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

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2024

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For The Transition Period From To

Commission file number: 001-40315

ONKURE THERAPEUTICS, INC.
(Exact name of registrant as specified in its charter)

Delaware	**47-2309515**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
6707 Winchester Circle, #400, Boulder, Colorado	**80301**
(Address of principal executive offices)	(Zip code)

Registrant's telephone number, including area code: (720) 307-2892

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

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, $0.0001 Par Value per Share	**OKUR**	**The Nasdaq Stock Market LLC**

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

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

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

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

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

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

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

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

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

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

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

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

Based on the closing price of $15.10 as reported on The Nasdaq Global Market, the aggregate market value of the registrant's common stock held by non-affiliates of the registrant on June 28, 2024 (the last business day of the registrant's most recently completed second fiscal quarter) was approximately $27.7 million. This calculation does not reflect a determination that certain persons are affiliates of the registrant for other purposes.

As of March 7, 2025, the registrant had 12,749,299 shares of Class A common stock, $0.0001 par value per share, and 686,527 shares of Class B common stock, $0.0001 par value per share, outstanding.

Auditor Firm Id: 185 Auditor Name: KPMG LLP Auditor Location: Denver, CO

TABLE OF CONTENTS

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EXPLANATORY NOTE

On October 4, 2024 (the "Closing Date"), the Delaware corporation formerly known as “Reneo Pharmaceuticals, Inc.” ("Reneo") completed its previously announced merger transaction pursuant to the terms of the Agreement and Plan of Merger, dated as of May 10, 2024 (the "Merger Agreement"), by and among Reneo, Radiate Merger Sub I, Inc., a Delaware corporation and a direct, wholly-owned subsidiary of Reneo ("Merger Sub I"), Radiate Merger Sub II, LLC, a Delaware limited liability company and a direct, wholly-owned subsidiary of Reneo ("Merger Sub II"), and OnKure, Inc., a Delaware corporation ("Legacy OnKure").

Pursuant to the Merger Agreement, on the Closing Date, (i) Reneo effected a reverse stock split of Reneo’s issued common stock at a ratio of 1:10 (the "Reverse Stock Split"), (ii) Reneo changed its name to “OnKure Therapeutics, Inc.”, (iii) Reneo reclassified all of its common stock as Class A Common Stock or Class B Common Stock, and (iv) Merger Sub I merged with and into Legacy OnKure (the "Merger"), with Legacy OnKure as the surviving company in the Merger and, after giving effect to such Merger, Legacy OnKure became a wholly-owned subsidiary of OnKure Therapeutics, Inc. (together, the "Combined Company"). Pursuant to the terms of the Merger Agreement, OnKure determined that the Merger would qualify for the intended tax treatment even if only the merger with Merger Sub I was consummated, and therefore the parties determined not to consummate the second merger with Merger Sub II contemplated by the Merger Agreement.

The financial statements included in this Annual Report on Form 10-K include historical financial information of OnKure Therapeutics, Inc., including as of and for the year ended December 31, 2024, unless otherwise indicated or as the context otherwise requires. In addition, except where otherwise indicated, the information in this Annual Report on Form 10-K as of and for the periods prior to the effective time of the Merger gives effect to the Merger.

Unless the context otherwise requires, “OnKure,” “we,” “us,” “our,” and the “Company” refer to the Combined Company. All references herein to the “Board” refer to the board of directors of OnKure Therapeutics, Inc.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this Annual Report on Form 10-K, including statements regarding our future results of operations and financial position, business strategy, development plans, planned preclinical studies and clinical trials, future results of clinical trials, expected research and development costs, regulatory strategy, timing and likelihood of success, as well as plans and objectives of management for future operations, are forward-looking statements. In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "would," "expect," "plan," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "potential" or "continue" or the negative of these terms or other similar expressions. Forward-looking statements contained in this Annual Report on Form 10-K include, but are not limited to, statements about:

- the ability of our clinical trials to demonstrate safety and efficacy of our product candidates, and other positive results;
- the beneficial characteristics, and the potential safety, efficacy, and therapeutic effects of OKI-219 and any other product candidates we have or may in the future develop;
- our future results of operations and financial position;
- our ability to obtain funding for our operations, including funding necessary to develop and commercialize our current and future product candidates, subject to regulatory approvals;
- our cash runway and our ability to extend our operating capital;
- the initiation, timing, progress and results of our preclinical and clinical activities for OKI-219 and any other product candidates we have or may in the future develop, including the timing of initiation and completion of studies or trials and related preparatory work, the period during which the results of the studies or trials may become available, research development programs, and the announcement of product candidates;
- the potential of our technologies and our ability to execute on our corporate strategy;
- expectations regarding the approval and use of our product candidates in combination with other drugs;
- our expectations regarding the market opportunities for our product candidates and PI3Kα inhibitors generally;
- our ability to obtain and adequately protect intellectual property rights for our product candidates;
- our ability to obtain regulatory approval for our product candidates and any related restrictions, limitations and/or warnings in the label of any approved product candidate;
- expectations regarding our reliance on third parties for the manufacture of our product candidates for clinical trials;
- our competitive position and the success of competing therapies that are or may become available;
- existing regulations and regulatory developments in the United States and other jurisdictions; and
- our ability to realize some or all of the anticipated benefits of the Merger.

We have based these forward-looking statements largely on our current expectations and projections about our business, the industry in which we operate and financial trends that we believe may affect our business, financial condition, results of operations and prospects, and these forward-looking statements are not guarantees of future performance or development. These forward-looking statements speak only as of the date of this Annual Report on Form 10-K and are subject to a number of risks, uncertainties and assumptions described in the section titled "Risk Factors" and elsewhere in this Annual Report on Form 10-K. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Except as required by applicable law, we do not plan to publicly update or revise

any forward-looking statements contained herein, whether as a result of any new information, future events or otherwise.

In addition, statements such as “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this Annual Report on Form 10-K, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and you are cautioned not to unduly rely upon these statements.

RISK FACTORS SUMMARY

We face many risks and uncertainties, as more fully described in Part I, Item 1A, under the heading "Risk Factors." Some of these risks and uncertainties are summarized below. The summary below does not contain all of the information that may be important to you, and you should read this summary together with the more detailed discussion of these risks and uncertainties contained in Part I, Item 1A, under the heading "Risk Factors." See also "Cautionary Note Regarding Forward-Looking Statements" in this Annual Report.

Our business operations are subject to numerous risks and uncertainties, including those outside of our control, that could cause our actual results to be harmed, including risks regarding the following:

- We are early in our development efforts and have no products approved for commercial sale, which may make it difficult for you to evaluate our current business and likelihood of success and future viability.
- We have incurred significant net losses in each period since inception, and expect to continue to incur significant net losses for the foreseeable future.
- We have never generated revenue from product sales and may never achieve or maintain profitability.
- We are substantially dependent on OKI-219. If we are unable to advance OKI-219 through clinical development, obtain regulatory approval and ultimately commercialize such product candidate, or experience significant delays in doing so, our business will be materially harmed.
- We have limited resources and are currently focusing our efforts on OKI-219 for development in particular indications and advancing our other discovery research programs. As a result, we may fail to capitalize on programs, product candidates or indications that may be more profitable or for which there is a greater likelihood of success.
- If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we would incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.
- The regulatory approval processes of the FDA, EMA and other comparable foreign regulatory authorities are lengthy, time-consuming and inherently unpredictable. If we are ultimately unable to obtain regulatory approval of our product candidates, we will be unable to generate product revenue and our business will be substantially harmed.
- If we experience delays or difficulties in the enrollment or retention of subjects in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.
- The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and the results of our clinical trials may not satisfy the requirements of the FDA, EMA or other comparable foreign regulatory authorities.
- If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market our product candidates on acceptable terms, we may be unable to successfully commercialize our product candidates that obtain regulatory approval.
- If we are unable to obtain and maintain sufficient intellectual property protection for our technology and products and product candidates we may develop, or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors or other third parties could develop and commercialize products similar or identical to ours, and our ability to successfully develop and, if approved, commercialize our product candidates may be adversely affected.
- We rely, and expect to continue to rely, on third parties, including independent clinical investigators and CROs, to conduct, supervise and monitor certain aspects of our clinical trials and preclinical studies. If these third parties do not successfully carry out their contractual duties, comply with applicable regulatory requirements and meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates, or such approval or commercialization may be delayed, and our business could be substantially harmed.

- Our success is highly dependent on our ability to attract and retain highly skilled executive officers and employees.
- The market price of our Class A Common Stock has been and is expected to continue to be volatile.
- We expect to incur losses for the foreseeable future and might never achieve profitability.
- We will need substantial additional funding before we can complete the development of our product candidates. If we are unable to obtain such additional capital on favorable terms, on a timely basis or at all, we would be forced to delay, reduce or eliminate our product development and clinical programs and may not have the capital required to otherwise operate our business.
- Our Amended Certificate of Incorporation and the Amended Bylaws and provisions under Delaware law could make an acquisition of our company more difficult and may prevent attempts by our stockholders to replace or remove our management.
- As a result of the Merger, we are subject to the SEC requirements applicable to reporting shell company business combinations. As a result, we are subject to more stringent reporting requirements, offering limitations and resale restrictions.
- An active trading market for our Class A Common Stock may not develop, and the holders of our Class A Common Stock may not be able to resell their shares of our Class A Common Stock for a profit, if at all.
- We could be subject to securities class action litigation, which is expensive and could divert management attention.
- Our executive officers, directors and principal stockholders have the ability to control or significantly influence all matters submitted to our stockholders for approval.

PART I

Item 1. Business

Overview

OnKure Therapeutics, Inc. (“OnKure”, “we”, “us” or the “Company”) is a clinical-stage biopharmaceutical company focused on the discovery and development of precision medicines that target biologically validated drivers of cancers underserved by available therapies. Using a structure- and computational chemistry-driven drug design platform, we are committed to improving clinical outcomes for patients by building a robust pipeline of small molecule drugs designed to selectively target specific mutations thought to be key drivers of cancer. By improving selectivity for the oncogenic and mutated form of these cancer-driver proteins, we aim to discover and develop drugs with improved safety and efficacy by sparing toxicity that arises from non-selective inhibition of the non-mutated (or wild-type) version of the protein. We work under the belief that inhibiting target proteins with specific mutations instead of wild-type variants should enable precise patient selection that will, in turn, improve the probability of clinical success. We designed our current product candidates utilizing disciplined medicinal chemistry, x-ray crystallography and computational chemistry to inhibit specified mutated versions of phosphoinositide 3-kinase alpha (“PI3Kα”), a key mediator in cancer growth signaling.

Our lead product candidate, OKI-219, is a highly selective inhibitor of PI3Kα harboring the H1047R mutation (“PI3Kα^{H1047R}”) that has a much smaller impact on wild-type PI3Kα (“PI3Kα^{WT}”). By minimizing the targeting of PI3Kα^{WT} (approximately 80-fold selectivity for PI3Kα^{H1047R} over PI3Kα^{WT}), we believe OKI-219 can achieve exposures required for activity in PI3Kα-mutated cancers with minimal effect on wild-type PI3Kα signaling, thus potentially limiting on-target toxicities, such as hyperglycemia, gastrointestinal ("GI") effects, fatigue, and rash. We plan to initially focus on the development of OKI-219 in patients with advanced breast cancer of genetic subtypes that are (a) both hormone receptor positive (“HR+”) and human epidermal growth factor receptor 2 negative (“HER2-”); and (b) human epidermal growth factor receptor 2 positive (“HER2+”). We believe we can potentially expand the application of OKI-219 by conducting appropriate clinical trials in earlier lines of treatment within breast cancer, other subtypes of breast cancer, and potentially in other solid tumors.

OKI-219 is currently being investigated in a first-in-human Phase 1a/1b open-label trial evaluating OKI-219 as a monotherapy and in combination with fulvestrant or trastuzumab in subjects with advanced solid tumors, including breast cancer harboring a PI3Kα^{H1047R} mutation (“PIKture-01”). In Phase 1a, subjects receive escalating oral doses of OKI-219 starting at 300 mg twice daily (commonly referred to as “BID”) continuously. In Phase 1b we are currently assessing OKI-219 in combination with fulvestrant in patients with HR+/HER2- breast cancer, and in the future, plan to assess OKI-219 in combination with HER2+ targeted agents (e.g., trastuzumab) in patients with HER2+ breast cancer.

In December 2024, we announced the preliminary safety, tolerability, and pharmacokinetic (“PK”) data from PIKture-01 with a cut off date of October 28, 2024. These data showed that OKI-219 was well tolerated across all dose levels with no hyperglycemia, stomatitis, or rash observed at any dose, and only grade 1 treatment-related adverse events (“TRAEs”) were reported. No dose interruptions, delays, reductions, or discontinuations were reported for any adverse events. OKI-219 dosed at 900 mg twice daily showed steady-state exposure levels with near-continuous coverage of the *in vivo* EC_{80} for pAKT inhibition. These data supported the initiation of Part 1b of PIKture-01 and we began enrolling patients in the fourth quarter of 2024 focusing initially on the evaluation of OKI-219 in combination with fulvestrant. To date, we have completed the enrollment of patients in the Part A monotherapy arm of PIKture-01 through the 1200 mg BID cohort level with no dose limiting toxicities observed in the completed cohorts. We are currently enrolling the last cohort with a top dose of 1500 mg BID and enrollment in Part A is almost complete. Additionally, we have enrolled patients in the Part B fulvestrant combination arm through the 900 mg BID cohort with no dose limiting toxicities observed for all completed cohorts through 600 mg BID and enrollment in the dose escalation portion of Part B is almost complete. We expect to report additional single-agent data and initial combination data with fulvestrant in the second half of 2025.

Pharmacokinetic and Selectivity Profile

OKI-219 has shown favorable PK data (Figure 1) in the PIKture-01 trial that support pharmacologically relevant exposures, potentially even at the lowest assessed dose levels, with a safety profile that is indicative of little or no inhibition of wild-type PI3Kα. At steady state, the exposures of OKI-219 exceed exposures associated with

robust antitumor activity in preclinical models. The PK data are considered preliminary with a data cut-off of October 28, 2024. We plan to provide updated PK data in the second half of 2025.

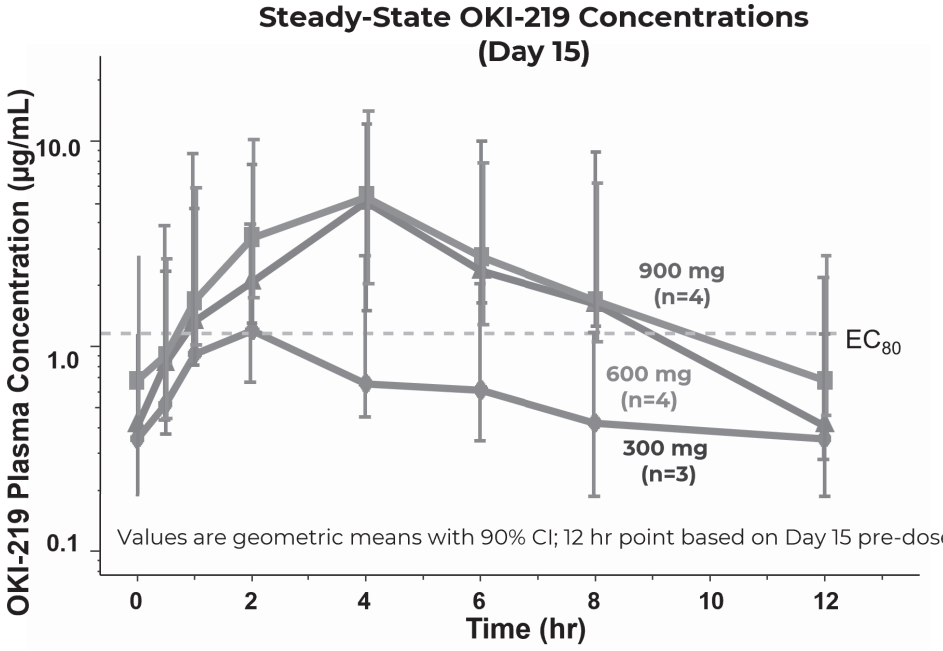


Figure 1. Steady-state concentrations of OKI-219 at Day 15 across three dose levels in PIKture-01 Part A. Data cut off October 28, 2024. Source: OnKure data.

As shown in Figure 2, 13 of the 14 patients that received a ≥600 mg dose twice a day remained in the study as of the cutoff date. In addition, two patients with HR+/HER2- breast cancer who received the 300 mg dose showed prolonged stable disease, including one patient who sustained >95% reduction in PIK3CA^{H1047R} ctDNA and was on treatment for more than seven months.

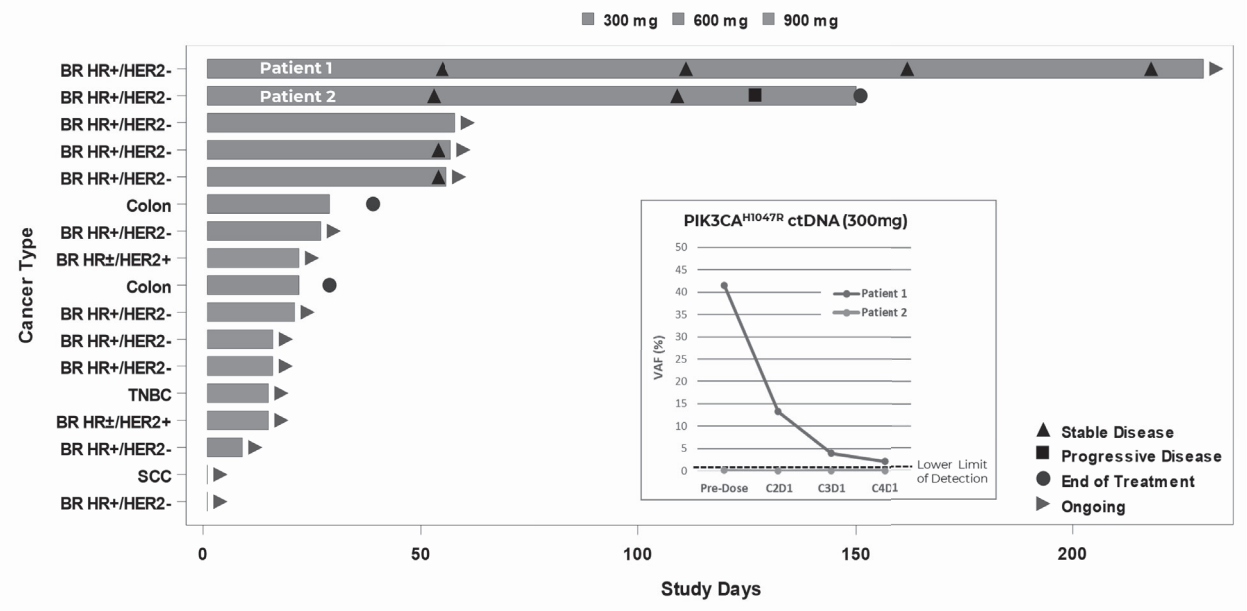


Figure 2. Time on treatment data from PIKture-01 trial. Data cut off October 28, 2024. Source: OnKure data.

Preclinical Data

Results from preclinical *in vivo* models (Figure 3 and 4 below) of OKI-219 used in combination with standard-of-care ("SOC") therapies for HR+ breast cancers show strong combination activity of OKI-219 in doublet combinations with SERDs and in triplet combinations with SERD + CDK4/6 inhibitors. Additionally, OKI-219 was well tolerated at doses well above those required for tumor regressions, supporting the ability to combine OKI-219 with SOC therapies in breast cancer. Additional preclinical combination studies are ongoing.

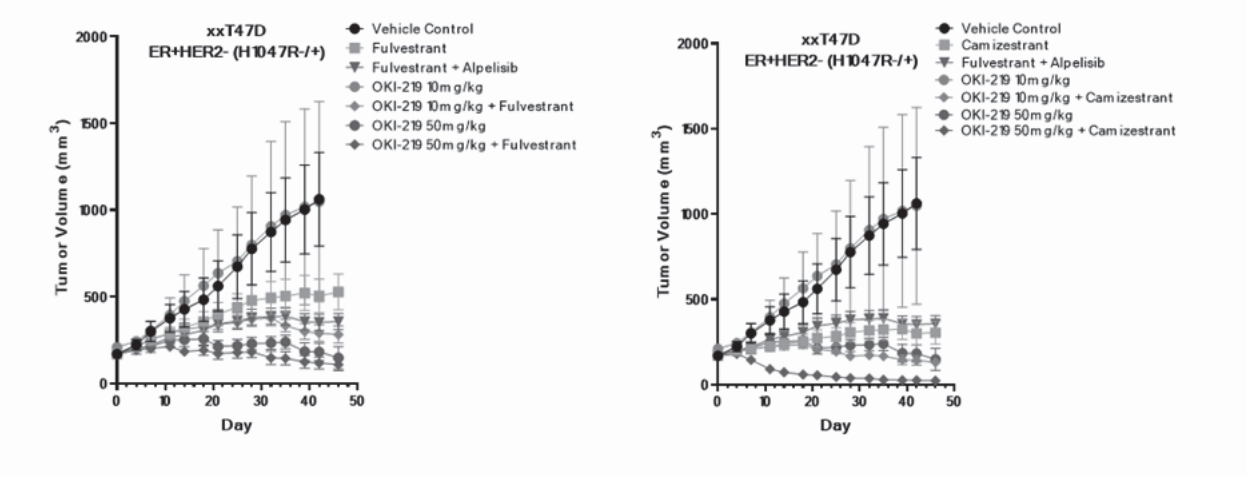


Figure 3. Preclinical comparison of tumor shrinkage for OKI-219 alone and in combination with fulvestrant or camizestrant vs. fulvestrant or camizestrant in an ER+HER2- breast cancer model. Source: OnKure data.

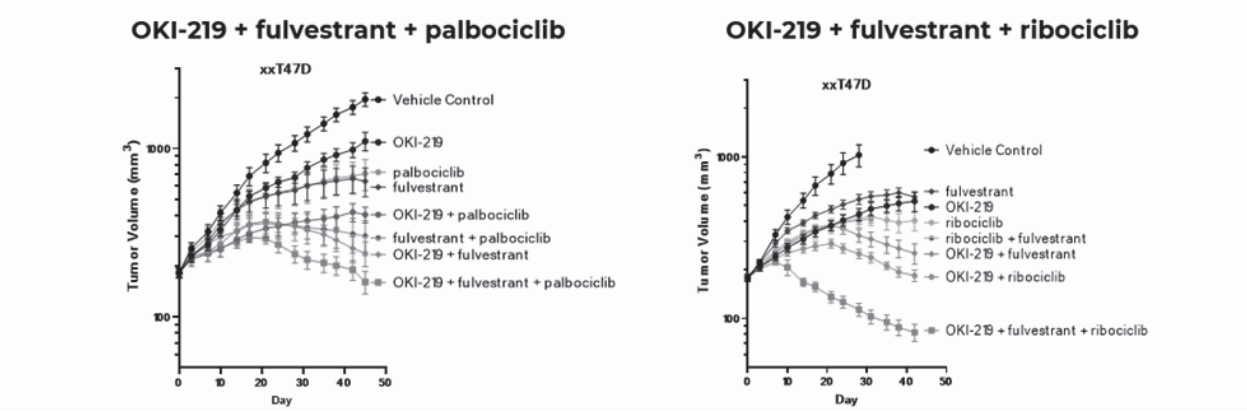


Figure 4. Preclinical comparison of tumor shrinkage for OKI-219 alone and in combination with fulvestrant plus CDK 4/6 inhibitors vs. CDK 4/6 inhibitors alone and in combination with fulvestrant. Source: OnKure data.

Genetic analysis of tumors has become standard-of-care in oncology and has enabled oncologists to characterize tumors much more precisely than simple segmentation based on the tissue of origin. A more precise understanding of the genetic alterations driving the growth of specific tumors has also created an opportunity for the industry to develop drugs that are intended to target mutated or oncogenic forms of proteins that drive cancer growth and survival. In a number of notable cases, this approach has profoundly changed how these tumors are treated and has significantly improved outcomes for patients with cancers that depend on these oncogenes for survival. However, in many cases, it has been challenging to effectively target the mutated oncogenic form of a target protein. In particular, non-selective inhibition of the wild-type protein in normal tissues often leads to toxic effects that can limit effective target inhibition of the intended oncogenic protein in cancers and, therefore, offers suboptimal clinical benefit. One such challenging target is the oncogene PI3Kα.

PI3Kα is an attractive target for cancer drugs because it is one of the most commonly mutated oncogenes in cancers and is a key mediator of abnormal cell growth. Furthermore, PI3Kα kinase mutations are clinically correlated with drug resistance and poor clinical outcomes. Single amino acid mutations such as E542K, E545K, H1047R, H1047L, and H1047Y account for over 70% of PI3Kα mutations. Notably, the PI3Kα^{H1047R} mutation is very common in breast cancer, being identified in approximately 14% of breast cancer cases. The PI3Kα inhibitor alpelisib has been approved to treat patients with advanced breast cancers harboring PI3Kα mutations. Alpelisib is non-selective for the key mutations, and its inhibition of not only mutant but also wild-type PI3Kα leads to significant toxicities in patients, such as hyperglycemia, rash and diarrhea. These toxicities can present significant challenges to optimal dosing and use in this patient population. We are focused on addressing the shortcomings of alpelisib and other first-generation PI3Kα inhibitors (e.g., inavolisib) by developing product candidates that target these genetic alterations selectively while sparing the wild-type PI3Kα.

Our Development Pipeline

We are focused on the discovery and development of precision oncology therapies that target biologically validated drivers of cancers underserved by available therapies. Currently, we are focused on delivering highly selective drug candidates that preserve wild-type PI3Kα while effectively targeting the PI3Kα-mutated cancers, initially in advanced breast cancer.

Our lead product candidate, OKI-219, is advancing in a Phase 1 clinical trial. We are also actively pursuing multiple additional discovery programs that target oncogenic mutations of PI3Kα. We expect to announce a pan-mutant development candidate in the second quarter of 2025 targeting the most common PI3Kα mutations (i.e., H1047R, E545K, and E542K). Additionally, we are developing an allosteric inhibitor molecule designed to be highly selective by specifically targeting the PI3Kα E545K and E542K mutations (which are also known as helical domain mutations or e-mutants) and expect to announce a development candidate in 2026.

Our Clinical Pipeline

Program/Target	Indication(s)	Discovery	Preclinical	Phase 1	Phase 2	Phase 3	Current Status	Next Anticipated Milestone
OKI-219 PI3Kα^{H1047R} mutant-selective inhibitor	Breast cancer & solid tumors	PIKture-01 Trial					Phase 1 enrolling	Data update (2H 2025)

Strategy

Our strategic objective is to conceive, develop and commercialize one or more mutation-specific PI3Kα inhibitors to address the needs of patients in breast cancer and beyond. With three PI3Kα inhibitor programs, we are committed to developing product candidates that address the needs of patients who suffer from diseases implicated by PI3Kα, a key mediator in cancer growth signaling. We rely on the experience of our team in precision kinase inhibitor drug design and development to carry out our strategy. In doing so, we intend to:

a) *Rapidly advance and expand the clinical development of our highly selective PI3KαH^{1047R} inhibitor, OKI-219*. The Phase 1 dose-escalation and expansion cohort trial, OKI-219-101, known as PIKture-01, is currently enrolling two arms: a) a monotherapy arm in patients with advanced solid tumors with a PI3Kα^{H1047R} mutation and b) a combination arm evaluating OKI-219 in combination with fulvestrant, a selective estrogen receptor degrader ("SERD"), in patients with PI3Kα^{H1047R}-mutated, HR+/HER2- advanced breast cancer. We also plan to initiate additional trials or arms of PIKture-01 to evaluate OKI-219 in combination with trastuzumab in patients with PI3Kα^{H1047R}-mutated, HER2+ advanced breast cancer, and certain combinations of OKI-219 with fulvestrant and CDK inhibitors in ER+ metastatic breast cancer.

b) *Discover and develop a PI3Kα inhibitor development candidate that selectively targets all the most common PI3Kα mutations*. We are actively pursuing a pan-mutant molecule to target all the most common PI3Kα mutations (i.e., H1047R, E545K, and E542K) that may have the potential to treat a

broader patient population. Our research and development team has extensive expertise in discovering early development candidates with favorable drug properties, and we plan to announce a pan-mutant development candidate in the second quarter of 2025.

c) *Discover and develop a PI3Kα inhibitor development candidate specifically targeting helical domain mutations*. We are also applying our precision drug design approach and our team's expertise to develop kinase inhibitors for PI3Kα E542K and E545K mutations (also known as helical domain mutations or e-mutants). These mutants are well known oncogenic drivers, and highly selective inhibitors targeting these mutations have the potential to further expand our addressable patient population. We anticipate announcing a development candidate in 2026.

d) *Conduct clinical and regulatory programs to support our global regulatory and commercialization strategy*. We retain worldwide rights to all our programs. We plan to expand our clinical development and seek regulatory approval for our current and future product candidates in the United States and abroad. Our long-term goal is to commercialize our products by establishing a commercial organization on our own and/or by leveraging the capabilities of potential commercial partners in the United States and outside the United States. We plan to evaluate strategic opportunities that we believe can maximize the commercial potential of our product candidates with collaborators whose development and commercial capabilities could be complementary.

Genetic Tumor Profiling is Unlocking Novel Targets for Cancer Therapy

Over the past 20 years, drug developers have translated findings from tumor genetic analysis into greater insight into tumor biology, a development that has led to a major improvement in anti-cancer therapies. Tumors are no longer simply classified based on their tissue of origin; rather, they are segmented based on genetic alterations, which frequently predict the likely pathogenesis of a specific malignancy and/or its sensitivity to treatment with specific targeted therapies. As a key part of this genetic analysis, mutations in critical signaling pathways have been identified, many of which are potential targets for precision medicines. The signaling axis encompassing PI3K/AKT and mammalian target of rapamycin ("mTOR") is believed to be a key growth driver of tumor cells and is often considered a master regulator of cancer. PI3K activity is upregulated by upstream oncogenes and growth factor receptors, or by activating mutations of PI3K itself, and aberrant PI3K activation is a common hallmark in tumor cell growth in both hematologic malignancies and solid tumors. PI3K activation is believed to contribute to cancer cell survival, angiogenesis, and tumor metastasis.

There are three subtypes of PI3K, known as Type I, Type II and Type III. Type I PI3K is believed to drive the proliferation of tumor cells and has been a key target for drug development. There are four biochemical variants, also known as isoforms or subtypes, of Type I PI3K: PI3Kα, PI3Kß, PI3Kγ and PI3Kδ. While they are differentiated from each other in sequence and structure, all these variants are based on the same fundamental kinase sequence, structure, and function.

PI3Kα is one of the most commonly mutated oncogenes in cancer. PI3Kα can be activated by oncogenic point mutations in the PI3Kα gene. The three most common mutations of PI3Kα are H1047R, E542K and E545K. Mutation of PI3Kα^{H1047R} in a mouse model has induced breast cancer tumorigenesis and is also associated with drug resistance to HER2-targeting agents in breast cancer. PI3Kα is mutated in up to 36% of breast cancer cases. Notably, the PI3Kα^{H1047R} mutation is also found in approximately 14% of breast cancer cases, making this an attractive target for novel therapeutics in metastatic breast cancer. In addition, targeting mutated PI3Kα is a clinically-validated approach following approvals of three drugs for patients with PI3Kα-mutated breast cancers: 1) the PI3Kα inhibitor alpelisib, marketed by Novartis as PIQRAY®, approved in combination with fulvestrant for the treatment of HR+, HER2-, locally advanced or metastatic breast cancer with PI3Kα mutations, 2) the AKT inhibitor capivasertib, marketed by AstraZeneca as TRUQAP®, also approved in combination with fulvestrant for the treatment of HR+, HER2-, locally advanced or metastatic breast cancer with PI3Kα mutations and 3) the PI3Kα-selective inhibitor inavolisib (Itovebi™) which was recently approved in combination with the SERD fulvestrant and the CDK4/6 inhibitor palbociclib (Ibrance™) in endocrine-resistant HR+/Her2- locally advanced or metastatic breast cancer.

Both alpelisib and inavolisib are ATP-competitive PI3Kα kinase inhibitors that do not distinguish between mutant and wild-type PI3Kα. Likewise, capivasertib inhibits the pathway downstream of PI3Kα, and also does not differentiate between inhibition of wild-type and mutated PI3Kα signaling. Unlike these drugs, OKI-219 is a specific and selective allosteric inhibitor of H1047R-mutated PI3Kα. OKI-219 is designed to bind at an allosteric

site located adjacent to the H1047R mutation which is distal from the active site. This has been shown in numerous x-ray images of OKI-219 bound to PI3Kα^{H1047R}.

Drug-related toxicities associated with non-selective PI3Kα pathway inhibitors such as alpelisib and capivasertib are caused by inhibiting the wild-type PI3Kα enzyme in normal tissues and limit the therapeutic dosing of these agents, resulting in sub-optimal dosing and limited efficacy. Adverse events commonly associated with PI3Kα inhibitors include hyperglycemia, rash, diarrhea, and stomatitis. Tumor sequencing analysis has led to the identification of specific mutations in the PI3Kα genes that offer novel drug targets for precision medicine with the potential to minimize the toxicities of non-selective PI3Kα inhibitors.

We are utilizing our precision medicine small molecule drug discovery platform to identify and develop therapeutic candidates that specifically bind to and inhibit the major PI3Kα mutations. We believe that by avoiding the targeting of wild-type PI3Kα, our product candidates have the potential to improve upon the safety, efficacy, or both, of other non-selective PI3Kα inhibitors.

Our Product Candidate

OKI-219, a Targeted Inhibitor of PI3Kα^{H1047R}

Our lead product candidate is OKI-219, an orally administered small molecule designed to selectively bind to and inhibit PI3Kα^{H1047R}, while avoiding inhibition of wild-type PI3Kα. As such, OKI-219 is designed to avoid the adverse effects of inhibiting wild-type PI3Kα in patients.

OKI-219 is currently being investigated in a first-in-human Phase 1a/1b trial. This is an open-label, international trial designed to evaluate OKI-219 for safety, tolerability, pharmacokinetics, pharmacodynamics, and efficacy with planned sites in the United States, European Union, and Asia. In December 2024, we reported preliminary safety, tolerability, and pharmacokinetic data from the PIKture-01 trial. OKI-219 was well tolerated across all dose levels tested with no hyperglycemia, and only grade 1 treatment-related adverse events were reported. No dose interruptions, delays, reductions, or discontinuations were reported for any adverse events. OKI-219 dosed at 900 mg twice daily showed steady-state exposure levels with near-continuous coverage of the in vivo EC_{80} for pAKT inhibition. These data supported the initiation of Part 1b of PIKture-01 evaluating OKI-219 in combination with fulvestrant in the fourth quarter of 2024. We expect to provide additional single agent data and initial combination data with fulvestrant in the second half of 2025. We will require additional Phase 2 and Phase 3 clinical trials to demonstrate that OKI-219 is safe and effective before we can seek regulatory approvals for the commercial sale of OKI-219.

Commercial Opportunity in Breast Cancer

Breast cancer is the most diagnosed cancer worldwide and is the leading cause of cancer death in women. In the United States, there were an estimated 300,590 new cases of breast cancer in 2023, resulting in 43,700 deaths. According to the National Cancer Institute, approximately 70% of breast cancer patients are HR+/HER2-, approximately 14% are HER2+ and approximately 11% are classified as triple negative, with the remaining 6% of patients being unclassified.

PI3Kα is the most commonly mutated oncogene in breast cancer. Mutations in the PI3K pathway are associated with increased failure of clinical treatments in advanced breast cancer, such HER2 therapy, endocrine therapy, and CDK inhibitor therapy. Notably, the activity of fulvestrant with or without CDK inhibitors in advanced or metastatic breast cancer is worse in PI3Kα^{H1047R} mutated tumors, suggesting that adding PI3Kα inhibitors to standard of care therapies in HR+ and HER2+ breast cancer may have strong clinical benefit in patients with PI3Kα-mutated cancers. The currently approved drugs, such as inavolisib and alpelisib show strong clinical benefit in combination with fulvestrant +/- CDK inhibitors in PI3Kα-mutated breast cancers, however these agents are still associated with significant toxicity from targeting the WT form of the enzyme, which is thought to limit the clinical benefit and quality of life for patients. While a number of molecules with modest selectivity for mutations versus WT PIK3CA are being developed, we believe that highly-selective inhibition of mutated PI3Kα is necessary to enable optimal target coverage and clinical benefit without eroding safety and quality of life due to inducing PI3Kα-related toxicity.

We believe the potential market opportunity for PI3Kα inhibitors is large. Total new HR+/HER2- advanced breast cancer patients each year with the most common PI3Kα mutations (i.e., H1047, E542 and E545) is approximately 29,000 in the U.S. and >60,000 in the U.S.+ EU5+Japan (see Figure 5). The single most common

PI3Kα mutation, PI3Kα^{H1047R} , is found in approximately 14% of all breast cancers. As a comparison, the HER2+ population in breast cancer also accounts for approximately 14% of all patients.

The other common PI3Kα mutations (i.e. PI3Kα^{E542K} and PI3Kα^{E545K}) are less prevalent, and combined are found in approximately 10% of breast cancers.

We believe that there is a significant market opportunity for a highly-selective PI3Kα^{H1047R} inhibitor, with the ability to target an annual population of ~17,000 patients in the United States and >35,000 patients in the United States+EU5 countries (UK, Spain, Italy, Germany and France)+Japan with PI3Kα^{H1047R}-mutated tumors across all lines of metastatic breast cancer (see Figure 5).

Based on the data from the PIKture-01 trial, as of the October 28, 2024 cutoff date, and the selectivity of OKI-219 (approximately 80-fold selectivity for PI3Kα^{H1047R} over PI3Kα^{WT}), we believe we have the opportunity with OKI-219 to optimize efficacy and safety in patients with PI3Kα^{H1047R}-mutated tumors, thus being well positioned to be an important therapeutic in this sizeable patient population.

	Assumption	US	EU5	Japan	China
Incidence	Annual Breast Cancer Incidence	305,000	290,000	100,000	380,000
	Total New HR+/HER2- Advanced Breast Cancer Patients Each Year	65,000	53,000	16,000	70,000
Biomarker Prevalence	% Patients with Kinase domain (H1047R or Helical Domain (E542K/E545K) Mutations	PI3Kα Kinase / PI3Kα Helical	PI3Kα Kinase / PI3Kα Helical	PI3Kα Kinase / PI3Kα Helical	PI3Kα Kinase / PI3Kα Helical
		~14% / *~10%*	*~14%* / *~10%*	*~14%* / *~10%*	*~14%* / *~10%*
Line of Therapy Progression	1L aBC Annual New Patient Starts	~9,000 / ~6,500	~7,300 / ~5,300	~2,300 / ~1,600	~9,700 / ~7,000
	2L aBC Annual New Patient Starts	~5,500 / ~3,600	~4,200 / ~3,200	~1,700 / ~1,200	~6,100 / ~4,500
	3L aBC Annual New Patient Starts	~2,500 / ~1,800	~2,000 / ~1,400	~1,100 / ~800	~3,200 / ~2,300

Figure 5. Estimated breast cancer incidence metrics across certain regions of the world. Source: OnKure third party research

Limitations of Currently Approved PI3K Inhibitors

Mutations in the PI3K/AKT/mTOR signaling axis occur frequently in many cancer types. PI3Kα is frequently mutated and activated in cancer, and aberrant PI3Kα activation is believed to be involved in tumor growth and metastasis. PI3Kα is composed of two components, a regulatory subunit, p85α, and catalytic subunit, p110α. An activating gain-of-function mutation in the catalytic p110α region of PI3Kα is one of the most common drivers of mutations in solid tumors.

Due to its role in mediating signaling in multiple cell types in humans, inhibition of the normal wild-type PI3Kα enzyme is associated with a diverse range of toxicities, including hyperglycemia, rash, diarrhea, nausea, and stomatitis, which present a challenge to maintenance of patients on therapy. Hyperglycemia is one of the readily monitorable key toxicities in both patients and animal models that limits the efficacy of currently approved PI3Kα inhibitors and is often used as a sentinel indicator of on-target activity vs wild-type PI3Kα, however other effects, such as rash and GI toxicities can also be severe and debilitating for patients.

Alpelisib (Piqray™) was the first PI3Kα inhibitor approved, in combination with fulvestrant for the treatment of adults with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, PIK3CA-mutated, advanced or metastatic breast cancer. At the approved dose in the SOLAR-1 trial for alpelisib, toxicities expected for inhibition of wild-type PI3Kα for the treatment of adults with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, PIK3CA-mutated, advanced or metastatic breast cancer were common. Other adverse events may be associated with the treatment of adults with

hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, PI3Kα-mutated, advanced or metastatic breast cancer. Increases in glucose were observed in 79% of patients treated with alpelisib (39% Grade 3 or 4) in this study. Other adverse events commonly associated with PI3K inhibition were also frequently observed: diarrhea (58%, 7% Gr3/4); nausea (45%, 2.5% Gr3/4); rash (52%, 20% Gr3/4); fatigue (42%, 5% Gr3/4) and stomatitis (30%, 2.5% Gr3/4).

Capivasertib (Truqap™) is an AKT inhibitor developed by AstraZeneca, indicated in combination with fulvestrant for the treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer with one or more PIK3CA/AKT1/PTEN-alterations. Capivasertib adverse events associated with PI3K pathway inhibition have also been commonly observed, highlighting the safety challenges of broadly inhibiting this pathway. Specifically, in the CAPItello-291 study that supported approval of capivasertib, while the rate of hyperglycemia (37% overall, 3.1% Gr3/4) was lower than observed with alpelisib, other PI3K-related AEs were more notable, including: diarrhea (77% overall, 12% Gr3/4); cutaneous (56%, 15% Gr3/4); fatigue (38%, 1.9% Gr3/4); stomatitis (25%, 1.9% Gr3/4) and nausea (35%, 1.3% Gr3/4).

Inavolisib (Itovebi™, Genentech) is a PI3Kα-selective inhibitor that was approved in 2024, in combination with fulvestrant and palbociclib in endocrine-resistant, PIK3CA-mutated, hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer. While the tolerability profile of inavolisib is considered to be manageable, this molecule still shows frequent adverse events associated with inhibition of the wild-type form of PI3Kα. These include increases in fasting glucose (85% overall, 22% Gr2 and 12.6% with Gr3/4); stomatitis (51% overall, 6% Gr3/4); diarrhea (48% overall, 3.7% Gr3/4); rash (26% overall, 0% Gr3/4), fatigue (38% overall, 1.9% Gr3/4) and nausea (28% overall, 0.6% Gr3/4).

While initial PI3Kα pathway inhibitors are active clinically, the frequent rate of adverse events due to inhibition of the wild-type PI3Kα pathway impact their use and are a challenge for patients, highlighting the need for more-selective inhibitors of mutated PI3Kα that can limit on-target toxicity. By minimizing the targeting of $PI3K\alpha^{WT}$ (approximately 80-fold selectivity for $PI3K\alpha^{H1047R}$ over $PI3K\alpha^{WT}$), we believe OKI-219 can achieve exposures required for activity in PI3Kα-mutated cancers with minimal effect on wild-type PI3Kα signaling, thus limiting the on-target toxicities, such as hyperglycemia, GI effects, fatigue, and rash. We believe that this is a key differentiator for OKI-219 compared to first-generation non-selective PI3Kα inhibitors.

In December 2024, we announced preliminary safety, tolerability, and PK data from PIKture-01 as of a data cut off on October 28, 2024. OKI-219 was well tolerated across all dose levels with no hyperglycemia, stomatitis, or rash observed with other PI3Kα inhibitors. Additionally, only grade 1 TRAEs were reported, with no dose interruptions, delays, reductions, or discontinuations reported for any adverse events.

	300 mg BID n = 3	600 mg BID n = 8	900 mg BID n = 6	ALL Pts n=17
Preferred Term	**Grade 1**	**Grade 1**	**Grade 1**	**Grade 1**
Diarrhoea	0 (0%)	3 (38%)	1 (17%)	4 (24%)
Nausea	0 (0%)	1 (13%)	1 (17%)	2 (12%)
Pruritus	1 (33%)	1 (13%)	0 (0%)	2 (12%)
Anaemia	0 (0%)	1 (13%)	0 (0%)	1 (6%)
Fatigue	0 (0%)	1 (13%)	0 (0%)	1 (6%)

Data cut-off - October 28, 2024

TRAEs: Treatment Related Adverse Events; DLT: Dose Limiting Toxicities; AEs: Adverse Events

Figure 6. Initial TRAEs observed across dose levels in PIKture-01 Part A. Data cutoff October 28, 2024. Source: OnKure data.

Blood-Brain Barrier Penetration

Brain metastases are estimated to occur in 98,000 to 170,000 cancer patients in the United States each year and in 10% to 26% of patients who die from their cancers. The observed growth in the incidence of brain metastasis over the last decade is believed to be partially attributed to the challenges of chemotherapeutic agents gaining access to the brain. While clinical outcomes for systemic malignancies have improved, the survival prognosis for brain metastasis has remained poor and for many patients remains at less than one year.

The blood-brain barrier (the "BBB") is a semi-permeable membrane that regulates the transfer of substances from the circulatory system into the brain and provides protection for the brain from potentially harmful substances present in the rest of the body. The BBB is composed of cells that line blood vessels, known as endothelial cells, which are joined to each other with tight junctions and are surrounded by a layer of cells known as pericytes found in the capillary basement membrane. The tight junctions limit the entry of most molecules greater than approximately four hundred Daltons in molecular weight. While it is protective of the brain and contributes to overall health, the BBB nonetheless presents a challenge to physicians seeking to deliver anti-cancer agents to the brain and to treat brain metastasis. Preclinical data for OKI-219 in a rat model suggest that OKI-219 is highly brain-penetrant, reaching free drug concentrations in the brain similar to those observed in plasma, indicating potential utility in central nervous system disease.

Distribution of OKI-219 through the BBB and into the brain has also been confirmed in both dogs and monkeys. We believe that the ability of OKI-219 to penetrate the BBB may enable it to effectively treat patients with brain metastasis in addition to those with systemic malignancies.

Current Standard-of-Care in Breast Cancer

Many cancers are treated with combinations of two or more anti-cancer drugs. Specifically, in breast cancer, the choice of therapy is dependent on the type and stage of disease. Breast cancers are segmented diagnostically based on growth drivers, including hormonal receptors such as estrogen and progesterone receptors and the HER2/neu receptor. Approximately 70% of breast cancers over-express an estrogen receptor ("ER") or progesterone receptor and are classified as HR+/HER2-. If diagnosed with early-stage disease, patients are usually treated with endocrine therapy, such as aromatase inhibitors or tamoxifen in the adjuvant setting, or they may receive chemotherapy before hormonal inhibitors if they are diagnosed with later-stage, intermediate or high-risk disease. For patients initially diagnosed with metastatic HR+/HER2- disease, and for those who have disease that has progressed to become metastatic HR+/HER2- disease, first-line treatment includes an aromatase inhibitor plus a CDK4/6 inhibitor, or the SERD, fulvestrant, plus a CDK4/6 inhibitor. In the second-line setting, treatment can vary depending on identified mutations in various genes. Patients with PI3Kα mutations are eligible to receive fulvestrant plus a PI3Kα- or AKT-targeting agent such as alpelisib or capivasertib. For patients with ESR1 mutations, physicians may prescribe a SERD such as elacestrant, a next-generation SERD marketed by Stemline Therapeutics, a subsidiary of Menarini Group, as Orserdu®. For other patients, fulvestrant with or without the mTOR inhibitor everolimus would be indicated.

Approximately 14% of breast cancer patients over-express the HER2/neu receptor and are classified as HER2+. These patients are treated with HER2-targeting agents such as trastuzumab, marketed by Roche as Herceptin®; generic biosimilars to trastuzumab; pertuzumab, marketed by Roche as Perjeta®; ado-trastuzumab emtansine or T-DM1, marketed by Roche as Kadcyla®; fam-trastuzumab deruxtecan-nxki or T-DXd, marketed by Daiichi Sankyo and AstraZeneca as Enhertu®; and tucatinib, marketed by Pfizer as Tukysa®. Typically, in early-stage or metastatic disease, the standard-of-care is trastuzumab plus chemotherapy, with or without pertuzumab. Ado-trastuzumab emtansine was the standard-of-care in second-line metastatic disease until the approval of trastuzumab deruxtecan in 2019. Trastuzumab deruxtecan is frequently prescribed in second-line HER2+ disease, whereas ado-trastuzumab emtansine is now typically used in the third-line setting. In patients with disease that progresses on all these therapy regimens, a triple combination of tucatinib, trastuzumab and capecitabine is often used in the fourth-line or salvage setting.

Approximately 10% of breast cancer patients do not over-express HR or HER2 receptors. These tumors are classified as triple negative breast cancer ("TNBC"). Patients with TNBC are treated with chemotherapy, sacituzumab govitecan, marketed by Gilead as Trodelvy®, immunotherapy such as pembrolizumab, marketed by Merck as Keytruda®, or atezolizumab, marketed by Genentech as Tecentriq®.

Beyond HR and HER2 receptors, breast cancer patients are also screened for PD-L1 positivity, which encompasses approximately 40% of patients, as well as for mutations in the germline BRCA1 or BRCA2 genes. The prevalence of a BRCA1 or BRCA2 mutation is only 3%–4% in HR+/HER2- patients but is approximately 15% in patients with TNBC. In PD-L1 positive, triple negative breast cancer, patients are treated with atezolizumab or pembrolizumab, while two Poly ADP Polymerase inhibitors ("PARP inhibitors") are approved for BRCA1/2 mutants: Olaparib, marketed by AstraZeneca as Lynparza®, and talazoparib, marketed by Pfizer as Talzenna®.

The PI3Kα-targeting agent alpelisib and the AKT-targeting agent capivasertib are currently approved in combination with fulvestrant in advanced HR+/HER2- breast cancer, providing a proof of concept for targeting mutated PI3Kα in this disease. These therapies have significant toxicity, however, which presents a challenge for their use. We believe that the ability to safely combine with fulvestrant or other SERDs is a critical advantage for any new therapy targeting PI3Kα-mutated HR+ breast cancer. OKI-219 was tested in combination with a next-generation SERD known as camizestrant in a preclinical breast cancer model utilizing the T47D cell line. T47D is an estrogen receptor-positive luminal A subtype breast cancer cell line that harbors the PI3Kα^{H1047R} mutation and is frequently utilized in research of hormonal signaling in breast cancer. In mouse xenograft models implanted with T47D cells, monotherapy treatment with camizestrant at 10mg/kg QD resulted in slower tumor growth than the control but did not result in significant tumor volume reduction from baseline. Similarly, monotherapy dosing with OKI-219 at 25mg/kg QID resulted in delay of tumor growth as well. The combination of OKI-219 and camizestrant resulted in significant and dose-dependent tumor shrinkage, supporting the potential for combination therapy of OKI-219 and SERDs in metastatic breast cancer.

We tested the combination of OKI-219 with tucatinib, an anti-HER2 small molecule tyrosine kinase inhibitor, in the HER2+ PI3Kα^{H1047R} HCC1954 breast cancer cell line. This cell line is resistant to tucatinib treatment, and in mouse xenograft models implanted with HCC1954 cells this was demonstrated by the continued tumor growth with 50mg/kg BID tucatinib dosing. OKI-219 monotherapy at 200mg/kg QD appears to limit the tumor's ability to grow but is not effective enough by itself to drive tumor shrinkage. The combination of tucatinib and OKI-291 resulted in tumor shrinkage, suggesting that inhibiting mutant PI3Kα in combination with targeting HER2 can overcome poor responses to HER2-targeting agents used alone.

We believe that breast cancer is an ideal tumor type for the initial development of mutant-selective PI3Kα inhibitors due to several factors:

- the fact that PI3Kα inhibitors have been approved in PI3Kα-mutated HR+ metastatic breast cancer;
- the high prevalence of the PI3Kα^{H1047R} mutation in breast cancer;
- the poor prognosis of patients with metastatic breast cancer who have PI3Kα mutations; and
- the fact that PI3Kα mutations appear to be truncal, meaning that they originate early in cancer development and, when mutated, are found in most cancer cells in a patient.

We believe that initially focusing on PI3Kα^{H1047R} in advanced breast cancer patients may enable the eventual development of OKI-219 in earlier lines of therapy as well as in patients with tumors with different tissues of origin besides breast and expanding the patient population that may benefit from treatment with OKI-219.

Phase 1 PIKture-01 Trial

OKI-219 is currently being investigated in the PIKture-01 trial, a Phase 1a/1b trial. This is an open-label international trial with sites in the United States, European Union, and Asia designed to evaluate the safety, tolerability, PK, PD, and preliminary antitumor activity of OKI-219 as monotherapy as well as in combination with fulvestrant or trastuzumab.

The PIKture-01 trial has three parts:

- **Part A** is a dose-ranging basket trial of solid tumors with a target enrollment of 24 subjects testing OKI-219 as a monotherapy. This part of the trial is enrolling patients with solid tumors with the

PI3Kα^{H1047R} mutation for whom there is no effective available therapy. The starting dose is 300mg BID, and this trial uses a Bayesian Optimal Interval design. We have dosed up to 1500mg BID.

- **Part B** is investigating OKI-219 in combination with fulvestrant in HR+/HER2- advanced breast cancer. These patients must have locally advanced, unresectable or metastatic cancer with the PI3Kα^{H1047R} mutation and have received at least one prior line of hormonal therapy and at least one prior line of CDK 4/6 inhibitor therapy in the advanced or metastatic setting unless contraindicated. Part B was initiated in the fourth quarter of 2024.
- **Part C** will investigate OKI-219 in combination with trastuzumab in HER2+ advanced breast cancer with the PI3Kα^{H1047R} mutation. These patients must have HER2+, locally advanced unresectable or metastatic breast cancer and also have received prior taxane, trastuzumab, pertuzumab, tucatinib or trastuzumab deruxtecan unless unavailable or contraindicated. Part C has not been initiated.

We expect that both Part B and Part C will initially enroll patients in a single-arm dose escalation trial and then would investigate high and low doses to comply with FDA's project OPTIMUS dose exploration requirement. The objective of a dose-finding trial is to find the optimum dose instead of utilizing the maximum tolerated dose, which historically has been the dose chosen for pivotal trials of cancer drugs.

The primary endpoint of Part A is to assess the safety of OKI-219 and to identify the maximum tolerated dose and pharmacologically active dose(s) ("PAD"). Secondary endpoints include additional measures of safety and tolerability designed to:

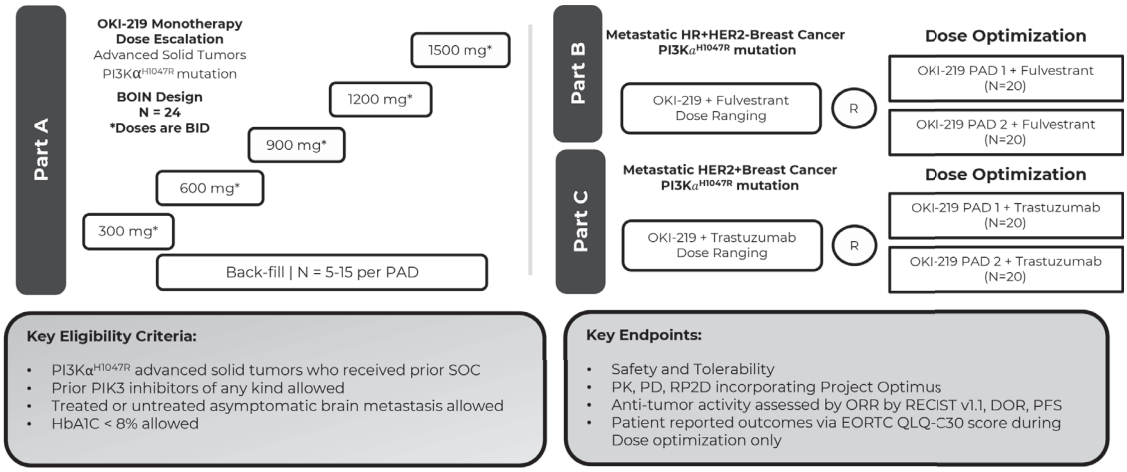
- assess plasma PK of OKI-219;
- assess the effect of food on the PK of OKI-219;
- estimate preliminary antitumor activity;
- assess the dose-response impact of circulating tumor DNA ("ctDNA"); and
- assess the PD activity of OKI-219 and its association with PK, safety, and efficacy.

For Parts B and C, the primary endpoints during dose-ranging are to assess the safety of OKI-219 when taken in combination with fulvestrant or trastuzumab and to identify two PAD doses that will be utilized during the dose optimization portion, for which the primary endpoint is to compare two PAD dose levels of OKI-219 plus a fixed dose of fulvestrant or trastuzumab in order to identify the recommended Phase 2 dose. Secondary endpoints include additional measures of safety and tolerability of OKI-219 when taken in combination with fulvestrant or trastuzumab, and are designed to:

- assess the plasma PK of OKI-219 when in combination with fulvestrant or trastuzumab;
- assess the effect of food on the PK of OKI-219 when in combination with fulvestrant or trastuzumab;
- estimate preliminary antitumor activity of OKI-219 when taken in combination with fulvestrant or trastuzumab;
- assess the dose-response impact of ctDNA of OKI-219 when taken in combination with fulvestrant or trastuzumab; and
- assess the PD activity of OKI-219 and, finally, determine the impact of OKI-219 dosing in combination with fulvestrant or trastuzumab on blood glucose and insulin.

Additionally, exploratory endpoints for all parts include an exploration of predictive biomarkers of response to OKI-219 in blood and tumor tissue as monotherapy and while in combination with fulvestrant and trastuzumab. For dose optimization only, we also seek to determine the impact of OKI-219 on quality of life.

During dose optimization, we anticipate that 20 participants will be randomized between two PAD levels in parts B and C. A sample size of 20 participants in each arm will provide 79% power to detect an increase in objective response rate from 5% to 20% within each PAD arm using a one-sided exact binomial test at the 10% level of significance. Monotherapy is not powered to assess efficacy.



BOIN: Bayesian Optimal Interval Design; DOR: Duration of Response; ORR: Objective Response Rate; PAD: Pharmacologically Active Dose; PD: Pharmacodynamics, PK: Pharmacokinetics; R: Randomization; RP2D: Recommended Phase 2 Dose; SOC: Standard of Care.

Figure 7. PIKture-01 trial design, key eligibility criteria and key endpoints as of October 28, 2024.

OKI-219 Potential Future Trials

OKI-219 was designed to target the PI3Kα^{H1047R} mutation to maintain or improve upon the efficacy and simultaneously to minimize the toxicities associated with first-generation PI3Kα^{WT} inhibitors. We anticipate that this precision targeting of the H1047R mutation and minimal inhibition of wildtype PI3Kα should enable OKI-219 to safely combine with one or two other cancer drugs and potentially result in synergistic clinical efficacy. We plan to explore OKI-219 in combination with other drugs in multiple lines of treatment in breast cancer. Based on initial data from these combination studies, a number of possible development strategies will be considered, including developing OKI-219 in combination with a SERD in second-line breast cancer patients; developing OKI-219 in patients who have disease that has progressed on prior inavolisib or alpelisib treatment; and development of OKI-219 in front-line metastatic breast cancer, in combination with CDK inhibitors, plus either an aromatase inhibitor or a SERD. With positive data in the metastatic setting, we would consider developing OKI-219 in combination with an AI+ a CDK inhibitor in the adjuvant setting.

Pan-mutant PI3Kα Precision Kinase Inhibitor Program

A key goal of cancer therapy is to improve efficacy, while maintaining a very well tolerated side effect profile, thus improving patient benefit and quality of life for patients. Our focus is on discovering and developing highly mutant-selective PI3Kα inhibitors that can improve target coverage and efficacy in PI3Kα-mutated cancers compared to existing agents, while also improving safety by sparing inhibition of wild type PI3Kα. OKI-219 has approximately 80-fold selectivity for PI3Kα^{H1047R} over the wild type form of the enzyme, a profile that may optimize the potential for efficacy and safety for treatment of tumors with a PI3Kα^{H1047R} mutation, the most common PI3Kα mutation in breast cancer.

We believe that to fully target all the most common PI3Kα mutations in SOC combinations in HR+ mBC a PI3Kα “Pan-mutant” inhibitor will need to demonstrate approximately 10-fold selectivity against each of the most common mutations (PI3Kα^{H1047X}, PI3Kα^{E542K} and PI3Kα^{E545K}). Currently, we are aware of no compounds in clinical development that can achieve this level of selectivity across all the most common mutations, leaving an opportunity for development and approval of a pan-mutant PI3Kα inhibitor for patients regardless of their PI3Kα mutation.

We are actively developing pan-mutant candidates with activity and selectivity (>10X) across the most common PI3Kα mutations (i.e., H1047R, E545K, and E542K). We believe a highly selective and potent pan-mutant inhibitor has the potential to achieve a maximal efficacy and safety profile in combinations in metastatic breast cancer, and may further enable sufficient activity as a single agent to target PI3Kα-mutated advanced cancer populations beyond breast cancer. This represents a significant patient population for which there are no current targeted therapies: Approximately 11% of all cancers harbor mutations in PI3Kα, and no PI3Kα-targeted therapies have shown sufficient efficacy to gain approval as a single-agent, potentially due to poor selectivity limiting the ability to get sufficient target inhibition without dose-limiting toxicities. We propose that a highly selective pan-

mutant inhibitor may have the efficacy to enable use in this underserved patient population beyond breast cancer. We expect to announce a pan-mutant development candidate in the second quarter of 2025.

Helical Domain PI3Kα Precision Kinase Inhibitor Program

Additionally, we are leveraging our discovery engine to develop a highly selective allosteric inhibitor molecule specifically targeting the PI3Kα E545K and E542K mutations (which are also known as helical domain mutations or e-mutants) and expect to announce a development candidate in 2026. Overall, the aim of our discovery engine is to deliver highly selective drug candidates that preserve wild-type PI3Kα while effectively targeting the vast majority of PI3Kα-mutated cancers, in breast and other cancers.

Competition

The pharmaceutical and biotechnology industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technology, the expertise of our team, and our development experience and scientific knowledge provide us with competitive advantages, we face increasing competition from many different sources, including pharmaceutical and biotechnology companies, academic institutions, governmental agencies, and public and private research institutions. Product candidates that we successfully develop and commercialize (whether alone or in partnership with others) may compete with existing therapies and new therapies that may become available in the future.

Many of our competitors, either alone or with their collaborators, have significantly greater financial resources, established presence in the market, and expertise in research and development, manufacturing, preclinical and clinical testing, obtaining regulatory approvals and reimbursement, and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel, in establishing clinical trial sites and patient registration for clinical trials, and in-licensing or acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with larger companies. Additional mergers and acquisitions may result in even more resources being concentrated in our competitors. Our commercial potential could be reduced or eliminated if our competitors develop and commercialize products that are safer or more effective, have fewer or less-severe side effects, or are more convenient or less expensive than products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we can, which could result in those competitors establishing a strong market position before we are able to enter the market or could otherwise make the development or commercialization of our products more complicated. The key competitive factors affecting the success of all of our programs are likely to be efficacy, safety and patient convenience.

There are multiple PI3Kα-pathway targeted agents either approved or under clinical development that may compete with OKI-219 and our PI3Kα-targeted portfolio. These include the marketed medicines alpelisib (Piqray®, a PI3Kα-selective inhibitor marketed by Novartis) and capivasertib (Truqap®, an AKT1 inhibitor marketed by Astra Zeneca), both of which are approved for the treatment of PI3Kα-mutated breast cancer patients in combination with the SERD fulvestrant. The PI3Kα-selective inhibitor inavolisib (Itovebi™) was recently approved in combination with the SERD fulvestrant and the CDK4/6 inhibitor palbociclib (Ibrance®) in endocrine resistant HR+/Her2- locally advanced or metastatic breast cancer. We are also aware of several novel PI3K-targeted therapies that are in clinical development. These include both multiple non-mutation-selective PI3K inhibitors such as gedatolisib (Celcuity Inc.), MEN1611 (Menarini), and TOS-358 (Totus Medicines), and inhibitors designed to have greater selectivity for mutated PI3Kα, including RLY-2608 (Relay Therapeutics), STX-473 (Scorpion Therapeutics) and SNV4818 (Synnovation Therapeutics). Multiple other companies have disclosed or published research efforts in PI3K inhibitors that are at an early stage but could potentially advance to the clinic.

Finally, there are numerous other investigational therapies, spanning many modalities that are being evaluated preclinically and in clinical trials for breast cancer.

Manufacturing

We do not own or operate, and currently have no plans to establish any manufacturing facilities. We rely, and expect to continue to rely, on third parties for the manufacture of our product candidates for preclinical and clinical testing, and expect to rely on third parties for commercial manufacturing should any of our product candidates obtain marketing approval. We believe that this strategy allows us to maintain a more efficient infrastructure by eliminating the need to invest in our own manufacturing facilities, equipment and personnel while

also enabling us to focus our expertise and resources on the discovery and development of our product candidates. In addition, we generally expect to rely on third parties for the manufacture of any companion diagnostics we may develop.

To date, we have obtained the regulatory starting materials and cGMP-compliant active pharmaceutical ingredients from three different suppliers, but could contract with other CMOs for these materials as the raw materials we use are commonly used and are available from multiple sources. We also currently rely on two CMOs, for the drug product for OKI-219, but may contract with other CMOs for the manufacture of drug product in the future. We are in the process of developing our supply chain for our product candidates and intend to put in place framework agreements under which third-party CMOs will generally provide us with necessary quantities of API and drug product on a project-by-project basis based on our development requirements.

As we advance our product candidates through development, we plan to explore adding backup suppliers for the API and drug product for OKI-219 and future product candidates in order to protect against any potential supply disruptions.

Intellectual Property

We strive to protect and enhance the proprietary technologies, inventions and improvements that are commercially important to our business by, among other methods, pursuing and obtaining patent protection in the United States and in jurisdictions outside of the United States directed to these technologies, inventions, improvements and to our drug candidates. We also rely on trade secrets, know-how, trademarks, continuing technological innovation and licensing opportunities to develop and maintain our proprietary and intellectual property position.

As of February 1, 2025, our owned and licensed patent portfolio included 150 patents and patent applications, including two licensed U.S. issued patents and six owned U.S. issued patents, covering various aspects of our proprietary technology, product candidates, and related inventions and improvements. The patent portfolio also includes 36 licensed patents issued in jurisdictions outside of the United States, and 30 owned patent applications pending in jurisdictions outside of the United States that, in many cases, are counterparts to the foregoing U.S. patents and patent applications. Our licensed patents relate to a patent family that is no longer material to our business.

PI3K Platform

We currently own 16 patent families directed to our PI3K platform technology as summarized below. The patent families are differentiated based on the chemical structures of the PI3K inhibitor compounds. All of the family members are currently at the application stage and exist as one or more U.S. provisional ("USP") applications, a Patent Cooperation Treaty ("PCT") application, or as U.S. and non-U.S. national phase applications. Several of our current patent applications relate to and include composition of matter claims for OKI-219. Four of the families which are at the PCT application stage also have a Taiwanese ("TW") application. The U.S. provisional applications secure an early filing date and provide an additional twelve months of patent protection beyond the normal 20-year lifetime of any patent granted thereon. The PCT applications are single-application placeholders for filings in a majority of the countries and geographic regions of the world. The types of claims for each application are listed, and an expiration year for each family based on the actual or projected PCT filing dates is also provided.

Family 1: 15 applications/product and method of treatment claims/2043 expiration

Family 2: PCT and TW applications/product and method of treatment claims/2043 expiration

Family 3: PCT application/product and method of treatment claims/2043 expiration

Family 4: PCT and TW applications/product and method of treatment claims/2043 expiration

Family 5: PCT and TW applications/product and method of treatment claims/2044 expiration

Family 6: USP application/product and method of treatment claims/2045 expiration

Family 7: USP application/product and method of treatment claims/2045 expiration

Family 8: 2 USP application/product and method of treatment claims/2045 expiration

Family 9: USP application/product and method of treatment claims/2045 expiration

Family 10: USP application/product and method of treatment claims/2045 expiration

Family 11: USP application/product and method of treatment claims/2045 expiration

Family 12: USP application/product and method of treatment claims/2045 expiration

Family 13: USP application/product and method of treatment claims/2045 expiration

Family 14: USP application/product and method of treatment claims/2046 expiration

Family 15: USP application/product and method of treatment claims/2046 expiration

Family 16: USP application/product and method of treatment claims/2046 expiration

We cannot guarantee that our owned pending patent applications, or any patent applications that we may in the future file or license from third parties, will result in the issuance of patents. We also cannot predict the scope of claims that may be allowed or enforced in our patents. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Consequently, we may not obtain or maintain adequate patent protection for any of our programs and product candidates.

The terms of individual patents depend upon the legal terms of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application. In the United States, the patent term of a patent that covers an FDA-approved drug may also be eligible for patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Hatch-Waxman Act permits a patent term extension of up to five years beyond the expiration of the patent. Similar provisions are available in Europe and other non-U.S. jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our products receive FDA approval, we expect to apply for patent term extensions on patents covering those products. We also plan to seek patent term extensions on any of our issued patents in any jurisdiction where available, but there is no guarantee that the applicable authorities, including the FDA in the United States, will agree with our assessment of whether such extensions should be granted, and if granted, the length of such extensions.

In addition to patent protection, we also rely on trademark registration, trade secrets, know how, other proprietary information, and continuing technological innovation to develop and maintain our competitive position. We protect and maintain the confidentiality of proprietary information to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. Although we take steps to protect our proprietary information and trade secrets, including through contractual means, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology. Therefore, we may not be able to meaningfully protect our trade secrets. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual during the course of the individual's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. Our agreements with employees also provide that all inventions conceived by the employee in the course of employment or from the employee's use of our confidential information are our exclusive property. However, such confidentiality agreements and invention assignment agreements can be breached and we may not have adequate remedies for any such breach.

The patent positions of biotechnology companies like us are generally uncertain and involve complex legal, scientific and factual questions. Our commercial success will also depend in part on not infringing upon the proprietary rights of third parties. It is uncertain whether the issuance of any third-party patent would require us to

alter our development or commercial strategies, alter our products or processes, obtain licenses, or cease certain activities. Our breach of any license agreements or our failure to obtain a license to proprietary rights required to develop or commercialize our future products may have a material adverse impact on us. If third parties prepare and file patent applications in the United States that also claim technology to which we have rights, we may have to participate in derivation proceedings in the USPTO to determine priority of invention. For more information, see the section entitled "*Risk Factors—Risks Related to our Intellectual Property*."

Government Regulation

Our product candidates and our operations are subject to extensive regulation by the FDA and other federal and state authorities in the United States, as well as comparable authorities in other countries.

The FDA and other federal, state, local and foreign authorities regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing, and export and import of drug and combination products. Generally, before a new drug can be marketed, considerable data demonstrating its quality, safety, and efficacy must be obtained, organized into a format specific for each regulatory authority, submitted for review and approved by the regulatory authority.

U.S. Drug Development

In the United States, the FDA regulates drugs under the Food, Drug, and Cosmetic Act ("FDCA") and its implementing regulations. Drug products and substances are subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local, and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process, or post-market may subject an applicant to administrative or judicial sanctions. These sanctions could include, among other actions, the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, untitled or warning letters, product recalls or market withdrawals, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement, and civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

Our current product candidates and any future small molecule product candidates must be approved by the FDA through the new drug application ("NDA") process before they may be legally marketed in the United States. The process generally involves the following:

- completion of extensive preclinical studies in accordance with applicable regulations, including the FDA's good laboratory practice requirements;
- submission to the FDA of an IND, which must become effective before clinical trials may begin;
- approval by an institutional review board ("IRB") or ethics committee at each clinical trial site before each trial may be initiated;
- performance of adequate and well controlled clinical trials in accordance with applicable Investigational New Drug Application ("IND") regulations, good clinical practice ("GCP") requirements and other clinical trial-related regulations to establish the safety and efficacy of an investigational product for each proposed indication;
- preparation and submission to the FDA of an NDA;
- a determination by the FDA within 60 days of its receipt of an NDA to file the application for review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities where the drug product will be produced to assess compliance with cGMP requirements to assure that the facilities, methods, and controls are adequate to preserve the drug identity, strength, quality, and purity;
- potential FDA audit of the preclinical study and/or clinical trial sites that generated the data in support of the NDA;

- FDA review and approval of the NDA, including consideration of the views of any FDA advisory committee, prior to any commercial marketing or sale of the drug in the United States; and
- compliance with any post-approval requirements, including the potential requirement to implement a risk evaluation and mitigation strategy ("REMS"), and the potential requirement to conduct post-approval studies.

Preclinical and Clinical Studies

The preclinical and clinical testing and approval process requires substantial time, effort, and financial resources, and we cannot be certain that any approvals for any future product candidates will be granted on a timely basis or at all. Preclinical tests generally involve laboratory evaluations of drug chemistry, formulation, and stability, as well as studies to evaluate toxicity in animals, including pharmacology, pharmacokinetics, toxicokinetic, and metabolism studies that support subsequent clinical testing in humans. The results of the preclinical studies, together with manufacturing information, analytical data, any available clinical data or literature, and a proposed clinical protocol, are submitted to the FDA as part of the IND. An IND is a request for authorization from the FDA to administer an investigational product to humans.

Long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted.

The central focus of an IND submission is the general investigation plan and the protocol(s) for human studies. An IND must become effective before clinical trials may begin. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

For each successive clinical trial conducted with the investigational drug, a separate, new protocol submission to an existing IND must be made, along with any subsequent changes to the investigational plan. Sponsors are also subject to ongoing reporting requirements, including submission of IND safety reports for any serious adverse experiences associated with use of the investigational drug or findings from preclinical studies suggesting a significant risk for human subjects, as well as IND annual reports on the progress of the investigations conducted under the IND.

Clinical studies involve the administration of the investigational product to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND.

Furthermore, each clinical trial must be reviewed and approved by an IRB for each institution at which the clinical trial will be conducted to ensure that the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative, and must monitor the clinical trial until completed. There also are requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries, including the website maintained by the U.S. National Institutes of Health, ClinicalTrials.gov.

A sponsor that wishes to conduct a clinical trial outside of the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of an NDA. The FDA will generally accept a well designed and well conducted foreign clinical trial not conducted under an IND if the trial was conducted in accordance with GCP requirements and the FDA is able to validate the data through an onsite inspection if deemed necessary.

Clinical trials in the United States generally are conducted in three phases, known as Phase 1, Phase 2, and Phase 3. Although the phases are usually conducted sequentially, they may overlap or be combined.

- Phase 1 clinical trials generally involve a small number of healthy volunteers or disease-affected patients who are initially exposed to a single dose and then multiple doses of the product candidate. The primary purpose of these clinical trials is to assess the metabolism, pharmacologic action, tolerability and safety of the drug.
- Phase 2 clinical trials typically involve studies in a limited population of disease-affected patients to determine possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance, optimal dosage, and dosing schedule.
- Phase 3 clinical trials generally involve a large number of patients at multiple sites and are designed to evaluate the effectiveness of the product for its intended use, its safety in use, and to establish the overall benefit/risk relationship of the product and provide an adequate basis for product approval. These trials may include comparisons with placebo and/or other comparator treatments.

Post-approval clinical trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA.

During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data, and clinical study investigators. Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the drug, findings from animal or *in vitro* testing that suggest a significant risk for human subjects, and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information.

Phase 1, Phase 2, and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether a trial may move forward at designated check-points based on access to certain data from the trial. Concurrent with clinical trials, companies usually complete additional animal safety studies and also must develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of our product candidates. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that our product candidates do not undergo unacceptable deterioration over their labeled shelf life.

NDA Review

Following completion of clinical trials, data are analyzed to assess whether the investigational product is safe and effective for the proposed indicated use or uses. The results of preclinical studies and clinical trials are then submitted to the FDA as part of an NDA, along with proposed labeling, chemistry, and manufacturing information in a request for approval to market the drug for one or more specified indications. The application must include both negative and ambiguous results of preclinical studies and clinical trials, as well as positive findings. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a product's use or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the investigational product to the

satisfaction of the FDA. FDA approval of an NDA must be obtained before a drug may be marketed in the United States.

Under the Prescription Drug User Fee Act, as amended (the "PDUFA"), each NDA must be accompanied by an application user fee. The FDA adjusts the PDUFA user fees on an annual basis. The PDUFA also imposes an annual program fee for each marketed human drug. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a qualifying small business.

The FDA reviews all submitted NDAs before it accepts them for filing to determine if they are sufficiently complete to permit a substantive review, and the FDA may request additional information rather than accepting the NDA for filing. In this event, the application must be resubmitted with the additional information and is subject to payment of additional user fees. The FDA must make a decision on accepting an NDA for filing within 60 days of receipt. Once the submission is accepted for filing, the FDA begins an in-depth substantive review of the NDA. Under the PDUFA, the FDA has agreed to certain performance goals in the review of NDAs through a two-tiered classification system: standard review and priority review. According to the PDUFA performance goals, the FDA endeavors to review applications subject to standard review within ten months, whereas the FDA's goal is to review priority review applications within six months. The FDA does not always meet its PDUFA goal dates for standard and priority NDAs, and the review process is often extended by FDA requests for additional information or clarification.

The FDA may refer applications for novel drug products or products which present difficult questions of safety or efficacy to an advisory committee for review, evaluation, and recommendation as to whether the application should be approved and under what conditions.

Before approving an NDA, the FDA will typically conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether they comply with cGMP requirements. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The FDA also may audit data from clinical trials to ensure compliance with GCP requirements. The FDA also closely analyzes the clinical trial data, which could result in extensive discussions between the FDA and the applicant during the review process. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

After the FDA evaluates an NDA and conducts inspections of manufacturing facilities, it will issue an Approval Letter or a Complete Response Letter. An Approval Letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application will not be approved in its present form. A Complete Response Letter usually describes all of the specific deficiencies in the NDA identified by the FDA. The Complete Response Letter may require additional clinical data, including the potential requirement to conduct additional pivotal Phase 3 clinical trial(s) and/or other significant and time-consuming requirements related to clinical trials, or to conduct additional preclinical studies or manufacturing changes. If a Complete Response Letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information are submitted, the FDA may decide that the NDA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive, and the FDA may interpret data differently than we interpret the same data.

Expedited Development and Review Programs

The FDA has a fast-track program that is intended to expedite or facilitate the process of reviewing new drugs that meet certain criteria. Specifically, new drugs are eligible for fast-track designation if they are intended to treat a serious or life-threatening condition and preclinical or clinical data demonstrate the potential to address unmet medical needs for the condition. Fast-track designation applies to both the product and the specific indication for which it is being studied. The sponsor can request that the FDA designate the product for fast-track status at any time before receiving NDA approval, but ideally no later than the pre-NDA meeting with the FDA. Any product submitted to the FDA for marketing, including under a fast-track program, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. Any product is eligible for priority review if it treats a serious or life-threatening condition and, if approved, would provide a significant improvement in safety and effectiveness compared to available therapies.

A product may also be eligible for accelerated approval if it treats a serious or life-threatening condition and generally provides a meaningful advantage over available therapies. In addition, such product must demonstrate an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality ("IMM"), which endpoint is reasonably likely to predict an effect on IMM or other clinical benefit. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform adequate and well controlled post-marketing clinical trials. The FDA may withdraw drug approval or require changes to the labeled indication of the drug if confirmatory post-market trials fail to verify clinical benefit or do not demonstrate sufficient clinical benefit to justify the risks associated with the drug. If the FDA concludes that a drug shown to be effective can be safely used only if distribution or use is restricted, it may require such post-marketing restrictions as it deems necessary to assure safe use of the drug. The Food and Drug Omnibus Reform Act made several changes to the FDA's authority and its regulatory framework, including, among other changes, reforms to the accelerated approval pathway, such as requiring the FDA to specify conditions for post-approval study requirements and setting forth procedures for the FDA to withdraw a drug on an expedited basis for non-compliance with post-approval requirements.

Additionally, a drug may be eligible for designation as a breakthrough therapy if (a) it is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening condition and (b) preliminary clinical evidence indicates that it may demonstrate substantial improvement over currently approved therapies on one or more clinically significant endpoints. The benefits of breakthrough therapy designation include the same benefits as fast-track designation, plus intensive guidance from the FDA to ensure an efficient drug development program. Fast-track designation, priority review, accelerated approval and breakthrough therapy designation do not change the standards for approval, but may expedite the development or approval process.

Post-Approval Requirements

Following approval of a new product, the product is subject to continuing regulation by the FDA, including, among other things, requirements relating to facility registration and drug listing monitoring and record-keeping adverse event and other periodic reporting, product sampling and distribution, and product promotion and advertising. The FDA strictly regulates marketing, labeling, advertising, and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not market or promote such uses. Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use or first publication.

After approval, if there are any changes to the approved product, including changes in indications, labeling or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new NDA or NDA supplement, which may require the development of additional data or preclinical studies and clinical trials. There also are continuing user fee requirements, under which FDA assesses an annual program fee for each product identified in an approved NDA. In addition, quality control, drug manufacture, packaging, and labeling products must continue to conform to cGMP requirements after approval. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products in accordance with cGMP regulations. Manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP requirements and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. The discovery of violative conditions, including failure to conform to cGMP regulations, could result in enforcement actions, and the discovery of problems with a product after approval may result in restrictions on a product, its manufacturer, or the NDA holder, including recalls.

The FDA may also place other conditions on approvals including the requirement for a REMS, to assure the safe use of the product. If the FDA concludes that a REMS is needed, the NDA sponsor must submit a proposed REMS. The FDA will not approve the product without an approved REMS, if required. A REMS could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries, and other risk minimization tools. Any of these limitations on approval or marketing

could restrict the commercial promotion, distribution, prescription, or dispensing of products. Product approvals may be withdrawn for non-compliance with regulatory standards or if problems occur following initial marketing.

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

- restrictions on the marketing or manufacturing of the product, suspension of the approval, complete withdrawal of the product from the market, or product recalls;
- fines, warning letters, or holds on clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications;
- suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of the product;
- mandated modifications of promotional materials and labeling and the issuance of corrective information;
- issuance of safety alerts, Dear Healthcare Provider letters, press releases, or other communications containing warnings or other safety information about the product; or
- injunctions or the imposition of civil or criminal penalties.

We also must comply with the FDA's advertising and promotion requirements, such as those related to direct-to-consumer advertising, the prohibition on promoting products for uses or in patient populations that are not described in the product's approved labeling, known as "off-label use," industry-sponsored scientific and educational activities, and promotional activities involving the internet and social media.

The FDA may also require post-approval studies and clinical trials if it finds that scientific data, including information regarding related drugs, make this appropriate. The purpose of such studies would be to assess a known serious risk or signals of serious risk related to the drug or to identify an unexpected serious risk when available data indicate the potential for a serious risk. The FDA may also require a labeling change if it becomes aware of new safety information that it believes should be included in the labeling of a drug.

Failure to comply with the applicable regulatory requirements at any time during the product development process, the approval process, or after approval may subject an applicant or manufacturer to, among other things, adverse publicity, warning letters, corrective advertising, and potential civil and criminal penalties. FDA sanctions could include refusal to approve pending applications, withdrawal of an approval, clinical hold, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, mandated corrective advertising or communications with doctors, debarment, restitution, disgorgement of profits, or civil or criminal penalties.

U.S. Patent-Term Restoration and Marketing Exclusivity

Depending upon the timing, duration, and specifics of FDA approval of any future product candidates, some of our U.S. patents may be eligible for limited patent term extension under the Hatch-Waxman Act. The Hatch-Waxman Act permits restoration of the patent term of up to five years as compensation for patent term lost during product development and FDA regulatory review process. Patent-term restoration, however, cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. An application for patent extension must be filed with the USPTO within 60 days of FDA approval of the drug product even if the product cannot be commercially marketed at that time.

The patent term restoration period is generally one-half the time between the effective date of an IND or the issue date of the patent, whichever is later, and the submission date of an NDA plus the time between the submission date of an NDA or the issue date of the patent, whichever is later, and the approval of the NDA

application, except that the review period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved drug is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may apply for restoration of patent term for our currently owned or licensed patents to add patent life beyond our current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA.

Market exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not approve an abbreviated new drug application ("ANDA"), or a 505(b)(2) NDA, submitted by another company for another version of such drug, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. Such three-year and five-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well controlled clinical trials necessary to demonstrate safety and effectiveness.

Other U.S. Regulatory Matters

Our current and future arrangements with healthcare providers, third-party payors, customers, and others may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations, which may constrain the business or financial arrangements and relationships through which we research, as well as, sell, market, and distribute any products for which we obtain marketing approval. The applicable federal, state, and foreign healthcare laws and regulations that may affect our ability to operate include, but are not limited to the following:

- The Anti-Kickback Statute ("AKS"), which makes it illegal for any person, including a prescription drug or medical device manufacturer (or a party acting on its behalf), to knowingly and willfully solicit, receive, offer or pay any remuneration that is intended to induce or reward referrals, including the purchase, recommendation, order or prescription of a particular drug, for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. Moreover, the Patient Protection and Affordable Care Act of 2010 ("ACA") provides that the government may assert that a claim including items or services resulting from a violation of the federal AKS constitutes a false or fraudulent claim for purposes of the federal False Claims Act ("FCA").

- The FCA, including the civil FCA that can be enforced by private citizens through civil whistleblower or qui tam actions, and civil monetary penalties prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease, or conceal an obligation to pay money to the federal government, and/or impose exclusions from federal health care programs and/or penalties for parties who engage in such prohibited conduct.

- The Health Insurance Portability and Accountability Act ("HIPAA") prohibits, among other things, executing or attempting to execute a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters.

- HIPAA also imposes obligations on covered entities such as health insurance plans, healthcare clearinghouses, and certain health care providers and their respective business associates and their

covered subcontractors, including mandatory contractual terms, with respect to safeguarding the privacy, security, and transmission of individually identifiable health information.

- The federal Physician Payments Sunshine Act requires applicable manufacturers of covered drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to annually report to the CMS information regarding certain payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists, and chiropractors), certain non-physician healthcare professionals (such as physician assistants and nurse practitioners, among others), and teaching hospitals, as well as information regarding ownership and investment interests held by physicians and their immediate family members.

- The federal Foreign Corrupt Practice Act ("FCPA") prohibits any U.S. individual or business from paying, offering, or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with: accounting provisions requiring them to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations; analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; state laws that require biotechnology companies to comply with the biotechnology industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; state and local laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures and require the registration of their sales representatives; state laws that require biotechnology companies to report information on the pricing of certain drug products; and state and foreign laws that govern the privacy and security of health information in some circumstances (such as Washington's My Health, My Data Act, which, among other things, provides for a private right of action), many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Pricing and rebate programs must also comply with the Medicaid rebate requirements of the U.S. Omnibus Budget Reconciliation Act of 1990 and more recent requirements in the ACA. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. Manufacturing, sales, promotion, and other activities also are potentially subject to federal and state consumer protection and unfair competition laws. In addition, the distribution of pharmaceutical and/or medical device products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage, and security requirements intended to prevent the unauthorized sale of pharmaceutical and/or medical device products. Products must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act of 1970 as well as other applicable consumer safety requirements.

The failure to comply with any of these laws or regulatory requirements could subject companies to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in significant civil, criminal, and administrative penalties, including damages, fines, disgorgement, imprisonment, exclusion from participation in government funded healthcare programs such as Medicare and Medicaid, integrity oversight and reporting obligations, contractual damages, reputational harm, diminished profits and future earnings, injunctions, requests for recall, seizure of products, total or partial suspension of production, denial or withdrawal of product approvals, or refusal to allow a firm to enter into supply contracts, including government contracts.

Coverage and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidate for which we may seek regulatory approval. Sales in the United States will depend, in part, on the availability of sufficient coverage and adequate reimbursement from third-party payors, which include government health programs such as Medicare, Medicaid, TRICARE, and the Veterans Administration, as well as managed care

organizations and private health insurers. Prices at which our customers may seek reimbursement for our product candidates can be subject to challenge, reduction, or denial by third-party payors.

The process for determining whether a third-party payor will provide coverage for a product is typically separate from the process for setting the reimbursement rate that the payor will pay for the product. A third-party payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be available. Additionally, in the United States there is no uniform policy among payors for coverage or reimbursement. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own coverage and reimbursement policies, but also have their own methods and approval processes. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. If coverage and adequate reimbursement are not available, or are available only at limited levels, successful commercialization of, and/or a satisfactory financial return on, any product we develop may not be possible.

Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. In order to obtain coverage and reimbursement for any product that might be approved for marketing, we may need to conduct expensive studies in order to demonstrate the medical necessity and cost-effectiveness of any products, which would be in addition to the costs expended to obtain regulatory approvals. Third-party payors may not consider our product candidates to be medically necessary or cost-effective compared to other available therapies, or the rebate percentages required to secure favorable coverage may not yield an adequate margin over cost or may not enable us to maintain price levels sufficient to realize an appropriate return on our investment in drug development.

In most foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing and reimbursement vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the European Union do not follow price structures of the United States and generally prices tend to be significantly lower. For more information, see the section entitled "*Risk Factors—We may face difficulties from changes to current regulations and future legislation. Healthcare legislative measures aimed at reducing healthcare costs may have a material adverse effect on our business and results of operations*."

Healthcare Reform

In the United States, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of product candidates, restrict or regulate post-approval activities and affect the profitable sale of product candidates. Among policy makers and payors in the United States, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. In March 2010, the ACA was passed, which substantially changed the way healthcare is financed by both the government and private insurers, and significantly impacts the U.S. pharmaceutical industry.

The ACA, among other things: (1) increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations; (2) created a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for certain drugs and biologics that are inhaled, infused, instilled, implanted, or injected; (3) established an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in certain government healthcare programs; (4) expanded the availability of lower pricing under the 340B drug pricing program by adding new entities to the program; (5) expanded the eligibility criteria for Medicaid programs; (6) created a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in and conduct comparative clinical effectiveness research, along with funding for such research; (7) created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (and 70% commencing January 1,

2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; and (8) established a Center for Medicare Innovation at the CMS, to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drugs.

Since its enactment, there have been executive, judicial, and congressional challenges to certain aspects of the ACA. For example, in June 2021 the U.S. Supreme Court held that Texas and other challengers had no legal standing to challenge the ACA, dismissing the case on procedural grounds without specifically ruling on the constitutionality of the ACA. Further, prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period in 2021 for purposes of obtaining health insurance coverage through the ACA marketplace.

This executive order also instructs certain governmental agencies to review existing policies and rules that limit access to health insurance coverage through Medicaid or the ACA, among others. It is possible that the ACA will be subject to judicial or congressional challenges in the future. It is unclear how any such challenges and healthcare measures promulgated by the Biden administration will impact the ACA, our business, financial condition, and results of operations. Complying with any new legislation or reversing changes implemented under the ACA could be time-intensive and expensive, resulting in a material adverse effect on our business.

Other legislative changes have been proposed and adopted since the ACA was enacted. These changes include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, effective April 1, 2013, which, due to subsequent legislative amendments, will stay in effect through 2032, unless additional congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on customers for our drugs, if approved, and accordingly, our financial operations.

Additionally, there has been heightened governmental scrutiny recently over the manner in which drug manufacturers set prices for their marketed products, which has resulted in several congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for drug products. For example, the American Rescue Plan Act of 2021 eliminated the statutory cap on Medicaid Drug Rebate Program rebates that manufacturers pay to state Medicaid programs. Elimination of this cap may require pharmaceutical manufacturers to pay more in rebates than they receive on the sale of products, which could have a material impact on our business. In August 2022, Congress passed the IRA, which includes prescription drug provisions that have significant implications for the pharmaceutical industry and Medicare beneficiaries, including allowing the federal government to negotiate a maximum fair price for certain high-priced single-source Medicare drugs, imposing penalties and excise tax for manufacturers that fail to comply with the drug price negotiation requirements, requiring inflation rebates for all Medicare Part B and Part D drugs, with limited exceptions, if their drug prices increase faster than inflation, and redesigning Medicare Part D to reduce out-of-pocket prescription drug costs for beneficiaries, among other changes. Only high-expenditure, single-source drugs that have been approved for at least seven years (11 years for single-source biologics) qualify for negotiation, with the negotiated price taking effect two years after the selection year. For 2026, the first year in which negotiated prices become effective, CMS selected 10 high-cost Medicare Part D drugs in 2023, negotiations began in 2024, and the negotiated maximum fair price for each drug has been announced. CMS has selected 15 additional Medicare Part D drugs for negotiated maximum fair pricing in 2027. For 2028, up to an additional 15 drugs, which may be covered under either Medicare Part B or Part D, will be selected, and for 2029 and subsequent years, up to 20 additional Part B or Part D drugs will be selected. Various industry stakeholders, including certain pharmaceutical companies and the Pharmaceutical Research and Manufacturers of America, have initiated lawsuits against the federal government asserting that the price negotiation provisions of the IRA are unconstitutional. The impact of these judicial challenges and other legislative, executive, and administrative actions of the government on us and the pharmaceutical industry as a whole is unclear.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access, and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. A number of states are considering or have

recently enacted state drug price transparency and reporting laws that could substantially increase our compliance burden and expose us to greater liability under such state laws once we begin commercialization after obtaining regulatory approval for any of our products. Further, the FDA has authorized the state of Florida to develop an importation program to import certain prescription drugs from Canada for a limited period to help reduce drug costs, provided that Florida's Agency for Health Care Administration meets the requirements set forth by the FDA. Other states may follow Florida. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our drug candidates or additional pricing pressures. We are unable to predict the future course of federal or state healthcare legislation in the United States directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our product candidates may lose regulatory approval that may have been obtained and we may not achieve or sustain profitability.

Foreign Regulation

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our product candidates to the extent we choose to develop or sell any product candidates outside of the United States. The approval process varies from country to country and the time may be longer or shorter than that required to obtain FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country.

Employees and Human Capital Resources

As of March 7, 2025, we had 46 employees, 35 of whom were engaged in research and development activities. We also engage contractors and consultants. None of our employees are represented by a labor union or covered under a collective bargaining agreement. We have not experienced any work stoppages due to employee disputes, and we consider our relationship with our employees to be good.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing, and integrating our existing and new employees, advisors, and consultants. The principal purposes of our equity and cash incentive plans are to attract, retain and reward personnel through the granting of stock-based and cash-based compensation awards, in order to increase stockholder value and the success of OnKure by motivating such individuals to perform to the best of their abilities and achieve our objectives.

Facilities

Our corporate headquarters is located in Boulder, Colorado, and consists of approximately 15,000 square feet of office and laboratory space pursuant to a lease that expires in December 2026, with the option to extend for a five-year period.

In the Merger, we assumed the lease of approximately 5,100 square feet of office space for the former Reneo headquarters in Irvine, California under a non-cancelable operating lease through November 2026. In January 2025, we subleased this space for the remaining duration of the lease.

We lease all of our facilities and do not own any real property. We believe that our existing facilities are adequate and suitable for our current needs and that, should it be needed, suitable additional or alternative space will be available as and when needed.

Corporate Information

We were incorporated under the laws of the State of Delaware in December 2014. Legacy OnKure was incorporated under the laws of the State of Delaware in March 2011. Pursuant to the Merger, we changed our name from Reneo Pharmaceuticals, Inc. to OnKure Therapeutics, Inc.

Our principal executive offices are located at 6707 Winchester Circle, Suite 400, Boulder, CO 80301, and our telephone number is (720) 307-2892.

Our website address is www.onkure.com. The information on, or that can be accessed through, our website is not part of this Annual Report or our other filings with the SEC. We have included our website address in this Annual Report solely as an inactive textual reference.

We use the OnKure logo and other marks as trademarks in the United States and other countries. This Annual Report contains references to our trademarks and service marks and to those belonging to other entities. Solely for convenience, trademarks and trade names referred to in this Annual Report, including logos, artwork and other visual displays, may appear without a trademark symbol, 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 or the rights of the applicable licensor to these trademarks and trade names. We do not intend our use or display of other entities' trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, any other entity.

Emerging Growth Company

We are an emerging growth company as defined in the Jumpstart Our Business Startups Act of 2012 (the "JOBS Act"). We will remain an emerging growth company until the earliest to occur of: the last day of the fiscal year in which we have more than $1.235 billion in annual revenues; the date we qualify as a "large accelerated filer," with at least $700 million of equity securities held by non-affiliates; the issuance, in any three-year period, by us of more than $1.0 billion in non-convertible debt securities; and the last day of the fiscal year ending after the fifth anniversary of Reneo's initial public offering (i.e., December 31, 2026).

Section 107 of the JOBS Act provides that an emerging growth company can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act of 1933, as amended (the "Securities Act"), for complying with new or revised accounting standards. In other words, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected not to opt out of such extended transition period, which means that when a standard is issued or revised and it has different application dates for public or private companies, we, as an emerging growth company, can adopt the new or revised standard at the time private companies adopt the new or revised standard. This may make comparison of our financial statements with certain other public companies difficult or impossible because of the potential differences in accounting standards used.

Smaller Reporting Company

Additionally, we are a "smaller reporting company" as defined in Item 10(f)(1) of Regulation S-K. Smaller reporting companies may take advantage of certain reduced disclosure obligations, including, among other things, providing only two years of audited financial statements. We may continue to be a smaller reporting company in any given year if either (i) the market value of our stock held by non-affiliates is less than $250 million as of June 30th in the most recently completed fiscal year, or (ii) our annual revenue is less than $100 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than $700 million as of June 30th in the most recently completed fiscal year.

Item 1A. Risk Factors

RISK FACTORS

An investment in shares of our Class A Common Stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this Annual Report, including our consolidated financial statements and the related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations" before deciding whether to purchase, hold or sell shares of our Class A Common Stock. The occurrence of any of the risks described below could harm our business, financial condition, results of operations, growth prospects, and/or stock price or cause our actual results to differ materially from those contained in forward-looking statements we have made in this Annual Report and those we may make from time to time. You should consider all of the risk factors described when evaluating our business. Certain statements below are forward-looking statements. See also "Cautionary Note Regarding Forward-Looking Statements" and "Risk Factor Summary" in this Annual Report.

Risks Related to Our Operating History, Financial Position and Need for Additional Capital

We are early in our development efforts and have no products approved for commercial sale, which may make it difficult for you to evaluate our current business and likelihood of success and future viability.

We are a clinical-stage biopharmaceutical company, have no products approved for commercial sale and have never generated any revenue. Our operations to date have been limited to organizing the company, raising capital and developing our product candidates. We have not yet demonstrated our ability to obtain marketing approvals, manufacture a commercial-scale product or arrange for a third-party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. As a result, it may be difficult for investors to accurately predict our likelihood of success and viability.

In addition, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors and risks frequently experienced by early-stage biopharmaceutical companies in rapidly evolving fields. We also expect that, as we advance our product candidates, we will need to transition from a company with a research and development focus to a company capable of supporting commercial activities. We have not yet demonstrated an ability to successfully overcome such risks and difficulties, or to make such a transition. If we do not adequately address these risks and difficulties or successfully make such a transition, our business will suffer.

We have incurred significant net losses in each period since inception, and we expect to continue to incur significant net losses for the foreseeable future.

We have incurred significant net losses in each reporting period since inception, have not generated any revenue from the sale of products, and have funded our operations primarily from the sale and issuance of equity securities and convertible debt. Our net losses were $52.7 million and $35.3 million for the years ended December 31, 2024 and 2023, respectively. As of December 31, 2024, we had an accumulated deficit of $154.7 million. We have no products approved for sale. As a result, we expect that it will be many years, if ever, before we have a commercialized product and generate revenue from product sales. Even if we succeed in receiving marketing approval for and commercializing one or more of our product candidates, we expect that we will continue to incur substantial research and development and other expenses to discover, develop and market additional product candidates.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue, if any. Our prior losses and expected future losses have had and will continue to have an adverse effect on our working capital, our ability to fund the development of our product candidates, our ability to achieve and maintain profitability and the performance of our stock.

We have never generated revenue from product sales and may never achieve or maintain profitability.

We have never generated any revenue from commercial product sales. To become and remain profitable, we must develop and eventually commercialize product candidates with significant market potential, which will require us to be successful in a range of challenging activities. These activities can include completing preclinical studies and clinical trials of our product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing and selling those products that are approved and satisfying any post-marketing requirements. We do not anticipate generating any revenue from product sales for many years. Our ability to generate revenue and achieve profitability depends significantly on our ability to achieve several objectives, including:

- successful and timely completion of clinical development of OKI-219 and preclinical and clinical development of other pipeline programs and any other future programs;
- establishing and maintaining relationships with contract research organizations (or "CROs") and clinical sites for the clinical development of OKI-219 and any other future programs;
- timely receipt of marketing approvals from applicable regulatory authorities for any product candidates for which we successfully complete clinical development;
- developing an efficient and scalable manufacturing process for our product candidates, including obtaining finished products that are appropriately packaged for sale;
- establishing and maintaining commercially viable supply and manufacturing relationships with third parties that can provide adequate, in both amount and quality, products and services to support clinical development and meet the market demand for our product candidates, if approved;
- successful commercial launch following any marketing approval, including the development of a commercial infrastructure, whether in-house or with one or more collaborators;
- a continued acceptable safety profile following any marketing approval of our product candidates;
- commercial acceptance of our product candidates by patients, the medical community and third-party payors;
- satisfying any required post-marketing approval commitments to applicable regulatory authorities;
- identifying, assessing and developing new product candidates;
- obtaining, maintaining and expanding patent protection, trade secret protection and regulatory exclusivity, both in the United States and internationally;
- defending against third-party interference or infringement claims, if any;
- entering into, on favorable terms, any collaboration, licensing or other arrangements that may be necessary or desirable to develop, manufacture or commercialize our product candidates;
- obtaining and maintaining coverage and adequate reimbursement by third-party payors for our product candidates;
- addressing any competing therapies and technological and market developments; and
- attracting, hiring and retaining qualified personnel.

We may never be successful in achieving our objectives and, even if we do, may never generate revenue that is significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease our value and could impair our ability to maintain or further our research and development efforts, raise additional necessary capital, grow our business and continue our operations.

Any changes in the manufacturing process, suppliers, or facilities will require further comparability analysis and approval by the U.S. Food and Drug Administration (the "FDA") before implementation, which could

delay our clinical trials and product candidate development, and could require additional clinical trials, including bridging studies, to demonstrate consistent and continued safety and efficacy.

We have not previously submitted an NDA to the FDA or similar approval filings to a comparable foreign regulatory authority for any product candidate. An NDA or other relevant regulatory filing must include extensive nonclinical and clinical data and supporting information to establish that the product candidate is safe and effective for each desired indication. The NDA or other relevant regulatory filing must also include significant information regarding the chemistry, manufacturing and controls for the product candidate. We cannot be certain that our current or future product candidates will be successful in clinical trials or receive regulatory approval. If we do not receive regulatory approvals for current or future product candidates, we may not be able to continue our operations. Even if we successfully obtain regulatory approval to market a product candidate, our revenue will depend, in part, upon the size of the markets in the territories for which we receive regulatory approval and have commercial rights, the availability of competitive therapies and whether there are sufficient levels of reimbursement and adoption by physicians.

We will need substantial additional funding before we can complete the development of our product candidates. If we are unable to obtain such additional capital on favorable terms, on a timely basis or at all, we would be forced to delay, reduce or eliminate our product development and clinical programs and may not have the capital required to otherwise operate our business.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is expensive. We have not generated any revenues from the commercial sale of products and will not be able to generate any product revenues until, and only if, we receive approval to sell our product candidates from the FDA or other regulatory authorities. Our cash, cash equivalents and short term investments are expected to fund operations into the fourth quarter of 2026. However, as we have not generated any revenue from commercial sales to date and do not expect to generate any revenue for several years, if ever, we will need to raise substantial additional capital in order to fund our general corporate activities and to fund our research and development, including our currently planned clinical trials and plans for new clinical trials and product development.

We may seek to raise additional funds through various potential sources, such as equity and debt financings, or through strategic collaborations and license agreements. We can give no assurances that we will be able to secure such additional sources of funds to support our operations or, if such funds are available, that such additional financing will be sufficient to meet our needs. Moreover, to the extent that we raise additional funds by issuing equity securities, our stockholders may experience additional significant dilution and new investors could gain rights, preferences and privileges senior to the holders of common stock. Debt financing, if available, may involve restrictive covenants. To the extent that we raise additional funds through collaboration and licensing arrangements, it may be necessary to relinquish some rights to our technologies or product candidates, or grant licenses on terms that may not be favorable.

Given our capital constraints, we will need to prioritize spending on our clinical and preclinical programs. If we are unable to raise sufficient funds to support our current and planned operations, we may elect to discontinue certain of our ongoing activities or programs. Our inability to raise additional funds could also prevent us from taking advantage of opportunities to pursue promising new or existing programs in the future.

Our forecasts regarding the sufficiency of our financial resources to support our current and planned operations are forward-looking statements and involve significant risks and uncertainties, and actual results could vary as a result of a number of factors, including the factors discussed elsewhere in this "*Risk Factors*" section. These estimates are based on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than currently expected.

Risks Related to Our Development and Commercialization of Our Product Candidates

We are substantially dependent on OKI-219. If we are unable to advance OKI-219 through clinical development, obtain regulatory approval and ultimately commercialize such product candidate, or experience significant delays in doing so, our business will be materially harmed.

We are currently evaluating OKI-219 in a Phase 1 clinical trial. We will be required to demonstrate thorough, adequate and well controlled clinical trials that OKI-219 is safe and effective, with a favorable benefit-risk profile, for use in its target indication before we can seek regulatory approvals for its commercial sale. Our initial

clinical trials will begin with relatively small cohorts before expanding in size in subsequent cohorts. If safety issues arise in an early cohort, we may be delayed or prevented from subsequently expanding into larger trial cohorts. Our ability to generate product revenue, which we do not expect will occur for many years, if ever, will depend heavily on the successful clinical development and eventual commercialization of OKI-219. We are not permitted to market or promote any product candidate before we receive marketing approval from the FDA, European Medicines Agency ("EMA") or any comparable foreign regulatory authorities, and we may never receive such marketing approvals.

We have limited resources and are currently focusing our efforts on OKI-219 for development in particular indications and advancing our other discovery research programs. As a result, we may fail to capitalize on programs, product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

We are currently focusing our resources and efforts on OKI-219 and advancing our other research programs. Because we have limited financial and managerial resources, we must focus on a limited number of research programs and product candidates and on specific indications. As a result, we may forgo or delay pursuit of opportunities for other indications or with other product candidates that may have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development activities for OKI-219 and our other research programs may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target markets for OKI-219 and our other research programs, or the product candidates we are currently developing in these programs, we may relinquish valuable rights to our product candidates or programs through collaboration, licensing or other strategic arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate or program.

If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we would incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct preclinical studies in animals and extensive clinical trials in humans to demonstrate the safety and efficacy of the product candidates. Clinical testing is expensive and difficult to design and implement, can take many years to complete and has uncertain outcomes. The outcome of preclinical studies and early clinical trials may not predict the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in advanced clinical trials due to lack of efficacy or unacceptable safety profiles, notwithstanding promising results in earlier trials. We do not know whether the clinical trials we may conduct will demonstrate adequate efficacy and safety to result in regulatory approval to market any of our product candidates in any jurisdiction. Our product candidates may fail to demonstrate efficacy in humans, and particularly across tumor types. A product candidate may fail for safety or efficacy reasons at any stage of the testing process. A major risk we face is the possibility that none of our product candidates under development will successfully gain market approval from the FDA, EMA or other comparable foreign regulatory authorities, resulting in our being unable to derive any commercial revenue from them after investing significant amounts of capital in their development.

If the results of our ongoing or future preclinical studies and future clinical trials are inconclusive with respect to the safety and efficacy of our product candidates, if our trials do not meet the clinical endpoints with statistical and clinically meaningful significance, or if there are safety concerns associated with our product candidates, we may be prevented or delayed in obtaining marketing approval for such product candidates. In some instances, there can be significant variability in safety or efficacy results between different preclinical studies and clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the clinical trial protocols and the rate of dropout among clinical trial participants.

Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or adverse events. In such an event, our trials could be suspended or terminated and the FDA, EMA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. Treatment-related side effects could also affect patient recruitment or

the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

Further, our product candidates could cause undesirable side effects in clinical trials related to on-target toxicity. If on-target toxicity is observed, or if our product candidates have characteristics that are unexpected, we may need to abandon their development or limit development to more narrow indications or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many compounds that initially showed promise in early stage testing for treating cancer have later been found to cause side effects that prevented further development of the compound.

The regulatory approval processes of the FDA, EMA and other comparable foreign regulatory authorities are lengthy, time-consuming and inherently unpredictable. If we are ultimately unable to obtain regulatory approval of our product candidates, we will be unable to generate product revenue and our business will be substantially harmed.

Our product candidates are and will continue to be subject to extensive governmental regulations relating to, among other things, research, testing, development, manufacturing, safety, efficacy, approval, recordkeeping, reporting, labeling, storage, packaging, advertising and promotion, pricing, marketing and distribution of drugs. Rigorous preclinical testing and clinical trials and an extensive regulatory approval process must be successfully completed in the United States and in many foreign jurisdictions before a new drug can be approved for marketing.

Obtaining approval by the FDA, EMA and other comparable foreign regulatory authorities is unpredictable, typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the type, complexity and novelty of the product candidates involved. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions, which may cause delays in the approval or the decision not to approve an application. For example, FDA's Oncology Center of Excellence initiated Project Optimus to reform the dose optimization and dose selection paradigm in oncology drug development and Project FrontRunner to help develop and implement strategies to support approvals in early clinical setting, among other goals. How the FDA plans to implement these goals and their impact on specific clinical programs and the industry are unclear. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other data. Even if we eventually complete clinical testing and receive approval for our product candidates, the FDA, EMA and other comparable foreign regulatory authorities may approve our product candidates for a more limited indication or a narrower patient population than originally requested or may impose other prescribing limitations or warnings that limit the product candidate's commercial potential. We have not submitted for, or obtained, regulatory approval for any product candidate, and it is possible that none of our product candidates will ever obtain regulatory approval. Further, development of our product candidates and/or regulatory approval may be delayed for reasons beyond our control.

Applications for our product candidates could fail to receive regulatory approval for many reasons, including the following:

- the FDA, EMA or other comparable foreign regulatory authorities may disagree with the design, implementation or results of our clinical trials;
- the FDA, EMA or other comparable foreign regulatory authorities may determine that our product candidates are not safe and effective, are only moderately effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use;
- the population studied in the clinical trial may not be sufficiently broad or representative to assure efficacy and safety in the full population for which we seek approval;
- the FDA, EMA or other comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- we may be unable to demonstrate to the FDA, EMA or other comparable foreign regulatory authorities that a product candidate's risk-benefit ratio for its proposed indication is acceptable;

- the FDA, EMA or other comparable foreign regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications or facilities of third-party manufacturers with which we contract for clinical and commercial supplies;
- the FDA, EMA or other comparable regulatory authorities may fail to approve companion diagnostic tests required for our product candidates; and
- the approval policies or regulations of the FDA, EMA or other comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

In addition, even if clinical trials are successfully completed, we cannot guarantee that the FDA or foreign regulatory authorities will interpret the results as we do, and more trials could be required before we submit our product candidates for approval. For example, although we have sought and received feedback from the FDA on the designs of our clinical trials and intend to continue to do so, the FDA may ultimately disagree that our trials support approval for OKI-219. Moreover, results acceptable to support approval in one jurisdiction may be deemed inadequate by another regulatory authority to support regulatory approval in that other jurisdiction. To the extent that the results of the trials are not satisfactory to the FDA or foreign regulatory authorities for support of a marketing application, we may be required to expend significant resources, which may not be available, to conduct additional trials in support of potential approval of our product candidates. Even if we secure regulatory approval for any of our product candidates, the terms of such approval may limit the scope and use of the product candidate, which may also limit its commercial potential.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- incur unplanned costs;
- be delayed in obtaining marketing approval for our product candidates or not obtain marketing approval at all;
- obtain marketing approval in some countries and not in others;
- obtain marketing approval for indications or patient populations that are not as broad as intended or desired;
- obtain marketing approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings;
- be subject to additional post-marketing testing requirements;
- be subject to changes in the way the product is administered; or
- have regulatory authorities withdraw or suspend their approval of the product.

We cannot be certain that our planned clinical trials or any other future clinical trials will be successful. Additionally, any safety concerns observed in any one of our clinical trials in our targeted indications could limit the prospects for regulatory approval of our product candidates in those and other indications, which could have a material adverse effect on our business, financial condition and results of operations.

In addition, the FDA and other regulatory authorities may change their policies, issue additional regulations or revise existing regulations, or take other actions, such as those implemented by the Department of Government Efficiency, which may prevent or delay approval of our products under development on a timely basis. Such policy or regulatory changes could impose additional requirements upon us that could delay our ability to obtain approvals, increase the costs of compliance or restrict our ability to maintain any marketing authorizations we may have obtained. In view of the overturning of the *Chevron* doctrine in *Loper Bright Enterprises v. Raimondo*, this Supreme Court decision may invite various stakeholders to bring lawsuits against the FDA to challenge longstanding decisions and policies. Additionally, changes in the leadership of the FDA and other federal agencies under the Trump administration may also lead to new policies and changes in the regulations and operations of the FDA, which may impact our clinical development plans.

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval of our product candidates in other jurisdictions.

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction. For example, even if the FDA grants marketing approval of a product candidate, comparable regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing and promotion and pricing of the product candidate in those countries. However, a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from those in the United States, including additional nonclinical studies or clinical trials, as clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, the pricing of a prescription drug candidate is subject to regulatory approval before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products is also subject to approval.

We may also submit marketing applications in other countries. Regulatory authorities in jurisdictions outside of the United States have requirements for approval of product candidates with which we must comply prior to marketing in those jurisdictions. Obtaining foreign regulatory approvals and establishing and maintaining compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we or any future collaborator fails to comply with the regulatory requirements in international markets or fails to receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our potential product candidates will be harmed.

If we experience delays or difficulties in the enrollment or retention of subjects in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

Trials may be subject to delays as a result of patient withdrawal or patient enrollment taking longer than anticipated. We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of subjects to participate to such trials' conclusion as required by the FDA, EMA or other comparable foreign regulatory authorities. Patient enrollment is a significant factor in the timing of clinical trials. While our Phase 1 dose-escalation and expansion cohort trial, OKI-219-101, known as PIKture-01, has begun enrollment, future difficulties we experience relating to enrollment in our clinical trials, or complications in the PIKture-01 trial or future clinical trials, could delay regulatory approval for OKI-219 or our future product candidates.

Patient enrollment may be affected if our competitors have ongoing clinical trials for product candidates that are under development for the same indications as our product candidates, and subjects who would otherwise be eligible for our clinical trials instead enroll in clinical trials of our competitors' product candidates. Patient enrollment for any of our future clinical trials may be affected by other factors, including:

- size and nature of the patient population, and process for identifying patients;
- severity and difficulty of diagnosing the condition under investigation;
- availability and efficacy of approved drugs and other competing therapeutic candidates for the condition under investigation;
- the eligibility and exclusion criteria for the trial in question as defined in the protocol;

- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- the design of the clinical trial;
- perceived risks and benefits of the product candidate under study;
- participants' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new products that may be approved for the indications we are investigating;
- efforts to facilitate timely enrollment in clinical trials;
- participant referral practices of doctors;
- the ability to monitor participants adequately during and after treatment;
- proximity and availability of clinical trial sites for prospective trial subjects;
- continued enrollment of prospective subjects by clinical trial sites; and
- the risk that subjects enrolled in clinical trials will drop out of the trials before completion.

Our inability to enroll a sufficient number of subjects for our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates and jeopardize our ability to obtain marketing approval for the sale of our product candidates. Furthermore, we expect to rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials, and we will have limited influence over their performance. Even if we are able to enroll a sufficient number of subjects for our clinical trials, we may have difficulty maintaining enrollment of such subjects in our clinical trials.

Our product candidates may cause significant adverse events, toxicities or other undesirable side effects when used alone or in combination with other approved products or investigational new drugs that may result in a safety profile that could prevent regulatory approval, prevent market acceptance, limit their commercial potential or result in significant negative consequences.

If our product candidates are associated with undesirable side effects or have unexpected characteristics in preclinical studies or clinical trials when used alone or in combination with other approved products or investigational new drugs, we may need to interrupt, delay or abandon their development or limit development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Treatment-related side effects could also affect patient recruitment or the ability of enrolled subjects to complete the trial or result in potential product liability claims. Any of these occurrences may prevent us from achieving or maintaining market acceptance of the affected product candidate and may harm our business, financial condition and prospects significantly.

Patients in our ongoing and planned clinical trials may suffer significant adverse events or other side effects not observed in our preclinical studies or previous clinical trials. Patients treated with our product candidates may also be undergoing surgical, radiation and chemotherapy treatments, which can cause side effects or adverse events that are unrelated to our product candidate but may still impact the success of our clinical trials. The inclusion of critically ill patients in our clinical trials may result in deaths or other adverse medical events due to other therapies or medications that such patients may be using or due to the gravity of such patients' illnesses. For example, it is expected that some of the patients enrolled in our clinical trials will die or experience major clinical events either during the course of our clinical trials or after participating in such trials.

If significant adverse events or other side effects are observed in any of our current or future clinical trials, we may have difficulty recruiting patients to the clinical trials, patients may drop out of our trials, or we may be required to abandon the trials or our development efforts of that product candidate altogether. We, the FDA, and other comparable regulatory authorities or an IRB may suspend clinical trials of a product candidate at any time for various reasons, including a belief that subjects in such trials are being exposed to unacceptable health risks or adverse side effects. Some potential therapeutics developed in the biotechnology industry that initially showed

therapeutic promise in early-stage trials have later been found to cause side effects that prevented their further development. Even if the side effects do not preclude the product candidate from obtaining or maintaining marketing approval, undesirable side effects may inhibit market acceptance due to its tolerability versus other therapies. Any of these developments could materially harm our business, financial condition and prospects. Further, if any of our product candidates obtains marketing approval, toxicities associated with such product candidates previously not seen during clinical testing may also develop after such approval and lead to a requirement to conduct additional clinical safety trials, additional contraindications, warnings and precautions being added to the drug label, significant restrictions on the use of the product or the withdrawal of the product from the market. We cannot predict whether our product candidates will cause toxicities in humans that would preclude or lead to the revocation of regulatory approval based on preclinical studies or early-stage clinical trials.

The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and the results of our clinical trials may not satisfy the requirements of the FDA, EMA or other comparable foreign regulatory authorities.

We will be required to demonstrate with substantial evidence through well controlled clinical trials that our product candidates are safe and effective for use in a diverse population before we can seek marketing approvals for their commercial sale. Success in preclinical studies and early-stage clinical trials does not mean that future clinical trials will be successful. For example, we previously decided to cease developing another product candidate, known as OKI-179, despite promising early data. In addition, in December 2024, we announced preliminary safety, tolerability and PK data from PIKture-01, with a cutoff date of October 28, 2024, which supported our initiation of Part 1b of PIKture-01. These data are considered preliminary, and we plan to provide updated data in the second half of 2025. We cannot predict whether these updated data will be consistent with the preliminary data announced in December 2024, or whether the data from Part 1b of PIKture-01 will be positive or consistent with our preliminary data from Part 1a of PIKture-01. If the updated data from Part 1a or the future data from Part 1b of PIKture-01 are not positive or fail to support further advancement of OKI-219, we could experience volatility or a substantial decline in our stock price. Further, even if such data are positive, future clinical trials of OKI-219 may not be successful.

Product candidates in later-stage clinical trials may fail to demonstrate sufficient safety and efficacy to the satisfaction of the FDA and other comparable foreign regulatory authorities despite having progressed through preclinical studies and early-stage clinical trials. Regulatory authorities may also limit the scope of later-stage trials until we have demonstrated satisfactory safety, which could delay regulatory approval, limit the size of the patient population to which we may market our product candidates, or prevent regulatory approval.

In some instances, there can be significant variability in safety and efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial protocols, differences in size and type of the patient populations, differences in and adherence to the dose and dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. Patients treated with our product candidates may also be undergoing surgical, radiation and chemotherapy treatments and may be using other approved products or investigational new drugs, which can cause side effects or adverse events that are unrelated to our product candidates. As a result, assessments of efficacy can vary widely for a particular patient, and from patient to patient and site to site within a clinical trial. This subjectivity can increase the uncertainty of, and adversely impact, our clinical trial outcomes.

We may also experience issues in conducting our clinical trials that would delay or prevent us from satisfying the applicable requirements of the FDA and other regulatory authorities, including:

- inability to generate sufficient preclinical, toxicology, or other in vivo or in vitro data to support the initiation of clinical trials for any future product candidates;
- delays in sufficiently developing, characterizing or controlling a manufacturing process suitable for advanced clinical trials;
- delays in reaching agreement with the FDA or other regulatory authorities as to the design or implementation of our clinical trials;
- obtaining regulatory authorization to commence a clinical trial;

- delays in reaching, or failing to reach, agreement on acceptable terms with clinical trial sites or prospective CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different clinical trial sites;
- obtaining approval at each trial site;
- recruiting suitable patients to participate in a clinical trial;
- having patients complete a clinical trial or return for post-treatment follow-up;
- inspections of clinical trial sites or operations by applicable regulatory authorities, or the imposition of a clinical hold;
- clinical sites, CROs or other third parties deviating from trial protocol or dropping out of a trial;
- failure to perform in accordance with applicable regulatory requirements, including the FDA's current GCP requirements, or applicable regulatory requirements in other countries;
- addressing patient safety concerns that arise during the course of a trial, including occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- adding a sufficient number of clinical trial sites;
- manufacturing sufficient quantities of product candidate for use in clinical trials; or
- suspensions or terminations by IRBs of the institutions at which such trials are being conducted, or by the FDA or other regulatory authorities due to a number of factors, including those described above.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates or significantly increase the cost of such trials, including:

- changes in regulatory requirements or guidance, or receive feedback from regulatory authorities that requires us to modify the design of our clinical trials;
- clinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon development programs;
- the number of patients required for clinical trials may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we or our investigators might have to suspend or terminate clinical trials for various reasons, including non-compliance with regulatory requirements, a finding that a product candidate has undesirable side effects or other unexpected characteristics, or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials may be greater than we anticipate and we may not have funds to cover the costs;
- the supply or quality of product candidates or other materials necessary to conduct clinical trials may be insufficient or inadequate;
- regulators may revise the requirements for approving our product candidates, or such requirements may not be as we anticipate; and
- any future collaborators that conduct clinical trials may face any of the above issues and may conduct clinical trials in ways they view as advantageous to them but that are suboptimal for us.

We do not know whether any clinical trials we may conduct will demonstrate efficacy and safety sufficient to obtain approval to market any of our product candidates.

Interim, initial, "top-line" and preliminary data from clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose interim, preliminary or top-line data from our preclinical studies and clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available or as patients from our clinical trials continue other treatments for their condition. Preliminary or top-line data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim, preliminary and top-line data should be viewed with caution until the final data are available. We also make assumptions, estimations, and calculations, and draw conclusions, as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the top-line or preliminary results that we report may differ from future results of the same studies or trials, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. For example, in December 2024, we announced preliminary safety, tolerability and PK data from PIKture-01, with a cutoff date of October 28, 2024, which supported our initiation of Part 1b of PIKture-01. These data are considered preliminary, and we plan to provide updated data in the second half of 2025. We cannot predict whether these updated data will be consistent with the preliminary data announced in December 2024, or whether the data from Part 1b of PIKture-01 will be positive or consistent with our preliminary data from Part 1a of PIKture-01. If the updated data from Part 1a or the future data from Part 1b of PIKture-01 are not positive or fail to support further advancement of OKI-219, we could experience volatility or a substantial decline in our stock price. Further, even if such data are positive, future clinical trials of OKI-219 may not be successful.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program or the approvability or commercialization of the particular product candidate, and could have a material adverse effect on the success of our business. In addition, the information we choose to disclose publicly regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure. If the interim, top-line or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for and commercialize our product candidates may be harmed, which could harm our business, results of operations, prospects or financial condition. Further, disclosure of interim, top-line or preliminary data by us or by our competitors could result in volatility in the price of our Class A Common Stock.

Changes in methods of product candidate manufacturing or formulation may result in additional costs or delay.

As product candidates progress through preclinical and clinical trials to marketing approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize yield and manufacturing batch size, minimize costs and achieve consistent quality and results. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the altered materials. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of product candidates and jeopardize our ability to commercialize our product candidates, if approved, and generate revenue.

We may develop programs in combination with other therapies, which exposes us to additional risks.

We intend to develop OKI-219, and may develop any other product candidate we develop, in combination with one or more currently approved cancer therapies or therapies in development. Patients may not be able to tolerate our product candidates in combination with other therapies, or dosing of our product candidates in combination with other therapies may have unexpected consequences. Even if any of our product candidates were to receive marketing approval or be commercialized for use in combination with other existing therapies, we would continue to be subject to risks that the FDA or other comparable foreign regulatory authorities could revoke

approval of the therapy used in combination with our product candidates, or safety, efficacy, manufacturing or supply issues could arise with these existing therapies. In addition, it is possible that existing therapies with which our product candidates may be approved for use could themselves fall out of favor or be relegated to later lines of treatment. This could result in the need to identify other combination therapies for our product candidates or our products being removed from the market or being less successful commercially. If the FDA or other comparable foreign regulatory authorities do not approve or revoke their approval of these other therapies, or if safety, efficacy, commercial adoption, manufacturing or supply issues arise with the therapies we choose to evaluate in combination with our product candidates, we may be unable to obtain approval of or successfully market any or all of the product candidates we develop.

Additionally, if the third-party providers of therapies or therapies in development used in combination with our product candidates are unable to produce sufficient quantities for clinical trials or for commercialization of our product candidates, or if the cost of combination therapies is prohibitive, our development and commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations and growth prospects.

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

The pharmaceutical and biotechnology industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We face increasing competition from many different sources, including pharmaceutical and biotechnology companies, academic institutions, governmental agencies and public and private research institutions. Product candidates that we successfully develop and commercialize may compete with existing therapies, and new therapies that may become available in the future.

Many of our competitors, either alone or with their collaborators, have significantly greater financial resources, established presence in the market and expertise in research and development, manufacturing, preclinical and clinical testing, obtaining regulatory approvals and reimbursement and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. Additional mergers and acquisitions may result in even more resources being concentrated in our competitors. As a result of these factors, our competitors may succeed in obtaining approval from the FDA, EMA or other comparable foreign regulatory authorities or in discovering, developing and commercializing product candidates in our field before we do.

There are multiple PI3Kα-pathway targeted agents either approved or under clinical development that will potentially compete with OKI-219 and our PI3Kα-targeted portfolio. Alpelisib (Piqray, a PI3Kα-selective inhibitor marketed by Novartis) and capivasertib (Truquap, an AKT1 inhibitor marketed by AstraZeneca) are marketed medicines, both of which are approved for the treatment of PI3Kα-mutated breast cancer patients in combination with the selective estrogen receptor degrader ("SERD") fulvestrant. Additionally, the PI3Kα-selective inhibitor inavolisib (Itovebi™) was recently approved in combination with the SERD fulvestrant and the CDK4/6 inhibitor palbociclib (Ibrance™) in endocrine resistant HR+/Her2- locally advanced or metastatic breast cancer.

We are also aware of several novel PI3K-targeted therapies that are in clinical development. This includes both multiple non-mutation-selective PI3K inhibitors (gedatolisib (Celcuity Inc.); MEN1611 (menarini) and TOS-358 (Totus Medicines)) and inhibitors designed to have greater selectivity for mutated PI3Kα, including RLY-2608 (Relay Therapeutics), STX-473 (Loxo Oncology). Multiple other companies have disclosed or published research efforts in PI3K inhibitors that are at an early stage, but could potentially advance to the clinical trial stage. Finally, there are numerous other investigational therapies, spanning many modalities that are being evaluated preclinically and in clinical trials for breast cancer.

Our commercial potential could be reduced or eliminated if our competitors develop and commercialize products that are safer or more effective, have fewer or less severe side effects or are more convenient or less expensive than products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we can, which could make our development more complicated or result in our competitors establishing a strong market position before we are able to enter the market.

Technological advances or products developed by our competitors may render our technologies or product candidates obsolete, less competitive or not economical. If we are unable to compete effectively, our opportunity to generate revenue from the sale of our product candidates, if approved, could be adversely affected.

Even if OKI-219 or any other product candidate receives marketing approval, they may fail to achieve market acceptance among physicians, patients, third-party payors and others in the medical community.

If OKI-219 or any other product candidate that we develop receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. The degree of market acceptance of OKI-219 or any other product candidate that we develop, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and potential advantages of our product candidates compared to alternative treatments, including the existing standard-of-care;
- our ability to offer products for sale at competitive prices;
- the clinical indications for which the product is approved;
- restrictions on the use of product candidates in the labeling approved by regulatory authorities, such as boxed warnings or contraindications in labeling, or a REMS, if any, which may not be required of alternative treatments and competitor products;
- the cost of treatment in relation to alternative treatments;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of doctors to prescribe these therapies;
- the strength of our marketing and distribution support;
- the timing of market introduction of competitive products;
- the availability of an approved product candidate for use as a combination therapy;
- the potential for our competitors to limit our access to the market through anti-competitive contracts or other arrangements;
- unfavorable publicity relating to our product candidates;
- the prevalence and severity of any side effects; and
- any restrictions on the use of our products together with other medications.

If any of our product candidates are approved but do not achieve an adequate level of market acceptance, we may not generate or derive sufficient revenue from that product candidate and our financial results could be negatively impacted.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market our product candidates on acceptable terms, we may be unable to successfully commercialize our product candidates that obtain regulatory approval.

If OKI-219 or another product candidate is approved, we must build marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services for each of the territories in which we intend to sell and market our product candidates. We may not be successful in accomplishing these required tasks.

Establishing and building out an internal sales and marketing team with technical expertise and supporting distribution capabilities to commercialize our product candidates will be expensive and time-consuming and will require significant attention of our executive officers to manage. Any failure or delay in the development of our internal sales, marketing and distribution capabilities could adversely impact the commercialization of any of our product candidates that we obtain approval to market, if we do not have arrangements in place with third parties to

provide such services on our behalf. Alternatively, if we choose to collaborate, either globally or on a territory-by-territory basis, with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems, we will be required to negotiate and enter into arrangements with such third parties relating to the proposed collaboration. If we are unable to enter into such arrangements when needed, on acceptable terms, or at all, we may not be able to successfully commercialize any of our product candidates that receive regulatory approval, or any such commercialization may experience delays or limitations. If we are unable to successfully commercialize our approved product candidates, either on our own or through collaborations with one or more third parties, our future product revenue will suffer, and we may incur significant additional losses.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our products, if approved.

Our business exposes us to significant product liability risks inherent in the development, testing, manufacturing and marketing of therapeutic treatments. Product liability claims could delay or prevent completion of our development programs. If our product candidates are approved for marketing, such claims could still result in an FDA, EMA or other regulatory authority investigation of the safety and effectiveness of such products, our manufacturing processes and facilities or our marketing programs. These investigations could potentially lead to a recall of our products or more serious enforcement actions, limitations on the approved indications for which they may be used or suspension or withdrawal of approvals. Regardless of the merits or eventual outcome, liability claims may also result in injury to our reputation, withdrawal of clinical trial participants, costs to defend the related litigation, a diversion of management's time and our resources, initiation of investigations by regulators, substantial monetary awards to patients or other claimants, the inability to commercialize our product candidates and decreased demand for our product candidates, if approved for commercial sale. We currently have product liability insurance that we believe is appropriate for our stage of development and may need to obtain higher levels prior to marketing any of our product candidates, if approved. Any insurance we have or may obtain may not provide sufficient coverage against potential liabilities and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business and cause the price of our Class A Common Stock to decline. Furthermore, clinical trial and product liability insurance is becoming increasingly expensive. As a result, we may be unable to maintain or obtain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses, including those caused by product liability claims.

Any product candidates we develop may become subject to unfavorable third-party coverage and reimbursement practices, as well as pricing regulations.

The availability and extent of coverage and adequate reimbursement by third-party payors, including government health administration authorities, private health coverage insurers, managed care organizations and other third-party payors is essential for most patients to be able to afford expensive treatments. Sales of any of our product candidates that receive marketing approval will depend substantially, both in the United States and internationally, on the extent to which the costs of such product candidates will be covered and reimbursed by third-party payors. If reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize an adequate return on investment. Coverage and reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we may not successfully commercialize any product candidate for which we obtain marketing approval.

There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved products. In the United States, for example, principal decisions about reimbursement for new products are typically made by the Centers for Medicare & Medicaid Services ("CMS"), an agency within the U.S. Department of Health and Human Services ("HHS"). CMS decides whether and to what extent a new product will be covered and reimbursed under Medicare, and private third-party payors often follow CMS's decisions regarding coverage and reimbursement to a substantial degree. However, one third-party payor's determination to provide coverage for a product candidate does not assure that other payors will also provide coverage for the product candidate. As a result, the coverage determination process is often time-consuming and costly. This process will require us to provide scientific and clinical support for the use of our products to each third-party payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Further, such payors are increasingly challenging the price, examining the medical necessity and reviewing the cost effectiveness of medical product candidates. There may be especially significant delays in obtaining coverage and reimbursement for newly approved drugs. Third-party payors may limit coverage to specific product candidates on an approved list, known as a formulary, which might not include all FDA-approved drugs for a particular indication. We may need to conduct expensive pharmaco-economic studies to demonstrate the medical necessity and cost effectiveness of our products. Nonetheless, our product candidates may not be considered cost effective. We cannot be sure that coverage and reimbursement will be available for any product that we commercialize and, if reimbursement is available, what the level of reimbursement will be.

Outside the United States, the commercialization of therapeutics is generally subject to extensive governmental price controls and other market regulations, and we believe that the increasing emphasis on cost containment initiatives in Europe, Canada and other countries has and will continue to put pressure on the pricing and usage of therapeutics such as our product candidates. In many countries, particularly the countries of the European Union, medical product prices are subject to varying price control mechanisms as part of national health systems. In these countries, pricing negotiations with governmental authorities can take considerable time after a product receives marketing approval. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost effectiveness of a product candidate to other available therapies. In general, product prices under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for products but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

If we are unable to establish or sustain coverage and adequate reimbursement for any product candidates from third-party payors, the adoption of those products and sales revenue will be adversely affected, which, in turn, could adversely affect the ability to market or sell those product candidates, if approved. Coverage policies and third-party payor reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

A variety of risks associated with marketing our product candidates internationally could materially adversely affect our business.

We are developing regulatory strategies for our product candidates outside the United States and, accordingly, we expect that we or our partners would seek regulatory approval of our product candidates outside of the United States. As such, we expect that we will be subject to additional risks related to operating in foreign countries if we or such partners obtain the necessary approvals, including:

- differing regulatory requirements and drug pricing regimes in foreign countries;
- unexpected changes in tariffs, trade barriers, price and exchange controls and other regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- difficulties staffing and managing foreign operations;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- potential liability under the FCPA or comparable foreign regulations;

- challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism.

These and other risks associated with our international operations or those of any applicable international partners may materially adversely affect our ability to attain or maintain profitable operations.

In particular, there is currently significant uncertainty about the future relationship between the United States and various other countries, most significantly China, with respect to trade policies, including sanctions, treaties, tariffs, taxes, regulatory requirements, and other limitations on cross-border operations. For example, the Trump administration has announced plans to significantly increase tariffs on foreign imports into the United States, particularly from Canada and Mexico, and has already increased tariffs on imports from China. The U.S. government has made and continues to make significant additional changes in U.S. trade policy and may continue to take future actions that could negatively impact U.S. trade. For example, legislation has been introduced in Congress to limit certain interactions with certain Chinese biotechnology companies. We cannot predict what actions may ultimately be taken with respect to trade relations between the United States and China or other countries, what interactions, including products or services, may be subject to such actions, or what actions may be taken by the other countries in retaliation. If our interactions with parties affected by any such actions are limited or no longer possible, our business, liquidity, financial condition, or results of operations could be materially and adversely affected.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain sufficient intellectual property protection for our technology and products and product candidates we may develop, or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors or other third parties could develop and commercialize products similar or identical to ours, and our ability to successfully develop and, if approved, commercialize our product candidates may be adversely affected.

We rely upon a combination of patents, trademarks, trade secret protection and confidentiality agreements to protect the intellectual property related to our development programs and product candidates. Our success depends in part on our ability to obtain and maintain patent protection in the United States and other countries with respect to OKI-219 and any future product candidates. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our development programs, product candidates and novel discoveries that are important to our business. The patent prosecution process is expensive and time-consuming, and we may not be able to file, prosecute, enforce or license all necessary or desirable patent applications at a reasonable cost or in a timely manner.

The patents and patent applications that we own may fail to result in issued patents with claims that protect OKI-219 or any future product candidate in the United States or in other foreign countries. There is no assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found, which can prevent a patent from issuing from a pending patent application, or be used to invalidate a patent. Even if patents do successfully issue and even if such patents cover OKI-219 or any future product candidate, third parties may challenge their validity, enforceability or scope, which may result in such patents being narrowed, invalidated or held unenforceable. Any successful opposition to these patents or any other patents owned by or licensed to us could deprive us of rights necessary for the successful commercialization of any product candidates that we may develop. Further, the scope and coverage of such patents may be so narrow that a third party could successfully design around our patents without materially impacting the therapeutic effectiveness of the resulting drug product. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced.

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our potential future collaborators will be successful in protecting our product candidates by obtaining and defending patents. These risks and uncertainties include the following:

- the United States Patent and Trademark Office (the "USPTO") and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process, the noncompliance with which can result in abandonment or lapse of a patent or patent application, and partial or complete loss of patent rights in the relevant jurisdiction;
- the USPTO requires us to disclose all material references to the patent examiner during prosecution of our patent applications, and failure to do so could result in a third party successfully challenging our ability to enforce a patent against an infringer;
- patent applications may not result in any patents being issued;
- patents may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable or otherwise may not provide any competitive advantage;
- our competitors, many of whom have substantially greater resources than we do and many of which have made significant investments in competing technologies, may seek or may have already obtained patents that will limit, interfere with or block our ability to make, use and sell our product candidates;
- there may be significant pressure on the U.S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for treatments of diseases or conditions that prove successful, as a matter of public policy regarding worldwide health concerns; and
- countries other than the United States may have patent laws that are less favorable to patentees, allowing foreign competitors a better opportunity to create, develop and market competing products.

The patent prosecution process is also expensive and time consuming, and we may not be able to file, prosecute, maintain, enforce or license all necessary or desirable patent applications or maintain or enforce patents that may issue based on our patent applications, at a reasonable cost or in a timely manner or in all jurisdictions where protection may be commercially advantageous. We may not be able to obtain or maintain patent applications and patents due to the subject matter claimed in such patent applications and patents in the public domain. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, if we choose to license certain patent rights in the future from third parties, we may not have the right to control the preparation, filing and prosecution of such patent applications, or to maintain the patents, directed to technology that we license from those third parties. We may also require the cooperation of our future licensor, if any, to enforce the licensed patent rights, and such cooperation may not be provided. Therefore, any licensed patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. We cannot be certain that patent prosecution and maintenance activities by any of our future licensors have been or will be conducted in compliance with applicable laws and regulations, which may affect the validity and enforceability of such patents or any patents that may issue from such applications. If they fail to do so, this could cause us to lose rights in any applicable intellectual property that we in-license, and as a result our ability to develop and commercialize products or product candidates may be adversely affected, and we may be unable to prevent competitors from making, using and selling competing products.

If the patent applications we hold or may in-license in the future with respect to our development programs and product candidates fail to issue, if their breadth or strength of protection is threatened, or if they fail to provide meaningful exclusivity for OKI-219 or any future product candidate, it could dissuade other companies from collaborating with us to develop product candidates, and threaten our ability to commercialize OKI-219 or future product candidates. Any such outcome could have a materially adverse effect on our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has been and will continue to be the subject of litigation and new legislation, resulting in court decisions, including U.S. Supreme Court decisions, which have increased uncertainties as to the ability to enforce patent rights in the future. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. For example, many countries restrict the patentability of methods of treatment of the human body. Publications in scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our own patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result of these and other factors, the issuance, scope, validity, enforceability, and

commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued that protect our technology or products, in whole or in part, or that effectively prevent others from commercializing competitive technologies and products.

Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. For example, the America Invents Act created new administrative post-grant proceedings, including post-grant review, inter partes review and derivation proceedings that allow third parties to challenge the validity of issued patents. This applies to all of our U.S. patents, even those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

Moreover, we may be subject to a third-party pre-issuance submission of prior art to the USPTO or become involved in opposition, derivation, reexamination, inter partes review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. The costs of defending patents or enforcing proprietary rights in post-issuance administrative proceedings and litigation can be substantial and the outcome can be uncertain. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize their technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents and patent applications may be challenged in the courts or patent offices in the United States and abroad. Even issued patents may later be found invalid or unenforceable or may be modified or revoked in proceedings instituted by third parties before various patent offices or in courts. An adverse decision in any such challenge may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Generally, issued patents are granted a term of 20 years from the earliest claimed non-provisional filing date. In certain instances, patent term can be adjusted to recapture a portion of delay incurred by the USPTO in examining the patent application (patent term adjustment). The scope of patent protection may also be limited.

Without patent protection for our current or future product candidates, we may be open to competition from generic versions of such products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.

Patent rights are of limited duration. In the United States, if all maintenance fees are paid timely, the natural expiration of a patent is generally 20 years after its first effective filing date. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such product candidates are commercialized. Even if patents covering our product candidates are obtained, once the patent life has expired for a product, we may be open to competition from biosimilar or generic products. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing product candidates similar or identical to ours. Upon issuance in the United States, the term of a patent can be increased by patent term adjustment, which is based on certain delays caused by the USPTO, but this increase can be reduced or eliminated based on certain delays caused by the patent applicant during patent

prosecution. The term of a U.S. patent may also be shortened if the patent is terminally disclaimed over an earlier-filed patent.

Depending upon the timing, duration and specifics of FDA marketing approval of OKI-219 and future product candidates, one or more of our U.S. patents may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years beyond the normal expiration of the patent as compensation for patent term lost during drug development and the FDA regulatory review process, which is limited to the approved indication (or any additional indications approved during the period of extension). This extension is based on the first approved use of a product and is limited to only one patent that covers the approved product, the approved use of the product or a method of manufacturing the product. Such patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval. However, the applicable authorities, including the FDA and the USPTO in the United States and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. We may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to extend the expiration date of our existing patents or obtain new patents with longer expiry dates, our competitors may be able to take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data to obtain approval of competing products following our patent expiration and launch their product earlier than might otherwise be the case.

Laws governing analogous patent term extension ("PTE") in foreign jurisdictions vary widely, as do laws governing the ability to obtain multiple patents from a single patent family. Additionally, we may not receive an extension if we fail to exercise due diligence during the testing phase or regulatory review process, apply within applicable deadlines, apply prior to expiration of relevant patents or otherwise satisfy applicable requirements. If we are unable to obtain PTE or restoration, or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our products will be shortened and our competitors may obtain approval of competing products following our patent expiration and may take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data to launch their product earlier than might otherwise be the case, and our revenue could be reduced, possibly materially.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for noncompliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other government fees on patents and patent applications will be due to the USPTO and other foreign patent agencies in several stages over the lifetime of our patents and patent applications. The USPTO and various foreign national or international patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment or lapse of patent rights include, but are not limited to, failure to timely file national and regional stage patent applications based on our international patent application, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we or any of our licensors fails to maintain the patents and patent applications covering OKI-219 or any future product candidate, our competitors may be able to enter the market, which would have an adverse effect on our business.

We may not identify relevant third-party patents or may incorrectly interpret the relevance, scope or expiration of a third-party patent, which might adversely affect our ability to develop and market our products.

As the biopharmaceutical industry expands and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties. There can be no assurance that our operations do not, or will not in the future, infringe, misappropriate or otherwise violate existing or future third-party patents or other intellectual property rights. Identification of third-party patent rights that may be relevant to our operations is difficult because patent searching is imperfect due to differences in terminology among patents,

incomplete databases and the difficulty in assessing the meaning of patent claims. We cannot guarantee that any of our patent searches or analyses, including the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and pending application in the United States and abroad that is relevant to or necessary for the commercialization of our current and future product candidates in any jurisdiction.

Numerous U.S. and foreign patents and pending patent applications exist in our market that are owned by third parties. Our competitors in both the United States and abroad, many of which have substantially greater resources and have made substantial investments in patent portfolios and competing technologies, may have applied for or obtained, or may in the future apply for and obtain, patents that will prevent, limit or otherwise interfere with our ability to make, use and sell our product candidates. We do not always conduct independent reviews of pending patent applications and patents issued to third parties. Patent applications in the United States and elsewhere are typically published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Certain U.S. applications that will not be filed outside the United States can remain confidential until patents issue. In addition, patent applications in the United States and elsewhere can be pending for many years before issuance, or unintentionally abandoned patents or applications can be revived. Furthermore, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our product candidates or the use of our product candidates. As such, there may be applications of others now pending or recently revived patents of which we are unaware. These patent applications may later result in issued patents, or the revival of previously abandoned patents, that may be infringed by the manufacture, use or sale of our product candidates or will prevent, limit or otherwise interfere with our ability to make, use or sell our product candidates.

The scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our products. For example, we may incorrectly determine that our product candidates are not covered by a third-party patent or may incorrectly predict whether a third party's pending application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect, and our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our products.

We may become involved in third-party claims of intellectual property infringement, which may delay or prevent the development and commercialization of OKI-219 and any future product candidate.

Our commercial success depends in part on us avoiding infringement and other violations of the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, derivation and administrative law proceedings, inter partes review and post-grant review before the USPTO, as well as oppositions and similar processes in foreign jurisdictions. We may be exposed to, or threatened with, future litigation by third parties having patent or other intellectual property rights and who allege that our product candidates, uses and/or other proprietary technologies infringe their intellectual property rights. Numerous U.S.- and foreign-issued patents and pending patent applications owned by third parties exist in the fields in which we and our collaborators are developing product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, and as we gain greater visibility and market exposure as a public company, the risk increases that our product candidates or other business activities may be subject to claims of infringement of the patent and other proprietary rights of third parties. Third parties may assert that we are infringing their patents or employing their proprietary technology without authorization.

Also, there may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our current and future product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our current or future product candidates may infringe.

In addition, third parties may obtain patent rights in the future and claim that use of our technologies infringes upon their rights. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our product candidates, any molecules formed during the manufacturing process, methods of treating certain diseases or conditions that we are pursuing with our product candidates, our formulations

including combination therapies, or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtain a license under the applicable patents, or until such patents expire. Such a license may not be available on commercially reasonable terms or at all. In addition, we may be subject to claims that we are infringing other intellectual property rights, such as trademarks or copyrights, or misappropriating the trade secrets of others, and to the extent that our employees, consultants or contractors use intellectual property or proprietary information owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our current and future product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful infringement or other intellectual property claim against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our affected products, which may be impossible or require substantial time and monetary expenditure. We cannot predict whether any such license would be available at all or whether it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates, and we have done so from time to time. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize one or more of our product candidates, which could harm our business significantly. We cannot provide any assurances that third-party patents do not exist which might be enforced against our product candidates, resulting in either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties or other forms of compensation to third parties.

During the course of any intellectual property litigation, there could be public announcements of the initiation of the litigation as well as results of hearings, rulings on motions, and other interim proceedings in the litigation. If securities analysts or investors regard these announcements as negative, the perceived value of our existing products, programs or intellectual property could be diminished. Accordingly, the price of our Class A Common Stock may decline. Such announcements could also harm our reputation or the market for our future products, which could have a material adverse effect on our business.

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

Competitors may infringe or otherwise violate our patents or other intellectual property rights, or those of our licensors. To counter infringement or unauthorized use or misappropriations, we or any future licensors may be required to file legal claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that one or more of our patents or any of our current or future licensors is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our or our licensors' patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing. The initiation of a claim against a third party may also cause the third party to bring counter claims against us, such as claims asserting that our patents are invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, non-enablement, insufficient written description or failure to claim patent-eligible subject matter. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant material information from the USPTO, or made a materially misleading statement, during prosecution. Third parties may also raise similar validity claims before the USPTO in post-grant proceedings such as ex parte reexaminations, inter partes review or post-grant review, or oppositions or similar proceedings outside the United States, in parallel with litigation or even outside the context of litigation. The outcome following legal assertions of invalidity and unenforceability is unpredictable. In any patent infringement proceeding, there is a risk that a court will decide that a patent of ours or a future licensor is invalid or unenforceable, in whole or in part, and that we do not have the right to stop the other party from using the invention at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our or any future licensors' patent claims do not cover the invention, or decide that the other party's

use of our or any future licensors' patented technology falls under the safe harbor to patent infringement under 35 U.S.C. §271(e)(1). An adverse outcome in a litigation or proceeding involving our or any future licensors' patents could limit our ability to assert our own or any future licensors' patents against those parties or other competitors and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. Any of these occurrences could adversely affect our competitive position and our business, financial condition, results of operations and prospects. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

We cannot be certain that there is no invalidating prior art of which we and the patent examiner were unaware during prosecution. For any patents and patent applications that we license from third parties, we may have limited or no right to participate in the defense of such licensed patents against challenge by a third party. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our current or future product candidates. Such a loss of patent protection could harm our business.

We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States. Our business could be harmed if in litigation the prevailing party does not offer us a license on commercially reasonable terms. Any litigation or other proceedings to enforce our intellectual property rights may fail, and even if successful, may result in substantial costs and distract our management and other employees.

Even if we establish infringement, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have an adverse effect on the price of our Class A Common Stock. Moreover, we cannot assure you that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings.

Because of the expense and uncertainty of litigation, we may not be in a position to enforce our intellectual property rights against third parties.

Because of the expense and uncertainty of litigation, we may conclude that even if a third party is infringing our patents, any patents that may be issued as a result of our future patent applications, or other intellectual property rights, the risk-adjusted cost of bringing and enforcing such a claim or action may be too high or not in our best interest or that of our stockholders. In such cases, we may decide that the more prudent course of action is to simply monitor the situation or initiate or seek some other non-litigious action or solution.

Changes in U.S. patent law or the patent law of other countries or jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining, defending, maintaining and enforcing patents in the biopharmaceutical industry involves both technological and legal complexity and is therefore costly, time-consuming and inherently uncertain. Changes in either the patent laws or interpretation of the patent laws in the United States could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents, and may diminish our ability to protect our inventions, obtain, maintain, enforce and protect our intellectual property rights and, more generally, could affect the value of our intellectual property or narrow the scope of our future owned and licensed patents. The United States has enacted and implemented wide-ranging patent reform legislation. The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on actions by Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in

unpredictable ways that would weaken our ability to obtain new patents or to enforce patents that we have licensed or that we might obtain in the future. Similarly, changes in patent law and regulations in other jurisdictions or changes in the governmental bodies that enforce them or changes in how the relevant governmental authority enforces patent laws or regulations may weaken our ability to obtain new patents or to enforce patents that we have licensed or that we may obtain in the future. For example, the complexity and uncertainty of European patent laws have also increased in recent years. In Europe, a new unitary patent system took effect June 1, 2023, which will significantly impact European patents, including those granted before the introduction of such a system. Under the unitary patent system, European applications have the option, upon grant of a patent, of becoming a Unitary Patent which will be subject to the jurisdiction of the Unitary Patent Court (the "UPC"). As the UPC is a new court system, there is no precedent for the court, increasing the uncertainty of any litigation. Patents granted before the implementation of the UPC have the option of opting out of the jurisdiction of the UPC over the first seven years of the court's existence and remaining as national patents in the UPC countries. Patents that remain under the jurisdiction of the UPC will be potentially vulnerable to a single UPC-based revocation challenge that, if successful, could invalidate the patent in all countries that are signatories to the UPC. We cannot predict with certainty the long-term effects of any potential changes.

We may not be able to protect our intellectual property rights throughout the world, which could impair our business.

Patents are of national or regional effect, and filing, prosecuting and defending patents covering OKI-219 and any future product candidate throughout the world would be prohibitively expensive. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States, even in jurisdictions in which we do pursue patent protection. Consequently, we may not be able to prevent third parties from practicing our or any future licensors' inventions in all countries outside the United States, even in jurisdictions where we or any future licensors do pursue patent protection, or from selling or importing products made using our or any future licensors' inventions in and into the United States or other jurisdictions. Competitors may use our or any future licensors' technologies in jurisdictions where we have not obtained patent protection to develop our own products and, further, may export otherwise infringing products to territories where we may have or obtain patent protection, but where patent enforcement is not as strong as in the United States. These unauthorized competitors' products may compete with our products in such jurisdictions and take away our market share where we do not have any issued or licensed patents, and any future patent claims or other intellectual property rights may not be effective or sufficient to prevent them from so competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biotechnology products. This could make it difficult for us to stop the infringement of our patents or the marketing of competing products in violation of our intellectual property and proprietary rights generally. In addition, certain jurisdictions do not protect to the same extent or at all inventions that constitute new methods of treatment.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

Furthermore, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws within the United States. We may need to share our trade secrets and proprietary know-how with current or future partners, collaborators, contractors and others located in countries at heightened risk of theft of trade secrets, including through direct intrusion by private parties or foreign actors and those affiliated with or controlled by state actors. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. In addition, some courts inside and outside of the United States may be less willing or unwilling to protect trade secrets. If we choose to go to court to stop a third party from using any of our trade secrets, we may incur substantial costs. Even if we are successful, such lawsuits would consume our time and other resources. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to the protection afforded by patents, we may seek to rely on trade secret protection to protect proprietary know-how that is not patentable, processes for which patents are difficult to enforce and any other elements of our product discovery and development processes that involve proprietary know-how, information or technology that is not covered by our patents. We may not be able to meaningfully protect our trade secrets. Although we require all of our employees to assign their inventions to us, and require all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information or technology to enter into confidentiality agreements, we cannot be certain that our trade secrets and other confidential proprietary information will not be disclosed to our competitors or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Furthermore, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws within the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, we will not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, operating results and financial condition.

Because we expect to rely on third parties to manufacture OKI-219 and any future product candidates, and we expect to collaborate with third parties on the continuing development of OKI-219 and any future product candidates, we must, at times, share trade secrets with them. We also expect to conduct R&D programs that may require us to share trade secrets under the terms of our partnerships or agreements with CROs. We seek to protect our proprietary technology in part by entering into agreements containing confidentiality and use restrictions and obligations, including material transfer agreements, consulting agreements, manufacturing and supply agreements, confidentiality agreements or other similar agreements with our advisors, employees, contractors, contract manufacturing organizations (or "CMOs"), CROs, other service providers and consultants prior to disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are intentionally or inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have an adverse effect on our business and results of operations.

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors CMOs, CROs, other service providers and consultants to publish data potentially relating to our trade secrets, although such agreements may contain certain limited publication rights. Despite our efforts to protect our trade secrets, our competitors may discover such trade secrets, either through breach of our agreements with third parties, independent development or publication of information by any of our third-party collaborators. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

Monitoring unauthorized disclosure and detection of unauthorized disclosure is difficult, and we do not know whether the steps we have taken to prevent such disclosure are, or will be, adequate. If we were to enforce a claim that a third party had illegally obtained and was using our trade secrets, it would be expensive and time-consuming, and the outcome would be unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets. If we choose to go to court to stop a third party from using any of our trade secrets, we may incur substantial costs. These lawsuits may consume our time and other resources even if we are successful. For example, significant elements of our products, including confidential aspects of sample preparation, methods of manufacturing, and related processes and software, are based on unpatented trade secrets. Although we take steps to protect our proprietary information and trade secrets, including through contractual means with our employees and consultants, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology.

We may become subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of their former employers or other third parties or claims asserting ownership of what we regard as our own intellectual property.

We employ individuals who were previously employed at other biotechnology or pharmaceutical companies, or at research institutions, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and advisors do not use the proprietary information or know-how of others in their work for us, we may become subject to claims that these individuals have or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of such individual's current or former employer. Further, although we seek to protect our ownership of intellectual property rights by ensuring that our agreements with our employees, collaborators, and other third parties with whom we do business include provisions requiring such parties to assign rights in inventions to us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed confidential information of our employees' former employers or other third parties. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. An inability to incorporate such technologies or features would harm our business and may prevent us from successfully commercializing our technologies or product candidates. In addition, we may lose personnel as a result of such claims, and any such litigation, or the threat thereof, may adversely affect our ability to hire employees or contract with independent contractors. A loss of key personnel or their work product could hamper or prevent our ability to commercialize our technologies or product candidates, which could adversely affect our business, financial condition, results of operations and prospects. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, we may also be subject to claims that former employers, consultants or other third parties have an ownership interest in our patents or patent applications as an inventor or co-inventor. The failure to name the proper inventors on a patent application can result in the patents issuing thereon being unenforceable. Inventorship disputes may arise from conflicting views regarding the contributions of different individuals named as inventors, the effects of foreign laws where foreign nationals are involved in the development of the subject matter of the patent, conflicting obligations of third parties involved in developing our product candidates or as a result of questions regarding co-ownership of potential joint inventions. Litigation may be necessary to resolve these and other claims challenging inventorship and/or ownership. Alternatively, or additionally, we may enter into agreements to clarify the scope of our rights in such intellectual property. There is no guarantee of success in defending these claims, and if we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such challenges may also result in our inability to develop, manufacture or commercialize our technologies and product candidates without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future technologies and product candidates. Even if we are successful, litigation could result in substantial costs and be a distraction to our management and other employees. Any of the foregoing could adversely affect our business, financial condition, results of operations and prospects.

If our future trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest, and our business may be adversely affected.

We intend to use registered or unregistered trademarks or trade names to brand and market ourselves and our products. Our trademarks or trade names may be challenged, infringed, circumvented, declared generic or determined to be infringing on other marks. During trademark registration proceedings, we may receive rejections of our applications by the USPTO or foreign agencies. Although we are given an opportunity to respond to such rejections, we may be unable to overcome them. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, which may not survive such proceedings.

We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to those of ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims

brought by owners of other trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively, and our business may be adversely affected. We may license our trademarks and trade names to third parties, such as distributors. Though these license agreements may provide guidelines for how our trademarks and trade names may be used, a breach of these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names. Our efforts to enforce or protect our proprietary rights related to trademarks, trade names, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our financial condition or results of operations.

In addition, any proprietary name we propose to use with our current or future product candidates in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of the potential for confusion with other product names. If the FDA objects to any of our proposed proprietary product names, we may be required to expend significant additional resources to identify a suitable proprietary product name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. Furthermore, in many countries, owning and maintaining a trademark registration may not provide an adequate defense against a subsequent infringement claim asserted by the owner of a senior trademark.

Our intellectual property rights do not necessarily address all potential threats to our competitive advantage.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business or permit us to maintain our competitive advantage. The following examples are illustrative:

- others may be able to make formulations or compositions that are the same as or similar to our current or future product candidates, but that are not covered by the pending patent applications or patents that we own or any pending patent applications or patents that we may in-license in the future;
- others may be able to make products that are similar to our current or future product candidates, but that are not covered by the patents that we own or exclusively license and have the right to enforce;
- we, or our future licensors or collaborators, may not have been the first to make the inventions covered by the issued patents or pending patent applications that we own or may in-license in the future;
- we, or our future licensors, may not have been the first to file patent applications covering certain of our or those licensors' inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing or otherwise violating our owned intellectual property rights or any patent applications that we may license in the future;
- it is possible that our pending patent applications or those that we may own or license in the future will not lead to issued patents;
- issued patents that we either own or that we may license in the future may be revoked, modified or held valid or unenforceable, as a result of legal challenges by our competitors;
- issued patents that we either own or may license in the future may not provide us with any competitive advantages;
- others may have access to the same intellectual property rights licensed to us in the future on a non-exclusive basis;
- our competitors may conduct research and development activities in the United States and other countries that provide a safe harbor from patent infringement claims for certain research and development activities, as well as in countries where we do not have patent rights, and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable;

- we cannot predict the scope of protection of any patent issuing based on our or any future licensors' patent applications, including whether the patent applications that we own or, in the future, in-license, will result in issued patents with claims directed to our product candidates or uses thereof in the United States or in other foreign countries;
- a court may not hold that our patents are valid, enforceable or infringed;
- we may need to initiate litigation or administrative proceedings to enforce or defend our patent rights, which will be costly whether we win or lose;
- we may choose not to file a patent application in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent application covering such intellectual property;
- we may fail to adequately protect and police our trademarks and trade secrets; and
- the patents of others may have an adverse effect on our business, including if others obtain patents claiming subject matter similar to or improving the subject matter covered by our patent applications.

Any collaboration or partnership arrangements that we may enter into in the future may not be successful, which could adversely affect our ability to develop and commercialize our products.

Any future collaborations that we enter into may not be successful. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborations are subject to numerous risks, which may include that:

- collaborators have significant discretion in determining the efforts and resources that they will apply to collaborations;
- collaborators may not pursue development and commercialization of our products or may elect not to continue or renew development or commercialization programs based on trial or test results, changes in our strategic focus due to the acquisition of competitive products, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our current and future product candidates;
- a collaborator with marketing, manufacturing and distribution rights to one or more products may not commit sufficient resources to or otherwise not perform satisfactorily in carrying out these activities;
- we could grant exclusive rights to our collaborators that would prevent us from collaborating with others;
- collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;
- disputes may arise between us and a collaborator that cause the delay or termination of the research, development or commercialization of current or future product candidates or that results in costly litigation or arbitration that diverts management attention and resources;
- collaborations may be terminated, and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable current or future product candidates;
- collaborators may own or co-own intellectual property covering our products that results from our collaborating with them, and in such cases, we would not have the exclusive right to develop or commercialize such intellectual property; and
- a collaborator's sales and marketing activities or other operations may not be in compliance with applicable laws resulting in civil or criminal proceedings.

If we fail to comply with our obligations under any license, collaboration or other agreement, such agreements may be terminated, we may be required to pay damages and could lose intellectual property rights that are necessary for developing and protecting our product candidates.

We may license or otherwise acquire development or commercialization rights to current and future product candidates or data from third parties. If any future licensors fail to prosecute, maintain, enforce and defend such patents, or lose rights to those patents, the rights we have licensed may be reduced or eliminated, and our right to develop and commercialize future product candidates that may be subject of such licensed rights could be adversely affected. In spite of our efforts, any future licensors might conclude that we are in material breach of obligations under our license agreements. If we breach any material obligations, or use the intellectual property licensed to us in an unauthorized manner, we may be required to pay damages and the licensor may have the right to terminate the license, which could result in us being unable to develop, manufacture and sell products that are covered by the licensed technology or enable a competitor to gain access to the licensed technology. If such in-licenses are terminated, or if the underlying patents fail to provide the intended exclusivity, our competitors will have the freedom to seek regulatory approval of, and to market, products identical to our product candidates, and the licensors to such in-licenses could prevent us from developing or commercializing product candidates that rely upon the patents or other intellectual property rights which were the subject matter of such terminated agreements. Any of these events could adversely affect our business, financial condition, results of operations and prospects.

Disputes may arise between us and our licensors regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- either party's financial or other obligations under the license agreement;
- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- our right to sublicense patents and other rights under our collaborative development relationships to third parties;
- our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates, and what activities satisfy those diligence obligations;
- our right to transfer or assign the license;
- the inventorship or ownership of inventions and know-how resulting from the joint creation or use of intellectual property by any of our licensors and us and our partners; and
- the priority of invention of patented technology.

If disputes over intellectual property that we license prevent or impair our ability to maintain our licensing arrangements on acceptable terms, we may not be able to successfully develop and commercialize the affected product candidates, which would have a material adverse effect on our business.

In addition, certain of our current or future agreements with third parties may limit or delay our ability to consummate certain transactions, may impact the value of those transactions, or may limit our ability to pursue certain activities.

Further, we or our current or future licensors may fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Therefore, we may miss potential opportunities to strengthen our patent position. It is possible that defects of form in the preparation or filing of our patents or patent applications may exist, or may arise in the future, for example with respect to proper priority claims, inventorship, ownership, claim scope or requests for patent term adjustments. If our current or future licensors are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised. If there are material defects in the form, preparation, prosecution or enforcement of our patents or patent applications, such patents may be invalid or unenforceable, and such applications may never result in valid, enforceable patents. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

In addition, even where we have the right to control patent prosecution of patents and patent applications under a license from third parties, we may still be adversely affected or prejudiced by actions or inactions of our predecessors or licensors and their counsel that took place prior to us assuming control over patent prosecution.

Our acquired technologies and current or future licensed technology may be subject to retained rights. Our predecessors or licensors may retain certain rights under their agreements with us, including the right to use the underlying technology for noncommercial academic and research use, to publish general scientific findings from research related to the technology and to make customary scientific and scholarly disclosures of information relating to the technology. It is difficult to monitor whether our predecessors or future licensors limit their use of the technology to these uses, and we could incur substantial expenses to enforce our rights to our licensed technology in the event of misuse.

If we are limited in our ability to utilize acquired technologies or current or future licensed technologies, or if we lose our rights to critical acquired or in-licensed technology, we may be unable to successfully develop, out-license, market and sell our products. Our business strategy may depend on the successful development of acquired technologies, and current or future licensed technology, into commercial products. Therefore, any limitations on our ability to utilize these technologies may impair our ability to develop, out-license or market and sell our product candidates.

We may not be able to license or acquire new or necessary intellectual property rights or technology from third parties.

Because our development programs may in the future require the use of proprietary rights held by third parties, the growth of our business may depend in part on our ability to acquire, in-license or use these third-party proprietary rights. Further, other parties, including our competitors, may have patents and have filed and are likely filing patent applications potentially relevant to our business. In order to avoid infringing these patents, we may find it necessary or prudent to obtain licenses to such patents from such parties. The licensing or acquisition of intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. No assurance can be given that we will be successful in-licensing any additional rights or technologies from third parties. Our inability to license the rights and technologies that we have identified, or that we may in the future identify, could have a material adverse impact on our ability to complete the development of our product candidates or to develop additional product candidates. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. Failure to obtain any necessary rights or licenses may detrimentally affect our planned development of our current or future product candidates and could increase the cost and extend the timelines associated with the development of such other product candidates, and we may have to abandon development of the relevant program or product candidate. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may enter into license agreements in the future with others to advance our existing or future research or allow commercialization of our existing or future product candidates. These licenses may not provide exclusive rights to use such intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and product candidates in the future. In that event, we may be required to expend significant time and resources to redesign our product candidates, or the methods for manufacturing them, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could harm our business, financial condition, results of operations and prospects significantly. We cannot provide any assurances that third-party patents do not exist which might be enforced against our current manufacturing methods, product candidates or future methods or product candidates, resulting in either an injunction prohibiting their manufacture or future sale or, with respect to their future sale, an obligation on our part to pay royalties or other forms of compensation to third parties, which could be significant.

Risks Related to Our Regulatory Approval and Other Legal Compliance Matters

Even if we receive regulatory approval of our product candidates, we will be subject to ongoing regulatory obligations and continued regulatory oversight, which may result in significant additional expense, and we may experience unanticipated problems with our product candidates or be subject to penalties if we fail to comply with regulatory requirements.

Even if we obtain regulatory approval for one or more of our product candidates, such product candidates will be subject to ongoing regulatory requirements applicable to manufacturing, labeling, packaging, storage, advertising, promoting, sampling, record-keeping and submission of safety or other post-market information, among other things. Any regulatory approvals that we receive for our product candidates will require surveillance to monitor safety and efficacy. The FDA may also require a REMS, limitations on the approved indicated uses for which the product candidate may be marketed or to the conditions of approval, or requirements that we conduct potentially costly post-market testing and surveillance studies, including Phase 4 trials and surveillance to monitor the quality, safety and efficacy of the product candidate. An unsuccessful post-marketing study or failure to complete such a study could result in requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools as conditions of approval.

Any new legislation addressing drug safety issues could result in delays in product development or commercialization or increased compliance costs. We must also comply with requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription drug products are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved label. As such, we will not be allowed to promote our products for indications or uses for which they do not have approval, commonly known as off-label promotion. The holder of an approved NDA must submit new or supplemental applications and obtain prior approval for certain changes to the approved product, product labeling or manufacturing process. A company that is found to have improperly promoted off-label uses of our products may be subject to significant civil, criminal and administrative penalties.

In addition, drug manufacturers are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with FDA's current Good Manufacturing Practices ("cGMPs") and adherence to commitments made in the NDA or foreign marketing application. If we, the FDA or a comparable foreign regulatory authority discovers previously unknown problems with our product candidates, such as adverse events of unanticipated severity or frequency, or problems with the facility where the drug was manufactured, or if a regulatory authority disagrees with the promotion, marketing or labeling of that drug, a regulatory authority may impose restrictions relative to that drug, the manufacturing facility or us, including requesting a recall or requiring withdrawal of the drug from the market or suspension of manufacturing.

Failure by us to comply with applicable regulatory requirements following approval of any product candidates may result in, among other things:

- restrictions on the marketing or manufacturing of our product candidates, withdrawal of the product from the market or voluntary or mandatory product recalls;
- manufacturing delays and supply disruptions where regulatory inspections identify observations of noncompliance requiring remediation;
- revisions to the labeling, including limitation on approved uses or the addition of additional warnings, contraindications or other safety information, including boxed warnings;
- imposition of a REMS, which may include distribution or use restrictions;
- requirements to conduct additional post-marketing clinical trials to demonstrate the safety of the product;
- suspension or withdrawal of regulatory approvals;
- issuance of fines, untitled letters, warning letters or holds on clinical trials;
- refusal by regulatory authorities to approve pending applications or supplements to approved applications filed by us, or suspension or revocation of approvals;

- product seizure or detention, or refusal to permit the import or export of a product candidates; and
- injunctions or the imposition of civil or criminal penalties.

The FDA's and other regulatory authorities' policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, and we may not achieve or sustain profitability. We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. It is difficult to predict how current and future legislation, executive actions and litigation, including the executive orders, will be implemented, and the extent to which they will impact our business and clinical development, and the FDA's and other agencies' ability to exercise their regulatory authority, including the FDA's pre-approval inspections and timely review of any regulatory filings or applications we submit to the FDA. To the extent any executive actions impose constraints on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

Disruptions at the FDA, the SEC or other government agencies caused by funding shortages or global health concerns could hinder their ability to hire and retain key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, statutory, regulatory and policy changes, and other events that may otherwise affect the FDA's ability to perform routine functions. Changes in the leadership of the FDA and other federal agencies under the Trump administration, as well as policy changes including return-to-office directives, hiring freezes, and layoffs, may also lead to changes in the operations of the FDA, which may have a material impact on the industry. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed or approved by necessary government agencies, which would adversely affect our business. If a prolonged government shutdown or other disruption occurs, or if global health or other concerns prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews or other regulatory activities in a timely manner, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns or delays could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Separately, in response to the COVID-19 pandemic, the FDA announced its intention to postpone most inspections of foreign and domestic manufacturing facilities at various points. Even though the FDA has since resumed standard inspection operations of domestic facilities, if a prolonged government shutdown occurs, either for global health related reasons or other reasons, preventing the FDA or other regulatory authorities from conducting business as usual or conducting inspections, reviews or other regulatory activities, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material effect on our business.

We may face difficulties from changes to current regulations and future legislation. Healthcare legislative measures aimed at reducing healthcare costs may have a material adverse effect on our business and results of operations.

The United States and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system that could prevent or delay marketing approval of our product candidates or any future product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell a product for which we obtain marketing approval. Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example:

- changes to our manufacturing arrangements;
- additions or modifications to product labeling;
- the recall or discontinuation of our products; or
- additional record-keeping requirements.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad, including as a result of the new presidential administration. Any such changes imposed on us could adversely affect the operation of our business.

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (as amended, the "ACA"), was passed, which substantially changed the way healthcare is financed by both governmental and private insurers and significantly impacted the U.S. pharmaceutical industry. The ACA contained provisions that may reduce the profitability of drug products through, among other things, increased rebates for drugs reimbursed by Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal health care programs.

There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. In August 2022, Congress passed the Inflation Reduction Act of 2022 (the "IRA"), which includes prescription drug provisions that have significant implications for the pharmaceutical industry and Medicare beneficiaries, including among other changes allowing the federal government to negotiate a maximum fair price for certain high-priced single-source Medicare drugs, imposing penalties and excise taxes for manufacturers that fail to comply with the drug price negotiation requirements, requiring inflation rebates for all Medicare Part B and Part D drugs, with limited exceptions, if their drug prices increase faster than inflation, and redesigning Medicare Part D to reduce out-of-pocket prescription drug costs for beneficiaries. HHS has issued and will continue to issue and update guidance as these programs are implemented. Only high-expenditure, single-source drugs that have been approved for at least seven years (11 years for single-source biologics) qualify for negotiation, with the negotiated price taking effect two years after the selection year. For 2026, CMS selected 10 high-cost Medicare Part D drugs in 2023 and the negotiated maximum fair price for each drug has been announced. CMS has selected 15 additional Medicare Part D drugs for negotiated maximum fair pricing in 2027. For 2028, up to an additional 15 drugs, which may be covered under either Medicare Part B or Part D, will be selected, and for 2029 and subsequent years, up to 20 additional Part B or Part D drugs will be selected. However, various industry stakeholders, including pharmaceutical companies, the U.S. Chamber of Commerce and the Pharmaceutical Research and Manufacturers of America, have initiated lawsuits against the federal government asserting that the price negotiation provisions of the IRA are unconstitutional. The impact of these judicial challenges, as well as future legislative, executive and administrative actions and any future healthcare measures and agency rules implemented by the government on us and the pharmaceutical industry as a whole, is difficult or impossible to predict. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our product candidates if approved.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control prescription drug pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures and, in some cases, designed to encourage bulk purchasing and importation from other countries. A number of states are considering or have recently enacted drug price transparency and reporting laws that could substantially increase our compliance burdens and expose us to greater liability under such state laws once we begin commercialization after obtaining regulatory approval for any of our products. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Our revenue prospects could be affected by changes in healthcare spending and policy in the United States and abroad. We operate in a highly regulated industry, and new laws, regulations or judicial decisions, or new interpretations of existing laws, regulations or decisions, related to healthcare availability, the method of delivery or

payment for healthcare products and services could negatively impact our business, operations and financial condition.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. We cannot predict what initiatives may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare or impose price controls may adversely affect:

- the demand for our product candidates, if we obtain regulatory approval;
- our ability to set a competitive price that we believe is fair for our products;
- our ability to generate revenue and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

The implementation of cost containment measures or other healthcare reforms may lower the pricing of competitor products or procedures, which in turn may constrain the pricing of our product candidates, if approved, and prevent us from being able to generate revenue, attain profitability or commercialize our product candidates.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for biotechnology products. We cannot be sure to what extent these legislative and regulatory proposals will be implemented by the federal and state governments, whether additional legislative changes will be enacted, whether FDA regulations, guidance or interpretations will be changed or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

We may be subject to federal and state healthcare fraud and abuse laws, false claims laws, transparency laws and health information privacy and security laws, which could expose us to, among other things, criminal sanctions, civil penalties, contractual damages, reputational harm, administrative burdens and diminished profits and future earnings.

Our current and future arrangements with healthcare professionals, clinical investigators, CROs and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we plan to market, sell and distribute products for which we obtain marketing approval.

Laws that may affect our ability to operate include, but are not limited to:

- the federal AKS, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, but the exceptions and safe harbors are drawn narrowly and require strict compliance in order to offer protection. Violations are subject to civil and criminal fines and penalties, plus up to three times the remuneration involved, imprisonment and exclusion from government healthcare programs;
- federal civil and criminal false claims laws, including the FCA, which can be enforced through civil "qui tam" or "whistleblower" actions, and civil monetary penalty laws, which impose criminal and civil penalties against individuals or entities for, among other things, knowingly presenting or causing to be presented claims for payment or approval from Medicare, Medicaid or other federal health care programs that are false or fraudulent; knowingly making or causing a false statement material to a false or fraudulent claim or an obligation to pay money to the federal government; or knowingly concealing or

knowingly and improperly avoiding or decreasing such an obligation. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. In addition, the government may assert that a claim including items or services resulting from a violation of the AKS constitutes a false or fraudulent claim for purposes of the FCA. The FCA also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery. When an entity is determined to have violated the federal civil FCA, the government may impose civil fines and penalties for each false claim, plus treble damages, and exclude the entity from participation in Medicare, Medicaid and other federal healthcare programs;

- HIPAA, which created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Similar to the AKS, a person or entity can be found guilty of violating HIPAA without actual knowledge of the statute or specific intent to violate it;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 ("HITECH"), and their respective implementing regulations, which impose requirements on certain covered healthcare providers, health plans and healthcare clearinghouses as well as their respective business associates and their subcontractors that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions;

- the federal Physician Payments Sunshine Act, created under the ACA and its implementing regulations, which requires manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to CMS information related to payments or other transfers of value made to covered recipients, including physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician healthcare professionals (such as physician assistants and nurse practitioners, among others) and teaching hospitals, as well as information regarding ownership and investment interests held by physicians and their immediate family members;

- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; and

- analogous and related state and foreign laws and regulations, such as state and foreign anti-kickback, false claims, consumer protection and unfair competition laws that may apply to pharmaceutical business practices, including but not limited to, research, distribution, sales and marketing arrangements as well as submitting claims involving healthcare items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government that otherwise restricts payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to file reports with states regarding pricing and marketing information, such as the tracking and reporting of gifts, compensations and other remuneration and items of value provided to healthcare professionals and entities; state and local laws requiring the registration of pharmaceutical sales representatives; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of available statutory exceptions and regulatory safe harbors, it is possible that some of our business activities, including our advisory board arrangements with

physicians and any sales and marketing activities after a product candidate has been approved for marketing in the United States, could be subject to legal challenge and enforcement actions. If our operations are found to be in violation of any of the federal and state laws described above or any other governmental regulations that apply to us, we may be subject to significant civil, criminal and administrative penalties, including, without limitation, damages, fines, disgorgement, imprisonment, additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs, suppliers and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk that our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs, suppliers and vendors may engage in misconduct or other improper activities. Misconduct by these parties could include failures to comply with FDA regulations, provide accurate information to the FDA, comply with federal and state health care fraud and abuse laws and regulations, accurately report financial information or data or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the health care industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Misconduct by these parties could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter misconduct by these parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, integrity oversight and reporting obligations, contractual damages, reputational harm, diminished profits and future earnings and the curtailment or restructuring of our operations.

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

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, or hazardous materials.

In addition, we may incur substantial costs to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or commercialization efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

We are subject to certain U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions and other trade laws and regulations and can face serious consequences for violations.

Among other matters, U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions and other trade laws and regulations prohibit companies and their employees, agents, clinical research organizations, legal counsel, accountants, consultants, contractors and other partners from authorizing, promising, offering,

providing, soliciting or receiving, directly or indirectly, corrupt or improper payments or anything else of value to or from recipients in the public or private sector. Violations of such trade laws can result in substantial criminal fines and civil penalties, imprisonment, the loss of trade privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm and other consequences. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities and other organizations. We also expect our non-U.S. activities to increase in time. We plan to engage third parties for clinical trials or to obtain necessary permits, licenses, patent registrations and other regulatory approvals, and we may be held liable for the corrupt or other illegal activities of our personnel, agents or partners even if we do not explicitly authorize or have prior knowledge of such activities.

Restrictive laws and regulations govern the collection, use, transfer, and other processing of personal information.

In conducting and enrolling patients in current or future clinical trials, we are subject to restrictions relating to privacy, data protection, and cybersecurity, and may be subject to additional restrictions associated with clinical operations in the future. For example, the collection, use, storage, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the General Data Protection Regulation ("GDPR"), which is wide-ranging in scope and imposes numerous requirements on companies that process personal data. The GDPR permits data protection authorities to impose large penalties for violations, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater, for the most serious violations. The GDPR also confers a private right of action on data subjects and consumer associations. Certain aspects of cross-border data transfers under the GDPR are uncertain as the result of legal proceedings in the EU, including a July 2020 decision by the Court of Justice for the European Union ("CJEU") that invalidated the EU-U.S. Privacy Shield and called into question the efficacy and legality of using standard contractual clauses ("SCCs"). To address certain concerns of the CJEU, the European Commission issued revised SCCs in June 2021. The EU also has enacted numerous new laws and regulations addressing cybersecurity.

In the United Kingdom ("UK"), the Data Protection Act of 2018 implements and complements the GDPR and is effective along with a version of the GDPR referred to as the UK GDPR. These regimes authorize significant fines, up to the greater of £17.5 million or 4% of global turnover, and expose us to two parallel regimes and potentially divergent enforcement actions. Further, aspects of data protection in the UK remain uncertain. On June 28, 2021, the European Commission issued an adequacy decision pursuant to which personal data generally may be transferred from the EU to the UK without restriction; however, this adequacy decision is subject to a four-year "sunset" period, after which it may be renewed. This decision may be revoked or modified at any time. Additionally, the UK's Information Commissioner's Office has issued standard contractual clauses to support personal data transfers out of the UK ("UK SCCs"). Regulatory guidance and other developments relating to cross-border personal data transfers, including the necessity of putting in place SCCs and UK SCCs, may increase the complexity of transferring personal data across borders and may require us to engage in additional contractual negotiations or to modify our policies and practices. Other jurisdictions also increasingly maintain laws and regulations addressing privacy, data protection, and cybersecurity. We may incur liabilities, expenses, and other operational losses under the GDPR and local laws of applicable EU member states, the UK, and other regions in connection with any measures we take to comply with them.

In the United States, in addition to HIPAA, HITECH, and state laws addressing health-related information, numerous federal and state laws and regulations govern the collection, use, disclosure, and other processing of information relating to individuals. In California, the California Consumer Privacy Act ("CCPA") requires covered companies to provide disclosures to consumers about such companies' data collection, use and sharing practices, provide such consumers ways to opt-out of certain sales or transfers of personal information, and provide consumers with additional causes of action in data breach situations. The CCPA went into effect on January 1, 2020, and was modified significantly by the California Privacy Rights Act ("CPRA"), which was approved by California voters in the 2020 election and became effective January 1, 2023. The CCPA has prompted numerous proposals for federal and state privacy legislation. Numerous U.S. states have proposed, and in certain cases enacted, laws addressing privacy and cybersecurity matters. Many of these laws are comprehensive privacy statutes imposing obligations similar to the CCPA. Certain U.S. states have also enacted laws and regulations addressing specific subject matter, such as Washington State's My Health, My Data Act which, among other things, provides for a private right of action.

Compliance with U.S. and international laws and regulations relating to privacy, data protection, and cybersecurity could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use, and disclose data, or, in some cases, impact our ability to operate in certain jurisdictions, and may increase our costs of doing business or require us to change our policies and practices. Any actual or alleged failure to comply with U.S. or international laws and regulations relating to privacy, data protection, or cybersecurity could result in governmental investigations, proceedings, and enforcement actions (which could include civil or criminal penalties), private litigation, adverse publicity, and harm to our reputation, and could negatively affect our operating results and business. Moreover, clinical trial subjects about whom we or our potential collaborators obtain information, as well as the providers who share this information with us, may contractually limit our ability to use and disclose such information or impose other obligations or restrictions in connection with our use, retention, or other processing of information, and we may otherwise face contractual restrictions applicable to these activities. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws, or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

Risks Related to Our Reliance on Third Parties

We rely, and expect to continue to rely, on third parties, including independent clinical investigators and CROs, to conduct, supervise and monitor certain aspects of our clinical trials and preclinical studies. If these third parties do not successfully carry out their contractual duties, comply with applicable regulatory requirements and meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates, or such approval or commercialization may be delayed, and our business could be substantially harmed.

We have relied upon, and plan to continue to rely upon, third parties, including independent clinical investigators and third-party CROs, to conduct certain aspects of our preclinical studies and clinical trials and to monitor and manage data for our ongoing clinical programs.

We rely on these parties for execution of our trials and generally do not control their activities. Nevertheless, we are responsible for ensuring that each of our studies and trials is conducted in accordance with the applicable clinical investigation plan and protocol as well as legal, regulatory and scientific standards, and our reliance on these third parties does not relieve us of our regulatory responsibilities. We and our third-party contractors and CROs are required to comply with GCPs, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities, for all of our products candidates in clinical development. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of these third parties or CROs fails to comply with applicable GCPs, the clinical data may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials complies with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be adversely affected if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

Further, these investigators and CROs are not our employees, and we will not be able to control, other than by contract, the amount of resources, including time, which they devote to our product candidates and clinical trials. These third parties may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other product development activities, which could affect their performance on our behalf. If independent investigators or CROs fail to devote sufficient resources to the development of our product candidates, or if CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed or precluded entirely.

In many cases, our CROs have the right to terminate their agreements with us in the event of an uncured material breach. In addition, some of our CROs have an ability to terminate their respective agreements with us if it can be reasonably demonstrated that the safety of the subjects participating in our clinical trials warrants such termination, if we make a general assignment for the benefit of our creditors or if we are liquidated. If any of our relationships with these third parties terminates, we may not be able to timely enter into arrangements with alternative third parties or to do so on commercially reasonable terms, if at all. Switching or adding CROs involves substantial cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet desired clinical development timelines. Though we intend to carefully manage our relationships with our CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

We contract with third parties for the manufacture of our product candidates for preclinical studies and clinical trials, and expect to continue to do so for additional clinical trials and ultimately for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not currently have the infrastructure or internal capability to manufacture supplies of our product candidates for use in development and commercialization and do not intend to develop such infrastructure and capabilities. We rely, and expect to continue to rely, on third party manufacturers for the production of our product candidates for preclinical studies and clinical trials under the guidance of members of our organization. Furthermore, we rely on single-source suppliers for our drug substance manufacturing (PharmaBlock Sciences (Nanjing), Inc.) and for our drug product manufacturing (STA Pharmaceutical Hong Kong Limited). We have entered into a master services agreement with each of these service providers; however, under the terms of the master services agreements, the service provider is not obligated to enter into any particular statement of work and there is no pre-determined pricing for the manufacturing services. If we were to experience an unexpected loss of supply of any of our product candidates or any of our future product candidates for any reason, whether as a result of manufacturing, supply or storage issues or otherwise, we could experience delays, disruptions, suspensions or terminations of, or be required to restart or repeat, any pending or ongoing preclinical studies and clinical trials.

We expect to continue to rely on third-party manufacturers for the commercial supply of any of our product candidates for which we obtain marketing approval. We may be unable to maintain or establish required agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- the failure of the third party to manufacture our product candidates according to our schedule, or at all, including if our third-party contractors give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of their agreements with us;
- the reduction or termination of production or deliveries by suppliers, or the raising of prices or renegotiation of terms;
- the termination or nonrenewal of arrangements or agreements by our third-party contractors at a time that is costly or inconvenient for us;
- the breach by the third-party contractors of their agreements with us;
- the failure of third-party contractors to comply with applicable regulatory requirements;
- the failure of third parties to manufacture product candidates according to our specifications;
- the mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or active drug or placebo not being properly identified;
- clinical supplies not being delivered to clinical sites on time, leading to clinical trial interruptions, or of drug supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales; and
- the misappropriation of our proprietary information, including our trade secrets and know-how.

We do not have complete control over all aspects of the manufacturing process of, and are dependent upon, our contract manufacturing partners for compliance with cGMP regulations for manufacturing both active drug substances and finished drug products. Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside of the United States. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA, EMA or others, we will not be able to secure and/or maintain marketing approval for our manufacturing facilities. In addition, we do not have control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA, EMA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain marketing approval for or market our product candidates, if approved. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates or drugs and harm our business and results of operations. Our current and anticipated future dependence upon others for the manufacture of our product candidates or drugs may adversely affect our future profit margins and our ability to commercialize any product candidates that receive marketing approval on a timely and competitive basis.

The manufacture of drugs is complex, and our third-party manufacturers may encounter difficulties in production. If any of our third-party manufacturers encounter such difficulties, our ability to provide adequate supply of our product candidates for clinical trials or our products for patients, if approved, could be delayed or prevented.

Manufacturing drugs, especially in large quantities, is complex and may require the use of innovative technologies. Each lot of an approved drug product must undergo thorough testing for identity, strength, quality, purity, potency and stability. Manufacturing drugs requires facilities specifically designed for and validated for this purpose, and sophisticated quality assurance and quality control procedures are necessary. Slight deviations anywhere in the manufacturing process, including filling, labeling, packaging, storage, shipping, quality control and testing, may result in lot failures, product recalls or spoilage. When changes are made to the manufacturing process, we may be required to provide preclinical and clinical data showing the comparable identity, strength, quality, purity or potency of the products before and after such changes. If microbial, viral or other contaminations are discovered at the facilities of our manufacturers, such facilities may need to be closed for an extended period of time to investigate and remedy the contamination, which could delay clinical trials and adversely harm our business. If our manufacturers are unable to produce sufficient quantities for clinical trials or for commercialization as a result of these challenges, or otherwise, our development and commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations and growth prospects.

Risks Related to Our Business Operations

Our success is highly dependent on our ability to attract and retain highly skilled executive officers and employees.

To succeed, we must recruit, retain, manage and motivate qualified executives, and we face significant competition for experienced personnel. We are highly dependent on the principal members of our management and need to add executives with operational and commercialization experience as we plan for commercialization of our product candidates and operations as a public company. Failure to attract and retain qualified personnel, particularly at the management level, could adversely affect our ability to execute our business plan and harm our operating results. In particular, the loss of one or more of our executive officers could be detrimental to us if we cannot recruit suitable replacements in a timely manner. The competition for qualified personnel in the biotechnology field is intense and, as a result, we may be unable to continue to attract and retain qualified personnel necessary for the future success of our business. We could in the future have difficulty attracting experienced personnel and may be required to expend significant financial resources in employee recruitment and retention efforts.

Many of the other biotechnology companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. They also may provide more diverse opportunities and better prospects for career advancement. Some of these characteristics may be more appealing to high-quality candidates than what we have to offer. If we are unable to continue to attract and

retain high-quality personnel, the rate and success at which we can discover, develop and commercialize our product candidates will be limited, and the potential for successfully growing our business will be harmed.

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

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

- increased operating expenses and cash requirements;
- the assumption of indebtedness or contingent liabilities;
- the issuance of equity securities resulting in dilution to our stockholders;
- assimilation of operations, intellectual property, products and product candidates of an acquired company, including difficulties associated with integrating new personnel;
- the diversion of management's attention from our existing product candidates and initiatives in pursuing such an acquisition or strategic partnership;
- loss of key personnel;
- uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and our existing products or product candidates; and
- our inability to generate revenue from acquired intellectual property, technology or products sufficient to meet our objectives or even to offset the associated transaction and maintenance costs.

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

Our internal computer systems, or those of any of our CROs, manufacturers, other contractors or consultants, or potential future collaborators, may fail or suffer actual or suspected security or privacy breaches or incidents or other unauthorized or improper access to, use of, or destruction of our proprietary or confidential data, employee data, or personal data, which could result in additional costs, significant liabilities, harm to our brand and material disruption of our operations, and potentially significant delays in our delivery to market.

Despite the implementation of security measures in an effort to protect systems that store our information, given their size and complexity and the increasing amounts of information maintained on our internal information technology systems and external processing and storage (e.g., cloud) systems, and those of our third-party CROs, other contractors (including sites performing our current or future clinical trials), consultants and other third-party service providers, these systems are potentially vulnerable to breakdown or other damage or interruption. Our systems and the systems of third parties who support our operations are vulnerable to service interruptions, system malfunction, natural disasters, terrorism, war (such as the ongoing conflicts in the Middle East and between Ukraine and Russia), and telecommunication and electrical failures, as well as security breaches and incidents arising from or caused by inadvertent or intentional actions by our employees, contractors, consultants, business partners, or other third parties, or from cyberattacks by malicious third parties (including the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering, and other means to affect service reliability and threaten the confidentiality, integrity, or availability of information), which may compromise our system infrastructure or lead to unauthorized access to or disruption of our or third-party systems and the unauthorized access to, misuse, disclosure, loss, destruction, alteration or dissemination of, or damage to, our data, including trade secrets or other confidential information, intellectual property, proprietary business information, and personal information. For example, companies have experienced an increase in phishing and social engineering attacks in recent years. Our employees generally work in a hybrid model in our offices and from home, and we may need to adjust our working model from time to time. As a result, we may have increased cyber security and data security risks, due to increased use of home wi-fi networks and virtual private networks. While we implement controls to reduce the risk of a resulting cyber security or data security incident or breach, we may experience data security incidents, and there is

no guarantee that the measures we have implemented will be adequate to safeguard all systems and data, especially with some employees working from home or in a hybrid model where it is more difficult for us to monitor.

Any disruption, security incident, or security breach resulting in any loss, destruction, unavailability, alteration or dissemination of, or damage to, our data (including confidential information) or other data we or any of our CROs, other contractors, consultants, potential future collaborators, or other third-party service providers maintain or otherwise process, or our applications, or for it to be believed or reported that any of these occurred, could result in us incurring liability and reputational damage, and the development and commercialization of our product candidates could be delayed. For example, if a security incident were to cause interruptions in our operations, it could result in a material disruption of our programs and the development of our product candidates could be delayed. In addition, the loss or unavailability of clinical trial data for our product candidates could result in delays in our marketing approval efforts and result in us incurring significant costs to recover or reproduce the data. Furthermore, disruptions of our internal information technology systems or those of third parties used in our business, or security breaches or incidents affecting us or any of our CROs, other contractors, consultants, potential future collaborators, or other third-party service providers, could result in the loss, misappropriation, or unauthorized access to, use or disclosure of, or the inability to access, data (including trade secrets or other confidential information, intellectual property, proprietary business information, and personal information), which could result in financial, legal, business, and reputational harm to us. Unauthorized access, use, or disclosure of personal information, including personal information regarding our clinical trial subjects or employees, could harm our reputation directly, compel us to notify individuals or regulators under data breach notification laws, cause us to incur costs related to investigation of the incident (including legal expenses, forensic examination costs, and remediation costs), subject us to mandatory corrective action, and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal information, which could result in significant legal and financial exposure and reputational damage that could have an adverse effect on our business. Our preclinical studies in China could increase our risk to such disruptions.

We expect to incur significant costs in our efforts to detect, prevent, and respond to security incidents. We also rely on third parties to manufacture our product candidates, and similar events relating to their systems could also have a material adverse effect on our business. There have been and may continue to be significant supply chain attacks and operational technology attacks globally, and we cannot guarantee that our systems or those of third-party service providers or other third parties that support us or our operations have not been breached or that they do not contain exploitable defects or bugs that could result in a security incident or breach of, or other disruption to, our systems or the systems of third parties that support us and our operations. To the extent that any disruption or security incident were to result in a loss, destruction or alteration of, or damage to, our data, or inappropriate disclosure of confidential or proprietary information, we could be exposed to litigation and governmental investigations, the further development and commercialization of our product candidates could be delayed, and we could be subject to significant fines or penalties for any noncompliance with certain state, federal or international laws relating to privacy, data protection, and information security. Litigation and governmental investigations could force us to spend money in defense or settlement, divert management's time and attention, increase our costs of doing business, and adversely affect our reputation. We could be required to fundamentally change our business activities and practices in response to such litigation or investigations, which could have an adverse effect on our business. Any actual or perceived inability to adequately protect data in our possession, custody, or control could have a material adverse effect upon our reputation, business, operations, or financial condition.

Our insurance policies may not be adequate to compensate us for the potential losses arising from any such disruption to, failure or security breach of, or incident impacting, our systems or third-party systems where information important to our business operations is stored. In addition, such insurance may not be available to us in the future on economically reasonable terms, or at all. Further, our insurance may not cover all claims made against us and could have high deductibles in any event, and defending a suit, regardless of its merit, could be costly and divert management attention.

Risks Related to Ownership of Our Class A Common Stock

The market price of our Class A Common Stock has been and is expected to continue to be volatile.

The market price of our Class A Common Stock has been and could continue to be subject to significant fluctuations. Some of the factors that may cause the market price of our Class A Common Stock to fluctuate include:

- price and volume fluctuations in the overall stock market from time to time;

- the timing and results of clinical trials for our current product candidates and any future product candidates that we may develop;
- commencement or termination of collaborations for our product development and research programs;
- failure to achieve development, regulatory or commercialization milestones under our collaborations;
- failure or discontinuation of any of our product development and research programs;
- results of preclinical studies, clinical trials or regulatory approvals of product candidates of our competitors, or announcements about new research programs or product candidates of our competitors;
- the level of expenses related to any of our research programs, clinical development programs or product candidates;
- the results of our efforts to develop additional product candidates;
- regulatory actions with respect to our or our competitors' product candidates or products;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- announced or completed acquisitions of businesses, products or intellectual property by us or our competitors;
- actual or anticipated changes in the financial projections or development timelines we may provide to the public or our failure to meet those projections or timelines;
- market conditions in the biotechnology and pharmaceutical sectors;
- changes in the structure of healthcare payment systems;
- sales of our Class A Common Stock by us or our stockholders, or expectations that such sales may occur, and the expiration of lock-up agreements;
- the recruitment or departure of key personnel;
- the public's reaction to our press releases, other public announcements and our filings with the SEC;
- rumors and market speculation involving us or other companies in our industry;
- fluctuations in the trading volume of our Class A Common Stock or the size of our public float;
- actual or anticipated changes or fluctuations in our results of operations;
- actual or anticipated developments in our business, our competitors' businesses or changes in the market valuations of similar companies and the competitive landscape generally;
- changes in the market valuations of similar companies;
- failure of securities analysts to maintain coverage of our Class A Common Stock, changes in actual or future expectations of investors or securities analysts or our failure to meet these estimates or the expectations of investors;
- litigation involving us, our industry or both;
- governmental or regulatory actions or audits;
- regulatory or legal developments in the United States and other countries;
- general economic conditions and trends;
- announcement or expectation of additional financing efforts;
- sales of securities by us or our securityholders in the future;

- if we do not achieve the perceived benefits of the Merger as rapidly or to the extent anticipated by financial or industry analysts; and
- changes in accounting standards, policies, guidelines, interpretations or principles.

Moreover, the stock markets in general have experienced substantial volatility that has often been unrelated to the operating performance of individual companies. These broad market fluctuations may also adversely affect the trading price of our Class A Common Stock. In addition, a recession, depression or other sustained adverse market event could materially and adversely affect our business and the value of our Class A Common Stock. Furthermore, market volatility may lead to increased shareholder activism if we experience a market valuation that activists believe is not reflective of our intrinsic value. Activist campaigns that contest or conflict with our strategic direction or seek changes in the composition of our Board could have an adverse effect on our operating results, financial condition and cash flows.

We expect to incur losses for the foreseeable future and might never achieve profitability.

We may never become profitable, even if we are able to complete clinical development for one or more product candidates and eventually commercialize such product candidates. We will need to successfully complete significant research, development, testing and regulatory compliance activities that, together with projected general and administrative expenses, is expected to result in substantial increased operating losses for at least the next several years. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis.

We may be unable to successfully integrate the businesses of Reneo and Legacy OnKure and realize the anticipated benefits of the Merger.

The Merger involved the combination of two companies that previously operated as independent companies. Following the Merger, we must devote significant management attention and resources to integrating the business practices and operations of the separate companies. We may fail to realize some or all of the anticipated benefits of the Merger if the integration process takes longer than expected or is more costly than expected. Potential difficulties in the integration process include the following:

- the inability to successfully combine the businesses of Reneo and OnKure in a manner that permits us to achieve the anticipated benefits from the Merger in the time frame currently anticipated or at all;
- creation of uniform standards, controls, procedures, policies and information systems; and
- potential unknown liabilities and unforeseen increased expenses, delays or regulatory conditions associated with the Merger.

Many of the other biotechnology companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. These competitors also may provide higher compensation, more diverse opportunities and better prospects for career advancement. Some of these characteristics may be more appealing to high-quality candidates than what we have to offer. If we are unable to continue to attract and retain high-quality personnel, the rate and success at which we can discover, develop and commercialize our product candidates will be limited and the potential for successfully growing our business will be harmed.

If we fail to attract and retain management and other key personnel, we may be unable to continue to successfully develop or commercialize our product candidates or otherwise implement our business plan.

Our ability to compete in the highly competitive pharmaceuticals industry depends on our ability to attract and retain highly qualified managerial, scientific, medical, legal, sales and marketing and other personnel. We will be highly dependent on our management and scientific personnel. The loss of the services of any of these individuals could impede, delay or prevent the successful development of our product pipeline, completion of our planned clinical trials, commercialization of our product candidates or in-licensing or acquisition of new assets and could impact negatively our ability to implement successfully our business plan. If we lose the services of any of these individuals, we might not be able to find suitable replacements on a timely basis or at all, and our business could be harmed as a result. We might not be able to attract or retain qualified management and other key personnel in the future due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses.

We will incur additional costs and increased demands upon management as a result of complying with the laws and regulations affecting public companies.

We will incur significant legal, accounting and other expenses as a public company that Legacy OnKure did not incur as a private company, including costs associated with public company reporting obligations under the Exchange Act. Our management team consists of the executive officers of Legacy OnKure prior to the Merger, some of whom have not previously managed and operated a public company. These executive officers and other personnel will need to devote substantial time to gaining expertise related to public company reporting requirements and compliance with applicable laws and regulations to ensure that we comply with all of these requirements. Any changes we make to comply with these obligations may not be sufficient to allow us to satisfy our obligations as a public company on a timely basis, or at all. These reporting requirements, rules and regulations, coupled with the increase in potential litigation exposure associated with being a public company, could also make it more difficult for us to attract and retain qualified persons to serve on our Board or board committees or to serve as executive officers, or to obtain certain types of insurance, including directors' and officers' insurance, on acceptable terms.

We will continue to be an emerging growth company and a smaller reporting company, and it cannot be certain if the reduced reporting requirements applicable to emerging growth companies and smaller reporting companies will make our Class A Common Stock less attractive to investors.

For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended (the "Sarbanes-Oxley Act"), reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding nonbinding advisory votes on executive compensation and stockholder approval of any golden parachute payments not previously approved. We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the closing of Reneo's initial public offering, (b) in which we have total annual gross revenue of at least $1.235 billion or (c) in which we are deemed to be a large accelerated filer, which requires, among other things, that the market value of our Class A Common Stock that is held by non-affiliates to exceed $700 million as of the prior June 30th, and (2) the date on which we have issued more than $1 billion in non-convertible debt during the prior three-year period.

Even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company," which would allow us to take advantage of many of the same exemptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act (if we are also a non-accelerated filer at that time) and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. It cannot be predicted if investors will find our Class A Common Stock less attractive because we may rely on these exemptions. If some investors find our Class A Common Stock less attractive as a result, there may be a less active trading market for our Class A Common Stock and the price of our Class A Common Stock may be more volatile.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. It is expected that we will continue to elect to use this extended transition period under the JOBS Act. As a result, our financial statements may not be comparable to the financial statements of issuers who are required to comply with the effective dates for new or revised accounting standards that are applicable to public companies, which may make comparison of our financials to those of other public companies more difficult. As a result, changes in rules of GAAP or their interpretation, the adoption of new guidance, or the application of existing guidance to changes in our business could significantly affect our financial position and results of operations.

Additionally, once we are no longer an emerging growth company or a smaller reporting company or otherwise no longer qualify for these exemptions, we will be required to comply with these additional legal and regulatory requirements applicable to public companies and will incur significant legal, accounting and other expenses to do so. If we are not able to comply with the requirements in a timely manner or at all, our financial condition or the market price of our Class A Common Stock may be harmed.

If we fail to maintain proper and effective internal controls, our ability to produce accurate financial statements on a timely basis could be impaired.

We are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act and the rules and regulations of Nasdaq. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting. We must perform system and process evaluation and testing of our internal control over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting in our Annual Report on Form 10-K filing for that year, as required by Section 404 of the Sarbanes-Oxley Act. As a private company, Legacy OnKure was not required to test its internal controls within a specified period. This will require that we incur substantial professional fees and internal costs to expand our accounting and finance functions and that we expend significant management efforts. We may experience difficulty in meeting these reporting requirements in a timely manner.

In addition to the matters described above in the context of Legacy OnKure being a private company, we may discover weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. Our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected.

If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act, or if we are unable to maintain proper and effective internal controls, we may not be able to produce timely and accurate financial statements. If that were to happen, the market price of our Class A Common Stock could decline and we could be subject to sanctions or investigations by Nasdaq, the SEC or other regulatory authorities.

Our Amended and Restated Certificate of Incorporation and the Amended and Restated Bylaws and provisions under Delaware law could make acquiring us more difficult and may prevent attempts by our stockholders to replace or remove our management.

Provisions in our Amended and Restated Certificate of Incorporation ("Amended Certificate of Incorporation") and our Amended and Restated Bylaws ("Amended Bylaws") may discourage, delay or prevent a merger, acquisition or other change in control of the Company that stockholders may consider favorable, including transactions in which holders of our Common Stock might otherwise receive a premium price for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our Common Stock, thereby depressing the market price of our Common Stock. In addition, because the Board will be responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove current management by making it more difficult for stockholders to replace members of the Board. Among other things, these provisions:

- authorize "blank check" preferred stock, which could be issued by the Board without stockholder approval and may contain voting, liquidation, dividend, and other rights superior to our Common Stock;
- provide for a classified board of directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by the Board;
- prohibit stockholder action by written consent;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of the stockholders, including proposed nominations of persons for election to the Board;
- provide that vacancies on the Board may be filled only by a majority of directors then in office, even though less than a quorum;
- provide that our directors may be removed (i) only for cause and (ii) only by the affirmative vote of the holders of 66 2/3% or more of the outstanding shares of capital stock then entitled to vote at an election of directors;
- expressly authorize the Board to make, alter, amend, or repeal the Amended Bylaws; and

- require supermajority votes of the holders of our Common Stock to amend specified provisions of our Amended Certificate of Incorporation and Amended Bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the DGCL, which prohibits stockholders owning in excess of 15% of our outstanding voting stock from merging or combining with us. Although we believe these provisions collectively will provide for an opportunity to receive higher bids by requiring potential acquirors to negotiate with the Board, they would apply even if the offer may be considered beneficial by some stockholders. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove then-current management by making it more difficult for stockholders to replace members of the Board, which is responsible for appointing the members of management.

Our Amended Bylaws provide that, unless we consent in writing to the selection of an alternative forum, certain designated courts will be the sole and exclusive forum for certain legal actions between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, employees or agents.

Our Amended Bylaws provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for the following types of actions or proceedings under Delaware statutory or common law: (i) any derivative claim or cause of action brought on our behalf; (ii) any claim or cause of action for breach of a fiduciary duty owed by any of our current or former directors, officers or other employees, to us or our stockholders; (iii) any claim or cause of action against us or any of our current or former directors, officers or employees arising out of or pursuant to any provision of the DGCL, our Amended Certificate of Incorporation or our Amended Bylaws; (iv) any claim or cause of action seeking to interpret, apply, enforce, or determine the validity of our Amended Certificate of Incorporation or our Amended Bylaws; (v) any claim or cause of action as to which the DGCL confers jurisdiction on the Court of Chancery of the State of Delaware; and (vi) any claim or cause of action against us or any of our current or former directors, officers or employees governed by the internal affairs doctrine or otherwise related to our internal affairs, in all cases to the fullest extent permitted by law and subject to the court having personal jurisdiction over the indispensable parties named as defendants. This provision would not apply to claims or causes of action brought to enforce a duty or liability created by the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction.

Unless we consent in writing to the selection of an alternate forum, the United States federal district courts shall be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. In addition, our Amended Bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock is deemed to have notice of and consented to these exclusive forum provisions. The forum selection provisions in our Amended Bylaws may limit our stockholders' ability to litigate disputes with us in a judicial forum that they find favorable for disputes with us or our directors, officers or employees, which may discourage the filing of lawsuits against us and our directors, officers and employees, even though an action, if successful, might benefit our stockholders. There is uncertainty as to whether a court would enforce such provisions, and investors cannot waive compliance with the federal securities laws and the rules and regulations thereunder. Furthermore, the enforceability of similar choice of forum provisions in other companies' charter documents has been challenged in legal proceedings. It is possible that a court could find these types of provisions to be inapplicable or unenforceable, and if a court were to find either exclusive-forum provision in our Amended Bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving the dispute in other jurisdictions, which could seriously harm our business. Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over actions brought under the Securities Act or the rules and regulations promulgated thereunder. In addition, these forum selection provisions may impose additional litigation costs for stockholders who determine to pursue any such lawsuits against us.

Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful third-party claims against us and may reduce the amount of money available to us.

Our Amended Certificate of Incorporation and Amended Bylaws provide that we will indemnify our directors and officers, in each case to the fullest extent permitted by Delaware law. In addition, as permitted by Section 145 of the DGCL, our Amended Bylaws and the indemnification agreements that we have entered with our directors and officers provide that:

- we may, in our discretion, indemnify employees and agents in those circumstances where indemnification is permitted by applicable law;
- we are required to advance expenses, as incurred, to our directors and officers in connection with defending a proceeding, except that such directors or officers shall undertake to repay such advances if it is ultimately determined that such person is not entitled to indemnification;
- we are not obligated pursuant to our Amended Bylaws to indemnify a person with respect to proceedings initiated by that person against us or our other indemnitees, except with respect to proceedings authorized by our Board or brought to enforce a right to indemnification;
- the rights conferred in our Amended Bylaws are not exclusive, and we are authorized to enter into indemnification agreements with our directors, officers, employees and agents and to obtain insurance to indemnify such persons; and
- we may not retroactively amend the provisions of our Amended Bylaws to reduce our indemnification obligations to directors, officers, employees and agents.

We will indemnify our directors and officers for serving us in those capacities or for serving other business enterprises at our request, to the fullest extent permitted by Delaware law. Delaware law provides that a corporation may indemnify such person if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of the registrant and, with respect to any criminal proceeding, had no reasonable cause to believe such person's conduct was unlawful.

To the extent that a claim for indemnification is brought by any of our directors or officers, it would reduce the amount of funds available for use in our business.

We do not anticipate that we will pay any cash dividends in the foreseeable future.

The current expectation is that we will retain our future earnings, if any, to fund the growth of our business as opposed to paying dividends. As a result, capital appreciation, if any, of our Class A Common Stock will be your sole source of gain, if any, for the foreseeable future.

An active trading market for our Class A Common Stock may not develop, and the holders of our Class A Common Stock may not be able to resell their shares of our Class A Common Stock for a profit, if at all.

Prior to the Merger, there had been no public market for shares of Legacy OnKure capital stock. An active trading market for our Class A Common Stock may never develop or be sustained. If an active market for our Class A Common Stock does not develop or is not sustained, it may be difficult for our stockholders to sell their shares of our Class A Common Stock at an attractive price or at all.

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

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because pharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business, operating results, or financial condition.

Reneo's winddown of its historical operations, the suspension of development activities and the Merger, resulting in the conversion of Legacy OnKure into a public company, made us subject to the SEC requirements applicable to reporting shell company business combinations. As a result, we are subject to more stringent reporting requirements, offering limitations and resale restrictions.

According to SEC guidance, the requirements applicable to reporting shell company business combinations apply to any company that sells or otherwise disposes of its historical assets or operations in connection with or as part of a plan to combine with a non-shell private company in order to convert the private company into a public one. Prior to the Merger, Reneo suspended its development activities and, as such, we are subject to the SEC requirements applicable to reporting shell company business combinations, which are as follows:

- we were required file a Current Report on Form 8-K to report the Form 10 type information (the "Super 8-K") after the closing of the Merger reflecting our status as an entity that is not a shell company;
- we are not eligible to use a Form S-3 until one year after the filing of the Super 8-K;
- we waited 60 calendar days after the filing of the Super 8-K to file a Form S-8 for our equity plans or awards;
- we are an "ineligible issuer" through October 4, 2026, which will prevent us from (i) incorporating by reference in our Form S-1 filings, (ii) using a free writing prospectus or (iii) taking advantage of the well-known seasoned issuer (also known as a "WKSI") status despite our public float;
- investors who (i) were affiliates of OnKure at the time the Merger were submitted for the vote or consent of OnKure stockholders, (ii) received securities in the Merger and (iii) publicly offer or sell such securities will be deemed to be engaged in a distribution of such securities, and therefore would be underwriters with respect to resales of those securities, and accordingly such securities may not be included in the Form S-1 resale shelf registration statement anticipated to be filed after the closing of the Merger unless such securities are sold only in a fixed price offering in which such investors are named as underwriters in the prospectus; and
- Rule 144(i)(2) limits the ability of holders of restricted securities and any affiliates of the public company to publicly resell Rule 145(c) securities per Rule 145(d), as well as any other of our "restricted" or "control" securities per Rule 144, until one year after the Super 8-K is filed with the SEC. Non-affiliate Reneo stockholders prior the Merger are not subject to such restrictions on public resales of their shares.

The foregoing SEC requirements will increase our time and cost of raising capital, offering stock under equity plans, and complying with securities laws. Furthermore, such requirements will add burdensome restrictions on the resale of our Class A Common Stock by our affiliates and any holders of our "restricted" or "control" securities.

Future sales of shares by existing stockholders could cause our Class A Common Stock price to decline.

If existing securityholders sell, or indicate an intention to sell, substantial amounts of our Class A Common Stock in the public market after legal restrictions on resale lapse, the trading price of our Class A Common Stock could decline. Of the outstanding shares of our Class A Common Stock, approximately 6,733,253 shares will be available for sale in the public market beginning 180 days after the closing of the Merger as a result of the expiration of lock-up agreements between Reneo and OnKure on the one hand and certain securityholders of Reneo and OnKure on the other hand. All other outstanding shares of our Class A Common Stock, other than shares held by our affiliates and shares of our Class A Common Stock issued in the Concurrent Financing, are currently freely tradable, without restriction, in the public market. In addition, shares of our Class A Common Stock that are subject to outstanding options or warrants will become eligible for sale in the public market to the extent permitted by the provisions of various vesting agreements and Rules 144 and 701 under the Securities Act. If these shares are sold, the trading price of our Class A Common Stock could decline.

Our executive officers, directors and principal stockholders have the ability to control or significantly influence all matters submitted to our stockholders for approval.

As of March 1, 2025, our executive officers, directors and principal stockholders, in the aggregate, beneficially own approximately 55.5% of the outstanding shares of our Class A Common Stock. As a result, if these stockholders were to choose to act together, they would be able to control or significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these stockholders, if they choose to act together, would control or significantly influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of voting power could delay or prevent an acquisition of us on terms that other stockholders may desire.

If equity research analysts do not publish research or reports, or publish unfavorable research or reports, about us, our business or our market, the stock price and trading volume of our Class A Common Stock could decline.

The trading market for our Class A Common Stock will be influenced by the research and reports that equity research analysts publish about us and our business. Equity research analysts may elect to not provide

research coverage of our Class A Common Stock, and such lack of research coverage may adversely affect the market price of our Class A Common Stock. In the event that we do have equity research analyst coverage, we will not have any control over the analysts or the content and opinions included in their reports. The price of our Class A Common Stock could decline if one or more equity research analysts downgrades our stock or issues other unfavorable commentary or research. If one or more equity research analysts ceases coverage of us or fails to publish reports on it regularly, demand for our Class A Common Stock could decrease, which in turn could cause our stock price or trading volume to decline.

We may be subject to adverse legislative or regulatory tax changes that could negatively impact our financial condition.

The rules dealing with U.S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service (the "IRS") and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or our stockholders. Any change in tax law will be accounted for in the period of enactment. We will assess the impact of various tax reform proposals and modifications to existing tax treaties in all jurisdictions where we have operations to determine the potential effect on our business and any assumptions we will make about our future taxable income. We cannot predict whether any specific proposals will be enacted, the terms of any such proposals or what effect, if any, such proposals would have on our business if they were to be enacted. Such changes, among others, may adversely affect our effective tax rate, results of operation and general business condition.

Our ability to use net operating loss carryforwards and other tax attributes may be limited, including as a result of the Merger.

As of December 31, 2024, we had U.S. federal net operating loss carryforwards of $219.4 million. Under current law, U.S. federal net operating loss carryforwards generated in taxable periods beginning after December 31, 2017, may be carried forward indefinitely, but the deductibility of such net operating loss carryforwards is limited to 80% of taxable income for taxable periods beginning after December 31, 2020. Net operating loss carryforwards may be subject to similar limitations under state law. In addition, under Sections 382 and 383 of the Code, U.S. federal net operating loss carryforwards and other tax attributes may become subject to an annual limitation in the event of certain cumulative changes in ownership. An "ownership change" pursuant to Section 382 of the Code generally occurs if one or more stockholders or groups of stockholders who own at least 5% of a company's stock increase their ownership by more than 50 percentage points (by value) over their lowest ownership percentage within a rolling three-year period. Legacy OnKure had not conducted a study to determine whether such an ownership change had occurred in the previous years to impair the use of its net operating loss carryforwards. Reneo may have experienced such ownership changes in the past, and we believe that Reneo experienced an ownership change in connection with the Merger and the Concurrent Financing. Our ability to utilize these net operating loss carryforwards and other tax attributes to offset future taxable income or tax liabilities may be limited as a result of ownership changes, including, as discussed above, in connection with the Merger and the Concurrent Financing or other transactions. Similar rules may apply under state tax laws. In addition, California has recently enacted a temporary suspension on the use of state net operating loss carryforwards for certain businesses, which may adversely affect us if we earn taxable income in the impacted tax years that is apportioned to California. Other state tax limitations may apply.

If we earn taxable income, such limitations could result in increased future income tax liability to us, and our future cash flows could be adversely affected.

Unfavorable global economic conditions could adversely affect our business, financial condition, results of operations or cash flows.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. A severe or prolonged economic downturn could result in a variety of risks to our business, including weakened demand for our product candidates and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, or cause our customers to delay making payments for our services. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

Item 1B. Unresolved Staff Comments

Not applicable.

Item 1C. Cybersecurity

Cybersecurity Risk Management and Strategy

We recognize the critical importance of cybersecurity in safeguarding our information systems, data, and operations. Our cybersecurity risk management framework is designed to identify, assess, mitigate, and respond to cybersecurity threats that could impact our business, financial condition, or operational results.

Cybersecurity Risk and Threat Landscape

As a company that relies on technology and digital assets, we are exposed to various cybersecurity risks, including unauthorized access to, or disruptions of, our systems and networks, and loss of, damage to, or unauthorized access to, or use, disclosure, or other processing of, data, cyberattacks such as ransomware and other malware, phishing and other forms of social engineering, and denial-of-service attacks, insider threats from employees or third-party service providers, supply chain vulnerabilities that may affect our software, hardware, or service providers, and other sources of security breaches and incidents. A security breach or incident, or any other system failure or disruption could result in operational disruptions, financial losses, reputational damage, regulatory penalties, and legal liabilities.

Cybersecurity Risk Management and Governance

Our cybersecurity risk management approach is integrated into our overall enterprise risk management program. We maintain a cybersecurity governance structure that includes oversight by executive leadership and our Board. Our Board, through the Audit Committee, receives updates on cybersecurity risks, threats, and mitigation strategies on at least a semi-annual basis. Our Chief Financial Officer (CFO) leads our cybersecurity initiatives, working closely with third-party cybersecurity service providers to implement security controls and response plans. We conduct periodic risk assessments and vulnerability analyses to evaluate and strengthen our security posture. Additionally, we maintain a cybersecurity incident response plan that defines procedures designed to identify, contain, mitigate, and recover from cybersecurity incidents. We also evaluate and monitor the security practices of our third-party vendors, partners, and service providers with access to our systems or processing sensitive data on our behalf.

Cybersecurity Strategy and Mitigation Measures

We implement a comprehensive cybersecurity strategy to address cybersecurity risks. We employ a multi-layered security approach that includes firewalls, intrusion prevention systems, endpoint protection, and network segmentation. We utilize access controls, including multi-factor authentication and role-based access management. To enhance employee awareness and reduce human error risks, we conduct regular cybersecurity training and phishing simulations. We utilize encryption technologies and secure backup systems to protect sensitive data. We adhere to certain frameworks such as the National Institute of Standards and Technology (NIST) Cybersecurity Framework. Furthermore, we leverage advanced threat intelligence and monitoring solutions designed to detect and respond to cyber threats in real time.

Cybersecurity Incident Disclosure

As of the date of this report, we have not identified any cybersecurity incidents that have materially affected our financial condition or operations. However, in light of the evolving nature of cyber threats, there is no assurance that we will not be subject to future cybersecurity incidents that could have a material impact on our business. Our cybersecurity risk management efforts are subject to ongoing evaluation and adaptation in response to emerging threats and factors such as regulatory developments. For additional information regarding whether any risks from cybersecurity threats, including as a result of any previous cybersecurity incidents, have materially affected or are reasonably likely to materially affect our company, including our business strategy, results of operations, or financial condition, please refer to Item 1A, “Risk Factors,” in this annual report on Form 10-K.

Item 2. Properties

We lease approximately 14,790 square feet of office space for our headquarters in Boulder, Colorado, and consists of office and laboratory space pursuant to a lease that expires in December 2026. In the Merger, we assumed the lease of approximately 5,100 square feet of office space for the former Reneo headquarters in Irvine, California under a non-cancelable operating lease through November 2026. In January 2025, we subleased this space for the remaining duration of the lease. We believe that our existing facilities are adequate to meet our current needs.

Item 3. Legal Proceedings

From time to time, we may become involved in legal proceedings relating to claims arising from the ordinary course of business. Information pertaining to legal proceedings is described in Item 8, "Financial Statements and Supplementary Data - Note 14: Commitments and Contingencies," and incorporated by reference herein.

Item 4. Mine Safety Disclosures

None.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Market Information

Our Class A common stock has been listed on The Nasdaq Global Market under the symbol "OKUR" since October 7, 2024. From April 9, 2021 through October 4, 2024, our common stock was listed on the Nasdaq Global Market under the symbol "RPHM".

As of March 7, 2025, there were 12,749,299 shares of our Class A common stock outstanding held by approximately 59 holders of record of our Class A common stock and there were 686,527 shares of our Class B common stock outstanding held by 1 holder of record of our Class B common stock. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees.

Dividend Policy

We have never declared or paid any cash dividends on our capital stock. We intend to retain future earnings, if any, to finance the operation of our business and do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to dividend policy will be made at the discretion of our Board and will depend on then-existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects and other factors our Board may deem relevant.

Securities Authorized for Issuance Under Equity Compensation Plans

See Item 12 of Part III of this Annual Report for information about our equity compensation plans which is incorporated by reference herein.

Recent Sales of Unregistered Securities

Except as previously reported in our Quarterly Reports on Form 10-Q and Current Reports on Form 8-K filed with the Securities and Exchange Commission ("SEC") during the year ended December 31, 2024, there were no unregistered sales of equity securities by us during the year ended December 31, 2024.

Stock Performance Graph

Not required for smaller reporting companies.

Use of Proceeds

On April 8, 2021, our registration statement on Form S-1 (File No. 333-254534) relating to our initial public offering ("IPO") was declared effective. On April 13, 2021, we completed our IPO and sold 6,250,000 shares of our common stock at a public offering price of $15.00 per share for aggregate gross proceeds of $93.8 million, before deducting underwriters' discounts and commissions and offering-related expenses. Net proceeds, after deducting underwriting discounts and commissions of $6.6 million and offering expenses of approximately $2.6 million, were $84.6 million. Jefferies LLC, SVB Securities LLC (now Leerink Partners LLC) and Piper Sandler & Co. acted as joint book-running managers. None of the offering proceeds were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning 10.0% or more of any class of our equity securities or to any other affiliates.

As of December 31, 2024, we have used all of the net proceeds from our IPO.

Item 6. [Reserved]

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

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and the related notes and other financial information included elsewhere in this Annual Report. This discussion and analysis contains forward-looking statements based upon our current beliefs, estimates, plans and expectations that involve risks, uncertainties and assumptions. Our actual results may differ materially from those contained in these forward-looking statements as a result of various factors, including those set forth under "Risk Factors" or in other parts of this Annual Report.

Overview

We are a clinical-stage biopharmaceutical company focused on the discovery and development of precision medicines that target biologically validated drivers of cancers underserved by available therapies. Using a structure- and computational chemistry-driven drug design platform, we are committed to improving clinical outcomes for patients by building a robust pipeline of small molecule drugs designed to selectively target specific mutations thought to be key drivers of cancer. By improving selectivity for the oncogenic and mutated form of these cancer-driver proteins, we aim to discover and develop drugs with improved safety and efficacy by sparing toxicity that arises from non-selective inhibition of the non-mutated (or wild-type) version of the protein. We work under the belief that inhibiting target proteins with specific mutations instead of wild-type variants should enable precise patient selection that will, in turn, improve the probability of clinical success. We designed our current product candidates utilizing disciplined medicinal chemistry, x-ray crystallography and computational chemistry to inhibit specified mutated versions of PI3Kα, a key mediator in cancer growth signaling. Our lead product candidate, OKI-219, is a highly selective inhibitor of $PI3K\alpha^{H1047R}$ that has a much smaller impact on $PI3K\alpha^{WT}$. We plan to initially focus on the development of OKI-219 in patients with advanced breast cancer of genetic subtypes that are (a) both HR+ and HER2-; and (b) HER2+. We believe we can potentially expand the application of OKI-219 by conducting appropriate clinical trials in earlier lines of treatment within breast cancer, other subtypes of breast cancer, and potentially in other solid tumors. OKI-219 is currently in a first-in-human Phase 1a/1b clinical trial.

Merger

On the Closing Date, Reneo consummated the previously announced Merger pursuant to the terms of the Merger Agreement, by and among Reneo, Merger Sub I, Merger Sub II, and Legacy OnKure.

Pursuant to the Merger Agreement, on the Closing Date, (i) Reneo effected a reverse stock split of Reneo's issued common stock at a ratio of 1:10, (ii) Reneo changed its name to "OnKure Therapeutics, Inc.", (iii) Reneo reclassified all of its common stock as "Class A Common Stock" or "Class B Common Stock", and (iv) Radiate Merger Sub I merged with and into Legacy OnKure, with Legacy OnKure as the surviving company in the Merger and, after giving effect to such Merger, Legacy OnKure becoming a wholly-owned subsidiary of OnKure Therapeutics, Inc..

Concurrently with the closing of the Merger, Reneo completed a private placement with certain investors (the "Concurrent Investors") to purchase 2,839,005 shares of Common Stock at a price per share of approximately $22.895 per share for an aggregate purchase price of approximately $65.0 million, including the conversion of outstanding convertible notes and accrued but unpaid interest thereon held by certain Legacy OnKure investors (the "Concurrent Financing"). In connection with the Concurrent Financing, Reneo entered into a registration rights agreement with certain investors, pursuant to which Reneo agreed to use commercially reasonably efforts to prepare and file a registration statement with the SEC within 45 calendar days after the Closing Date, registering the resale of the shares of Common Stock issued pursuant to the Concurrent Financing, which was filed in October 2024. Immediately after the effective time of the Merger, following the consummation of the Concurrent Financing, shares received by Legacy OnKure stockholders represented approximately 53.6%, pre-Merger Reneo shares outstanding represented approximately 25.1%, and the shares purchased in the Concurrent Financing represented approximately 21.3% of our outstanding Common Stock.

As of the open of trading on October 7, 2024, our Common Stock began trading on Nasdaq under the symbol "OKUR."

Financial Overview

Since our inception, our operations have primarily focused on raising capital, establishing and protecting our intellectual property portfolio, organizing and staffing our company, business planning, and conducting preclinical

and clinical development of and manufacturing development for our product candidates. We do not have any product candidates approved for sale, have not generated any revenue from product sales, and do not expect to generate revenues from the commercial sale of any products for the foreseeable future, if ever. Since inception, we have incurred significant operating losses. Our net losses were $52.7 million and $35.3 million for the years ended December 31, 2024 and 2023, respectively. As of December 31, 2024, we had an accumulated deficit of $154.7 million, and cash and cash equivalents of $110.8 million.

We have funded our operations primarily through private placements of our common stock, preferred stock and issuance of convertible debt. As of December 31, 2024, we believe our cash resources are sufficient to fund our planned operations for at least the next 12 months from the date of issuance of these financial statements.

Components of Our Results of Operations

Operating Expenses

Research and Development Expenses

Research and development expenses primarily relate to expenses incurred in connection with the discovery and development of our product candidates.

Research and development expenses include:

- employee-related expenses, including salaries, severance, retention, benefits, insurance, and share-based compensation expense;
- expenses incurred under agreements with CROs, which are investigative sites that conduct our clinical trials, other clinical trial-related vendors and clinical consultants;
- the costs of acquiring, developing, and manufacturing and testing clinical and preclinical materials, including costs incurred under agreements with CMOs;
- costs associated with non-clinical activities and regulatory operations; and
- facilities, depreciation, market research, and other expenses, which include allocated expenses for rent and maintenance of facilities, depreciation of leasehold improvements and equipment, and laboratory supplies.

We make non-refundable advance payments for goods and services that will be used in future research and development activities. These payments are recorded as expenses in the period in which we receive or take ownership of the goods or when the services are performed. At any one time, we are working on multiple research or drug discovery programs and internal resources. Employees and infrastructure are not directly tied to any one program and are typically deployed across multiple programs; therefore, we do not track our research and development expenses on a program-specific basis.

Conducting preclinical studies and clinical trials necessary to obtain regulatory approval is costly and time-consuming. As we initiate new clinical trials, our research and development expenses may increase. Product candidates in later stages of development generally have higher development costs than those in earlier stages. As a result, we expect that our research and development expenses will increase substantially over the next several years as we advance product candidates through preclinical studies into and through clinical trials, continue to discover and develop additional product candidates, undertake activities to expand, maintain, protect and enforce our intellectual property portfolio, and hire additional research and development personnel.

Successful development of product candidates is highly uncertain and may not result in approved products. The probability of success for each product candidate may be affected by numerous factors, including clinical data, preclinical data, competition, manufacturability, and commercial viability. Completion dates and completion costs can vary significantly for each product candidate and are difficult to predict. We anticipate that we will make determinations as to which programs to pursue and how much funding to direct to each program on an ongoing basis in response to our ability to enter strategic alliances with respect to each program or product candidate, the scientific and clinical success of each product candidate, and ongoing assessments as to each product candidate's commercial potential. We will need to raise additional capital and may seek strategic alliances in the future to advance our various programs.

General and Administrative

General and administrative expenses consist primarily of salaries, bonuses and related benefits, share-based compensation, and severance and retention benefits related to our executive, finance and administrative functions, professional fees for auditing, tax, consulting and legal services, as well as insurance, board of director compensation, consulting and other administrative expenses. We recognize general and administrative expenses in the periods in which they are incurred.

We expect that our general and administrative expenses will increase over the next several years as we hire additional personnel to support the growth of our business. In addition, we will incur significant additional expenses associated with being a public company, including expenses related to accounting, audit, legal, regulatory, public company reporting and compliance, director and officer insurance, investor and public relations, and other administrative and professional services.

Other Income

Interest Income

Interest income primarily consists of interest income generated from our cash equivalents in interest-bearing money market accounts.

Interest and Other Expense

Interest expense consists primarily of interest expense generated from our convertible notes payable, which were converted at the time of the Merger.

Results of Operations

Comparison of the Year Ended December 31, 2024 and 2023

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

	Year Ended December 31,		
	2024	2023	$ Change
	(in thousands)		
Operating expenses:			
Research and development	$ 43,795	$ 32,115	$ 11,680
General and administrative	10,591	4,819	5,772
Total operating expenses	54,386	36,934	17,452
Loss from operations	(54,386)	(36,934)	(17,452)
Other income and (expense):			
Interest income	2,013	1,623	390
Interest and other expense	(300)	—	(300)
Total other income and (expense)	1,713	1,623	90
Net loss and comprehensive loss	$ (52,673)	$ (35,311)	$ (17,362)

Research and Development Expenses

Research and development expenses were $43.8 million for the year ended December 31, 2024 compared to $32.1 million for the year ended December 31, 2023, an increase of $11.7 million. This increase was primarily due to an increase in research and development costs, consisting of a $6.3 million increase in clinical trial and manufacturing expenses and a $6.2 million increase in personnel-related costs due to an increase in headcount, and higher severance, and share-based compensation charges. These increases were partially offset by a decrease in outsourced research of $0.9 million.

We expect research and development expenses in 2025 to be higher than 2024 due to the continued efforts to advance of our clinical and preclinical programs.

General and Administrative Expenses

General and administrative expenses were $10.6 million for the year ended December 31, 2024 and $4.8 million for the year ended December 31, 2023, an increase of $5.8 million. The increase was primarily related to increased personnel-related and consulting costs of $3.0 million, increased professional service costs, which includes legal, audit and tax services, of $2.1 million, and a $0.4 million increase related to insurance and outside director compensation during 2024.

We expect general and administrative expenses in 2025 to be higher than 2024 as we operate as a public company for the full year in 2025.

Other Income (Expense)

Other income (expense) was $1.7 million for the year ended December 31, 2024 compared to $1.6 million for the year ended December 31, 2023. The change was primarily due to an increase in interest income due to an increase in cash and cash equivalents available to invest during the year ended December 31, 2024 and increased interest expense related to convertible notes payable issued in 2024.

We expect other income (expense) in 2025 to be higher than 2024 with higher average available cash available to invest during 2025.

Liquidity and Capital Resources

Since inception, we have not generated any revenue from product sales and have incurred significant operating losses and negative cash flows from our operations. We expect to continue to incur significant expenses and operating losses for the foreseeable future as we advance the clinical development of our product candidates. We expect that our research and development and general and administrative costs will continue to increase significantly, including in connection with conducting clinical trials and manufacturing our product candidates to support commercialization and providing general and administrative support for our operations, including the costs associated with operating as a public company following the Closing. As a result, we will need additional capital to fund our operations, which we may seek to obtain from equity or debt financings, collaborations, licensing arrangements or other sources.

We have funded our operations primarily through private placements of equity and convertible debt. Based on our current operating plan, we believe that our existing cash, cash equivalents and marketable securities will be sufficient to fund our planned operations for at least the next 12 months from the date of filing this Annual Report.

Funding Requirements

Our primary uses of cash to date have been to fund our research and development activities, including with respect to our PI3Kα and other programs, business planning, establishing and maintaining our intellectual property portfolio, hiring personnel, raising capital and providing general and administrative support for these activities.

We have never generated any revenue from product sales and do not expect to generate any meaningful product revenue unless and until we obtain regulatory approval for our product candidates, and management does not know when, or if, that will occur. Until we can generate significant revenue from product sales, if ever, we will continue to require substantial additional capital to develop our product candidates and fund operations for the foreseeable future. We are subject to all the risks inherent in the development of new biopharmaceutical products, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may harm our business.

In order to complete the development of our product candidates and to build the sales, marketing and distribution infrastructure that we believe will be necessary to commercialize product candidates, if approved, we will require substantial additional capital. Accordingly, until such time that we can generate a sufficient amount of revenue from product sales or other sources, we expect to seek to raise any necessary additional capital through equity financings, debt financings or other capital sources, which could include income from collaborations, partnerships, licensing or other strategic arrangements with third parties. To the extent that we raise additional capital through equity financings or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our stockholders. Debt financing and equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, including restricting our operations and limiting

our ability to incur liens, issue additional debt, pay dividends, repurchase our own Common Stock, make certain investments or engage in merger, consolidation, licensing or asset sale transactions. If we raise capital through collaborations, partnerships and other similar arrangements with third parties, we may be required to grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. We may be unable to raise additional capital from these sources on favorable terms, or at all.

Our ability to secure capital is dependent upon a number of factors, including our success in developing our product candidates. The failure to obtain sufficient capital on acceptable terms when needed could have a material adverse effect on our business, results of operations or financial condition, including requiring us to delay, reduce or curtail our research, product development or future commercialization efforts. We may also be required to license rights to product candidates at an earlier stage of development or on less favorable terms than we would otherwise choose. We cannot provide assurance that we will ever generate positive cash flow from operating activities.

Our future funding requirements will depend on many factors, including:

- the scope, timing, progress, results and costs of researching and developing OKI-219, and conducting preclinical studies and clinical trials;
- the scope, timing, progress, results and costs of researching and developing other product candidates that we may pursue;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs of future activities, including product sales, medical affairs, marketing, manufacturing and distribution for our product candidates for which we receive marketing approval;
- the costs of manufacturing commercial-grade products and producing sufficient inventory to support commercial launch;
- the revenue, if any, received from commercial sales of our products, should our product candidates receive marketing approval;
- the cost and timing of attracting, hiring and retaining skilled personnel to support our operations and continued growth;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- our ability to establish, maintain and derive value from collaborations, partnerships or other marketing, distribution, licensing or other strategic arrangements with third parties on favorable terms, if at all;
- the extent to which we acquire or in-licenses other product candidates and technologies, if any; and
- the costs associated with operating as a public company.

A change in the outcome of any of these or other factors with respect to the development of OKI-219 or any of our future product candidates could significantly change the costs and timing associated with the development of that product candidate. Furthermore, our operating plans may change in the future, and we may need additional capital to meet the capital requirements associated with such operating plans.

Cash Flows

The following table summarizes our cash flows for the years ended December 31, 2024 and 2023 (in thousands):

	Years Ended December 31,	
	2024	2023
	(in thousands)	
Net cash provided by (used in):		
Operating activities	$ (51,117)	$ (34,546)
Investing activities	15,873	(246)
Financing activities	116,129	53,125
Net increase in cash and cash equivalents	$ 80,885	$ 18,333

Cash Flows from Operating Activities

Net cash used in operating activities during the year ended December 31, 2024 was $51.1 million. This consisted primarily of a net loss of $52.7 million, a net decrease in operating assets and liabilities of $4.0 million, and an increase in non-cash share-based compensation of $4.3 million.

Net cash used in operating activities during the year ended December 31, 2023 was $34.5 million. This consisted primarily of a net loss of $35.3 million, reduced by non-cash charges for share-based compensation, depreciation and amortization.

Cash Flows from Investing Activities

Net cash provided by investing activities for the year ended December 31, 2024 was $15.9 million and consisted primarily of $15.9 million of proceeds from the sale of available-for-sale securities.

Net cash used in investing activities for the year ended December 31, 2023 was $0.2 million for the purchase of property and equipment.

Cash Flows from Financing Activities

Net cash provided by financing activities was $116.1 million during the year ended December 31, 2024 and primarily consisted of $54.6 million of net proceeds from the Concurrent Financing, $57.7 million of cash acquired in connection with the Merger, and $5.9 million of net proceeds from the issuance of convertible notes payable. These amounts were partially offset by payment of $2.0 million of reverse recapitalization transaction costs in connection with the Merger.

Net cash provided by financing activities during the year ended December 31, 2023 was $53.1 million. This consisted primarily of proceeds of $53.8 million from the sale of shares of Legacy OnKure's preferred stock, partially offset by the payment of $0.7 million of issuance costs.

Material Cash Requirements

The discussion below summarizes our significant contractual obligations and commitments as of December 31, 2024.

Leases. See Note 5 of Notes to Consolidated Financial Statements included in this Annual Report for information regarding our leases, including the future operating lease minimum payments.

Critical Accounting Policies and Estimates

Our management’s discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States of America. The preparation of these consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, and expenses and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements. We base our estimates on historical experience, known trends and events, and various other factors that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and

liabilities that are not readily apparent from other sources. Actual results may differ materially from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this Annual Report, we believe the following accounting policies are the most critical for fully understanding and evaluating our financial condition and results of operations.

Accrued Research and Development Expenses

We record research and development expenses in the period in which we receive or take ownership of the applicable goods or when the applicable services are performed. We are required to estimate our expenses resulting from our obligations under contracts with vendors, consultants, and contract research organizations, in connection with conducting research and development activities. The financial terms of these contracts are subject to negotiations, which vary from contract to contract and may result in payment flows that do not match the periods over which materials or services are provided under such contracts. We reflect research and development expenses in our financial statements by matching those expenses with the period in which services and efforts are expended. We account for these expenses according to the progress of the preclinical studies or clinical trials, as measured by the timing of various aspects of the study or related activities. We determine accrual estimates through a review of the underlying contracts along with the preparation of financial models considering discussions with research and other key personnel as to the progress of studies, trials, or other services being conducted. During a study or trial, we adjust our rate of expense recognition if actual results differ from our estimate. Nonrefundable advance payments for goods and services, including fees for process development or manufacturing and distribution of clinical supplies that will be used in future research and development activities, are deferred and recognized as an expense in the period that the related goods are consumed, or services are performed.

Share-Based Compensation

We maintain an equity incentive compensation plan under which incentive stock options and nonqualified stock options to purchase Common Stock, and restricted stock units for Common Stock, are granted to employees, board of directors, and non-employee consultants. Stock-based compensation cost is measured at the grant date, based on the fair value of the award, and is recognized as expense over the requisite service or performance period. The fair value of stock options granted to employees is estimated using the Black-Scholes option pricing model.

The Black-Scholes valuation method requires certain assumptions be used as inputs, such as the fair value of the underlying Common Stock, expected term of the option before exercise, expected volatility of our Common Stock, risk-free interest rate and expected dividend. Options granted have a maximum contractual term of 10 years. We have limited historical stock option activity and therefore estimate the expected term of stock options granted using the simplified method, which represents the arithmetic average of the original contractual term of the stock option and its weighted-average vesting term. The expected volatility of stock options is based on the historical volatility of several publicly traded companies in similar stages of clinical development. We will continue to apply this process until enough historical information regarding the volatility of our stock price becomes available. The risk-free interest rates used are based on the U.S. Treasury yield in effect at the time of grant for zero-coupon U.S. treasury notes with maturities approximately equal to the expected term of the stock options. We have historically not declared or paid any dividends and do not currently expect to do so in the foreseeable future, and therefore have estimated the dividend yield to be zero.

Stock-based compensation expenses year-over-year have increased due to more equity grants awarded in 2024 to attract and retain key scientific or management personnel.

Recent Accounting Pronouncements

A description of recent accounting pronouncements that may potentially impact our financial position, results of operations or cash flows is disclosed in Note 2 to our consolidated financial statements included elsewhere in this Annual Report.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

We are a smaller reporting company, as defined by Rule 12b-2 under the Exchange Act and in Item 10(f)(1) of Regulation S-K, and are not required to provide the information under this item.

Item 8. Financial Statements and Supplementary Data

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and Board of Directors of
OnKure Therapeutics, Inc.:

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of OnKure Therapeutics, Inc. and subsidiaries (the Company) as of December 31, 2024 and 2023, the related consolidated statements of operations and comprehensive loss, changes in stockholders' equity, and cash flows for the years then ended and the related notes (collectively, the consolidated financial statements). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2024 and 2023, and the results of its operations and its cash flows for the years then ended, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

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

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ KPMG LLP

We have served as the Company's auditor since 2021.

Denver, Colorado
March 10, 2025

ONKURE THERAPEUTICS, INC.

Consolidated Balance Sheets
(In thousands, except par value and share data)

	December 31, 2024	December 31, 2023
ASSETS		
Current assets:		
Cash and cash equivalents	$ 110,761	$ 29,876
Prepaid expenses and other current assets	2,242	3,890
Total current assets	113,003	33,766
Property and equipment, net	1,025	1,432
Operating lease right-of-use asset	770	478
Other assets	109	58
Total assets	$ 114,907	$ 35,734
LIABILITIES, CONVERTIBLE PREFERRED STOCK, AND STOCKHOLDERS' EQUITY (DEFICIT)		
Current liabilities:		
Accounts payable	$ 2,968	$ 3,417
Accrued expenses	7,026	3,660
Operating lease liabilities, current portion	536	208
Total current liabilities	10,530	7,285
Long-term operating lease liabilities	549	466
Total liabilities	11,079	7,751
Commitments and contingencies (Note 14)		
Convertible preferred stock, Series C, $0.0001 par value; no shares and 7,404,919 shares authorized; no shares and 6,840,620 shares issued and outstanding at December 31, 2024 and December 31, 2023, respectively; liquidation preference of $195,823 as of December 31, 2023	—	129,825
Stockholders' equity (deficit):		
Preferred stock, $0.0001 par value; 10,000,000 shares authorized; no shares issued or outstanding at December 31, 2024	—	—
Common stock, Class A, $0.0001 par value; 200,000,000 and 943,840 shares authorized; 12,660,590 and 313,747 shares issued and outstanding at December 31, 2024 and December 31, 2023, respectively	1	—
Common stock, Class B, $0.0001 par value; 10,000,000 and 226,285 shares authorized; 686,527 and no shares issued and outstanding at December 31, 2024 and December 31, 2023, respectively	—	—
Additional paid-in capital	258,551	209
Accumulated deficit	(154,724)	(102,051)
Total stockholders' equity (deficit)	103,828	(101,842)
Total liabilities, convertible preferred stock, and stockholders' equity (deficit)	$ 114,907	$ 35,734

The accompanying notes are an integral part of these consolidated financial statements.

ONKURE THERAPEUTICS, INC.

Consolidated Statements of Operations and Comprehensive Loss
(In thousands, except share and per share data)

	Years Ended December 31,	
	2024	**2023**
	(in thousands, except share and per share amounts)	
Operating expenses:		
Research and development	$ 43,795	$ 32,115
General and administrative	10,591	4,819
Total operating expenses	54,386	36,934
Loss from operations	(54,386)	(36,934)
Other income and (expense):		
Interest income	2,013	1,623
Interest and other expense	(300)	—
Total other income and (expense)	1,713	1,623
Net loss and comprehensive loss	$ (52,673)	$ (35,311)
Net loss per share attributable to common stockholders:		
Basic and diluted	$ (15.28)	$ (124.41)
Weighted average shares outstanding:		
Basic and diluted	3,447,071	283,817

The accompanying notes are an integral part of these consolidated financial statements.

ONKURE THERAPEUTICS, INC.

Consolidated Statements of Changes in Stockholders' Equity
(In thousands, except share data)

	Convertible Preferred Stock		Class A Common stock		Class B Common stock		Additional Paid-In Capital	Accumulated Deficit	Total Stockholders' Deficit
	Shares	Amount	Shares	Amount	Shares	Amount			
Balance, December 31, 2022	**3,738,936**	**$ 64,389**	**182,769**	**$ —**	**—**	**$ —**	**$ 2,656**	**$ (57,074)**	**$ (54,418)**
Issuance of Series C Preferred Stock under a stock purchase agreement, net of issuance costs of $0.7 million	2,818,192	53,059	—	—	—	—	—	—	—
Issuance of Class A Common Stock and Series C Preferred Stock in exchange for Series A, A-1, and Series B Preferred Stock under a stock purchase agreement	283,492	12,377	127,476	—	—	—	(2,711)	(9,666)	(12,377)
Issuance of Class A Common Stock for cash upon the exercise of stock options	—	—	3,502	—	—	—	65	—	65
Share-based compensation expense	—	—	—	—	—	—	199	—	199
Net loss	—	—	—	—	—	—	—	(35,311)	(35,311)
Balance, December 31, 2023	**6,840,620**	**129,825**	**313,747**	**$ —**	**—**	**$ —**	**$ 209**	**$ (102,051)**	**$ (101,842)**
Conversion of Convertible Preferred Stock for Class A and B Common Stock in connection with the Merger	(6,840,620)	(129,825)	6,154,093	1	686,527	—	129,824	—	129,825
Issuance of Class A Common Stock in the Concurrent Financing, less issuance costs	—	—	2,571,736	—	—	—	54,428	—	54,428
Issuance of common stock to former stockholders of Reneo Pharmaceuticals, Inc. in the reverse recapitalization	—	—	3,343,604	—	—	—	65,499	—	65,499
Reverse recapitalization transaction costs of OnKure	—	—	—	—	—	—	(2,085)	—	(2,085)
Issuance of Class A Common Stock for the conversion of Convertible Promissory Notes	—	—	267,269				6,120		6,120
Issuance of Class A common stock for the settlement of restricted stock units	—	—	7,700	—	—	—	—	—	—
Issuance of Class A Common Stock from the exercise of stock options	—	—	2,476	—	—	—	26	—	26
Adjustment for fractional shares in the reverse recapitalization	—	—	(35)	—	—	—	—	—	—
Share-based compensation	—	—	—	—	—	—	4,530	—	4,530
Net loss	—	—	—	—	—	—	—	(52,673)	(52,673)
Balance, December 31, 2024	**—**	**$ —**	**12,660,590**	**$ 1**	**686,527**	**$ —**	**$ 258,551**	**$ (154,724)**	**$ 103,828**

The accompanying notes are an integral part of these consolidated financial statements.

ONKURE THERAPEUTICS, INC.

Consolidated Statements of Cash Flows
(In thousands)

	Years Ended December 31,	
	2024	2023
	(in thousands)	
Cash flows from operating activities:		
Net loss	$ (52,673)	$ (35,311)
Adjustments to reconcile net loss to net cash used in operating activities:		
Share-based compensation expense	4,530	199
Depreciation and amortization	459	417
Amortization of right-of-use asset - operating	203	143
Amortization of debt issuance costs	142	—
Non-cash interest expense	120	—
Loss on sales of available-for-sale securities	54	—
Change in operating assets and liabilities:		
Prepaid and other assets	2,256	(1,497)
Accounts payable, accrued and other liabilities	(5,927)	1,713
Lease liabilities	(281)	(210)
Net cash used in operating activities	(51,117)	(34,546)
Cash flows from investing activities:		
Proceeds from sales of marketable securities	15,925	—
Purchases of property and equipment	(52)	(246)
Net cash provided by (used in) investing activities	15,873	(246)
Cash flows from financing activities:		
Proceeds from the issuance of common stock in Concurrent Financing	58,881	—
Payment of issuance costs associated with the Concurrent Financing	(4,327)	—
Cash acquired in connection with the reverse recapitalization	57,736	—
Payment of reverse recapitalization transaction costs	(2,045)	—
Proceeds from the issuance of Convertible Preferred Stock	—	53,783
Payment of issuance costs associated with the issuance of Convertible Preferred Stock	—	(723)
Proceeds from issuance of convertible notes payable	6,000	—
Payment of issuance costs associated with the issuance of convertible notes payable	(142)	—
Proceeds from the issuance of common stock in connection with equity plans	26	65
Net cash provided by financing activities	116,129	53,125
Net increase in cash and cash equivalents	80,885	18,333
Cash and cash equivalents, beginning of period	29,876	11,543
Cash and cash equivalents, end of period	$ 110,761	$ 29,876
Supplemental cash flow information:		
Interest paid	$ —	$ —
Supplemental disclosure of noncash financing activities:		
Right-of-use asset obtained in exchange for new operating lease liability	$ —	$ 219
Issuance of Series C Preferred Stock conversion	$ —	$ 23,313
Conversion of Series C Preferred Stock	$ 129,825	$ —
Conversion of convertible note payable	$ 6,120	$ —
Assets acquired in connection with the reverse recapitalization	$ 17,222	$ —
Other liabilities assumed in connection with the reverse recapitalization	$ 9,459	$ —
Reverse recapitalization transaction costs included in accounts payable	$ 40	$ —
Concurrent Financing issuance costs included in accounts payable	$ 37	$ —
Concurrent Financing issuance costs paid by Reneo prior to Merger	$ 89	$ —

The accompanying notes are an integral part of these consolidated financial statements.

1. Organization and Business

OnKure Therapeutics, Inc., ("OnKure" or the "Company") is a clinical-stage biopharmaceutical company focused on the discovery and development of precision medicines that target biologically validated drivers of cancers that are underserved by available therapies. Using a structure- and computational chemistry-driven drug design platform, OnKure is committed to improving clinical outcomes for patients by building a pipeline of small molecule drugs designed to selectively target specific mutations thought to be key drivers of cancer. The Company was formed in 2014 as Reneo Pharmaceuticals, Inc. (“Reneo”) under the laws of the State of Delaware. On October 4, 2024, the Company changed its name to OnKure Therapeutics, Inc.

Merger with Reneo

On October 4, 2024, Radiate Merger Sub I, Inc. ("Merger Sub I") a wholly-owned subsidiary of Reneo completed its merger with and into OnKure, Inc. (referred to herein as “Legacy OnKure”), with Legacy OnKure continuing as the surviving entity as a wholly-owned subsidiary of Reneo. This transaction is referred to as the “Merger.” Following the Merger, Reneo changed its name to OnKure Therapeutics, Inc. Legacy OnKure remains as a wholly-owned subsidiary of the Company. The Merger was effected pursuant to an Agreement and Plan of Merger, dated as of May 10, 2024 (the "Merger Agreement"), by and among Reneo, Radiate Merger Sub I, Inc., a Delaware corporation Radiate Merger Sub II, LLC, a Delaware limited liability company ("Merger Sub II"), and Legacy OnKure. In connection with the Merger Agreement, certain parties entered into a subscription agreement with the Company to purchase shares of Reneo’s common stock for an aggregate purchase price of $65.0 million contingent upon the concurrent consummation of the Merger (the “Concurrent Financing”). On October 4, 2024 (the “Closing Date”), the Merger and the Concurrent Financing closed.

The Merger was accounted for as a reverse recapitalization in accordance with accounting principles generally accepted in the United States of America (“GAAP”). For accounting purposes, Legacy OnKure is considered the accounting acquirer and Reneo is the acquired company based on the terms of the Merger Agreement and other factors, such as relative voting rights and the composition of the combined company’s board of directors and senior management. Accordingly, the Merger was treated as the equivalent of Legacy OnKure issuing stock to acquire the net assets of Reneo. As a result of the Merger, the net assets of Reneo were recorded at their acquisition-date fair value in the financial statements of the combined company and the reported operating results prior to the Merger are those of Legacy OnKure. Legacy OnKure’s historical financial statements became the historical consolidated financial statements of the combined company. All issued and outstanding Legacy OnKure common stock, convertible preferred stock, restricted stock units, and options to purchase common stock prior to the effective date of the Merger have been retroactively adjusted to reflect the exchange ratio for all periods presented.

See Note 3 for further discussion.

Risks and Uncertainties

The board of directors of the Company discusses with management macroeconomic and geopolitical developments, including inflation, instability in the banking and financial services sector, tightening of the credit markets, international conflicts, cybersecurity, and sanctions so that the Company can be prepared to react to new developments as they arise. The board of directors and the management of the Company are carefully monitoring these developments and the resulting economic impact on its financial condition and results of operations.

Liquidity and Capital Resources

The Company had recurring losses from operations, an accumulated deficit of $154.7 million and cash and cash equivalents of $110.8 million as of December 31, 2024. The Company’s ability to fund its ongoing operations is highly dependent upon raising additional capital through the issuance of equity securities, issuing debt or other financing vehicles.

As of December 31, 2023, the Company had determined that substantial doubt about the Company’s ability to continue as a going concern for a period of at least 12 months from the date of the issuance of those financial

statements did exist. However, following the completion of the Merger and Concurrent Financing, as described in more detail in Note 3, management believes the Company's cash and cash equivalents will be sufficient to fund its current operating plan for at least the next 12 months from the date of issuance of these consolidated financial statements and as such substantial doubt has been alleviated.

The Company's ability to secure capital is dependent upon success in discovering and developing its drug candidates. The Company cannot provide assurance that additional capital will be available on acceptable terms, if at all. The issuance of additional equity or debt securities will likely result in substantial dilution to the Company's stockholders. Should additional capital not be available to the Company in the near term, or not be available on acceptable terms, the Company may be unable to realize value from the Company's assets or discharge liabilities in the normal course of business, which may, among other alternatives, cause the Company to delay, substantially reduce, or discontinue operational activities to conserve cash, which could have a material adverse effect on the Company's ability to achieve its intended business objectives.

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern, which contemplates the realization of assets and the settlement of liabilities and commitments in the normal course of business. The financial statements do not reflect any adjustments relating to the recoverability and reclassification of assets and liabilities that might be necessary if the Company is unable to continue as a going concern.

Failure to raise capital as and when needed, on favorable terms or at all, would have a negative impact on the Company's financial condition and its ability to discover and develop its product candidates. Changing circumstances may cause the Company to consume capital significantly faster or slower than currently anticipated. If the Company is unable to acquire additional capital or resources, it will be required to modify its operational plans. The estimates included herein are based on assumptions that may prove to be wrong, and the Company could exhaust its available financial resources sooner than currently anticipated.

2. Summary of Significant Accounting Policies

Basis of Presentation and Consolidation

The Company's consolidated financial statements are prepared in accordance with GAAP and reflect the operation of the Company and its wholly owned subsidiaries, OnKure, Inc. and Merger Sub II. All intercompany balances and transactions among the consolidated entities have been eliminated in consolidation.

Segment Information

The Company operates in one operating segment: clinical research. All equipment and other property and equipment are physically located within the United States.

Use of Estimates

The preparation of the Company's consolidated financial statements in accordance with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and contingent liabilities at the date of the financial statements, and the reported amounts of expenses during the reporting period. Although these estimates are based on the Company's knowledge of current events and actions it may take in the future, actual results may ultimately differ from these estimates. The most significant estimates relate to external research and development expenses, and the fair value of stock options and restricted stock awards and units.

Comprehensive Loss

Comprehensive loss is defined as a change in equity during a period from transactions and other events and circumstances from non-owner sources. The Company's comprehensive loss was the same as its reported net loss for all periods presented.

Research and Development Expenses

Research and development ("R&D") costs are expensed as incurred in performing research and development activities. The costs include employee-related expense, including salaries, severance, benefits, share-

based compensation, fees for acquiring and maintaining licenses under third-party license agreements, consulting fees, costs of research and development activities conducted by third parties on the Company's behalf, costs to manufacture or have manufactured clinical trial materials, depreciation, and facilities and overhead costs.

Accrued Research and Development Expenses

The Company records research and development expenses in the period in which the Company receives or takes ownership of the applicable goods or when the applicable services are performed. The Company is required to estimate its expenses resulting from its obligations under contracts with vendors, consultants, and contract research organizations, in connection with conducting research and development activities. The financial terms of these contracts are subject to negotiations, which vary from contract to contract and may result in payment flows that do not match the periods over which materials or services are provided under such contracts. The Company reflects research and development expenses in its financial statements by matching those expenses with the period in which services and efforts are expended. The Company accounts for these expenses according to the progress of the preclinical studies or clinical trials, as measured by the timing of various aspects of the study or related activities. The Company determines accrual estimates through a review of the underlying contracts along with the preparation of financial models considering discussions with research and other key personnel as to the progress of studies, trials, or other services being conducted. During a study or trial, the Company adjusts its rate of expense recognition if actual results differ from its estimate. Nonrefundable advance payments for goods and services, including fees for process development or manufacturing and distribution of clinical supplies that will be used in future research and development activities, are deferred and recognized as an expense in the period that the related goods are consumed, or services are performed.

Patent Costs

The Company expenses all costs as incurred in connection with patent applications (including direct application fees and the legal and consulting expenses related to making such applications) and such costs are included in general and administrative expenses in the statements of operations and comprehensive loss.

Share-Based Compensation

The Company maintains an equity incentive compensation plan under which incentive stock options and nonqualified stock options to purchase common stock, and restricted stock units for common stock, are granted to employees, board of directors, and non-employee consultants. Stock-based compensation cost is measured at the grant date, based on the fair value of the award, and is recognized as expense over the requisite service or performance period. The fair value of stock options granted to employees is estimated using the Black-Scholes option pricing model.

The Black-Scholes valuation method requires certain assumptions be used as inputs, such as the fair value of the underlying common stock, expected term of the option before exercise, expected volatility of the Company's common stock, risk-free interest rate and expected dividend. Options granted have a maximum contractual term of 10 years. The Company has limited historical stock option activity and therefore estimates the expected term of stock options granted using the simplified method, which represents the arithmetic average of the original contractual term of the stock option and its weighted-average vesting term. The expected volatility of stock options is based on the historical volatility of several publicly traded companies in similar stages of clinical development. The Company will continue to apply this process until enough historical information regarding the volatility of its stock price becomes available. The risk-free interest rates used are based on the U.S. Treasury yield in effect at the time of grant for zero-coupon U.S. treasury notes with maturities approximately equal to the expected term of the stock options. The Company has historically not declared or paid any dividends and does not currently expect to do so in the foreseeable future, and therefore has estimated the dividend yield to be zero. (See Note 12).

The Company recognizes stock-based compensation expense for grants under its various Equity Incentive Plans and employee stock purchase plan ("ESPP"). The Company accounts for all stock-based awards granted to employees and directors at their fair value and recognizes compensation expense over the award's vesting period. Determining the amount of stock-based compensation to be recorded requires the Company to develop estimates of fair values of stock options as of the grant date. The Company calculates the grant date fair values of stock options using the Black-Scholes valuation model, which requires the input of subjective assumptions, including but not limited to expected stock price volatility over the term of the awards and the expected term of stock options. The fair

value of restricted stock awards granted to employees is based on the quoted closing market price per share on grant date.

Common Stock Valuation

Due to the lack of marketability for the Company's common stock prior to the Merger, the Company utilized methodologies, approaches and assumptions consistent with the American Institute of Certified Public Accountants' Audit and Accounting Practice Guide: Valuation of Privately-Held Company Equity Securities Issued as Compensation to estimate the fair value of its common stock. In determining the exercise prices for options granted prior to the Merger, the Company had considered the fair value of the common stock as of the grant date. The fair value of the common stock has been determined based upon a variety of factors, including the prices at which the Company sold shares of its convertible preferred stock to outside investors in arms-length transactions, and the superior rights, preferences and privileges of the preferred stock relative to the common stock at the time of each grant; the progress of the Company's research and development programs, including their stages of development, and the Company's business strategy; external market and other conditions affecting the biotechnology industry, and trends within the biotechnology industry; the Company's financial position, including cash on hand, and its historical and forecasted performance and operating results; the lack of an active public market for the Company's common stock; and the market performance of peer companies in the biopharmaceutical industry.

Significant changes to the key assumptions underlying the factors used could result in different fair values of common stock at each valuation date.

Fair Value of Financial Instruments

The Company is required to disclose information on all assets and liabilities reported at fair value that enables an assessment of the inputs used in determining the reported fair values.

The carrying amounts of the Company's financial assets and liabilities, such as cash, receivables, prepaid and other current assets, accounts payable, and accrued expenses approximate their fair values because of the short maturity of these instruments.

Cash and Cash Equivalents

All highly liquid investments with maturities of 90 days or less, at the time of purchase, are classified as cash equivalents. Cash equivalents are reported at cost, which approximates fair value. The Company's cash and cash equivalents consist of money held in demand depository accounts and money market funds. The carrying amount of cash and cash equivalents was $110.8 million and $29.9 million as of December 31, 2024, and 2023, respectively, which approximates fair value and was determined based upon Level 1 inputs. The money market account is valued using quoted market prices with no valuation adjustments applied and is categorized as Level 1.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to concentrations of credit risk consist primarily of cash and cash equivalents. The Company maintains accounts in federally insured financial institutions above federally insured limits of $250,000 as of December 31, 2024 and 2023. Management believes the Company is not exposed to significant credit risk due to the financial position of the depository institutions in which these deposits are held and of the money market funds in which these investments are made.

Property and Equipment, Net

The Company carries its property and equipment at cost, less accumulated depreciation, amortization and impairment, if any. Expenditures for renewals or betterments that materially extend the useful life of an asset or increase its productivity, such as leasehold improvements, are capitalized. Depreciation is computed using the straight-line method over the estimated useful lives of the assets, generally between three to seven years. Leasehold improvements are amortized over the shorter of the life of the lease (including any renewal periods that are deemed to be reasonably assured) or the estimated useful life of the assets. Repair and maintenance costs are expensed as incurred and expenditures for major improvements are capitalized.

Impairment of Long-Lived Assets

The Company assesses the carrying amount of its property and equipment whenever events or changes in circumstances indicate the carrying amount of such assets may not be recoverable. No impairment charges were recorded during the years ended December 31, 2024 and 2023.

Leasing – Lessee Accounting

The Company determines if an arrangement is a lease at inception. The Company's operating lease agreements are primarily for office space and research labs.

For operating leases with a term greater than one year, the Company recognizes the right-of-use ("ROU") assets and lease liabilities related to the lease payments on its balance sheet. The lease liabilities are initially and subsequently measured at the present value of the unpaid lease payments at the lease commencement date. The ROU assets represent the Company's right to use the underlying assets for the term of the lease and the lease liabilities represent the Company's obligation to make lease payments arising for the agreements. ROU assets are initially measured at cost, which comprises the initial amount of the lease liability adjusted for lease payments made at or before the lease commencement date, plus any initial direct costs incurred less any lease incentives received. The ROU asset is periodically reviewed for impairment unless a triggering event occurs. Lease expense for lease payments is recognized on a straight-line basis over the lease term. Variable lease payments, except for the ones that depend on index or rate, are excluded from the calculation of the ROU assets and lease liabilities and are recognized as variable lease expense in the statements of operations and comprehensive loss in the period in which they are incurred.

As the interest rate implicit in the Company's leases is not readily determinable, the Company uses its estimated incremental borrowing rate in its present value calculations. One of the Company's lessee agreements include an option to extend the lease, which the Company does not include in its minimum lease term unless it is reasonably certain to exercise such option. Operating leases with a term of less than one year are recognized as a lease expense over the term of the lease, with no asset or liability recognized on the balance sheet.

Income Taxes

Income taxes are provided for the tax effects of transactions reported in the financial statements and consist of taxes currently payable and deferred taxes. The Company accounts for income taxes using the asset and liability method of accounting for deferred income taxes. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax basis, and operating losses and tax credit carryforwards.

A valuation allowance is recorded to the extent it is more likely than not that some portion of a deferred tax asset will not be realized. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in operations in the period that includes the enactment date. The Company's significant deferred tax assets are net operating loss carryforwards, tax credits, and accruals. The Company has provided a valuation allowance equal to its net deferred tax assets since inception as, due to its history of operating losses, the Company has concluded that it is more likely than not that most of its deferred tax assets will not be realized.

Accounting for uncertain tax positions requires a more likely than not threshold for recognition in the financial statements. The Company recognizes a tax benefit based on whether it is more likely than not that a tax position will be sustained. The Company records a liability to the extent that a tax position taken or expected to be taken on a tax return exceeds the amount recognized in the financial statements.

The Company has no unrecognized tax benefits as of December 31, 2024 and 2023. The Company classifies interest and penalties arising from the underpayment of income taxes in the statements of operations as general and administrative expenses. No such expenses have been recognized during the years ended December 31, 2024 and 2023.

The Company is subject to taxation in the United States and the United Kingdom ("UK"). As of December 31, 2024, the Company's tax years since inception are subject to examination by taxing authorities in the United States, and the UK tax returns from 2018 forward are subject to examination.

Recently Issued Accounting Pronouncements

In November 2023, the FASB issued ASU 2023-07, *Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures* to update reportable segment disclosure requirements, primarily through enhanced disclosures about significant segment expenses and information used to assess segment performance. This update is effective beginning with the Company's 2024 fiscal year annual reporting period, with early adoption permitted. The disclosure related to this ASU are in Note 4 below.

In December 2023, the FASB issued ASU 2023-09, *Income Taxes (Topic 740): Improvements to Income Tax Disclosures* ("ASU 2023-09"), which requires enhanced income tax disclosures, including specific categories and disaggregation of information in the effective tax rate reconciliation, disaggregated information related to income taxes paid, income or loss from continuing operations before income tax expense or benefit, and income tax expense or benefit from continuing operations. The requirements of the ASU are effective for annual periods beginning after December 15, 2024, with early adoption permitted. The Company is currently evaluating the impact of this pronouncement.

In November 2024, the FASB issued ASU 2024-03, *Income Statement—Reporting Comprehensive Income—Expense Disaggregation Disclosures (Subtopic 220-40): Disaggregation of Income Statement Expenses*. This ASU requires more detailed disclosures, on an annual and interim basis, about specified categories of expenses (including employee compensation, depreciation, and amortization) included in certain expense captions presented on the face of the income statement. This ASU is effective for fiscal years beginning after December 15, 2026, and interim periods within fiscal years beginning after December 15, 2027. Early adoption is permitted. This ASU may be applied either prospectively or retrospectively. The Company is currently evaluating the impact of this pronouncement.

The Company continues to monitor new accounting pronouncements issued by the FASB and does not believe any accounting pronouncements issued through the date of this report will have a material impact on its financial statements.

3. Merger Agreement and Concurrent Financing

As described in Note 1, Merger Sub I merged with and into Legacy OnKure, with Legacy OnKure surviving as a wholly-owned subsidiary of the Company on October 4, 2024.

At the Closing, each then-outstanding share of Legacy OnKure common stock was converted into the right to receive 0.023596 shares of common stock of Reneo based on the Common Exchange Ratio, which was reclassified as Class A Common Stock in connection with the Merger, and each then-outstanding share of Legacy OnKure preferred stock was converted into the right to receive 0.144794 shares of Class A Common Stock based on the Preferred Exchange Ratio; provided that one holder of Legacy OnKure preferred stock elected to receive 686,527 shares that it would otherwise have received in the form of Class A Common Stock in an equal number of shares of Class B Common Stock. Upon the closing of the Merger, (i) an aggregate of 6,470,281 shares of Class A Common Stock and 686,527 shares of Class B Common Stock of the combined company were issued in exchange for the shares of Legacy OnKure capital stock outstanding as of immediately prior to the Closing and (ii) outstanding shares of Reneo common stock were reclassified into an aggregate of approximately 3,343,604 shares of Class A Common Stock.

In addition, each then-outstanding option to purchase shares of Legacy OnKure common stock was assumed and converted into an option to purchase Class A Common Stock based on the Common Exchange Ratio, and each then-outstanding RSU of Legacy OnKure corresponding to shares of Legacy OnKure preferred stock was assumed and converted into RSUs covering 213,254 shares of Class A Common Stock based on the Preferred Exchange Ratio.

Each share of Reneo common stock, each option to purchase shares of Reneo common stock and each RSU award covering shares of Reneo common stock that was issued and outstanding as of immediately prior to the Closing remained issued and outstanding in accordance with its terms and such shares, options and RSUs, subject to the Reverse Stock Split, were reclassified as Class A Common Stock but were otherwise unaffected by the Merger; provided that, to the extent not previously vested, all such options and RSUs held by Reneo's directors and executive officers vested at Closing.

In connection with the Merger Agreement, Reneo entered into a subscription agreement with certain investors, pursuant to which the investors subscribed for and purchased, concurrent with the closing of the Merger, an aggregate of 2,839,005 shares of Class A Common Stock at a price of approximately $22.895 per share for aggregate gross proceeds of approximately $65.0 million, including the conversion of previously funded Convertible Promissory Notes principal of $6.0 million and accrued interest there on of $120 thousand, on October 4, 2024.

At the effective time of the Merger, the authorized shares of Class A Common Stock of the Company are 200,000,000 with par value of $0.0001 and Class B Common Stock of the Company are 10,000,000 with par value of $0.0001.

In addition, in October 2024 the Company adopted the 2024 Equity Incentive Plan (the "2024 Plan") and 2024 Employee Stock Purchase Plan (the "2024 ESPP"). Under the 2024 Plan a total of 2,480,000 shares of Class A Common Stock were initially reserved for issuance. In addition, shares reserved for issuance under the 2024 Plan will include shares of Class A Common Stock equity awards granted under the Reneo 2021 Plan and any shares of Class A Common Stock equity awards that were assumed in the Merger. Under the 2024 ESPP, an aggregate of 137,500 shares of Class A Common Stock are currently reserved and available for issuance.

The Merger was accounted for as a reverse recapitalization in accordance with GAAP, with Legacy OnKure as the accounting acquirer of Reneo. Legacy OnKure was determined to be the accounting acquirer based on the terms of the Merger Agreement and other factors, such as relative voting rights and the composition of the combined company's board of directors and senior management.

As a result, Legacy OnKure's historical financial statements became the historical consolidated financial statements of the combined company for accounting purposes together with a deemed issuance of shares, equivalent to the shares held by the former stockholders Reneo, the legal acquirer, and a recapitalization of the equity of Legacy OnKure, the accounting acquirer. The final transaction amounts have been recorded as a reduction of proceeds in stockholders' equity.

At the effective time of the Merger, the net assets of Reneo were recorded at their acquisition-date fair value in the financial statements of the combined company, which approximated book value due to the short-term nature. Reneo's development programs had ceased prior to the Merger and were deemed to be de minimis in value at the transaction date. No goodwill or intangible assets were recognized.

As part of the recapitalization, excluding the Concurrent Financing, the Company acquired the assets and liabilities listed below (in thousands):

	Amount
Cash and cash equivalents	$ 57,736
Short-term investments	15,979
Other current assets	690
Other assets	553
Accrued expenses	(9,072)
Long-term operating lease liability	(387)
Net assets acquired	$ 65,499

4. Segment

The Company is a publicly listed company with a single reportable segment: clinical research. Because the Company has one reportable segment, before adopting the ASU, it provided only the entity-wide disclosures required by ASC 280.

The clinical research segment has no revenues. The accounting policies of the clinical research segment are the same as those described in the summary of significant accounting policies.

The Chief Operating Decision Maker ("CODM") assesses the performance for the clinical research segment and decides how to allocate resources based on operating expenses as reported on the income statement.

The measure of segment assets is reported on the balance sheets as total consolidated assets. The CODM considers a variety of factors, including actual and projected expenses in deciding whether to invest funds in the clinical research segment or into other parts of the entity, such as for acquisitions or to pay dividends. The Company does not have intra-entity sales or transfers.

The Company's CODM is the senior executive committee that is comprised of the Chief Financial Officer and the Chief Executive Officer.

	Clinical Research Segment
Operating expenses:	
Direct program expense	$ 27,398
Indirect program expense	2,157
Workforce salaries and benefits	15,102
Stock-based compensation expense	4,530
General corporate expenses	5,199
Interest and other expense	300
Segment net loss	54,686
Reconciliation of loss:	
Interest income	(2,013)
Adjustments and reconciling items	(2,013)
Net loss	$ 52,673

5. Leases

The Company’s headquarters are located in Boulder, Colorado, where it leases 14,790 square feet of office and lab facilities under operating leases that expire in December 2026, with rights to extend for a 5 year period. In the Merger with Reneo, the Company assumed the lease in Irvine, California, where it leases office space under a lease agreement that expires in November 2026 ("Irvine lease"). In January 2025, the Company entered into a sublease agreement on the Irvine lease. See Note 16 for further discussion.

Right-of-use assets and lease liabilities for operating leases as included in the Company’s financial statements are as follows (in thousands):

	December 31, 2024	December 31, 2023
Operating lease right-of-use assets	$ 770	$ 478
Current operating lease liabilities	536	208
Noncurrent operating lease liabilities	549	466
Total lease liabilities	$ 1,085	$ 674

Lease expense for operating leases as included in the Company’s financial statements are as follows (in thousands):

	December 31,	
	2024	2023
Operating lease cost	$ 236	$ 173
Variable lease expense	187	201

Lease term, discount rates, and additional information for operating leases are as follows (in thousands):

	As of December 31,	
	2024	2023
Weighted-average remaining lease term - operating leases (years)	1.87	2.92
Weighted-average discount rate - operating leases	4.5%	4.5%
Cash paid for amounts included in the measurement of lease liabilities:		
Operating cash flows for operating leases	$ 315	$ 210

The aggregate maturities of the Company's operating lease liabilities were as follows as of December 31, 2024 (in thousands):

2025	$ 571
2026	560
Total future minimum lease payments	1,131
Less: imputed interest	(46)
Less: Current portion	(536)
Operating lease liability, net of current portion	$ 549

6. Net Loss Per Share

The Company computes basic loss per share by dividing the net loss attributable to common stockholders by the weighted average number of common shares outstanding for the period, without consideration for common stock equivalents. Diluted net loss per share assumes the conversion, exercise or issuance of all potential common stock equivalents, unless the effect of inclusion would be anti-dilutive. For purposes of this calculation, common stock shares to be issued upon if-converted method for the convertible Series C Preferred Stock, if-converted method for the convertible promissory note, exercise of all outstanding stock options and restricted stock units were excluded from the diluted net loss per share calculation for the twelve months ended December 31, 2024 and 2023 because such shares are anti-dilutive.

Anti-dilutive securities outstanding during the period not included in the diluted net loss per share calculation include the following:

	December 31,	
	2024	2023
Convertible Series C Preferred Stock	5,191,375	6,135,306
Convertible Promissory Notes	149,650	—
Outstanding stock options	2,393,824	178,232
Unvested restricted stock units	213,254	214,436
Unreleased restricted stock units assumed in the Merger	17,000	—
	7,965,103	6,527,974

7. Fair Value Measurements

ASC Topic 820, *Fair Value Measurement*, establishes a fair value hierarchy for instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and the Company's own assumptions (unobservable inputs). Observable inputs are inputs that market participants would use in pricing an asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the asset or liability and are developed based on the best information available in the circumstances.

ASC Topic 820 identifies fair value as the exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As a basis for considering market participant assumptions in fair value measurements, ASC Topic 820 establishes a three-tier fair value hierarchy that distinguishes between the following:

- Level 1 – Observable inputs such as quoted prices in active markets for identical assets or liabilities.
- Level 2 – Inputs, other than quoted prices in active markets, which are observable for the asset or liability, either directly or indirectly.
- Level 3 – Unobservable inputs in which there is little or no market data, which requires the Company to develop its own assumptions.

Assets and liabilities measured at fair value are classified in their entirety based on the lowest level of input that is significant to the fair value measurement. The Company's assessment of the significance of a particular input to the fair value measurement in its entirety requires management to make judgments and consider factors specific to the asset or liability. The Company's financial assets are subject to fair value measurements on a recurring basis.

The Company categorizes its money market funds as Level 1, using the quoted prices in active markets. The fair value of the Company's investments in certain money market funds is their face value and such instruments are classified as Level 1 and are included in cash and cash equivalents on the consolidated balance sheets.

No assets or liabilities were transferred into or out of their classifications during the years ended December 31, 2024 and 2023.

As part of the Merger, the Company acquired certain short-term investments in debt securities that were carried at fair value and classified as current assets available-for-sale and represented the investment of funds available for current operations. During the year ended December 31, 2024, the Company sold these short-term investments for proceeds of $15.9 million which resulted in a realized loss of approximately $54,000. The Company had no available-for-sale securities as of December 31, 2024 or 2023.

8. Prepaid expenses and other current assets

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

	December 31, 2024	December 31, 2023
Prepaid clinical trial expenses	$ 152	$ 3,192
Prepaid insurance expense	537	68
Other prepaid expenses	1,553	630
Total prepaid expenses	$ 2,242	$ 3,890

9. Property and Equipment, Net

Property and equipment, net, consisted of the following (in thousands):

	December 31, 2024	December 31, 2023
Lab equipment	$ 705	$ 706
Leasehold improvements	1,090	1,090
Computer hardware and software	189	141
Furniture and fixtures	160	160
Property and equipment, gross	2,144	2,097
Less: Accumulated depreciation and amortization	(1,119)	(665)
Property and equipment, net	$ 1,025	$ 1,432

Depreciation and amortization expense for the years ended December 31, 2024 and 2023 was $459,000 and $417,000, respectively.

10. Accrued Expenses

Accrued expenses consisted of the following (in thousands):

	December 31, 2024	December 31, 2023
Accrued compensation	$ 3,173	$ 1,663
Accrued contract manufacturing costs	1,565	1,627
Accrued clinical trial costs	1,302	—
Accrued other	986	370
Total accrued expenses	$ 7,026	$ 3,660

Accrued compensation includes severance costs. For further information see Note 14.

11. Equity

Common Stock

The Company is authorized to issue 210,000,000 shares of common stock, of which 200,000,000 shares have been designated as Class A Common Stock and 10,000,000 shares have been designated as Class B Common Stock, both with a par value of $0.0001 per share.

The number of authorized shares of common stock may be increased or decreased by the affirmative vote of the holders of a majority of the Company's stock who are entitled to vote. Each share of Class A Common Stock is entitled to one vote. Class B Common Stock is not entitled to vote on any matter on which the holders of Class A Common Stock or Preferred Stock are entitled to vote. All holders of common stock are entitled to receive dividends when and as declared or paid by the Company's board of directors, subject to the preferential rights of the holders of preferred stock.

Class B Common Stock is convertible into a corresponding number of shares of Class A Common Stock upon written notice of the holder, subject to defined beneficial ownership limitations.

Preferred Stock

The Company is authorized to issue 10,000,000 shares of preferred stock, with a par value of $0.0001 per share. As of December 31, 2024, none of these shares of preferred stock have been designated or issued.

Convertible Preferred Stock

As of December 31, 2023, the Company's Preferred Stock was classified as temporary equity in the accompanying consolidated balance sheets given that the holders of the convertible preferred stock could cause certain events to occur that were outside of the Company's control whereby the Company could be obligated to redeem the convertible preferred stock. The carrying value of the convertible preferred stock is not adjusted to the redemption value until the contingent redemption events are considered probable to occur.

Series C Preferred Stock

In March 2023, the Company entered into a Series C Purchase Agreement pursuant to which the Company issued 2,818,192 shares of Series C Preferred Stock at a purchase price of $19.06 per share, which resulted in gross proceeds of approximately $53.8 million, as well as the conversion of all Series A Preferred Stock, Series A-1 Preferred Stock, and Series B Preferred Stock. In conjunction with the Merger, immediately following the Closing, each then-outstanding share of Legacy OnKure preferred stock converted into Class A or Class B Common Stock. No Convertible Preferred Shares are authorized, issued or outstanding at December 31, 2024.

The Company's convertible preferred stock had the following characteristics as of December 31, 2023:

Conversion of Preferred Stock into Common Stock

Each share of preferred stock, at the option of the holder, was convertible into a number of shares of common stock as determined by multiplying the number of shares of preferred stock being converted by the conversion rate. The conversion rate in effect at any time for conversion of preferred stock is determined by dividing the Original Issue Price by the Conversion Price. The Original Issue Price for the Series C Preferred Stock was

$19.06 per share. The Conversion Price was subject to certain adjustments as provided in the Company's restated certificate of incorporation.

The preferred stock would have automatically converted to common stock upon the closing of an initial public offering of the Company's common stock in which the per-share price is at least $38.19 and gross proceeds of not less than $75 million, or the date and time specified by vote or the written consent of the holders of at least a majority of the then outstanding shares of Series C Preferred Stock voting or consenting as a separate class on an as-converted basis.

Voting Rights

Each preferred stockholder was entitled to the number of votes equal to the number of shares of Class A Common Stock into which such holder's shares are convertible. At any time when a defined number of shares of Series C Preferred Stock are outstanding, the Company was restricted from certain actions described in the Company's restated certificate of incorporation without the vote or written consent of the holders of a majority of the then outstanding shares of Series C Preferred Stock voting or consenting as a separate class on an as-converted basis.

Dividends

The Company could not have declared, paid or set aside any dividends on any shares of any other class or series of capital stock unless each holder of the preferred stock first received a dividend based upon a formula in the Company's restated certificate of incorporation. No dividends were declared during the years ended December 31, 2024 or 2023.

Liquidation Preference

Upon any liquidation, dissolution or winding up of the Company, certain qualifying mergers, sales or transactions with a special purpose acquisition companies, and other deemed liquidation events as defined in the Company's restated certificate of incorporation, unless the holders of a majority of the then outstanding shares of Series C Preferred Stock, voting as a separate class on an as-converted basis, elected otherwise, prior to and in preference to any distribution to the holders of common stock, holders of Series C Preferred Stock were entitled to be paid out of the assets of the Company legally available for distribution, or the consideration received in such transaction, an amount per share of Series C Preferred Stock equal to the greater of: i) 1.50 times the Series C Original Issuance Price plus all declared and unpaid dividends on Series C Preferred Stock or ii) such amount per share that would have been payable had all shares of Series C Preferred Stock been converted into common stock immediately prior to such event. If upon liquidation, dissolution, or winding up of the Company, the assets and funds of the Company are insufficient to permit the payment of the full preferential amounts to the holders of preferred stock, then the holders shall share ratably in any distribution of the assets available for distribution, in proportion to the respective amounts which would otherwise be payable in respect of the shares held by the preferred stockholders.

After the payment of all preferential amounts required to be paid to the holder of shares of preferred stock, the remaining assets available for distribution to its stockholders would have been distributed to the holders of shares of common stock, pro rata based on the number of shares held by each holder. The liquidation preference as of December 31, 2023 was $195.8 million.

12. Share-Based Compensation

The Company's share-based compensation plans are described below:

2024 Equity Incentive Plan

In October 2024, the Company established an equity incentive plan (the "2024 Plan"). The 2024 Equity Incentive Plan became effective upon the closing of the Merger, and will continue in effect for a period of ten years from its effectiveness, unless terminated earlier by the administrator. The 2024 Plan provides for the grant of stock options, RSUs and RSAs to employees, non-employee directors, advisors, and consultants. Under the 2024 Plan a total of 2,480,000 shares of Class A Common Stock were initially reserved for issuance. In addition, shares reserved for issuance under the 2024 Plan will include shares of Class A Common Stock equity awards granted under the Reneo 2021 Plan and any shares of Class A Common Stock equity awards that were assumed in the Merger. As of the effective date of the 2024 Plan, awards granted under the 2011, 2021 and 2023 Plans that are forfeited or otherwise become available will be included and available for issuance under the 2024 Plan. Under the 2024 Plan,

the Company may grant stock options, stock appreciation rights, restricted stock awards, restricted stock units, and other awards to individuals who are employees, officers, directors or consultants of the Company and its affiliates. The Company issues new shares in settlement of equity awards under the 2024 Plan. See Note 16 for discussion of the increase to the available for issuance as of January 1, 2025.

2023 RSU Equity Incentive Plan

In September 2023, the Company established an equity incentive plan (the "2023 Plan"). The 2023 Plan provided for the grant of restricted stock units ("RSU") to employees, directors, and consultants. Upon the close of the Merger, all shares available for issuance under the 2023 Plan were cancelled.

2021 Equity Incentive Plan

In February 2021, the Company established an equity incentive plan (the "2021 Plan"). The 2021 Plan provided for the grant of stock options and RSA to employees, non-employee directors, advisors, and consultants. Upon the close of the Merger, all shares available for issuance under the 2021 Plan were cancelled.

2011 Equity Incentive Plan

In October 2011, the Company established an equity incentive plan (the "2011 Plan"). The 2011 Plan provided for the grant of stock options and restricted stock awards ("RSA") to employees, non-employee directors, advisors, and consultants. Shares are no longer available for issuance under the 2011 Plan, which was subsequently terminated in March 2023. Upon the close of the Merger, all shares available for issuance under the 2011 Plan were cancelled.

In addition, as part of the Merger with Reneo discussed in Note 1, the Company assumed outstanding awards under the following Reneo Equity Incentive Plans and certain awards not issued pursuant to a Reneo Equity Plan:

Reneo 2021 and 2014 Equity Incentive Plans

In March 2021, the Reneo Board of Directors adopted the Reneo 2021 Equity Incentive Plan ("Reneo 2021 Plan"), which is the successor to Reneo's 2014 Equity Incentive Plan and UK Sub-Plan ("2014 Plan").

2024 ESPP

In October 2024, the Company established the 2024 ESPP. Under the 2024 ESPP, an aggregate of 137,500 shares of Class A Common Stock are currently reserved and available for issuance. As of December 31, 2024, no offering periods have been established under the 2024 ESPP. See Note 16 for discussion of the increase to the available for issuance as of January 1, 2025.

Shares Reserved for Future Issuance

As of December 31, 2024, the Company had reserved shares of its common stock for future issuance as follows:

	Shares Reserved
Common stock options outstanding	2,393,824
Unvested restricted stock units under the 2023 Plan	213,254
Unreleased restricted stock units assumed in the Merger	17,000
Available for future grants under the 2024 Equity Incentive Plan	747,867
Available for future grants under the 2024 Employee Stock Purchase Plan	137,500
Total shares of common stock reserved for future issuance	3,509,445

Stock Options

Options granted under the Company's equity incentive plans have an exercise price equal to or in excess of the market value of the Class A Common Stock at the date of grant and expire no more than 10 years from the date of grant. Generally, options become exercisable ratably over a period of three to four years from the date of grant. Stock options granted to non-employees generally vest quarterly over two to three years.

A summary of the Company's stock option activity and related information for the year ended December 31, 2024 is as follows:

	Options Outstanding			
	Number of Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Options outstanding - December 31, 2023	178,232	$ 16.74	8.88	$ 16
Assumed in reverse recapitalization	467,100	47.39		
Granted	1,775,318	18.13		
Exercised	(2,476)	10.19		
Expired	(740)	21.62		
Forfeited	(23,610)	38.34		
Options outstanding - December 31, 2024	2,393,824	$ 23.54	7.90	$ 1
Options exercisable - December 31, 2024	654,636	$ 38.08	3.07	$ 1

All outstanding options as of December 31, 2024 are expected to vest.

As of December 31, 2024, the Company had unrecognized compensation cost for unvested stock options of $26.5 million, expected to be recognized over a weighted-average period of approximately 2.8 years.

The aggregate intrinsic value is calculated as the difference between the exercise price and the estimated fair value of the Company's common stock as of December 31, 2024.

The weighted-average grant-date fair value of options granted for the years ended December 31, 2024, and 2023 was $16.05 and $5.51, respectively.

The Company has granted performance-based stock options. During the year ended December 31, 2023, the Company granted 8,449 performance-based shares, which are included in the table above. The company recognized $30,000 and $13,000 in performance-based compensation expense for the years ended December 31, 2024 and 2023, respectively.

The Company estimates stock awards fair value on the date of grant using the Black-Scholes valuation, with the vesting being subject to service requirements. The Company accounts for forfeitures when they occur. The weighted-average assumptions used in the Black-Scholes option pricing model to determine the fair value of the employee stock option grants were as follows:

	Year Ended December 31,	
	2024	2023
Expected term (years)	5.77	5.73
Expected volatility	126.2%	32.0%
Risk-free interest rate	3.80%	4.31%
Expected dividend yield	0%	0%

Risk-free interest rate. The Company bases the risk-free interest rate assumption on the U.S. Treasury's rates for U.S. Treasury zero-coupon bonds with maturities similar to those of the expected term of the award being valued.

Expected volatility. The expected volatility assumption was based on the volatilities of a peer group of similar companies whose share prices are publicly available. The peer group was developed based on companies in the biotechnology industry.

Expected term. The expected term represents the period of time that options are expected to be outstanding. Because the Company does not have historical exercise behavior, it determines the expected life assumption using the simplified method, which is an average of the contractual term of the option and its vesting period.

Expected dividend yield. The Company bases the expected dividend yield assumption on the fact that it has never paid cash dividends and has no present intention to pay cash dividends.

Restricted Stock Awards (RSAs) and Restricted Stock Units (RSUs)

RSA typically vests 25% on the first anniversary of the issuance date and incrementally vest monthly for the three-year period thereafter. In the event of a termination of services, all unvested shares are forfeited, and the Company has the option to purchase all outstanding vested shares at their fair market value.

RSU vests based on a service-based requirement and a liquidity event plus service requirement. No RSU had vested as of December 31, 2023. The following table summarizes RSU and RSA activities during the year ended December 31, 2024:

	Number of Shares	Weighted Average Grant Date Fair Value
Unvested balance as of December 31, 2023	214,436	$ 22.88
Granted	—	—
Vested (RSA)	(638)	0.83
Forfeited	(544)	22.88
RSUs outstanding - December 31, 2024	213,254	$ 22.88
Unvested balance as of December 31, 2024	213,254	$ 22.88

As of December 31, 2024, the Company had unrecognized compensation cost for unvested RSU awards of $2.8 million, expected to be recognized over a weighted-average period of approximately 2.0 years.

In addition to the RSUs in the table above, in connection with the Merger, the Company assumed 24,700 RSUs which were fully vested at the time of the Merger. The RSUs were releasable upon set time frames after completion of the Merger. From the Merger through December 31, 2024, 7,700 RSUs were released. The remaining 17,000 RSUs were released in January 2025. There was no unamortized compensation cost related to these RSUs as of the Merger or December 31, 2024.

2024 Employee Stock Purchase Plan

In October 2024, the Company's Board of Directors adopted the ESPP, which became effective immediately upon completion of the Merger with Reneo. As of December 31, 2024, no shares have been issued under the ESPP.

Share-Based Compensation Expense

The following table shows the allocation of share-based compensation expense related to the company's share-based awards (in thousands):

	December 31,	
	2024	2023
Research and development	$ 2,896	$ 98
General and administrative	1,634	101
Total	$ 4,530	$ 199

The Company recorded accelerated share-based compensation expenses related to modifications of RSUs under certain separation agreements of $1.7 million during the year ended December 31, 2024, which is reflected in the above table. See Note 14 for further discussion on severance. There were no such modifications during the year ended December 31, 2023.

13. Income Taxes

Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which the temporary differences are expected to be recovered or settled.

The components of the income tax benefit are as follows:

	Years ended December 31,	
	2024	2023
Federal tax at statutory rate	21.0 %	21.0 %
State taxes, net of federal deduction	3.2 %	3.6 %
R&D credits	0.1 %	0.2 %
Other	(2.3)%	(0.1)%
Change in valuation allowance	(22.0)%	(24.7)%
Income tax benefit	0.0 %	0.0 %

Significant components of deferred income taxes are as follows (in thousands):

	As of December 31,	
	2024	2023
Deferred tax assets:		
Net operating loss carryforwards	$ 53,984	$ 9,027
R&D tax credit	837	837
Deferred R&D expenses	32,729	11,123
Accrued expenses	1,903	783
Share-based compensation	978	104
Other	424	337
Total deferred tax assets	90,855	22,211
Valuation allowance	(90,855)	(22,211)
Deferred tax assets, net of valuation allowance	—	—

As of December 31, 2024, the Company had approximately $3.1 million of net operating loss carryforwards ("NOLs") and $0.8 million of research and experimental credits which expire through 2037, and approximately $216.5 million of federal and state net operating loss carryforwards which have an indefinite life.

At December 31, 2024, the Company had federal and state tax credit carry forwards of approximately $6.9 million. The Company has not performed a formal research and development credit study with respect to these credits. The federal credits will begin to expire in 2034, if unused.

Pursuant to Internal Revenue Code ("IRC") Sections 382 and 383, the Company's ability to use NOLs and research tax credit carry forwards to offset future taxable income may be limited if the Company experiences a cumulative change in ownership of more than 50% within a three-year testing period. The Company has not completed an ownership change analysis pursuant to IRC Section 382. If ownership changes within the meaning of IRC Section 382 are identified as having occurred, the amount of NOLs and research tax carryforwards available to offset future taxable income and income tax liabilities in future years may be significantly restricted or eliminated. Further, deferred tax assets associated with such NOLs and research tax credits could be significantly reduced upon realization of an ownership change within the meaning of IRC Section 382.

In assessing the realizability of deferred tax assets, management considers whether it is more likely than not that some portion or all of the deferred tax assets will not be realized. The ultimate realization of deferred tax assets is dependent upon the generation of future taxable income during periods in which those temporary differences become deductible. Management considers projected future taxable income and tax planning strategies in making this assessment.

At December 31, 2024 and 2023, the Company has not accrued any interest or penalties related to uncertain tax positions. The Company does not anticipate that there will be a significant change in the amount of unrecognized

tax benefits over the next 12 months. The Company recognizes interest and penalties related to uncertain tax positions in income tax expense.

The Company is subject to taxation in the United States and the UK. The UK subsidiary operations ceased in 2024. The Company's federal and state income tax returns for all years will remain open to examination by federal and state tax authorities for three years from the date of utilization of any net operating loss carryforwards. The Company's federal and state returns since inception are subject to examination due to the carryover of net operating losses. The Company has not been, nor is it currently, under examination by any tax authorities. The UK tax returns from 2018 through 2024, are subject to examination by the UK tax authorities.

14. Commitments and Contingencies

Legal Proceedings

Merger Proceedings

In connection with the Merger, two complaints were filed in the Supreme Court of the State of New York, County of New York, captioned *Thomas v. Reneo Pharmaceuticals, Inc., et al.*, Index No. 654628/2024 (filed September 5, 2024) and *Kent v. Reneo Pharmaceuticals, Inc., et al.*, Index No. 654642/2024 (filed September 6, 2024) (together, the "Complaints"). The Complaints generally allege that the Proxy Statement/Prospectus filed by Reneo with the SEC misrepresented and/or omitted certain purportedly material information relating to Reneo management's financial projections for Reneo and OnKure, the data and inputs underlying the financial valuation analyses that support the fairness opinion provided by Leerink Partners, Reneo's financial advisor, and potential conflicts of interest with Leerink Partners LLC, Evercore Group L.L.C., and LifeSci Capital LLC, which were the placements agents for the Concurrent Financing that closed concurrently with the Merger. The Complaints assert violations of negligent misrepresentation and concealment in violation of New York common law and negligence in violation of New York common law. The Complaints sought orders enjoining the proposed Merger, or in the event that the Merger was consummated, orders rescinding the Merger or awarding actual and punitive damages, as well as all of the plaintiffs' fees and expenses in connection with the litigation, including reasonable attorneys' and experts' fees and expenses.

We cannot predict the outcome of the Complaints or any other litigation that might be filed arising out of the Merger or the Concurrent Financing. The Company and the individual defendants intend to vigorously defend against the Complaints and any subsequently filed, similar actions. It is possible additional lawsuits may be filed arising out of the Merger or the Concurrent Financing. Absent new or significantly different allegations, the Company will not necessarily disclose such additional filings.

From time-to-time in the future, the Company could be involved in disputes, including litigation, relating to claims arising out of operations in the normal course of business, which may have a material adverse effect on the Company's consolidated results of operations or financial position.

Clinical Trial Collaboration and Supply Agreement with Pfizer

In August 2020, as amended in December 2024, the Company entered into a clinical trial collaboration and supply agreement under which Pfizer Inc. ("Pfizer") agreed to supply drug product in connection with a clinical trial. The agreement continues until the earlier of the completion of all obligations of the parties or the termination of the contract by either party as defined in the agreement. The Company may terminate the agreement if the clinical trial is deemed to be unsafe, regulatory authorities raise concerns, or if Pfizer does not uphold its obligations outlined in the agreement.

Indemnification

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, business partners and other parties with respect to certain matters including, but not limited to, losses arising of breach of such agreements or from intellectual property infringement claims made by third parties. In addition, the Company has entered into indemnification agreements with members of its board of directors that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is, in many cases, unlimited. To date, the Company has not incurred any material costs because of such indemnifications. The Company is not aware of any claims under

indemnification arrangements, and it has not accrued any liabilities related to such obligations in its financial statements as of December 31, 2024.

Severance

A former officer of the Company terminated his employment with the Company on May 24, 2024 and entered into a separation agreement and release on that date. The separation agreement and release provides for payments and benefits including continuing payments of base salary for a period of 14 months following termination of employment, payment for or reimbursement for COBRA premiums for up to 14 months following termination of employment, a full accelerated vesting of his equity awards and extension of the post-termination exercise period applicable to his Options through the earlier of 12 months following termination of service or the applicable option expiration date. During the year ended December 31, 2024, the Company recorded an expense of $622,000 for these severance benefits in research and development expense, of which $326,000 remains unpaid and is included in accrued compensation. See Note 12 for discussion of stock-based compensation recorded for the modifications of equity awards discussed above. The related RSU shares were released in January 2025.

Certain Reneo employees became employees of the Company to assist with the Merger transition through the end of the year December 31, 2024 at which time they were terminated and received severance benefits in accordance with the Reneo severance agreements. The Company recorded expense of $225,000 for severance benefits for these employees for the year ended December 31, 2024, which is included in General and Administrative expenses and of which, approximately $154,000 remains unpaid as of December 31, 2024 and is included in accrued compensation.

Employee Benefit Plan

The Company established a qualified 401(k) plan in June 2021 which covers all employees who meet eligibility requirements. The Company matches its employee contributions up to a maximum amount of 4% of the participant's compensation. During the years ended December 31, 2024, and 2023, the Company made matching contributions of approximately $360,000 and $294,000, respectively. See Note 16.

15. Convertible Promissory Notes

In June 2024, the Company entered into convertible promissory note agreements with certain of its existing investors for up to $12.0 million. At closing, the Company received total proceeds of $6.0 million and had the ability to draw up to an additional $6.0 million in the event the Merger with Reneo had not closed by September 30, 2024, but no additional draw was made. The notes bore interest at rates from 6% per annum. All unpaid principal and accrued interest were due in December 2025, unless earlier converted. In October 2024, the unpaid notes and accrued unpaid interest automatically converted into shares issued in the Concurrent Financing at the price per share paid by investors in the Concurrent Financing. See Note 3 for further discussion. The Company incurred $142,000 of debt issuance costs related to the convertible promissory notes during the year ended December 31, 2024. Debt issuance costs are amortized as a component of interest expense over the term of the related debt using the straight-line method, which approximates the interest method. The Company recognized $148,000 in interest expense related to the amortization of the debt issuance costs for the year ended December 31, 2024 and a $114,000 loss on the conversion for the year ended December 31, 2024, both of which are recorded in interest and other expense in the Statement of Operations. As of December 31, 2024, the Company had no accrued interest related to the convertible promissory notes.

16. Subsequent Events

Sublease

In January 2025, the Company entered into a sublease on the Irvine lease for all of the leased square footage. The sublease rent payments will be approximately $450,000 over the term of the lease, which expires in November 2026.

Available for Issuance Increase

The Company's 2024 Plan provides that on the first day of each fiscal year, the number of shares of our Class A common stock available for issuance thereunder is automatically increased by a number equal to the least of (i) 2,407,100 shares, (ii) 5% of the outstanding shares of all classes of common stock as of the last day of the

immediately preceding fiscal year, or (iii) such other amount as the Company's board of directors may determine. The Company's ESPP provides that on the first day of each fiscal year, the number of shares of Class A common stock available for issuance thereunder is automatically increased by a number equal to the least of (i) 481,500 shares, (ii) 1% of the outstanding shares of all classes of common stock as of the last day of the immediately preceding fiscal year, or (iii) such other amount as the board of directors may determine. On January 1, 2025, the number of shares of Class A common stock available for issuance under the 2024 Plan and the ESPP increased by 667,355 and 133,471 shares, respectively, pursuant to these provisions.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Our management, with the participation and supervision of our principal executive officer and our principal financial officer, have evaluated our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act), as of the end of the period covered by this Annual Report. Based on that evaluation, our principal executive officer and our principal financial officer have concluded that as of December 31, 2024, our disclosure controls and procedures were effective to provide reasonable assurance that information we are required to disclose in reports that we file or submit under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in SEC rules and forms, and that such information is accumulated and communicated to our management, including our principal executive officer and our principal financial officer, as appropriate, to allow timely decisions regarding required disclosure.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rule 13a-15(f) and 15(d)-15(f) under the Exchange Act. Our management conducted an evaluation of the effectiveness of our internal control over financial reporting based on the 2013 framework in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO framework). Management believes that the COSO framework is a suitable framework for its evaluation of financial reporting because it is free from bias, permits reasonably consistent qualitative and quantitative measurements of our internal control over financial reporting, is sufficiently complete so that those relevant factors that would alter a conclusion about the effectiveness of our internal control over financial reporting are not omitted, and is relevant to an evaluation of internal control over financial reporting.

Based on its evaluation under the COSO framework, our management concluded that we maintained effective internal control over financial reporting at a reasonable assurance level as of December 31, 2024, based on those criteria.

Attestation Report of the Independent Registered Public Accounting Firm

This Annual Report does not include an attestation report of our independent registered public accounting firm due to an exemption established by the JOBS Act for "emerging growth companies."

Changes in Internal Control over Financial Reporting

There have been no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the quarter ended December 31, 2024 that materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

During the fiscal quarter ended December 31, 2024, none of our officers or directors, as defined in Rule 16a-1(f), informed us of the adoption, modification or termination of any "Rule 10b5-1 trading arrangement" or a "non-Rule 10b5-1 trading arrangement," as those terms are defined in Item 408 of Regulation S-K.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The following table sets forth the names, ages, and positions of our executive officers and members of the Board as of March 1, 2025:

Name	Age	Position(s)
Executive Officers		
Nicholas A. Saccomano, Ph.D.	66	President and Chief Executive Officer and Class I Director (4)
Jason Leverone, C.P.A.	51	Chief Financial Officer
Samuel Agresta, M.D.	52	Chief Medical Officer
Dylan Hartley, Ph.D.	56	Chief Scientific Officer
Non-Employee Directors		
Isaac Manke, Ph.D. (1) (2) (3)*	48	Class I Director (4)
R. Michael Carruthers (1)*	67	Class II Director (4)
Andrew Phillips, Ph.D. (1) (2)*	54	Class III Director (4)
Valerie M. Jansen, M.D., Ph.D. (3)	47	Class II Director (4)
Michael Grey	72	Class III Director (4)
Edward T. Mathers (2)	64	Class II Director (4)

* Committee Chair
(1) Member of the Audit Committee of the Board
(2) Member of the Compensation Committee of the Board
(3) Member of the Nominating and Corporate Governance Committee of the Board
(4) See "Board of Directors" below for discussion of Class I – III Director service terms.

Executive Officers

Nicholas Saccomano, Ph.D. has served as our Chief Executive Officer and President and a member of the Board since the closing of the Merger. He previously served as Legacy OnKure's Chief Executive Officer since September 2023, as President since May 2024, and as a member of the Legacy OnKure board of directors since March 2021. Dr. Saccomano has over 30 years of experience in pharmaceutical and biotechnology research and development, with expertise in discovery research, clinical development, portfolio strategy, technology and clinical candidate licensing, and scientific partnering. Prior to joining Legacy OnKure, he was the Chief Science Officer at Pfizer Inc.'s Boulder facility (previously Array BioPharma, Inc. prior to its acquisition by Pfizer, Inc. in 2019) from August 2019 to January 2022, the Chief Scientific Officer at Array BioPharma Inc. from May 2014 to August 2019, and the Chief Technology Officer at SomaLogic from July 2009 to May 2014. Dr. Saccomano currently serves on the board of directors of BioLoomics, Inc., Gyges Therapeutics, Kestrel Therapeutics Inc., and Modulo Bio, Inc. Dr. Saccomano holds a B.S. from the State University of New York at Buffalo and a Ph.D. in organic chemistry from Columbia University. We believe Dr. Saccomano is qualified to serve on the Board because of his role as our President and Chief Executive Officer and his extensive leadership and operational experience within the pharmaceutical and biotech industries.

Jason Leverone, C.P.A. has served as our Chief Financial Officer since the closing of the Merger. He previously served as Legacy OnKure's Chief Financial Officer since January 2022. Prior to joining Legacy OnKure, Mr. Leverone was the Chief Financial Officer and Secretary of Viridian Therapeutics (NASDAQ: VRDN) (formerly miRagen Therapeutics prior to a reverse merger that closed in October 2020) from November 2008 to May 2021, and Senior Director of Finance and Controller of Replidyne, Inc., a publicly traded biotechnology company, from November 2005 to February 2009. He began his professional career in public accounting at Ernst & Young LLP and continued with Arthur Andersen LLP. Mr. Leverone is a Certified Public Accountant and holds a B.S. in business administration from Bryant University.

Samuel Agresta, M.D. has served as our Chief Medical Officer since the closing of the Merger. He previously served as Legacy OnKure's Chief Medical Officer since February 2024. Prior to joining Legacy OnKure, he was Chief Medical Officer at Foghorn Therapeutics Inc. from September 2019 to September 2023, Director and Chief Medical Officer at Infinity Pharmaceuticals, Inc. from August 2018 to August 2019, and Vice President and

Head of Clinical Development at Agios Pharmaceuticals Inc. from December 2011 to August 2018. Prior to these roles, Dr. Agresta served as Senior Medical Director at Merrimack Pharmaceuticals, Inc. and Genentech, Inc. Dr. Agresta holds a B.S. from Georgetown University, an M.P.H. and T.M. from Tulane School of Public Health and Tropical Medicine, an M.D. from Tulane University Medical School and an M.S. in clinical investigation from the University of South Florida.

Dylan Hartley, Ph.D. has served as our Chief Scientific Officer since the closing of the Merger. He previously served as Legacy OnKure's Chief Scientific Officer since July 2024. Dr. Hartley has over 20 years of experience in drug research and development, including expertise in pharmacology, toxicology, drug metabolism and pharmacokinetics. Most recently, Dr. Hartley served as Vice President, Head of Research at Pfizer, Inc.'s Boulder facility (previously Array BioPharma, Inc. prior to its acquisition by Pfizer, Inc. in 2019) from September 2021 to July 2024. Dr. Hartley held a succession of roles of increasing responsibility at Array BioPharma, Inc. since 2011. He holds a B.A. in biological sciences from the University of Northern Colorado and a Ph.D. in pharmaceutical sciences from the University of Colorado Health Sciences Center.

Non-Employee Directors

Isaac Manke, Ph.D. has been a member of the Board since the closing of the Merger and previously served on the Legacy OnKure board of directors since March 2021. Dr. Manke has more than 15 years of experience in the life science industry as an investor, research analyst, consultant and scientist. Dr. Manke has served as a General Partner at Acorn Bioventures since April 2020, where he focuses on investing in small cap public and private biotechnology companies. Prior to Acorn, Dr. Manke spent 11 years at New Leaf Venture Partners (NLV) through 2019. In addition to private venture investments, during his time at NLV, he also led the firm's public investment activities. Dr. Manke has been a board member for several biotechnology companies, including Q32 Bio Inc. (NASDAQ: QTTB) since October 2020, True North Therapeutics (acquired by Bioverativ), Karos Pharmaceuticals (acquired by an undisclosed company), and Addex Therapeutics Ltd (NASDAQ: ADXN) since 2016. Dr. Manke holds a B.A. in biology and a B.A. in chemistry from Minnesota State University (Moorhead), and a Ph.D. in biophysical chemistry and molecular structure from the Massachusetts Institute of Technology. We believe Dr. Manke is qualified to serve on the Board because of his education and his experience in the life sciences industry and in venture capital.

Andrew Phillips, Ph.D. has been a member of the Board since the closing of the Merger and previously served on the Legacy OnKure board of directors since March 2021. He was appointed as Chairman in connection with the closing of the Merger. Dr. Phillips has served as President and Chief Executive Officer of Aleksia Therapeutics, Inc., a biotechnology company, and Nexo Therapeutics, Inc., a biotechnology company, since August 2022. Previously, Dr. Phillips served as a Managing Director at Cormorant Asset Management, an investment manager, from August 2020 to August 2022. Dr. Phillips has served as on the board of directors of Enliven Therapeutics, Inc. (NASDAQ: ELVN) since December 2020, and MoonLake Immunotherapeutics, Inc. (NASDAQ: MLTX), since April 2021. He has also served as the Chief Financial Officer of Helix Acquisition Corp. from April 2021 to April 2022, and since June 2021, he has served as Chief Executive Officer of Blossom Bioscience Ltd. From January 2016 to March 2020, Dr. Phillips was with C4 Therapeutics, Inc. (NASDAQ: CCCC), a clinical-stage biopharmaceutical company focused on therapeutics for the treatment of cancer and other diseases, where he served as Chief Executive Officer from May 2018 to March 2020, President from September 2016 to May 2018 and Chief Scientific Officer from January 2016 to May 2018. From July 2014 to January 2016, he served as Senior Director, Center for Development of Therapeutics at the Broad Institute, a biomedical and genomic research organization. From June 2010 to January 2015, Dr. Phillips was a Professor of Chemistry at Yale University, and from July 2001 to June 2010, he was Assistant Professor, Associate Professor, and Professor of Chemistry and Biochemistry at the University of Colorado. He holds a B.Sc. in biochemistry and a Ph.D. in chemistry from the University of Canterbury in New Zealand. We believe Dr. Phillips is qualified to serve on the Board because of his extensive experience in the biotechnology industry, his education and his leadership experience as a senior executive.

R. Michael Carruthers has been a member of the Board since the closing of the Merger and previously served on the Legacy OnKure board of directors since March 2021. Mr. Carruthers has served as the Chief Financial Officer of Edgewise Therapeutics, Inc. (NASDAQ: EWTX), a publicly traded biopharmaceutical company, since September 2020. Mr. Carruthers consulted as Chief Financial Officer of OnKure between March 2019 and May 2021, and has served on the board of directors of Elevation Oncology (NASDAQ: ELEV), a publicly traded biopharmaceutical company, since May 2021. Mr. Carruthers previously served as Chief Financial Officer of Brickell Biotech, Inc., a publicly traded biopharmaceutical company, from December 2017 to October 2020, and

ClinOne, Inc., clinical trial management company, from August 2018 to May 2020. He also served as Interim President of Nivalis Therapeutics, Inc., a publicly traded biopharmaceutical company, from January 2017 to August 2017 and Chief Financial Officer and Secretary from February 2015 to August 2017. From December 1998 to February 2015, he served as Chief Financial Officer of Array BioPharma Inc. a publicly traded biopharmaceutical company. Prior to Array, he served as Chief Financial Officer of Sievers Instruments, Inc., a water purification technology company, Treasurer and Controller for the Waukesha division of Dover Corporation, a global manufacturing company, and a Senior Auditor with Coopers & Lybrand, LLP. Mr. Carruthers studied accounting at Western Colorado University, and received a B.S. in accounting from the University of Colorado Boulder and a M.B.A. from the University of Chicago. We believe Mr. Carruthers is qualified to serve on the Board because of his experience serving as chief financial officer for publicly traded biopharmaceutical companies and his extensive knowledge of corporate finance and strategic planning.

Valerie M. Jansen, M.D., Ph.D., joined the Board in connection with the closing of the Merger. She has served as the Chief Medical Officer of Elevation Oncology, Inc. (NASDAQ: ELEV) since October 2021 and as the Vice President of Clinical Development from April 2021 to October 2021. Prior to that, she served as Executive Medical Director of Mersana Therapeutics (NASDAQ: MRSN) from January 2020 to April 2021. Prior to Mersana Therapeutics, Dr. Jansen was employed at Eli Lilly and Company (NYSE: LLY), where she served as Senior Medical Advisor from September 2017 to January 2020. Prior to Eli Lilly, Dr. Jansen was employed at the Vanderbilt University Medical Center from July 2010 to July 2018 serving, most recently, as Adjunct Instructor in Medicine. Dr. Jansen received a B.A. in Chemistry from Maryville College, a Ph.D. in Molecular Sciences from the University of Tennessee Health Science Center and an M.D. from the University of Chicago Pritzker School of Medicine. We believes Dr. Jansen is qualified to serve on the Board because of her experience serving as chief medical officer and other clinical development roles for biopharmaceutical companies.

Michael Grey has been a member of the Board since the closing of the Merger. He previously served as Executive Chairman of Reneo's board of directors from December 2017 until the closing of the Merger, and as Chairman of Reneo's board of directors and Reneo's Chief Executive Officer from September 2014 to December 2017. Mr. Grey has served as the Executive Chairman of the board of the following life science companies: Spruce Biosciences, Inc. (NASDAQ: SPRB) since March 2018, Plexium, Inc., a private company, since August 2020, and Theolytics Ltd., a private company, since November 2023. Mr. Grey has served as Chairman of Sorriso Pharmaceuticals, Inc., a private company, since April 2022 and as Chief Executive Officer from April 2021 to April 2022. Additionally, Mr. Grey previously served in the below listed capacities for the following life science companies: Executive Chairman and Chief Executive Officer of Mirum Pharmaceuticals, Inc. (NASDAQ: MIRM) from May 2018 to March 2019, Chief Executive Officer of Amplyx Pharmaceuticals, Inc., a private company, from September 2014 to December 2017 and then as Executive Chairman from January 2018 until April 2020, and as Executive Chairman of Curzion Pharmaceuticals, Inc., a private company, from May 2019 to April 2020. Mr. Grey has served on the board of directors of Mirum Pharmaceuticals since May 2018 and as Chair since March 2019. Mr. Grey also previously served on the board of directors of the following publicly traded life science companies: BioMarin Pharmaceuticals (NASDAQ: BMRN) from December 2005 until May 2021, Horizon Therapeutics plc (NASDAQ: HZNP) from January 2011 until October 2023, and Mirati Therapeutics Inc. from November 2014 to June 2021. Mr. Grey has also served as a venture partner at Pappas Ventures, a venture capital firm, since January 2010. Mr. Grey has more than 45 years of experience in the pharmaceutical and biotechnology industries and has held senior positions at a number of companies, including President and Chief Executive Officer of SGX Pharmaceuticals, Inc. (sold to Eli Lilly in 2008), President and Chief Executive Officer of Trega Biosciences, Inc. (sold to LION Bioscience, Inc. in 2001) and President of BioChem Therapeutic Inc. Prior to these, Mr. Grey served in various roles with Glaxo, Inc., and Glaxo Holdings PLC, culminating in his position as Vice President, Corporate Development and director of international licensing. Mr. Grey received a B.S. in chemistry from the University of Nottingham in the United Kingdom. We believe that Mr. Grey’s extensive experience managing and leading both early stage and established companies within the pharmaceutical and biotechnology industries qualify him to serve on the Board.

Edward T. Mathers has been a member of the Board since the closing of the Merger and previously served as a member of Reneo's board of directors from December 2017 until the closing of the Merger. Mr. Mathers is Partner at New Enterprise Associates, Inc. (NEA), a private venture capital firm focusing on technology and healthcare investments. Mr. Mathers serves on the board of directors of the following publicly traded life science companies: Trevi Therapeutics, Inc. (NASDAQ: TRVI) since July 2017, Inozyme Pharma, Inc. (NASDAQ: INZY) since January 2017, Rhythm Pharmaceuticals, Inc. (FSE: 1RV.F) since March 2010, Synlogic, Inc. (NASDAQ:

SYBX) since October 2012, Senti Biosciences, Inc. (NASDAQ: SNTI) since July 2016 and MBX Biosciences, Inc. (NASDAQ: MBX) since July 2020. Mr. Mathers previously served on the board of directors of the following publicly traded companies: ObsEva SA (OTC: OBSEF) from November 2015 to June 2023, Mirum Pharmaceuticals, Inc. (NASDAQ: MIRM) from November 2018 to September 2022, Akouos, Inc. from October 2017 to December 2022, Lumos Pharma, Inc. from January 2014 to March 2020, Ra Pharmaceuticals, Inc. from February 2010 to April 2020, and Liquidia Technologies, Inc. from July 2009 to May 2019. From 2002 to 2008, Mr. Mathers served as Executive Vice President, Corporate Development and Venture at MedImmune, Inc., a biopharmaceutical company, and led its venture capital subsidiary, MedImmune Ventures, Inc. Before Joining MedImmune in 2002, Mr. Mathers was Vice President, Marketing and Corporate Licensing and Acquisitions at Inhale Therapeutic Systems, a biotechnology company. Previously, Mr. Mathers spent 15 years a Glaxo Wellcome, Inc. (GlaxoSmithKline), where he held various sales and marketing positions. Mr. Mathers received a B.S. in Chemistry from North Carolina State University. We believe that Mr. Mathers' experience as a venture capitalist, as an executive and in business development and his experience in serving on the board of directors for several public and private pharmaceutical and life sciences companies qualifies him to serve on the Board.

Family Relationships

There are no family relationships among any of our directors or executive officers.

Board of Directors

Our business and affairs are organized under the direction of the Board. Our executive officers are appointed by and serve at the discretion of our Board. The Board currently consists of seven directors divided into three staggered classes, with one class to be elected at each annual meeting to serve for a three-year term. Andrew Phillips serves as Chairman of our Board. The primary responsibilities of the Board are to provide oversight, strategic guidance, counseling and direction to our management. The Board meets on a regular basis and additionally as required.

In accordance with the terms of our Amended Certificate of Incorporation and the Amended Bylaws, the Board is divided into three classes, Class I, Class II and Class III, with members of each class serving staggered three-year terms. The members of the classes are divided as follows:

- the Class I directors are Nicholas Saccomano and Isaac Manke, and their terms will expire at the annual meeting of stockholders to be held in 2025;
- the Class II directors are R. Michael Carruthers, Valerie M. Jansen and Edward T. Mathers, and their terms will expire at the annual meeting of stockholders to be held in 2026; and
- the Class III directors are Andrew Phillips and Michael Grey, and their terms will expire at the annual meeting of stockholders to be held in 2027.

Committees of the Board

The Board has three standing committees: an audit committee, a compensation committee and a nominating and corporate governance committee. Each committee operates pursuant to a charter, which is available at investors.onkuretherapeutics.com. The Board may establish other committees from time to time.

Audit Committee

The audit committee of the Board (the "Audit Committee"), was established by the Board in accordance with Section 3(a)(58)(A) of the Securities and Exchange Act of 1934 (the "Exchange Act"), to oversee our corporate accounting and financial reporting processes and audits of our financial statements. For this purpose, the audit committee performs several functions. The Audit Committee is responsible for the following activities, among other things:

- select, retain, compensate, evaluate, oversee and, where appropriate, terminate our independent registered public accounting firm;
- review and pre-approve the scope and plans for the audits and the audit fees and pre-approve all non-audit and tax services to be performed by the independent auditor;

- evaluate the independence and qualifications of our independent registered public accounting firm;
- review our financial statements, and discuss with management and our independent registered public accounting firm the results of the annual audit and the quarterly reviews, including a review of our disclosures under the "Management's Discussion and Analysis of Financial Condition and Results of Operations" discussion in our Annual Reports on Form 10-K and Quarterly Reports on Form 10-Q;
- review and discuss with management and our independent registered public accounting firm the quality and adequacy of our internal controls and our disclosure controls and procedures;
- discuss with management our procedures regarding the presentation of our financial information, and review earnings press releases and guidance;
- oversee the design, implementation and performance of our internal audit function, if any;
- set hiring policies with regard to the hiring of employees and former employees of our independent auditor and oversee compliance with such policies;
- review, approve and monitor related party transactions;
- adopt and oversee procedures to address complaints regarding accounting, internal accounting controls and auditing matters, including confidential, anonymous submissions by our employees of concerns regarding questionable accounting or auditing matters;
- review and discuss with management and our independent auditor the adequacy and effectiveness of our legal, regulatory and ethical compliance programs; and
- review and discuss with management and our independent auditor our guidelines and policies to identify, monitor and address enterprise risks, including the oversight of risks from cybersecurity threats.

The members of the Audit Committee are R. Michael Carruthers, Andrew Phillips and Isaac Manke. R. Michael Carruthers is the Chair of the Audit Committee and is a financial expert under the rules of the SEC. To qualify as independent to serve on the Audit Committee, listing standards of Nasdaq and the applicable SEC rules require that a director not accept any consulting, advisory or other compensatory fee from us, other than for service as a director, or be an affiliated person of us. The composition of the Audit Committee complies with the applicable requirements of the rules and regulations of Nasdaq and the SEC. The Audit Committee met four times during the fiscal year. References to the "Audit Committee" in this Annual Report on Form 10-K refer to our Audit Committee and, with respect to pre-Merger actions, its predecessor committee of the Reneo board of directors. The Board has adopted a written charter of the Audit Committee that is available to stockholders on our website at investors.onkuretherapeutics.com.

Compensation Committee

The compensation committee of our Board (the "Compensation Committee") is responsible for the following activities, among other things:

- review, approve or make recommendations to the Board regarding the compensation for our executive officers, including our chief executive officer;
- review, approve and administer our employee benefit and equity incentive plans;
- establish and review the compensation plans and programs of our employees, and ensure that they are consistent with our general compensation strategy;
- determine or make recommendations to the Board regarding non-employee director compensation; and
- approve or make recommendations to the Board regarding the creation or revision of any clawback policy.

The members of the Compensation Committee are Andrew Phillips, Isaac Manke, and Edward Mathers. Dr. Phillips is the Chair of the Compensation Committee. Each member of the Compensation Committee is a "non-employee" director within the meaning of Rule 16b-3 of the rules promulgated under the Exchange Act and independent within the meaning of the independent director guidelines of Nasdaq. The composition of the Compensation Committee complies with the applicable requirements of the rules and regulations of Nasdaq. The Compensation Committee met two times during the fiscal year. References to the "Compensation Committee" in this Annual Report on Form 10-K refer to our Compensation Committee and, with respect to pre-Merger actions, its predecessor committee of the Reneo board of directors. The Compensation Committee has adopted a written charter that is available to stockholders on our website at investors.onkuretherapeutics.com.

Compensation Committee Processes and Procedures

Typically, the Compensation Committee meets as it deems appropriate. The agenda for each meeting is usually developed by the Chair of the Compensation Committee. However, from time to time, various members of management and other employees as well as outside advisors or consultants may be invited by the Compensation Committee to make presentations, to provide financial or other background information or advice or to otherwise participate in Compensation Committee meetings. The Chief Executive Officer may not participate in, or be present during, any deliberations or determinations of the Compensation Committee regarding his compensation or individual performance objectives. The Compensation Committee has the sole authority to retain compensation consultants to assist in its evaluation of executive and director compensation, including the authority to approve the consultant's reasonable fees and other retention terms. In general, the Compensation Committee has set executive compensation to be competitive with compensation provided by peer companies identified by the Compensation Committee, to promote retention of our executive officers and to incentivize our executive officers in achieving our short- and long-term corporate goals.

In 2024, in connection with the Merger, the Legacy OnKure board of directors and its compensation committee and Reneo's board of directors reviewed our current employee and director compensation. As part of this review, the Legacy OnKure compensation committee recommended approval of the OnKure Therapeutics, Inc. 2024 Equity Incentive Plan (the "Plan"), and the Plan was subsequently approved by the boards of directors of Legacy OnKure and Reneo and by Reneo's stockholders on September 26, 2024, and ratified by the Board following the completion of the Merger.

The current compensation for the Named Executive Officers was recommended by the Legacy OnKure compensation committee, approved by the boards of directors of Legacy OnKure and Reneo in 2024, and ratified by the Board following the completion of the Merger. See "*New OnKure Employment Agreements"* below for discussion of current compensation for the Named Executive Officers.

Historically, the Compensation Committee has made most of the significant adjustments to annual compensation, determined bonus and equity awards and established new performance objectives at one or more meetings held during the first quarter of the year. However, the Compensation Committee also considers matters related to individual compensation, such as compensation for new executive hires, as well as high-level strategic issues, such as the efficacy of our compensation strategy, potential modifications to that strategy and new trends, plans or approaches to compensation, at various meetings throughout the year. Generally, the Compensation Committee's process comprises two related elements: the determination of compensation levels and the establishment of performance objectives for the current year. The Legacy OnKure compensation committee in conjunction with the Legacy OnKure's board of directors served similar functions with respect to the assessment and determination of compensation for the Legacy OnKure executives.

The Compensation Committee reviews and approves the compensation of our Chief Executive Officer and our other executive officers, including annual base salaries, annual and long-term incentive or bonus awards, employment agreements, and severance and change in control agreements/provisions, in each case as, when and if appropriate, and any special or supplemental benefits. For executives other than the Chief Executive Officer, the Compensation Committee solicits and considers evaluations and recommendations submitted to the Compensation Committee by the Chief Executive Officer. The Compensation Committee evaluates the performance of the Chief Executive Officer in light of Company and individual goals and objectives, and makes appropriate recommendations for improving performance. In performing the evaluation, the Chair of the Compensation Committee may solicit comments from the other non-employee members of the Board and lead the Board in an overall review of the Chief Executive Officer's performance in an executive session of non-employee members of the Board. If the compensation for the Chief Executive Officer or any other executive officer is governed by an employment

agreement, the Compensation Committee approves such employment agreement and any amendments thereto. In connection with the Merger, the Legacy OnKure board of directors and the Reneo board of directors approved and we entered into new employment agreements with the Chief Executive Officer and other executive officers, and these agreements were ratified by the Board following the completion of the Merger. See "*New OnKure Employment Agreements"* below for discussion of current compensation for the Named Executive Officers.

For all executives as part of its deliberations, the Compensation Committee may review and consider, as appropriate, materials such as financial reports and projections, operational data, tax and accounting information, tally sheets that set forth the total compensation that may become payable to executives in various hypothetical scenarios, executive and director stock ownership information, company stock performance data, analyses of historical executive compensation levels and current Company-wide compensation levels.

Nominating and Corporate Governance Committee

The nominating and corporate governance committee of the Board (the "Nominating and Corporate Governance Committee") has responsibility for the following activities, among other things:

- review and assess and make recommendations to the Board regarding desired qualifications, expertise and characteristics sought of Board members;
- identify, evaluate, select or make recommendations to the Board regarding nominees for election to the Board;
- develop policies and procedures for considering stockholder nominees for election to the Board;
- review our succession planning process for our chief executive officer and any other members of our executive management team;
- review and make recommendations to the Board regarding the composition, organization and governance of the Board and its committees;
- review and make recommendations to the Board regarding our corporate governance guidelines and corporate governance framework;
- oversee director orientation for new directors and continuing education for the Board;
- oversee the evaluation of the performance of the Board and its committees;
- review and monitor compliance with our code of business conduct and ethics, and review conflicts of interest of the director and officers other than related party transactions reviewed by the Audit Committee; and
- administer policies and procedures for communications with the non-management members of the Board.

The members of the Nominating and Corporate Governance Committee are Isaac Manke and Valerie M. Jansen. Dr. Manke is the Chair of the Nominating and Corporate Governance committee. The composition of the Nominating and Corporate Governance Committee meets the requirements for independence under, and complies with, any applicable requirements of the rules and regulations of Nasdaq. The Nominating and Corporate Governance Committee did not meet during the 2024 fiscal year. References to the "Nominating and Corporate Governance Committee" in this Annual Report on Form 10-K refer to our Nominating and Corporate Governance Committee and, with respect to pre-Merger actions, its predecessor committee of the Reneo board of directors. The Nominating and Corporate Governance Committee has adopted a written charter that is available to stockholders on our website at investors.onkuretherapeutics.com.

The Nominating and Corporate Governance Committee periodically reviews the compensation of non-employee Directors for service on the Board and committees thereof. In 2024, the Nominating and Corporate Governance Committee began a review of its Director compensation levels considering general market conditions in the life science industry, and in comparison to other clinical stage biopharmaceutical companies, and the Nominating and Corporate Governance Committee recommended, and the Board approved, revised compensation for non-employee Directors, discussed in "Director Compensation" below.

It is the responsibility of the Nominating and Corporate Governance Committee to adopt a process for identifying and evaluating director nominees, including stockholder nominees. Before recommending an individual to the Board for membership on the Board, the Nominating and Corporate Governance Committee will canvass its members and our management team for potential candidates for the Board. The Nominating and Corporate Governance Committee also uses its network of contacts to identify potential candidates and, if it deems appropriate, may also engage a professional search firm. The Nominating and Corporate Governance Committee will consider stockholders' recommendations for nominees to serve as director if notice is timely received by our Secretary. Candidates nominated by stockholders will be evaluated in the same manner as other candidates. The Nominating and Corporate Governance Committee keeps the Board apprised of its discussions with potential nominees, and the names of potential nominees received from our current directors, management and stockholders, if the stockholder notice of nomination is timely made.

Although the Board has not adopted a fixed set of minimum qualifications for candidates for membership on the Board, the Nominating and Corporate Governance Committee generally considers several factors in its evaluation of a potential member, such as the candidate's character, professional ethics and integrity, judgment, business acumen, education, professional background and field of expertise including industry or academic experience in the pharmaceutical and biotechnology fields, experience in corporate governance and management, understanding of our business, the reasonable availability of the potential member to devote time to our affairs, as well as any other criteria deemed relevant by the Board or the Nominating and Corporate Governance Committee. However, the Nominating and Corporate Governance Committee retains the right to modify these qualifications from time to time. Candidates for director nominees are reviewed in the context of the current composition of the Board, our operating requirements and the long-term interests of stockholders. In conducting this assessment, the Nominating and Corporate Governance Committee typically considers diversity, age, skills and such other factors as it deems appropriate given our current needs and the current needs of the Board, to maintain a balance of knowledge, experience and capability. The Nominating and Corporate Governance Committee believes it is essential that Board members come from a variety of backgrounds and experiences.

In the case of incumbent directors whose terms of office are set to expire, the Nominating and Corporate Governance Committee reviews these directors' overall contributions to us and the Board during their terms, including level of attendance, level of participation, quality of performance and contribution to the Board's responsibilities and actions, and any relationships and transactions that might impair the directors' independence. In the case of new director candidates, the Nominating and Corporate Governance Committee also determines whether the nominee is independent for Nasdaq and SEC purposes, which determination is based upon applicable Nasdaq listing standards, applicable SEC rules and regulations and the advice of counsel, if necessary. The Nominating and Corporate Governance Committee conducts any appropriate and necessary inquiries into the backgrounds and qualifications of possible candidates after considering the function and needs of the Board. The Nominating and Corporate Governance Committee meets to discuss and consider the candidates' qualifications and then determines whether to recommend a nominee to the Board by majority vote.

Stockholders who wish to recommend individuals for consideration by the Nominating and Corporate Governance Committee to become nominees for election to the Board may do so by delivering a written recommendation to our Corporate Secretary. The recommendation must include the candidate's name, home and business contact information, detailed biographical data, relevant qualifications, a signed letter from the candidate confirming willingness to serve, information regarding any relationships between the candidate and us and evidence of the recommending stockholder's ownership of Company stock. Such recommendations must also include a statement from the recommending stockholder in support of the candidate. Stockholders may also nominate candidates directly for election to the Board at our annual meeting of stockholders by following the notice, deadline and other requirements set forth in our Bylaws. To date, the Nominating and Corporate Governance Committee has not rejected a timely director nominee from a stockholder.

In 2024, the Nominating and Corporate Governance Committee did not pay any fees to assist in the process of identifying or evaluating director candidates.

Stockholder Communications with the Board

Stockholders who wish to communicate with the Board may do so by written message to our General Counsel or Chief Financial Officer at our offices. Communications sent in accordance with this process will be transmitted by us to the appropriate Board members.

Compensation Committee Interlocks and Insider Participation

Each member of the Compensation Committee is a "non-employee" director within the meaning of Rule 16b-3 of the rules promulgated under the Exchange Act and is independent within the meaning of the independent director guidelines of Nasdaq. None of our executive officers serves as a member of the Board or Compensation Committee of any entity that has one or more executive officers who serves on our Board or Compensation Committee.

Non-Employee Director Compensation

We maintain an outside director compensation policy that is designed to provide a total compensation package that enables us to attract and retain, on a long-term basis, high-caliber directors. See "*Director Compensation"* below for discussion of current compensation for our non-employee directors.

Code of Business Conduct and Ethics

We maintain a Code of Business Conduct and Ethics that applies to all our employees, officers and directors. This includes our principal executive officer, principal financial officer and principal accounting officer or controller, or persons performing similar functions. The full text of our Code of Business Conduct and Ethics is posted on our website at investors.onkuretherapeutics.com. Our website and the information contained on, or that can be accessed through, the website will not be deemed to be incorporated by reference in, and are not considered part of, this Annual Report. If we make any substantive amendments to the Code of Business Conduct and Ethics or grant any waiver from a provision of the Code of Business Conduct and Ethics to any executive officer or director that are required to be disclosed pursuant to SEC rules, we will promptly disclose the nature of the amendment or waiver on our website or in a current report on Form 8-K.

Insider Trading Policy

We have adopted an Insider Trading Policy that governs the purchase, sale and/or other dispositions of our securities by our directors, officers and employees, as well as their immediate family members and entities owned or controlled by them, and that is designed to promote compliance with insider trading laws, rules and regulations.

Item 11. Executive Compensation

Executive Compensation

The following table shows for the fiscal years ended December 31, 2024 and December 31, 2023, compensation awarded to, paid to, or earned by our current and former principal executive officer and our two most highly compensated executive officers as of December 31, 2024, collectively, the Named Executive Officers:

Name and Principal Position	Year	Salary ($)(1)	Bonus ($)(2)(6)	Stock Awards ($)(3)	Option Awards ($)(3)	All Other Compensation ($)(4)(6)	Total ($)
Nicholas A. Saccomano, Ph.D. (1).....	2024	462,145	279,598	—	8,773,422	—	9,515,165
President and Chief Executive Officer							
	2023	67,709	22,000	86,958	132,185	—	308,852
Samuel Agresta, M.D. (5).....	2024	416,727	183,360	—	2,228,619	12,362	2,841,068
Chief Medical Officer							
Jason Leverone, C.P.A.....	2024	382,958	168,501	—	2,113,312	13,799	2,678,570
Chief Financial Officer							
	2023	346,500	91,476	311,684	28,972	13,315	791,947
Gregory J. Flesher (6).....	2024	453,365	—	—	—	1,326,242	1,779,607
Former President and Chief Executive Officer							
	2023	563,942	—	—	—	5,762	569,704

(1) The amounts reported under "Salary" in the above table represent the actual amounts paid during the calendar year. For Dr. Saccomano's 2023 Salary, the amount reported represents a prorated salary following Dr. Saccomano's appointment as Chief Executive Officer in September 2023.

(2) The amounts reported represent discretionary bonuses paid based upon the achievement of Legacy OnKure company goals for the years ended December 31, 2024 and 2023, as determined by the Legacy OnKure board of directors and our Board, as applicable. Cash bonuses earned and reported above in 2023 were paid in 2024, and cash bonuses earned and reported above in 2024 for Drs. Saccomano and Agresta and Mr. Leverone were paid in 2025. See "Executive Compensation" for descriptions of the bonuses.

(3) In accordance with SEC rules, this column reflects the aggregate grant date fair value of the stock option awards granted during 2024 and 2023, computed in accordance with FASB ASC 718, Compensation—Stock Compensation. The assumptions used in calculating the grant date fair value of the awards disclosed in this column are set forth in Note 12 to the audited financial statements included elsewhere in this Annual Report. These amounts do not reflect the actual economic value that will be realized by the Named Executive Officer upon the vesting of the stock options, the exercise of the stock options, or the sale of the common stock underlying such stock options.

(4) The amounts reported for Drs. Saccomano and Agresta and Mr. Leverone represent matching contributions under Legacy OnKure's 401(k) plan. For Mr. Flesher, all Other Compensation includes (i) matching contributions under Reneo's 401(k) plan, (ii) premiums paid for group term life insurance and (iii) fringe benefits paid on behalf Reneo's named executive officers in 2023.

(5) Dr. Agresta was hired in February 2024.

(6) Mr. Flesher ceased providing services as President and Chief Executive Officer concurrent with the close of Merger on October 4, 2024. Mr. Flesher received a one-time separation payment equal to 150% of his 2024 base salary ($894,992) plus 150% of his 2024 target annual bonus ($431,250) pursuant to the terms of his participation in the Reneo Severance Plan (as defined below).

Narrative Disclosure to Summary Compensation Table

Executive Compensation Elements

The following describes the material terms of the elements of our compensation program for our Named Executive Officers during 2024:

Annual Base Salary

Our Board and Compensation Committee recognize the importance of base salary as an element of compensation that helps to attract and retain the named executive officers. We provide a base salary as a fixed source of income for our Named Executive Officers for the services they provide to us during the year, which allows us to maintain a stable executive team.

See "New OnKure Employment Agreements" below for a discussion of 2024 base salary for Dr. Saccomano, Dr. Agresta and Mr. Leverone. See "Pre-Merger Employment Agreement with Mr. Flesher; Consulting Agreement with Mr. Flesher" for a discussion of 2024 base salary for Mr. Flesher.

New OnKure Employment Agreements

Reneo and Legacy OnKure entered into new employment agreements with certain eligible employees of OnKure, including Dr. Saccomano, Dr. Agresta and Mr. Leverone related to their continued employment with OnKure and as executive officers of the Combined Company on an at-will basis, each of which includes terms for base salary, benefits, target annual bonus opportunities and eligibility to participate the benefit plans, and which agreements became effective as of the Closing (the "New Employment Agreements").

Pursuant to the New Employment Agreements, Dr. Saccomano's annual base salary became $600,000 and he has a target annual bonus opportunity equal to 55% of his base salary ($330,000); Dr. Agresta's annual base salary became $482,000 and he has a target annual bonus opportunity equal to 40% of his base salary ($192,800); and Mr. Leverone's annual base salary became $444,000 and he has a target annual bonus opportunity equal to 40% of his base salary ($177,600).

Pre-Merger Employment Agreement with Mr. Flesher; Consulting Agreement with Mr. Flesher

During the period in 2024 prior to the closing the Merger, Mr. Flesher's annual base salary was $575,000 and had a target annual bonus of 50% of his base salary, which was subject to his continued employment through the payment date. Mr. Flesher ceased providing services as President and Chief Executive Officer concurrent with the close of Merger on October 4, 2024.

The Reneo board of directors approved a consulting agreement with Mr. Flesher that became effective on that same date, pursuant to which Mr. Flesher agreed to provide consulting services to OnKure to assist with transition and post-transaction integration efforts for approximately five hours per month for a period of six months following the Effective Time (as defined in the Merger Agreement) of the Merger in exchange for a one-time cash payment in the gross amount of $20,000, payable within ten days following the six-month anniversary of the closing the Merger, unless the consulting agreement was terminated for "cause" (as defined therein) prior to such time in accordance with its terms).

Termination and Change of Control Arrangements

Dr. Saccomano, Dr. Agresta and Mr. Leverone

Each of the New Employment Agreements entered into with Dr. Saccomano, Dr. Agresta and Mr. Leverone provides that if, other than during the period beginning three months before a "change in control" (as defined in each such New Employment Agreement) through the one-year anniversary of a change in control (the "CIC Period"), the applicable executive officer's employment with the Combined Company is terminated either (x) by the Combined Company without "cause" (as defined in each such New Employment Agreement, and excluding by reason of death or "disability" (as defined in each such New Employment Agreement)) or (y) by the executive officer for "good reason" (as defined in each such New Employment Agreement), then the executive officer will receive the following severance payments and benefits if he timely executes and does not revoke a separation agreement and release of claims in the Combined Company's favor:

- A lump sum cash payment equal to 100% of the executive officer's base salary as in effect immediately before such termination (or, if the termination is due to a resignation for good reason based on a material reduction in the executive's base salary, then executive's annual base salary in effect immediately prior to the reduction); and
- Combined Company payment or reimbursement of the premiums required for continued coverage pursuant to the Consolidated Omnibus Budget Reconciliation Act of 1985, as amended ("COBRA") under the Combined Company's group health, dental and vision care plans for the executive officer and his eligible dependents for up to 12 months.

If, during the CIC Period, the applicable executive officer's employment with the Combined Company is terminated either (x) by the Combined Company without cause (and excluding by reason of his death or disability) or (y) by the executive officer for good reason, the executive officer will receive the following severance payments and benefits if he timely executes and does not revoke a separation agreement and release of claims in the Combined Company's favor:

- A lump sum cash payment equal to 100% (or 150% for Dr. Saccomano) of the executive officer's base salary as in effect immediately before such termination (or, if the termination is due to a resignation for

good reason based on a material reduction in the executive's base salary, then executive's annual base salary in effect immediately prior to the reduction), or if greater, the base salary in effect immediately before the change in control;

- A lump sum cash payment equal to 100% (or 150% for Dr. Saccomano) of the executive officer's target bonus opportunity as in effect immediately before such termination or if greater, the target bonus opportunity in effect immediately before the change in control;
- Combined Company payment or reimbursement of the premiums required for continued coverage pursuant to COBRA under the Combined Company's group health, dental and vision care plans for the executive officer and his eligible dependents for up to 12 months (or 18 months for Dr. Saccomano); and
- 100% accelerated vesting and exercisability of the outstanding and unvested equity awards (other than equity awards subject to performance-based vesting criteria) granted to the executive officer.

Such New Employment Agreements also provide that, if any of the amounts provided for under the New Employment Agreement or otherwise payable to the executive officer would constitute "parachute payments" within the meaning of Section 280G of the Internal Revenue Code or 1986, as amended, and could be subject to the related excise tax, the executive officer would receive (to the extent he is entitled to such receipt) either the full payment of benefits under the executive officer's New Employment Agreement or such lesser amount that would result in no portion of the payments and benefits being subject to the excise tax, whichever results in the greater amount of after-tax benefits to the executive officer. The New Employment Agreements do not provide for any tax gross-ups in connection with a change in control.

Mr. Flesher

In connection with the Merger, the Reneo board of directors approved the acceleration of vesting, to the extent not previously vested, of all Reneo stock options and Reneo restricted stock units held by Reneo's directors and executive officers, including Mr. Flesher, effective as of the Effective Time (as defined in the Merger Agreement and which Effective Time was the closing of the Merger). In addition, in connection with the Merger, the Reneo board of directors approved an amendment to all Reneo stock options held by certain Reneo optionholders, including Mr. Flesher, to provide that the applicable exercise window following termination of service with Reneo (or its affiliates) other than for Cause (as defined in the applicable Reneo Equity Plan) is the longer of (a) a period of three months following termination of service; or (b) a period commencing on the date of termination of service and ending on the six-month anniversary of the Effective Time (but in no event may an option be exercised beyond its maximum term). In the event that the Merger Agreement had been terminated pursuant to its terms, the applicable exercise window would have been the longer of: (i) a period of three months following termination of service; or (ii) a period of three months following termination of the Merger Agreement.

Mr. Flesher ceased providing services as President and Chief Executive Officer concurrent with the close of Merger on October 4, 2024. Mr. Flesher received a one-time separation payment of $894,992 pursuant to the terms of his employment agreement.

Equity Incentive Plans

Under the Plan and the Legacy OnKure 2023 RSU Equity Incentive Plan, if, in the event of a merger or change in control (as defined in the applicable plan) a successor (or an affiliate thereof) does not assume, substitute for or continue an award (or portion thereof), then such award (or its applicable portion) will fully vest, all restrictions on such award (or its applicable portion) will lapse, all performance goals or other vesting criteria applicable to such award (or its applicable portion) will be deemed achieved at 100% of target levels and such award (or its applicable portion) will become fully exercisable, if applicable, for a specified period before the transaction, unless specifically provided otherwise under the applicable award agreement or other written agreement with the participant authorized by the administrator.

In addition, unless specifically provided otherwise under the applicable award agreement or other written agreement with the participant authorized by the administrator, if an option or stock appreciation right (or a portion of such award) granted under the Plan is not assumed, substituted or continued, the administrator will notify the participant that such option or stock appreciation right (or its applicable portion) will be exercisable for a period of time determined by the administrator in its sole discretion and the option or stock appreciation right (or its applicable portion) will terminate upon the expiration of such period.

With respect to awards granted to a non-employee director under the Plan while such individual was a non-employee director that are assumed or substituted for in the merger or change in control and the service of such non-employee director is terminated (other than upon his or her voluntary resignation that does not include a resignation at the request of the acquirer) on or following the merger or change in control, all such awards will fully vest, all restrictions on such awards will lapse, all performance goals or other vesting criteria applicable to such awards will be deemed achieved at 100% of target levels and such awards will become fully exercisable, if applicable, unless specifically provided otherwise under the applicable award agreement or other written agreement with the non-employee director authorized by the administrator. Under our Outside Director Compensation Policy, as described more fully below, in the event of a change in control, each non-employee will fully vest in his or her outstanding awards granted under such policy, as of immediately prior to the change in control, provided that the non-employee director continues to be a non-employee through immediately prior to such change in control.

Under the Legacy OnKure 2021 Stock Incentive Plan, in the event of Corporate Transaction (as defined in the Legacy OnKure 2021 Stock Incentive Plan), the administrator is not obligated to accelerate the vesting of equity awards in the event the awards are not assumed or substituted for. The administrator also has discretion to suspend the right of grantees to exercise outstanding awards during a limited period of time preceding the closing of a Corporate Transaction if such suspension is administratively necessary to facilitate the closing of the transaction, and may terminate optionholders' right to early exercise options, such that following closing of a Corporate Transaction an option may only be exercised to the extent vested.

Each of the Named Executive Officers' options and restricted stock units granted in 2023 provides that, if during the period beginning three months prior to through (and inclusive of) the date 12 months following a "change in control" (as defined in the 2023 RSU Plan for the restricted stock unit), and in the award agreement for the options; provided that the Merger did not constitute a change in control for purposes of these awards), the Named Executive Officer's service provider status is terminated by Legacy OnKure or its successor without "cause" (as defined in the applicable award agreement) (and excluding by reason of the Named Executive Officer's death or disability (as defined in the applicable equity plan), or by the Named Executive Officer for "good reason" (as defined in the applicable award agreement), 100% of the then-unvested options or restricted stock units under the award will immediately vest.

2024 Annual Cash Bonuses

Each Named Executive Officer was eligible to participate in an annual cash incentive compensation program that provides participants with an opportunity to earn variable cash incentive compensation based on individual and company performance. For 2024, Dr. Saccomano's target bonus was 55% of his earned salary, Dr. Agresta's target bonus was 40% of his earned salary and Mr. Leverone's target bonus was 40% of his earned salary.

The determination of the 2024 bonus amounts was discretionary based on the Board's assessment of Company performance against corporate goals.

The actual annual cash bonuses awarded to each of Dr. Saccomano, Dr. Agresta and Mr. Leverone for 2024 performance are set forth in the "Bonus" column of the Summary Compensation Table for Fiscal 2024 above. Mr. Flesher did not remain employed through the payment date of 2024 bonuses and therefore did not receive an annual bonus in 2024. However, he did become entitled to a severance payment that was calculated, in part, by reference to his 2024 target annual bonus as described above.

Mr. Flesher received a bonus related to the closing of the Merger equal to 150% of his target annual bonus for 2024 pursuant to the terms of his employment agreement with Reneo.

Special Performance Bonus

Pursuant to his employment agreement with Reneo, Mr. Flesher had the opportunity to earn a special performance bonus in the amount of $7.5 million in the event that during Mr. Flesher's continued service to Reneo, either (i) Reneo's market value exceeds $750 million utilizing the volume-weighted average of the Nasdaq closing sale price of Reneo Common Stock for each of the 30 trading days immediately prior to the measurement date, or (ii) the fair market value of the net proceeds available for distribution to Reneo Stockholders in connection with a Change in Control (as defined in the Reneo Severance Plan) exceeds $750 million, as determined in good faith by the Reneo Board.

Although the Merger constituted a Change in Control for purposes of Mr. Flesher's bonus opportunity, the required net proceeds threshold was not met in connection with the Merger and thus Mr. Flesher did not receive this bonus.

Executive Incentive Compensation Plan

Prior to the completion of the Merger, the Reneo board of directors and the Legacy OnKure board of directors approved an Executive Incentive Compensation Plan (the "Incentive Compensation Plan"), and the Board ratified the Incentive Compensation Plan following the closing of the Merger, to provide periodic incentive bonus opportunities to our employees (or employees of our subsidiaries). The Incentive Compensation Plan became effective at the Effective Time (as defined in the Merger Agreement). The Compensation Committee administers the Incentive Compensation Plan. Bonuses to our Named Executive Officers for 2024 were not governed by the Incentive Compensation Plan; however, it is expected that from time to time certain employees, including our Named Executive Officers, may be eligible and selected, subject to their continued employment, to participate in the Incentive Compensation Plan.

No Nonpublic Material Information Taken into Account for Executive Compensation

Our Board and Compensation Committee do not take material nonpublic information into account when determining the timing and terms of any stock option grant. The timing of any stock option grants to recipients in connection with new hires, promotions or other non-routine grants is tied to the event giving rise to the award (such as an employee's commencement of employment or promotion effective date). We have not timed the disclosure of material nonpublic information for the purpose of affecting the value of executive compensation.

During fiscal year 2024, and in connection with the closing of the Merger, we awarded options to certain of our Named Executive Officers in the period beginning four business days before the filing of a report on Form 8-K that disclosed material nonpublic information, and ending one business day after such filing. The following table provides information concerning each such award:

Name	Grant Date	Number of securities underlying the award	Exercise price of the award ($/sh)	Grant date fair value of the award	Percentage change in the closing market price of the securities underlying the award between the trading day ending immediately prior to the disclosure of material nonpublic information and the trading day beginning immediately following the disclosure of material nonpublic information
Nicholas A. Saccomano, Ph.D.	10/4/2024	542,232	$ 18.20	$ 16.18	-1.2%
Jason Leverone, C.P.A.	10/4/2024	130,611	$ 18.20	$ 16.18	-1.2%
Samuel Agresta, M.D.	10/4/2024	131,396	$ 18.20	$ 16.18	-1.2%

Employee Benefit Plans

401(k) Plan

Reneo had maintained a 401(k) retirement savings plan that was terminated prior to the Merger. Through 2024, eligible employees of Legacy OnKure and, following the Merger, us and our subsidiaries, were eligible to participate in a tax-qualified defined contribution plan under Section 401(k) of the Code sponsored by Insperity, a professional employer organization, on the terms applicable to such plan. Effective as of December 31, 2024, we and our subsidiaries ceased participating in the Insperity 401(k) plan and, effective in March 2025, we adopted a new 401(k) plan in which eligible employees of us and our subsidiaries may participate. Under the Insperity 401(k) plan and the new Company 401(k) plan, eligible employees were able to elect or may elect, as applicable, to defer a portion of their compensation, within the limits prescribed by the Code, on a pre-tax (traditional) or post-tax (Roth) basis, through contributions to the applicable 401(k) plan. As a tax-qualified retirement plan, pre-tax contributions to the applicable 401(k) plan and earnings on those pre-tax contributions are not taxable to the employees until

distributed from the applicable 401(k) plan, and earnings on Roth contributions are not taxable when distributed from the applicable 401(k) plan.

Health and Welfare Benefits

All of our full-time employees, including our Named Executive Officers, are eligible to participate in our health and welfare benefits, including medical, dental and vision insurance, medical and dependent care flexible spending accounts, group life and disability insurance and 401(k) plan. Named Executive Officers are eligible to participate in all our employee benefit plans on the same basis as other employees.

We do not offer any defined benefit pension plans or nonqualified defined compensation arrangements for our employees, including our Named Executive Officers.

Outstanding Equity Awards at Fiscal Year-End

The following table shows for the fiscal year ended December 31, 2024, certain information regarding outstanding equity awards at fiscal year-end for the Named Executive Officers.

A description of the equity incentive plans we maintain is set forth in Note 12 to our financial statements included in this Annual Report on Form 10-K.

		Option Awards (1)				
Name	Grant Date	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable		Option Exercise Price ($) (2)	Option Expiration Date
Nicholas A. Saccomano, Ph.D.	1/11/2022	2,359	—		21.20	1/10/2032
	8/30/2023	618	867	(3)	13.99	8/29/2033
	10/15/2023	8,449	—		13.99	10/14/2033
	10/15/2023	16,898	—		13.99	10/14/2033
	10/4/2024	30,124	512,108	(4)	18.20	10/3/2034
Jason Leverone	1/11/2022	4,215	1,566	(5)	21.20	1/10/2032
	8/30/2023	2,217	3,105	(3)	13.99	8/29/2033
	10/4/2024	7,256	123,355	(4)	18.20	10/3/2034
Samuel Agresta, M.D.	2/6/2024	—	18,588	(6)	13.99	2/5/2034
	10/4/2024	7,299	124,097	(4)	18.20	10/3/2034
Gregory J. Flesher	1/21/2021	105,264	—		48.80	1/20/2031
	12/10/2021	19,999	—		66.90	12/9/2031
	12/9/2022	29,999	—		18.00	12/8/2032

(1) All of the outstanding stock option awards granted on October 4, 2024 were granted under and subject to the terms of the 2024 Equity Incentive Plan and cover shares of Class A Common Stock and all of the outstanding stock option awards listed that were granted to Dr. Saccomano, Mr. Leverone and Dr. Agresta prior to October 4, 2024 were granted under and subject to the terms of the Legacy OnKure 2021 Stock Incentive Plan and cover shares of Company Class A Common Stock. Mr. Flesher's January 21, 2021 stock option award was granted under and subject to the terms of the 2014 Reneo Stock Incentive Plan and the December 10, 2021 and December 9, 2022 stock option awards were granted under and subject to the terms of the 2021 Reneo Stock Incentive Plan.

(2) The stock option awards listed that were granted Dr. Saccomano, Mr. Leverone and Dr. Agresta prior to October 4, 2024 were granted with a per share exercise price equal to the fair market value of one share of Legacy OnKure Class A Common Stock on the date of grant, as determined in good faith by the Legacy OnKure board of directors based on third party valuations of Legacy OnKure Class A Common Stock. Exercise prices and share numbers are disclosed on a post-Merger basis.

(3) 1/48th of the shares subject to the award vested on May 1, 2023 and 1/48th of the shares subject to the option vest monthly thereafter, subject to the optionee continuing to be a service provider to us through each such date. The award also is subject to certain acceleration of vesting provisions as described under "Termination and Change in Control Arrangements" above.

(4) 1/36th of the shares subject to the option shall vest on November 4, 2024 and each month thereafter, subject to the optionee continuing to be a service provider to us through each such date. The award also is subject to certain acceleration of vesting provisions as described under "Termination and Change in Control Arrangements" above.

(5) 1/4th of the shares subject to the option vested on January 3, 2023 and 1/48th of the shares subject to the option vest on the first day of each month thereafter, subject to the optionee continuing to be a service provider to us through each such date. The award also is subject to certain acceleration of vesting provisions as described under "Termination and Change in Control Arrangements" above.

(6) 1/4th of the shares subject to the option vested on February 5, 2025 and 1/48th of the shares subject to the option vest on the first day of each month thereafter, subject to the optionee continuing to be a service provider to us through each such date. The award also is subject to certain acceleration of vesting provisions as described under "Termination and Change in Control Arrangements" above.

	Stock Awards (1)		
Name	Number of Shares or Units of Stock That Have Not Vested (#) Unvested		Market Value of Shares or Units of Stock That Have Not Vested Price ($)
Nicholas A. Saccomano, Ph.D.	4,556	(2)	39,182
Jason Leverone	16,331	(2)	140,447
Gregory J. Flesher	10,000	(3)	86,000

(1) All of the outstanding restricted stock unit awards for Dr. Saccomano and Mr. Leverone were granted under and subject to the terms of the Legacy OnKure 2023 RSU Equity Incentive Plan and cover shares of Class A Common Stock.

(2) Both a "Service-Based Requirement" and a "Liquidity Event Plus Service Requirement" must be met in order for the RSU to vest. 1/16th of the RSUs met the "Service-Based" requirement on June 20, 2023 and 1/16th of the RSUs are scheduled to meet the Service-Based Requirement on each three-month anniversary thereafter, subject to the optionee continuing to be a service provider to us through each such date. The Liquidity Event Plus Service Requirement will be satisfied on the 181st day following the closing of the Merger. The award also is subject to certain acceleration of vesting provisions as described under "Termination and Change in Control Arrangements" above.

(3) The vesting of Mr. Flesher's stock award was accelerated such that the award became fully vested at the time of the Merger.

Director Compensation

Legacy OnKure's policy was to provide each director who is neither an employee nor affiliated with funds invested in Legacy OnKure preferred stock with an annual retainer of $40,000, which generally was paid in quarterly installments, subject to the director's continued service to Legacy OnKure. Dr. Saccomano was not eligible to receive this retainer for fiscal 2024 given his status as chief executive officer of Legacy OnKure. Legacy OnKure also reimbursed its directors for expenses associated with attending meetings of the Legacy OnKure board of directors and its committees.

Dr. Saccomano is Legacy OnKure's only director who was an employee director during 2024. See the section entitled "*Executive Compensation*" above for information about Dr. Saccomano's compensation that he received for serving as Legacy OnKure's Chief Executive Officer during 2024.

During the portion of 2024 prior to the Merger, Michael Grey and Edward Mathers served on the Reneo board of directors, and each was compensated for such services pursuant to Reneo's Non-Employee Director Compensation Policy (the "Reneo Director Policy"). Pursuant to the Reneo Director Policy, Mssrs. Grey and Mathers were entitled to an annual retainer of $40,000 plus, for Mr. Grey, an additional annual retainer of $30,000 for his service as non-executive Chair of the Reneo board of directors and, for Mr. Mathers, an additional annual retainer of $5,000 for his services on the Reneo compensation committee. Mr. Grey received an annual fee of $100,000 for his services as Reneo Executive Chairman in lieu of the cash fees he would otherwise receive as a non-employee member of Reneo's board of directors pursuant to the Reneo Director Policy. The annual retainers were paid in equal annual installments in arrears on the last day of each fiscal quarter in which the service occurred. Neither of Mssrs. Grey and Mathers received any Reneo equity awards in 2024 pursuant to the Reneo Director Policy. Upon the closing of the Merger, no further payments were made under the Reneo Director Policy. In connection with the Merger, the Reneo board of directors approved the acceleration of vesting, to the extent not previously vested, of all Reneo stock options and Reneo restricted stock units held by Reneo's directors and executive officers, including Mssrs. Grey and Mathers, effective as of the Effective Time.

The following table presents the total compensation that each of our then non-employee directors received during the fiscal year ended December 31, 2024.

Name	Fees Earned or Paid in Cash ($)	Option Awards ($)(1)	Nonqualified Deferred Compensation Earnings ($)	All Other Compensation ($)	Total ($)
Isaac Manke, Ph.D.	14,752	247,557	—	—	262,309
R. Michael Carruthers	43,740	247,557	—	—	291,297
Andrew Phillips, Ph.D.	21,336	247,557	—	—	268,893
Valerie M. Jansen, M.D., Ph.D.	10,729	247,557	—	—	258,286
Michael Grey	85,849	247,557	—	—	333,406
Edward Mathers	49,021	247,557	—	—	296,578

(1) In accordance with SEC rules, this column reflects the aggregate grant date fair value of the equity awards granted during 2024, computed in accordance with FASB ASC Topic 718, Compensation-Stock Compensation. The assumptions used in calculating the grant date fair value of the awards disclosed in this column are set forth in Note 12 to our audited financial statements included elsewhere in this Annual Report. These amounts do not reflect the actual economic value that will be realized by the non-employee director upon vesting, settlement or exercise of equity awards or the sale of the common stock underlying such equity awards.

(2) Includes $76,096 of cash fees paid by Reneo prior to the Merger. Mr. Grey received an annual fee of $100,000 for his services as Reneo Executive Chairman in lieu of the cash fees he would otherwise receive as a non-employee member of Reneo's board of directors pursuant to the Reneo Director Policy.

(3) Includes $38,048 of cash fees earned by Mr. Mathers for his service as a non-employee director of Reneo for January 1, 2024 through the Merger that were paid directly to NEA by Reneo.

The following table lists all outstanding stock and option awards held by non-employee directors as of December 31, 2024.

Name	Number of Shares Underlying Outstanding RSU Awards	Number of Shares Underlying Outstanding Options
Isaac Manke, Ph.D.	—	15,300
R. Michael Carruthers	4,065	18,384
Andrew Phillips, Ph.D.	—	15,300
Valerie M. Jansen, M.D., Ph.D.	—	15,300
Michael Grey	—	40,236
Edward Mathers	—	20,200

Director Compensation Policy

In 2024, the compensation committee of the Legacy OnKure board of directors retained Pearl Meyer & Partners, LLC, a third-party compensation consultant, to provide the Legacy OnKure board of directors and its compensation committee with an analysis of publicly available market data regarding practices and compensation levels at comparable companies and assistance in determining compensation to be provided to our non-employee directors. Based on the discussions with and assistance from the compensation consultant with Legacy OnKure's compensation committee, in connection with the Merger, the Legacy OnKure board of directors and the Reneo board of directors approved an Outside Director Compensation Policy that provides for certain compensation to non-employee directors of the Combined Company, with the Outside Director Compensation Policy becoming effective as of immediately prior to the Effective Time. The Outside Director Compensation Policy was ratified by our Board following the closing of the Merger.

Cash Compensation

The Outside Director Compensation Policy provides for the following cash compensation program for non-employee directors following the closing of the Merger:

- $40,000 per year for service as a non-employee director;
- $30,000 per year for service as non-employee chair;
- $15,000 per year for service as Chair of the Audit Committee;
- $7,500 per year for service as a member of the Audit Committee;
- $10,000 per year for service as Chair of the Compensation Committee;
- $5,000 per year for service as a member of the Compensation Committee;
- $8,000 per year for service as Chair of the Nominating and Corporate Governance Committee; and
- $4,000 per year for service as a member of the Nominating and Corporate Governance Committee.

RSU Award in Lieu of Cash Retainers

Under the Outside Director Compensation Policy, a non-employee director may elect to convert 100% of his or her retainer fees with respect to services to be performed in a future fiscal year (or portion of a fiscal year with respect to certain initial elections) into an award of RSUs (a "Retainer Award"), in accordance with the election procedures under the Outside Director Compensation Policy, and in addition, (i) individuals who were non-employee directors as of immediately following the closing of the Merger has the option to make such election with respect to retainer fees payable for services provided as a non-employee director in fiscal year 2024, and (ii) individuals who become non-employee directors following the closing of the Merger may make such election with respect to retainer fees payable for services provided as a non-employee director for their initial year of service as a non-employee director. Retainer Awards will be granted automatically on the last day of the fiscal quarter to which such election relates, subject to continued service through such date. The number of shares subject to a Retainer Award will be determined by dividing (x) the aggregate annual amount of cash fees described above applicable to the non-employee director as of the last day of the applicable fiscal quarter for which the non-employee director receives the Retainer Award, by (y) the fair market value of a share of our Class A Common Stock on the date of grant of the Retainer Award (which, under the Plan generally is the closing sales price of a share of our Class A Common Stock on the date of the grant of the Retainer Award (or, if no closing sales price was reported on that date, on the last trading day such closing sales price was reported)). Each Retainer Award will be fully vested as of the date of grant. No outside directors elected to receive Retainer Awards for services provided as a non-employee director in fiscal year 2024.

Equity Compensation

Each individual serving as a non-employee director as of immediately following the Effective Time was granted an award of stock options to purchase 15,300 shares of Class A Common Stock (the "Closing Award"). The Closing Award was granted automatically on the date of the closing of the Merger. Each Closing Award is scheduled to vest in equal monthly installments over the next 36 months on the same day of each relevant month as the applicable vesting date, in each case subject to the non-employee director continuing to be a service provider through the applicable vesting date. The Closing Awards were not permitted to be exercised prior to the time that a Registration Statement on Form S-8 relating to the issuance of our Class A Common Stock under the Plan became effective, which occurred on December 9, 2024.

Initial Award. Each individual who first becomes a non-employee director following the closing of the Merger will receive, on the first trading day on or after the date on which such individual first becomes a non-employee director, an award of stock options to purchase 15,300 shares of our Class A Common Stock (an "Initial Award"), provided that if an individual was an employee director, becoming a non-employee director due to termination of the individual's status as an employee will not entitle such individual to an Initial Award. Further, such stock options were not permitted to be exercised prior to the time that a Registration Statement on Form S-8 relating to the

issuance of our Class A Common Stock under the Plan became effective, which occurred on December 9, 2024. Each Initial Award will be scheduled to vest as to 1/36th of the shares subject to the Initial Award each month following the Initial Award's grant date on the same day of the month as such grant date (or on the last day of the month, if there is no corresponding day in such month), in each case subject to continued services through the applicable vesting dates.

Annual Award. On the first trading day immediately following each Annual Meeting of our stockholders (an "Annual Meeting") that occurs after the closing of the Merger, each non-employee director will receive an award of stock options to purchase 7,650 shares of our Class A Common Stock (the "Annual Award"). If an individual commenced service as a non-employee director after the date of the Annual Meeting that occurred immediately prior to such Annual Meeting (or if there is no such prior Annual Meeting, then after the closing of the Merger), then such Annual Award will be prorated based on the number of whole months that the individual served as a non-employee director prior to the Annual Award's grant date during the 12-month period immediately preceding such Annual Meeting (with any resulting fractional share rounded down to the nearest whole share). The Annual Award will be scheduled to vest in full on the earlier of the one-year anniversary of the Annual Award's grant date or the day immediately prior to the date of the next Annual Meeting that occurs after the Annual Award's grant date, subject to continued services through the applicable vesting dates.

Change in Control. In the event of a change in control (as defined in the Plan), each non-employee director's then-outstanding equity awards that were granted to him or her while a non-employee director will accelerate vesting in full, provided that he or she remains a non-employee director through immediately prior to such change in control.

Other Award Terms. Each Retainer Award, Closing Award, Initial Award and Annual Award will be granted under the Plan (or its successor plan, as applicable) and applicable forms of award agreement under such plan. Other than Retainer Awards, awards will have a maximum term to expiration of ten years from their grant and a per-share exercise price equal to 100% of the fair market value of a share of our Class A Common Stock on the award's grant date.

Director Compensation Limits. The Outside Director Compensation Policy will provide that in any fiscal year, a non-employee director may be granted equity awards (with the value of equity awards based on its grant date fair value determined in accordance with U.S. GAAP for purposes of this limit) and be provided any cash retainers or fees with an aggregate value of no more than $750,000, provided that such amount is increased to $1,000,000 in the fiscal year of initial service as a non-employee director. Equity awards granted or other compensation provided to a non-employee director for services provided as an employee or consultant (other than a non-employee director), or provided before the closing of the Merger, will not count toward this annual limit. For purposes of determining when cash retainers or fees are provided, any deferral elections to delay payout timing will be disregarded.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

EQUITY COMPENSATION PLAN INFORMATION

The following table sets forth information as of December 31, 2024, for all of our equity compensation plans:

Plan Category	Number of Securities to be Issued Upon Exercise of Outstanding Options or Upon Vesting of Restricted Stock Units (a) (1)	Weighted Average Exercise Price of Outstanding Options ($) (b) (2)	Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans (Excluding Securities Reflected in Column (a)) Price (c) (3)
Equity compensation plans approved by security holders	2,606,078	$ 23.05	885,367
Equity compensation plans not approved by security holders	18,000	88.50	—
Total	2,624,078	$ 23.54	885,367

(1) See Note 12 of the audited consolidated financial statements for a description of our equity plans. Consists of (i) options to purchase a total of 2,375,824 shares of our Class A common stock under the 2024 Plan, the 2021 Plan, the Reneo 2021 Plan, the 2014 Plan and the 2011 Plan, (ii) 213,254 shares of our Class A common stock that are subject to outstanding RSUs under the 2023 Plan and (ii) 17,000 shares of our Class A common stock that are subject to outstanding RSUs under the Reneo 2021 Plan. As of December 31, 2024, no purchase rights have accrued under the 2024 ESPP. Equity compensation plans not approved by security holders consists of inducement awards of outstanding stock options to purchase 18,000 shares, which were adopted by the Reneo Compensation Committee without stockholder approval in accordance with Rule 5635(c)(4) of the Nasdaq Listing Rules, which were assumed in the Merger.

(2) The weighted average exercise price is calculated based solely on outstanding stock options. It does not take into account the shares of our Class A common stock subject to outstanding RSUs, which have no exercise price.

(3) Consists of 747,867 shares of our Class A common stock reserved for issuance under the Plan and 137,500 shares of our Class A common stock reserved for issuance under our ESPP. The Plan provides that on the first day of each fiscal year, the number of shares of our Class A common stock available for issuance thereunder is automatically increased by a number equal to the least of (i) 2,407,100 shares, (ii) 5% of the outstanding shares of all classes of our common stock as of the last day of our immediately preceding fiscal year, or (iii) such other amount as our Board may determine. Our ESPP provides that on the first day of each fiscal year, the number of shares of our Class A common stock available for issuance thereunder is automatically increased by a number equal to the least of (i) 481,500 shares, (ii) 1% of the outstanding shares of all classes of our common stock as of the last day of our immediately preceding fiscal year, or (iii) such other amount as our Board may determine. On January 1, 2025, the number of shares of our Class A common stock available for issuance under our 2024 Plan and our ESPP increased by 667,355 and 133,471 shares, respectively, pursuant to these provisions. These increases are not reflected in the table above.

Security Ownership of Certain Beneficial Owners

The following table sets forth information regarding the beneficial ownership of Class A Common Stock as of March 1, 2025:

- each person known by us to be the beneficial owner of more than 5% of our outstanding Class A Common Stock;
- each of our executive officers and directors; and
- all of our directors and executive officers as a group.

Beneficial ownership is determined according to the rules of the SEC, which generally provide that a person has beneficial ownership of a security if such person possesses sole or shared voting or investment power over that security. Under those rules, beneficial ownership includes securities that such person has the right to acquire, such as through the exercise of stock options, within 60 days of the closing date of the Merger. Shares subject to warrants and options that are currently exercisable or exercisable within 60 days of the closing date are considered outstanding and beneficially owned by the person holding such warrant and/or options for the purpose of computing the percentage ownership of that person but are not treated as outstanding for the purpose of computing the percentage ownership of any other person.

Except as noted by footnote, and subject to community property laws where applicable, based on the information provided to us, we believe that the individuals and entities named in the table below have sole voting and investment power with respect to all shares shown as beneficially owned by them. Unless otherwise noted, the business address of each of our directors and executive officers is 6707 Winchester Circle, Suite 400, Boulder, CO 80301. The percentage of beneficial ownership of the Combined Company is calculated based on 12,749,299 shares of Class A Common Stock and 686,527 shares of non-voting Class B Common Stock outstanding.

Beneficial Owner	Shares Beneficially Owned	Percentage Shares Beneficially Owned
Directors and Named Executive Officers		
Nicholas A. Saccomano, Ph.D. (1)	129,223	1.0%
Samuel Agresta, M.D. (2)	30,132	*
Jason Leverone, C.P.A. (3)	41,353	*
Dylan Hartley, Ph.D. (4)	2,812	*
Gregory J. Flesher (5)	167,582	1.2%
Isaac Manke, Ph.D. (6)	2,550	*
R. Michael Carruthers (7)	7,004	*
Andrew Phillips, Ph.D. (8)	2,550	*
Valerie M. Jansen, M.D., Ph.D. (9)	2,550	*
Michael Grey (10)	95,370	*
Edward Mathers (11)	7,450	*
All current directors and executive officers as a group (10 persons) (12)	320,994	2.3%
5% Stockholders		
Entities affiliated with Cormorant Asset Management LP (13)	1,837,739	13.7%
Acorn Bioventures, L.P. (14)	1,439,674	10.7%
Entities affiliated with Citadel Advisors (15)	1,330,146	9.9%
Perceptive Life Sciences Master Fund, Ltd. (16)	1,004,439	7.5%
Samsara BioCapital, L.P. (17)	824,155	6.1%
The Vanguard Group (18)	706,733	5.3%

* Represents beneficial ownership of less than 1%.

(1) Consists of 126,945 shares of Class A Common Stock subject to options held by Dr. Saccomano exercisable within 60 days of March 1, 2025 and 2,278 restricted stock units that vest within 60 days of March 1, 2025.

(2) Consists of 30,132 shares of Class A Common Stock subject to options held by Dr. Agresta exercisable within 60 days of March 1, 2025.

(3) Consists of 33,188 shares of Class A Common Stock subject to options held by Mr. Leverone exercisable within 60 days of March 1, 2025 and 8,165 restricted stock units that vest within 60 days of March 1, 2025.

(4) Consists of 2,812 shares of Class A Common Stock subject to options held by Dr. Hartley exercisable within 60 days of March 1, 2025.

(5) Mr. Flesher ceased providing services as President and Chief Executive Officer on October 4, 2024. Consists of (i) 12,320 shares of Class A Common Stock and (ii) 155,262 shares of Class A Common Stock subject to options held by Mr. Flesher that are exercisable within 60 days of March 1, 2025.

(6) Consists of 2,550 shares of Class A Common Stock subject to options held by Dr. Manke exercisable within 60 days of March 1, 2025.

(7) Consists of 4,972 shares of Class A Common Stock subject to options held by Mr. Carruthers exercisable within 60 days of March 1, 2025 and 2,032 restricted stock units that vest within 60 days of March 1, 2025.

(8) Consists of 2,550 shares of Class A Common Stock subject to options held by Dr. Phillips exercisable within 60 days of March 1, 2025.

(9) Consists of 2,550 shares of Class A Common Stock subject to options held by Dr. Jansen exercisable within 60 days of March 1, 2025.

(10) Consists of (i) 49,476 shares of Class A Common Stock held by The Grey Family Trust dated November 12, 1999 (the Grey 1999 Trust), (ii) 13,408 shares of Class A Common Stock held by Michael Grey and Rondi Rauch Grey, Co-Trustees of The Grey 2014 Irrevocable Children's Trust u/a/d 12/17/14 (the Grey 2014 Trust), and (iii) 32,486 shares of Class A Common Stock subject to options held by Mr. Grey exercisable within 60 days of March 1, 2025. Mr. Grey, Reneo's former Executive Chairman and a member of the Board of the Combined Company, is trustee of each of the Grey 1999 Trust and Grey 2014 Trust, and in such capacity has the power to vote and dispose of such shares held by the Grey 1999 Trust and Grey 2014 Trust.

(11) Consists of 7,450 shares of Class A Common Stock subject to options held by Mr. Mathers exercisable within 60 days of March 1, 2025.

(12) See Notes (1) through (11) above.

(13) Based on information taken from Schedule 13G/A filed on October 16, 2024. Consists of (i) 434,934 shares of Class A Common Stock held by Cormorant Global Healthcare Master Fund, LP ("Master Fund"); (ii) 1,109,451 shares of Class A Common Stock held by Cormorant Private Healthcare Fund III, LP ("Fund III"); (iii) 235,480 shares of Class A Common Stock held by Cormorant Private Healthcare Fund IV, LP ("Fund IV"); (iv) 7,945 shares of Class A Common Stock held by CRMA SPV, LP ("CRMA"); (v) 49,929 shares of Class A Common Stock held by Cormorant Private Healthcare Fund V, LP ("Fund V"). Cormorant Global Healthcare GP, LLC serves as the general partner of Master Fund, Cormorant Private Healthcare GP III, LLC

serves as the general partner of Fund III, Cormorant Private Healthcare GP IV, LLC serves as the general partner of Fund IV, Cormorant Private Healthcare GP V, LLC serves as the general partner of Fund V, and Cormorant Asset Management, LP ("Cormorant") serves as the investment manager to Master Fund, Fund III, Fund IV, Fund V and CRMA. Bihua Chen serves as the managing member of Cormorant Global Healthcare GP, LLC, Cormorant Private Healthcare GP III, LLC, Cormorant Private Healthcare GP IV, LLC and Cormorant Private Healthcare GP V, LLC, and the general partner of Cormorant and therefore may be deemed to share voting and investment power over such shares. Each of the reporting persons disclaims beneficial ownership of the shares except to the extent of its pecuniary interest therein. The address for each of reporting person is 200 Clarendon Street 52nd Floor, Boston, Massachusetts 02116.

(14) Based on information taken from Schedule 13G filed on October 9, 2024. Consists of (i) 1,439,674 shares of Class A Common Stock held by Acorn Bioventures, L.P.. Acorn Capital Advisors, GP, LLC ("Acorn GP") is the general partner of Acorn Bioventures L.P. Acorn GP has discretionary authority to vote and dispose of the shares held by Acorn Bioventures L.P. and, accordingly, Acorn GP may be deemed to have beneficial ownership of such shares. Anders Hove is the manager of Acorn GP and, in his capacity as such, may be deemed to beneficially own the shares held by Acorn Bioventures L.P. Dr. Isaac Manke, a member of the Board, is a partner at Acorn GP. Each of Acorn GP, Dr. Hove and Dr. Manke disclaim beneficial ownership of the shares held by Acorn Bioventures L.P., except to the extent of their respective pecuniary interests therein. The business address for these persons is 420 Lexington Avenue, Suite 2626, New York, NY 10170.

(15) Based on information taken from Schedule 13G filed on October 11, 2024. Consists of (i) 702,044 shares of Class A Common Stock held by Citadel Multi-Strategy Equities Master Fund Ltd. ("CM"), (ii) 267,310 shares of Class A Common Stock issuable upon conversion of Class B Common Stock held by CM, and (iii) 360,792 shares of Class A Common Stock held by Citadel CEMF Investments Ltd. ("CEMF Investments"). Does not include 419,217 shares of Class A Common Stock otherwise issuable to CM upon conversion of Class B Common Stock due to a 9.9% beneficial ownership limit. The Class B Common Stock is non-voting. Citadel Advisors LLC ("Citadel Advisors") is the portfolio manager of CM and CEMF Investments. Citadel Advisors Holdings LP ("CAH") is the sole member of Citadel Advisors. Citadel GP LLC ("CGP") is the general partner of CAH. Kenneth Griffin owns a controlling interest in CGP. Mr. Griffin, as the owner of a controlling interest in CGP, may be deemed to have shared power to vote or direct the vote of, and/or shared power to dispose or to direct the disposition of, the shares held by CEMF. This response is not and shall not be construed as an admission that Mr. Griffin or any of the Citadel related entities listed above is the beneficial owner of any securities of the Combined Company other than the securities actually owned by such person (if any). The address for each of these persons is c/o Citadel Enterprise Americas, Southeast Financial Center, 200 S. Biscayne Blvd., Suite 3300, Miami, FL 33131.

(16) Based on information taken from Schedule 13G filed on October 10, 2024. Consists of 1,004,439 shares of Class A Common Stock held by Perceptive Life Sciences Master Fund, Ltd. Perceptive Advisors LLC (the "Advisor") serves as the investment manager to Perceptive Life Sciences Master Fund, Ltd. (the "Master Fund"). Joseph Edelman is the managing member of the Advisor. Each of Mr. Edelman and the Advisor disclaims, for purposes of Section 16 of the Exchange Act, beneficial ownership of the shares held by the Master Fund, except to the extent of his/its indirect pecuniary interest therein, and this report shall not be deemed an admission that either Mr. Edelman or the Advisor is the beneficial owner of such securities. The address for Perceptive Life Sciences Master Fund, Ltd. and Perceptive Advisors LLC is 51 Astor Place, 10th Floor, New York, NY 10003.

(17) Based on information taken from Schedule 13G filed on October 11, 2024. Consists of 824,155 shares of Class A Common Stock held by Samsara BioCapital, L.P. Samsara BioCapital GP, LLC ("Samsara LLC") is the general partner of by Samsara BioCapital, L.P. ("Samsara LP") and therefore may be deemed to beneficially own the shares held by Samsara LP. Dr. Srinivas Akkaraju, MD, Ph.D. has voting and investment power over the shares held by Samsara LLC and, accordingly, may be deemed to beneficially own the shares held by Samsara LP. Samsara LLC disclaims beneficial ownership in these shares except to the extent of its respective pecuniary interest therein. The address for Samsara LP is 628 Middlefield Road, Palo Alto, CA 94301.

(18) Based on information taken from Schedule 13G filed on January 31, 2025. The Vanguard Group reported that it has sole dispositive power with respect to 705,988 shares and shared dispositive power with respect to 745 shares. The address for the Vanguard Group is 100 Vanguard Blvd., Malvern, PA 19355.

Item 13. Certain Relationships and Related Transactions, and Director Independence

Independence of the Board

As required under the Nasdaq listing standards, a majority of the members of a listed company's board of directors must qualify as "independent," as affirmatively determined by the board of directors. Our Board consults with counsel to ensure that its determinations are consistent with relevant securities and other laws and regulations regarding the definition of "independent," including those set forth in pertinent listing standards of the Nasdaq, as in effect from time to time.

Consistent with these considerations, after review of all relevant identified transactions or relationships between each director, or any of his or her family members, and us, our senior management and our independent registered public accounting firm, the Board has affirmatively determined that the following five directors are independent directors within the meaning of the applicable Nasdaq listing standards: Mr. R. Michael Carruthers, Dr. Isaac Manke, Dr. Andrew Phillips, Mr. Edward T. Mathers and Dr. Valerie M. Jansen. In making this determination, the Board found that none of the directors had a material or other disqualifying relationship with us. Dr. Saccomano, our President and Chief Executive Officer is not an independent director by virtue of his employment relationship with us. Mr. Grey is not considered an independent director because of his recent former service as Reneo's Executive Chairman.

Certain Transactions With or Involving Related Persons

The following is a summary of transactions since January 1, 2023, or any currently proposed transaction, in which we were or are a participant and the amount involved exceeds the lesser of $120,000 or one percent of the average of our total assets at fiscal year-end for 2024 and 2023, and in which any of our executive officers, directors or holders of more than 5% of our capital stock, or any member of the immediate family of any of the foregoing persons, had or will have a direct or indirect material interest, other than compensation arrangements disclosed in "Item 11. Executive Compensation" of this Annual Report on Form 10-K.

Director and Officer Indemnification

We have entered into indemnification agreements with each of our directors and executive officers. These agreements, among other things, require us or will require us to indemnify each director (and in certain cases their related venture capital funds) and executive officer to the fullest extent permitted by Delaware law, including indemnification of expenses such as attorneys' fees, judgments, fines, and settlement amounts incurred by the director or executive officer in any action or proceeding, including any action or proceeding by or in right of us, arising out of the person's services as a director or executive officer.

Our amended and restated certificate of incorporation and our Bylaws provide that we will indemnify each of our directors and officers to the fullest extent permitted by the DGCL. Further, we have purchased a policy of directors' and officers' liability insurance that insures our directors and officers against the cost of defense, settlement, or payment of a judgment under certain circumstances.

Sublease Agreement

On January 10, 2025, we entered into a sublease agreement with Ambros Therapeutics, Inc. ("Ambros Therapeutics"), pursuant to which we subleased certain office space to Ambros Therapeutics for their corporate headquarters. Mr. Flesher, the President and Chief Executive Officer of Reneo prior to the Merger, is acting President and the Chief Executive Officer and a stockholder of Ambros Therapeutics. The premises are located in Irvine, California. The approximate value of the transaction is $450,000 over the term of the Sublease. The Sublease was considered by us in accordance with our Related Person Transactions Policy, and approved by Audit Committee.

Policies and Procedures for Related Person Transactions

We have adopted a formal, written policy regarding related person transactions. This policy provides that a related person transaction is a transaction, arrangement or relationship or any series of similar transactions, arrangements or relationships, in which we are a participant and in which a related person has, had or will have a direct or indirect material interest and in which the aggregate amount involved exceeds $120,000. For purposes of this policy, a related person means any of our executive officers and directors (including director nominees), in each case at any time since the beginning of our last fiscal year, or holders of more than 5% of any class of our voting

securities and any member of the immediate family of, or person sharing the household with, any of the foregoing persons.

Our Audit Committee has the primary responsibility for reviewing and approving, ratifying, or disapproving related person transactions. In determining whether to approve, ratify, or disapprove any such transaction, our Audit Committee will consider, among other factors, (1) whether the transaction is fair to us and on terms no less favorable than terms generally available to unaffiliated third parties under the same or similar circumstances, (2) the extent of the related person's interest in the transaction, (3) whether there are business reasons for us to enter into such transaction, (4) whether the transaction would impair the independence of any of our outside directors, and (5) whether the transaction would present an improper conflict of interest for any of our directors or executive officers.

The policy grants standing pre-approval of certain transactions, including (1) certain compensation arrangements for our directors or executive officers, (2) transactions with another company at which a related person's only relationship is as a non-executive employee, director, or beneficial owner of less than 10% of that company's shares, provided that the aggregate amount involved does not exceed the greater of $200,000 or 5% of such company's total annual revenues and the transaction is on terms no less favorable than terms generally available to unaffiliated third parties under the same or similar circumstances, (3) charitable contributions by us to a charitable organization, foundation or university at which a related person's only relationship is as a non-executive employee or director, provided that the aggregate amount involved does not exceed the greater of $200,000 or 5% of such organization's total annual receipts, (4) transactions where a related person's interest arises solely from the ownership of our common stock and all holders of our common stock received the same benefit on a pro rata basis and (5) any indemnification or advancement of expenses made pursuant to our organizational documents or any agreement. In addition to our policy, our Audit Committee charter provides that our Audit Committee shall review and approve or disapprove any related person transactions.

Item 14. Principal Accountant Fees and Services

KPMG LLP ("KPMG") served as the independent registered public accounting firm of Legacy OnKure prior to the consummation of the Merger. On November 7, 2024, the Audit Committee engaged KPMG as our independent registered public accounting firm to audit our consolidated financial statements for the year ending December 31, 2024. Accordingly, Ernst & Young LLP ("EY"), our independent registered public accounting firm prior to the Merger, was informed on November 7, 2024 that it was dismissed as our independent registered public accounting firm.

The following table represents aggregate fees billed, or expected to be billed, to us by KPMG and EY for the fiscal years ended December 31, 2024 and December 31, 2023:

	2024 (4)	2024 (5)	2023 (6)
Audit Fees (1)	$ 595,000	$ 275,300	$ 613,412
Audit-related Fees (2)	—	15,000	—
Tax Fees	—	—	—
All Other Fees (3)	23,985	—	2,000
Total Fees	$ 618,985	$ 290,300	$ 615,412

(1) Audit Fees include fees for the (i) audit of the financial statements included in our Form 10-K for our fiscal years ended December 31, 2024, and December 31, 2023, (ii) review of Legacy OnKure, Inc.'s interim financial statements included on Forms S-4, S-1 and 8-K and (iii) attest, consent and review services normally provided by the accountant in connection with SEC filings. Included in the 2023 audit fees are $135,622 of fees billed in connection with the Reneo public offering that closed in May 2023.
(2) Audit-related Fees include fees for accounting consultations.
(3) Consists of non-audit fees in connection with access to the EY on-line accounting research and disclosures database.
(4) Represents fees from KPMG for audit of fiscal year 2024.
(5) Represents fees from EY for audit of fiscal year 2024.
(6) Represents fees from EY for audit of fiscal year 2023.

All fees described above were approved by the Audit Committee.

Pre-Approval Policies and Procedures

The above services performed by the independent registered public accounting firm were pre-approved in accordance with the pre-approval policy and procedures adopted by the Audit Committee. This policy describes the permitted audit, audit-related, tax, and other services that our independent registered public accounting firm may perform. The policy also requires that our independent registered public accounting firm provide in writing:

- an annual description of all relationships between the independent registered public accounting firm and the client that may reasonably be thought to bear on independence;
- confirmation that, in the independent registered public accounting firm's professional judgment, it is independent of the client under SEC requirements; and
- discussion of its independence and the potential effects on its independence of performing any non-audit related services.

The services expected to be performed by our independent registered public accounting firm during the subsequent fiscal year are presented to the Audit Committee for pre-approval. Any pre-approval must describe, in writing, the particular service or category of services.

Requests for audit, audit-related, tax, and other services not contemplated by those pre-approved services must be submitted to the Audit Committee for specific pre-approval. Generally, pre-approval is considered at the Audit Committee's regularly scheduled meetings. However, the authority to grant specific pre-approval between meetings, as necessary, has been delegated to the Chair of the Audit Committee. If the Chair is not available, the other two Audit Committee members together have the authority to grant specific pre-approval between meetings. The Chair or the other members must update the Audit Committee at the next regularly scheduled meeting of any services that were granted specific pre-approval.

The Audit Committee pre-approved all audit related services rendered in 2024 and did not rely on the waiver of pre-approval requirement provided by paragraph (c)(7)(i)(C) of Rule 2-01 of Regulation S-X promulgated under the Exchange Act.

PART IV

Item 15. Exhibit and Financial Statement Schedules

(a) The following documents are filed as part of this Annual Report:

(1) Financial statements

The financial statements filed as part of this Annual Report are included in Part II, Item 8 of this Annual Report.

(2) Financial statement schedules

Financial statement schedules have been omitted in this Annual Report because they are not applicable, not required under the instructions, or the information requested is set forth in the financial statements or related notes thereto.

(3) Exhibits

The exhibits listed in the accompanying Exhibit Index are filed as part of, or incorporated by reference into, this Annual Report.

EXHIBIT INDEX

		Incorporated by Reference			
Exhibit Number	**Description**	**Form**	**Filing Date**	**Number**	**Filed Herewith**
2.1	Agreement and Plan of Merger, dated May 10, 2024, by and among Reneo Pharmaceuticals, Inc., Radiate Merger Sub I, Inc., Radiate Merger Sub II, LLC and OnKure, Inc.	8-K	5/13/2024	2.1	
3.1	Certificate of Amendment to Amended and Restated Certificate of Incorporation.	8-K	10/8/2024	3.1	
3.2	Amended and Restated Certificate of Incorporation, as amended.	8-K	10/8/2024	3.2	
3.3	Amended and Restated Bylaws.	8-K	10/8/2024	3.3	
4.1	Amended and Restated Investors' Rights Agreement, by and among the Registrant and certain of its stockholders, dated December 9, 2020.	S-1	3/19/2021	4.2	
4.2	Description of Capital Stock of the Registrant.				X
10.1+	Form of Indemnity Agreement by and between the Registrant and its directors and executive officers.	S-1/A	4/5/2021	10.8	

Exhibit Number	Description	Form	Filing Date	Number	Filed Herewith
10.2	Registration Rights Agreement dated October 4, 2024 by and among OnKure Therapeutics, Inc. and certain parties thereto.	8-K	10/8/2024	10.23	
10.3	Sales Agreement, dated November 13, 2023, by and between the Registrant and Leerink Partners LLC.	10-Q	11/13/2023	10.1	
10.4+	Reneo Pharmaceuticals, Inc. 2014 Equity Incentive Plan, as amended, and UK Sub-Plan.	S-1/A	4/5/2021	10.1	
10.5+	Forms of Grant Notice, Stock Option Agreement and Notice of Exercise under the Reneo Pharmaceuticals, Inc. 2014 Equity Incentive Plan, as amended, and UK Sub-Plan.	S-1/A	4/5/2021	10.2	
10.6+	Reneo Pharmaceuticals, Inc. 2021 Equity Incentive Plan.	S-1/A	4/5/2021	10.3	
10.7+	Forms of (i) Stock Option Grant Notice, Stock Option Agreement and Notice of Exercise, (ii) Stock Option Grant Notice - International, Stock Option Agreement - International and Notice of Exercise - International and (iii) Non-Employee Director Stock Option Grant Notice, Stock Option Agreement and Notice of Exercise – Non-Employee Director under the Reneo Pharmaceuticals, Inc. 2021 Equity Incentive Plan.	10-K	3/27/2023	10.18	
10.8+	Forms of (i) Restricted Stock Unit Award Grant Notice and Award Agreement and (ii) Restricted Stock Unit Award Grant Notice - International and Award Agreement - International under the Reneo Pharmaceuticals, Inc. 2021 Equity Incentive Plan.	S-1/A	4/5/2021	10.5	
10.9+	Forms of Stock Option Grant Notice, Stock Option Agreement and Notice of Exercise for Inducement Grant Outside of the Reneo Pharmaceuticals, Inc. 2021 Equity Incentive Plan.	10-Q	11/12/2021	10.4	
10.10+	Reneo Pharmaceuticals, Inc. Severance Benefit Plan, as amended as of September 27, 2022, and form of Participation Agreement thereunder.	10-Q	11/8/2022	10.2	

Exhibit Number	Description	Form	Filing Date	Number	Filed Herewith
10.11+	OnKure Therapeutics, Inc. 2024 Equity Incentive Plan, and forms of agreement thereunder.	8-K	10/8/2024	10.4	
10.12+	OnKure Therapeutics, Inc. 2024 Employee Stock Purchase Plan.	8-K	10/8/2024	10.15	
10.13+	OnKure, Inc. 2011 Stock Incentive Plan, as amended, and forms of agreement thereunder.	8-K	10/8/2024	10.16	
10.14+	OnKure, Inc. 2021 Stock Incentive Plan, as amended, and forms of agreement thereunder.	8-K	10/8/2024	10.17	
10.15+	OnKure, Inc. 2023 RSU Equity Incentive Plan, as amended, and forms of agreement thereunder.	8-K	10/8/2024	10.18	
10.16+	OnKure Therapeutics, Inc. Executive Incentive Compensation Plan.	8-K	10/8/2024	10.19	
10.17+	OnKure Therapeutics, Inc. Form of Executive Employment Agreement.	8-K	10/8/2024	10.20	
10.18+	OnKure Therapeutics, Inc. Outside Director Compensation Policy.	8-K	10/8/2024	10.21	
10.19	Form of Indemnification Agreement.	8-K	10/8/2024	10.22	
10.20	Form of Reneo Support Agreement.	8-K	5/13/2024	10.1	
10.21	Form of OnKure Support Agreement.	8-K	5/13/2024	10.2	
10.22	Form of Lock-Up Agreement.	8-K	5/13/2024	10.3	
10.23	Subscription Agreement dated May 10, 2024.	8-K	5/13/2024	10.4	
19	Insider Trading Policy.				X
21.1	Subsidiaries of the Registrant.				X
23.1	Consent of independent registered public accounting firm.				X
24.1	Power of Attorney (see signature page).				X

Exhibit Number	Description	Form	Filing Date	Number	Filed Herewith
31.1	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				X
31.2	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				X
32.1†	Certification of Principal Executive Officer and Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				X
97	OnKure Therapeutics, Inc. Compensation Recovery Policy.				X
101. INS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document				X
101.SCH	Inline XBRL Taxonomy Extension Schema Document				X
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101).				X

† This certification shall not be deemed filed for purposes of Section 18 of the Exchange Act or otherwise subject to the liability of that Section, nor shall it be deemed incorporated by reference into any filing under the Securities Act or the Exchange Act.
+ Indicates Management contract or compensatory plan.
# Pursuant to Item 601(b)(10) of Regulation S-K, certain portions of this exhibit have been omitted by means of marking such portions with asterisks because the Registrant has determined that the information is not material and is the type that the Registrant treats as private or confidential.

Item 16. Form 10-K Summary

None.

SIGNATURES

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

ONKURE THERAPEUTICS, INC.

March 10, 2025

By: /s/ Nicholas A. Saccomano
Nicholas A. Saccomano
President & Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Nicholas A. Saccomano and Jason Leverone and each of them, as his or her true and lawful attorneys-in-fact and agents, each with the full power of substitution, for him or her and in his or her name, place or stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or their or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

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

Signature	Title	Date
/s/ Nicholas A. Saccomano Nicholas A. Saccomano	Chief Executive Officer, President and Director *(Principal Executive Officer)*	March 10, 2025
/s/ Jason Leverone Jason Leverone	Chief Financial Officer *(Principal Financial and Accounting Officer)*	March 10, 2025
/s/ R. Michael Carruthers R. Michael Carruthers	Director	March 10, 2025
/s/ Michael Grey Michael Grey	Director	March 10, 2025
/s/ Valerie M. Jansen Valerie M. Jansen	Director	March 10, 2025
/s/ Isaac Manke Isaac Manke	Director	March 10, 2025
/s/ Edward T. Mathers Edward T. Mathers	Director	March 10, 2025
/s/ Andrew Phillips Andrew Phillips	Director	March 10, 2025