fees under the Pharmakon Senior Secured Notes was \$136.0 million.

As part of the A&R Note Purchase Agreement, the Pharmakon Senior Secured Notes now bear interest at the 3-month Secured Overnight Financing Rate (subject to a 2.50% floor), determined as of the date that is two business days prior to the commencement of each quarter, plus 8.50% per annum, which interest rate shall be increased by an additional 3.00% per annum upon the occurrence and during the continuation of any event of default. Pursuant to the A&R Note Purchase Agreement, certain modifications to the affirmative and negative covenants, events of default and other terms were made, including, without limitation, (i) the requirement for us to deliver quarterly and annual financial statements that, commencing with our financial statements for the year ending December 31, 2023, are not subject to a "going concern" statement and (ii) the removal of certain exceptions to the negative covenants which previously permitted us to enter into certain transactions without the consent of the holders of the Pharmakon Senior Secured Notes, including permitted acquisitions, swap contracts, convertible bonds and revolving credit facilities. The financial covenants requiring us to achieve minimum trailing twelve-month consolidated XHANCE net product sales and royalties were also modified as follows (shown in millions):

Trailing Twelve-Months Ending	Requirement Prior to A&R Note Purchase Agreement	Requirement Under A&R Note Purchase Agreement
September 30, 2022	N/A	N/A
December 31, 2022	N/A	N/A
March 31, 2023	\$98.75	N/A
June 30, 2023	102.50	N/A
September 30, 2023	106.25	N/A
December 31, 2023	110.00	N/A
March 31, 2024	113.75	\$82.50
June 30, 2024	117.50	90.00
September 30, 2024	N/A	102.50
December 31, 2024	N/A	110.00
March 31, 2025	N/A	115.00
June 30, 2025	N/A	120.00
September 30, 2025	N/A	125.00
December 31, 2025	N/A	130.00
March 31, 2026	N/A	135.00
June 30, 2026	N/A	140.00
September 30, 2026	N/A	145.00
December 31, 2026	N/A	150.00
March 31, 2027	N/A	155.00
June 30, 2027	N/A	160.00
September 30, 2027	N/A	165.00

In conjunction with the A&R Note Purchase Agreement, a modification was made to the "make-whole" premium payment due in connection with any principal prepayments (whether mandatory or voluntary) made prior to November 23, 2025. On any such prepayment date, we will be required to pay a make-whole premium in the amount of (i) for any prepayment date occurring on or before May 23, 2024, the foregone interest from such prepayment date through the 18-month anniversary of such prepayment date; and (ii) for any prepayment after May 23, 2024, the foregone interest from such prepayment date through November 23, 2025; provided, however, that in no event shall the amount of all make-whole premium payments exceed \$24.0 million in the aggregate.

DESCRIPTION OF OUR UNITS

The following description, together with the additional information we include in any applicable prospectus supplement, summarizes the material terms and provisions of the units that we may offer under this prospectus. Units may be offered independently or together with common stock, preferred stock, debt securities and/or warrants offered by any prospectus supplement, and may be attached to or separate from those securities. While the terms we have summarized below will generally apply to any future units that we may offer under this prospectus, we will describe the particular terms of any series of units that we may offer in more detail in the applicable prospectus supplement. The terms of any units offered under a prospectus supplement may differ from the terms described below.

We will incorporate by reference into the registration statement of which this prospectus forms a part the form of unit agreement, including a form of unit certificate, if any, that describes the terms of the series of units we are offering before the issuance of the related series of units. The following summaries of material provisions of the units, and the unit agreements, are subject to, and qualified in their entirety by reference to, all the provisions of the unit agreement applicable to a particular series of units. We urge you to read the applicable prospectus supplements related to the units that we sell under this prospectus, as well as the complete unit agreements that contain the terms of the units.

General

We may issue units comprised of one or more shares of our common stock or preferred stock, debt securities and warrants in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date.

We will describe in the applicable prospectus supplement the terms of the series of units, including:

- the designation and terms of the units and of the securities comprising the units, including whether, and under what circumstances, those securities may be held or transferred separately;
- · the rights and obligations of the unit agent, if any;
- · any provisions of the governing unit agreement that differ from those described below; and
- · any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units.

The provisions described in this section, as well as those described under "Description of Our Common Stock," "Description of our Preferred Stock," "Description of Our Debt Securities" and "Description of Our Warrants," will apply to each unit and to any common stock, preferred stock, debt securities or warrants included in each unit, respectively.

Issuance in Series

We may issue units in such amounts and in numerous distinct series as we determine.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the Commission. The Commission maintains an Internet website at www.sec.gov that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the Commission. Our reports on Forms 10-K, 10-Q and 8-K, and amendments to those reports, are also available for download, free of charge, as soon as reasonably practicable after these reports are filed with, or furnished to, the Commission, in the investor section of our website at www.optinose.com. Information contained on or accessible through our website is not a part of this prospectus or any prospectus supplement, and the inclusion of our website address in this prospectus is an inactive textual reference only.

INCORPORATION BY REFERENCE

The Commission allows us to "incorporate by reference" into this prospectus the information in other documents that we file with it. This means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be a part of this prospectus, and information in documents that we file later with the Commission will automatically update and supersede information contained in documents filed earlier with the Commission or contained in this prospectus. We incorporate by reference in this prospectus (i) the documents listed below, (ii) all documents that we file with the Commission under Section 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of the initial filing of the registration statement of which this prospectus is included and prior to the effectiveness of such registration statement, and (iii) and any future filings that we may make with the Commission under Sections 13(a), 13(c), 14, or 15(d) of the Exchange Act prior to the termination of the offering under this prospectus; provided, however, that we are not incorporating, in each case, any documents or information deemed to have been furnished and not filed, including any information that we disclose under Items 2.02 or 7.01 of any Current Report on Form 8-K, in accordance with Commission rules:

- Our Annual Report on Form 10-K for the year ended December 31, 2022 filed with the Commission on March 7, 2023;
- Our Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2023 filed with the Commission on May 11, 2023 and our Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2023 filed with the Commission on August 10, 2023;
- Our Current Reports on Form 8-K filed with the Commission on <u>January 31, 2023</u> (other than Item 2.02 and Exhibit 99.1), <u>March 7, 2023</u> (other than Item 2.02 and Exhibit 99.1), <u>March 28, 2023</u>, <u>May 4, 2023</u>, <u>May 11, 2023</u> (other than Item 2.02 and Exhibit 99.1), <u>June 13, 2023</u> and <u>August 10, 2023</u> (other than Item 2.02 and Exhibit 99.1);
- · Our Definitive Proxy Statement on Schedule 14A, filed with the Commission on May 1, 2023 (other than the portions thereof that are furnished and not filed); and
- The description of our common stock contained in our registration statement on Form 8-A (File No. 001-38241) filed with the Commission on October 10, 2017, as updated by Exhibit 4.5 to our Annual Report on Form 10-K for the year ended December 31, 2022, including any further amendment or report filed for the purpose of updating such description.

You may request, orally or in writing, a copy of any or all of the documents incorporated herein by reference. These documents will be provided to you at no cost by contacting: OptiNose, Inc., 1020 Stony Hill Road, Suite 300, Yardley, PA 19067, Attention: Chief Legal Officer, or by calling (267) 364-3500. In addition, copies of any or all of the documents incorporated herein by reference may be accessed at our website at www.optinose.com. The information on such website is not incorporated by reference and is not a part of this prospectus.

LEGAL MATTERS

The validity of the issuance of the securities offered hereby will be passed upon for us by Hogan Lovells US LLP. As appropriate, legal counsel representing the underwriters, dealers or agents will be named in the accompanying prospectus supplement and may opine to certain legal matters.

EXPERTS

The consolidated financial statements of OptiNose, Inc. appearing in OptiNose, 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 (which contains an explanatory paragraph describing conditions that raise substantial doubt about the Company's ability to continue as a going concern as described in Note 2 to the consolidated financial statements), included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

31,800,000 Shares of Common Stock

and

Pre-Funded Warrants to purchase up to 23,700,000 shares of Common Stock



PROSPECTUS SUPPLEMENT

May 8, 2024

The prospectus supplement to which this exhibit is attached is a final prospectus for the related offering. The maximum aggregate offering price of that offering is \$200,000,000.					