

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, 2022
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 001-39866

eFFECTOR Therapeutics, Inc.
(Exact name of Registrant as specified in its Charter)

Delaware
(State or other jurisdiction of
incorporation or organization)
142 North Cedros Avenue, Suite B
Solana Beach, CA
(Address of principal executive offices)

85-3306396
(I.R.S. Employer
Identification No.)
92075
(Zip Code)

Registrant's telephone number, including area code: (858) 925-8215

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	EFTR	Nasdaq Capital Market
Warrants to purchase common stock	EFTRW	Nasdaq Capital Market

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

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

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

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

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, 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	<input type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input checked="" type="checkbox"/>	Smaller reporting company	<input checked="" type="checkbox"/>
Emerging growth company	<input checked="" type="checkbox"/>		

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 ☒

As of June 30, 2022, the aggregate market value of the common stock held by non-affiliates of the Registrant, based on the closing price of the shares of common stock on the Nasdaq Capital Market of \$1.42 per share, was approximately \$47.7 million.

The number of shares of Registrant's common stock outstanding as of February 28, 2023 was 42,401,219.

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS AND MARKET DATA

This Annual Report on Form 10-K ("Annual Report") contains forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and Section 27A of the Securities Act of 1933, as amended (the "Securities Act"). All statements other than statements of historical facts contained in this Annual Report, including statements regarding our future results of operations or financial condition, research and development plans, the anticipated timing, costs, design and conduct of our ongoing and planned preclinical studies and planned clinical trials for our product candidates, the timing and likelihood of regulatory filings and approvals for our product candidates, our ability to commercialize our product candidates, if approved, the impact of the COVID-19 pandemic on our business, the potential to develop future product candidates, the potential benefits of strategic collaborations, the timing and likelihood of success, plans and objectives of management for future operations, and future results of anticipated product development efforts, are forward-looking statements. In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "could," "expect," "intend," "target," "plan," "anticipate," "believe," "estimate," "predict," "potential," "continue," or the negative of these terms or other similar expressions. These forward-looking statements are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this Annual Report and are subject to a number of risks, uncertainties and assumptions, including those described in Part I, Item 1A, "Risk Factors". 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, changed circumstances or otherwise. All forward-looking statements are qualified in their entirety by this cautionary statement, which is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

This Annual Report includes trademarks, tradenames and service marks that are the property of other organizations. Solely for convenience, trademarks and tradenames referred to in this Annual Report appear without the ® and ™ symbols, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights, or that the applicable owner will not assert its rights, to these trademarks and tradenames.

This Annual Report also contains industry, market and competitive position data from our own internal estimates and research, as well as from independent market research, industry and general publications and surveys, governmental agencies and publicly available information. In some cases, we do not expressly refer to the sources from which this data is derived. In that regard, when we refer to one or more sources of this type of data in any paragraph, you should assume that other data of this type appearing in the same paragraph is derived from the same sources, unless otherwise expressly stated or the context otherwise requires. In addition, while we believe the industry, market and competitive position data included in this report is reliable and based on reasonable assumptions, such data involve risks and uncertainties and are subject to change based on various factors, including those discussed in the section titled "Risk Factors." These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties or by us.

Item 1. Business.




Overview

We are a clinical-stage biopharmaceutical company focused on pioneering the development of a new class of oncology drugs we refer to as selective translation regulator inhibitors (“STRIs”). Translation is the process in cells whereby the synthesis of proteins is directed by information contained in genetic sequences. We utilized our proprietary selective translation regulation technology platform to internally discover a portfolio of small molecule STRI product candidates. Our product candidates target the eIF4F complex and its activating kinase, MNK. The eIF4F complex is a central node where two of the most frequently mutated signaling pathways in cancer, the PI3K-AKT and RAS-MEK pathways, converge to activate the translation of select messenger RNA (“mRNA”) into proteins that are frequent culprits in key disease-driving processes. Inhibition of these targets simultaneously downregulates multiple disease-driving proteins before they are synthesized. Each of our product candidates is designed to act on a single protein that drives the expression of multiple functionally related proteins, including oncoproteins, which are proteins whose aberrant function can cause cancer, immunosuppressive proteins in T cells and proteins known to drive drug resistance that together control tumor growth, survival and immune evasion.

Our lead product candidate, tomivosertib, is an inhibitor of MNK, and is currently being evaluated in combination with KEYTRUDA® (also known as pembrolizumab), an FDA-approved inhibitor of programmed cell death protein 1 (“PD-1”) in a randomized Phase 2b clinical trial in patients with metastatic non-small cell lung cancer (“NSCLC”). Our second product candidate, zotatifin, is an inhibitor of eIF4A, a component of the eIF4F complex, and is currently being evaluated in a Phase 1/2 clinical trial in patients with certain solid tumors. We have completed the initial dose escalation portion of this trial and are currently evaluating zotatifin in combination with fulvestrant and abemaciclib in a Phase 2a open-label expansion cohort in patients with ER+ breast cancer. In light of the favorable safety results observed to date in the Phase 1/2 clinical trial, we have also resumed dose escalation of zotatifin in combination with fulvestrant in patients with ER+ breast cancer to determine if a higher dose of zotatifin can be utilized in future clinical studies. We have also completed a Phase 1b clinical trial evaluating zotatifin as an antiviral agent against SARS-CoV-2. We have entered into a global collaboration and license agreement with Pfizer for our earliest stage program, inhibitors of eIF4E, and Pfizer is currently conducting investigational new drug application (“IND”) enabling studies for this program. We believe each of our product candidates has the potential to improve patient outcomes and expand the utility of cancer treatments such as checkpoint inhibitors and targeted therapies.

The following table summarizes our current programs:

Figure 1: Our Pipeline

Program (Target)	Discovery	Preclinical	Phase 1	Phase 2a	Phase 2b	Phase 3	Global Rights	Anticipated Milestones
Tomivosertib (MNKi)	1L NSCLC PD-L1 ≥50% - 1L in combo with pembro							H2 2023 Topline data readout
Zotatifin Oncology (eIF4Ai)	Solid Tumors ER+ BC and KRAS NSCLC							H1 2023 Topline data from remaining 11 patients in ECRF+A P2a (n=18) expansion cohort H2 2023 Data from P1b dose escalation cohorts
Zotatifin COVID-19 (eIF4Ai)	Anti-SARS-CoV-2 Dose Escalation							Topline data from Phase 1b trial reported at CROI 2023
eIF4Ei	Solid Tumors						 <small>eFFECTOR Option to Co-Develop / Profit Share in US</small>	

Targeting the eIF4F Complex and MNK

The eIF4F complex plays a critical role in the production of certain proteins that promote cell growth and division. During normal cellular function, extracellular factors such as growth factors or antigens, bind to cell surface receptors such as receptor tyrosine kinases (“RTKs”) and T cell receptors (“TCRs”) which initiate signaling through the PI3K-AKT and RAS-MEK pathways to stimulate growth. Under normal conditions, RTKs and TCRs are stimulated only transiently when cell growth and proliferation are required. However, when eIF4F activation is excessive and continuous, either because of oncogenic mutations that activate the PI3K-AKT and RAS-MEK pathways or the continuous presentation of antigens to TCRs in cancer, this results in a sustained upregulation of protein synthesis. This sustained upregulation leads to uncontrolled growth of tumor cells and exhaustion of T cells, which causes T cells to become less effective cancer fighters. Inhibiting targets in the eIF4F complex downregulates production of disease-driving proteins before they are synthesized. Proteins in tumor cells that are controlled by the eIF4F complex include: (1) multiple oncoproteins currently addressed by targeted therapies, such as RTKs and KRAS; (2) oncoproteins for which there are currently no targeted therapies available, such as MYC and Cyclin D1; and (3) certain proteins that are often upregulated in response to targeted therapies as a resistance mechanism, such as Cyclin D1, CDK4/6, RTKs, and KRAS. In T cells, MNK controls the production of multiple immunosuppressive factors including PD-1, PD-L1, TIM3, LAG3 and IL-10 that serve to exhaust the T cells and attenuate an immune response.

We believe there are several potential advantages of targeting MNK and the eIF4F complex. First, we can simultaneously aim to inhibit the production of multiple key disease -driving proteins that tumor cells have hijacked for growth, proliferation and survival. Rather than inhibiting a single target oncoprotein, our product candidates are each designed to downregulate multiple target oncoproteins that are often co-produced in cancer cells, or multiple immunosuppressive factors produced in activated T cells. In addition, our product candidates are designed to downregulate many proteins that are frequently over-produced by feedback pathways as resistance mechanisms that cause tumors to become less responsive to targeted therapies. Moreover, some of the disease-driving proteins such as MYC and Cyclin D1 that our product candidates are designed to downregulate are not currently addressable by any existing marketed agents due to the cellular location and complex shape of these targets. Lastly, our product candidates are designed to preserve normal cell function while at the same time enhancing tumor cell killing because these over-produced disease-driving proteins, which are dependent on MNK and the eIF4F complex for their production, are more critical for the growth and survival of tumor cells than normal cells.

Tomivosertib, a Potent and Highly Selective MNK Inhibitor

Our lead product candidate, tomivosertib, is an oral small molecule inhibitor of MNK that we are developing in combination with inhibitors of PD-1 and programmed cell death ligand 1 (“PD-L1”), collectively what we refer to as anti PD-(L)1 therapy, for the treatment of patients with solid tumors. MNK is a kinase that phosphorylates, or modifies by the enzymatic addition of a phosphate chemical group, a key protein within the eIF4F complex. Through inhibition of MNK, tomivosertib is designed to downregulate production of multiple immune-suppressive proteins and to reprogram T cells to delay exhaustion and dysfunction, increasing their ability to combat tumor cells. Tomivosertib has been shown to downregulate production of multiple immunosuppressive proteins, including PD-1, PD-L1, TIM3, LAG3 and IL-10, in preclinical studies. MNK plays a crucial role in the development of many tumors, including by controlling in a coordinated manner the expression of multiple factors that attenuate an immune response. Immune attenuation is a normal biological process that prevents overstimulation of the immune system. However, tumors frequently exploit the attenuation process in order to evade immune control. In preclinical studies, tomivosertib inhibited MNK, and enhanced the ability of the immune system to attack tumors. Immune checkpoints, such as PD-1, PD-L1, TIM3 and LAG3, are signaling molecules expressed on immune and tumor cells that can activate multiple mechanisms to attenuate an anti-tumor immune response. Over the past several years, a class of drugs called checkpoint inhibitors, primarily anti PD-(L)1 therapies, have emerged as an important new class of therapeutics in the treatment of cancer with the ability to block these immune checkpoint pathways. In 2022, the worldwide market value for anti PD-(L)1 therapies was greater than \$35 billion, of which nearly half accounted for the treatment of patients with metastatic NSCLC. While checkpoint inhibitor treatment is very effective in patients for a variety of cancers, these agents are generally not curative, and a large majority of patients ultimately

progress on their checkpoint inhibitor therapy, emphasizing the need for novel frontline combination treatments that may increase the proportion of patients that experience long term durable benefit, and delay progression in other patients. We are currently using PD-L1 expression level greater than or equal to 50% ("PD-L1 \geq 50%") as a biomarker to enroll patients in the ongoing KICKSTART Phase 2b clinical trial of tomivosertib. There are an estimated 27,000 new U.S. patients per year with metastatic NSCLC that have PD-L1 \geq 50%, which we estimate represents a \$4 billion market opportunity in the United States. We also believe tomivosertib can be used to treat patients with PD-L1 expression levels 1-49%, which we estimate to represent another \$5 billion dollar market opportunity in the United States.

Based on the encouraging results in our Phase 2a clinical trial, we are currently enrolling in KICKSTART, a double-blind, randomized, placebo-controlled Phase 2b trial of tomivosertib combined with pembrolizumab in patients with metastatic NSCLC, with PD-L1 \geq 50%. Pembrolizumab is owned and marketed by Merck for frontline NSCLC and several other indications. We initiated this trial in the second quarter of 2021 and anticipate reporting topline data from the KICKSTART trial in the second half of 2023.

In our completed Phase 2a CPI-A clinical trial evaluating tomivosertib in combination with anti PD-(L)1 therapy in 17 patients with metastatic, NSCLC tomivosertib substantially extended the median progression free survival ("mPFS"), the time duration during which patients remain alive and experience no disease progression, defined as an increase in their tumor assessment of greater than 20% or appearance of new lesions, in patients that were previously not responding to their anti PD-(L)1 therapies. In addition, as of study completion in September 2020, two of those 17 patients (12%) had confirmed partial responses, or decreases in tumor assessments of greater than or equal to 30% from baseline ("PRs"), one of which went on to achieve a confirmed complete response, or no detectable tumor lesions ("CR") with a third patient showing 28% tumor regression. Tomivosertib was generally well tolerated in this clinical trial. In these 17 patients, once tomivosertib was added without any change or break in the anti PD-(L)1 therapy, there was a mPFS of 20 weeks. In this trial, patients with positive PD-L1 expression, a biomarker of T cell infiltration into tumors, as determined by post-hoc analysis of available data from diagnostic assays conducted during their treatment history, had mPFS of 53 weeks relative to 9 weeks for PD-L1 negative patients. Tomivosertib has been tested in over 200 patients in completed studies, including approximately 80 in combination with checkpoint inhibitors, and has demonstrated a favorable adverse event profile both as a single agent and in combination with checkpoint inhibitors.

We are enrolling NSCLC patients in KICKSTART with PD-L1 \geq 50%. Patients with PD-L1 \geq 50% are the most responsive to pembrolizumab monotherapy in the frontline setting. In this setting, pembrolizumab monotherapy is a standard-of-care and pembrolizumab is the most widely used checkpoint treatment. Beyond this initial KICKSTART patient population, we plan to pursue additional clinical trials of tomivosertib NSCLC patients with PD-L1 expression 1-49% and in other indications where anti PD-(L)1 therapy is the standard-of-care, including other cancers where PD-(L)1 therapy is approved such as renal, bladder, triple negative breast cancer, or tumors with high microsatellite instability ("MSI-H").

Our preclinical studies suggest combining tomivosertib with anti PD-(L)1 treatments can overcome mechanisms of resistance to checkpoint inhibitors, resulting in enhanced and durable sensitivity. In addition, our preclinical data demonstrated that tomivosertib, either as a single agent or in combination with anti PD-1 treatment, promoted anti-tumor immunity that persisted after stopping drug treatment. We believe that a key advantage of our approach is that by inhibiting MNK, tomivosertib is designed to downregulate the production of multiple immune checkpoint and immunosuppressive cytokine proteins in a coordinated manner to activate an immune response against tumors. Our preclinical data demonstrated that tomivosertib activity addressed key mechanisms of checkpoint inhibitor resistance by:

- increased target cell killing;
- simultaneous downregulation of several key checkpoint proteins associated with T cell exhaustion and dysfunction, including PD-1, PD-L1, LAG-3 and TIM-3;
- decreased production of immunosuppressive IL-10; and
- increased memory T cell population.

Collectively, these effects may complement checkpoint inhibitors by increasing tumor recognition, restoring immune response, improving durability of response and preserving antitumor immunity.

Zotatifin—A Potent and Selective eIF4A mRNA Helicase Inhibitor

Our second product candidate, zotatifin, is a small molecule designed to inhibit eIF4A, and is currently being evaluated in a Phase 1/2 clinical trial in patients with solid tumors. eIF4A is a helicase and is responsible for unwinding complex secondary structures, found in the 5' untranslated region ("UTR") of certain mRNA. This unwinding is a regulatory control step that leads to efficient stimulated production of important proteins that enable normal cells to respond to growth signals, and which are upregulated in tumor cells. Proteins in tumor cells that are controlled by eIF4A include multiple oncoproteins currently addressed by targeted therapies, oncoproteins for which there are currently no targeted therapies available and certain proteins that are often upregulated in response to targeted therapies as a resistance mechanism. Several of these oncoproteins can function in concert within a vertical signaling pathway to drive tumor growth, proliferation and survival in cancer, including certain breast cancers and NSCLC. In our preclinical studies, we discovered that most proteins inhibited by zotatifin have common distinct translation initiation regulatory elements in the 5' UTR of the mRNA recognized by zotatifin. Our preclinical data showed that zotatifin inhibition at physiologic concentrations in vitro only impacted translation of approximately 5% of mRNAs in a cell. Further, because these translation initiation regulatory elements are located in the mRNA prior to and independent from the coding sequences that dictate the amino acids included in protein synthesis, their inhibition is independent of protein mutation variants. We have initiated multiple Phase 2a expansion cohorts with zotatifin both as a single agent and in combination with targeted agents in ER+ breast cancer, FGFR+ breast cancer, and KRAS mutant NSCLC, and are currently focused on combinations in ER+ breast cancer. Together, we believe the estimated target population of breast cancer and NSCLC patients that meet the enrollment criteria in our Phase 2a expansion cohorts totals approximately 82,000 in the United States.

Zotatifin as an Antiviral Agent for COVID-19

In collaboration with the Quantitative BioSciences Institute ("QBI") at UCSF, which received a \$5 million cooperative agreement sponsored by DARPA, a research and development agency within the U.S. Department of Defense, we evaluated zotatifin as a potential host-directed anti-viral therapy in patients with mild to moderate COVID-19. Zotatifin inhibits the eIF4A-dependent translation of select mRNA into proteins. eIF4A is required to unwind the complex secondary structures within the 5' UTR of coronaviruses, and other RNA viruses, to translate viral RNA and replicate. Zotatifin was evaluated as one of 69 compounds tested for in vitro antiviral activity against severe acute respiratory syndrome coronavirus ("SARS CoV-2") the virus that causes COVID-19, by independent groups at Mount Sinai Hospital in New York and Institut Pasteur in Paris. Results from the study, published in Nature in April 2020, revealed that zotatifin was one of the most active antiviral agents against SARS-CoV-2 among all the compounds tested. In subsequent studies using normal human bronchoepithelial cells, zotatifin demonstrated potent inhibition of SARS-CoV-2 as well as Middle East respiratory syndrome coronavirus ("MERS-CoV"). Overall, these studies showed that zotatifin was approximately 10 times more potent than remdesivir or nirmatrelvir, two agents authorized by the FDA for treatment of patients infected with SARS-CoV-2. We've completed a Phase 1b double-blind, randomized dose escalation trial of zotatifin in non-hospitalized patients with mild to moderate COVID-19 funded by DARPA in approximately 36 patients evaluating three different doses of zotatifin. In this trial, zotatifin was found to be safe and well-tolerated, and demonstrated favorable trends in several assessments of viral clearance compared to placebo. This trial began utilizing the same IV formulation currently being used in our cancer trials but switched to a newly developed sub-cutaneous formulation for the last 34 patients enrolled. Pharmacokinetics results show a profile of drug concentrations in blood over time virtually identical to the IV formulation, suggesting the more convenient sub-cutaneous formulation could be used in future COVID or cancer trials. We have exhausted the full \$5.0 million of allowable costs under our agreement with UCSF as of December 31, 2022.

eIF4E—Global Collaboration with Pfizer

Our third program is focused on developing inhibitors of eIF4E and is currently being developed by Pfizer under the Pfizer Agreement. Pfizer is currently conducting IND-enabling studies for the lead product candidate. We have received \$42 million to date under the Pfizer Agreement with the potential to receive up to an additional \$465 million in future milestone payments as well as potential royalties on sales.

Our Proprietary STRIs—Invented Using Our Translation Regulation Technology Platform

We discovered our product candidates using our proprietary selective translation regulation technology platform. In addition, we assembled a team of founders and collaborators that are experts in the eIF4F complex and growth-dependent translation control. The importance of translation regulation in disease has become increasingly recognized in the pharmaceutical industry, and we believe we remain at the forefront of developing approaches to cancer therapy focused on STRIs. Utilizing our proprietary selective translation regulation technology platform, we developed an understanding of genes that are translationally upregulated in multiple tumor types and other diseases. This has enabled us to identify specific points of therapeutic intervention that may have a meaningful clinical effect and to identify patient populations most likely to respond to product candidates acting at these points of intervention. We believe our in-depth understanding of translation regulation biology combined with our sophisticated and dedicated structure-based design and computational chemistry approach to medicinal chemistry gave us a key advantage in pioneering the emerging field of translation regulation therapeutics and creates significant barriers to entry. We currently plan to focus our resources on the clinical development of our existing product candidates.

We have strong composition of matter and other intellectual property positions covering our product candidates and their uses and strive to protect our product candidates and our technology platform through an intellectual property estate in major markets throughout the world.

Strategy

Our goal is to continue to pioneer the development of and ultimately commercialize STRIs for the treatment of multiple types of cancer. To achieve our goal, we intend to pursue the following strategies:

- ***Advance our lead product candidate, tomivosertib, through clinical development and regulatory approval.*** We are currently enrolling patients in KICKSTART, a randomized Phase 2b clinical trial evaluating tomivosertib in combination with pembrolizumab in patients with metastatic NSCLC, including patients with PD-L1 expression $\geq 50\%$ in the frontline setting. We expect to report topline data from the KICKSTART trial in the second half of 2023. If we obtain positive results from this Phase 2b clinical trial, we plan to follow this trial with subsequent Phase 3 registration trials, with the ultimate goal of securing marketing approval in order to enable treatment of cancer patients for whom current treatments are inadequate. We also plan to further expand our clinical development program with tomivosertib in additional tumor types.
- ***Develop zotatifin in patients with selected breast cancer and NSCLC tumors.*** We plan to advance our clinical trials of zotatifin in patients who we believe could most benefit from zotatifin's potential ability to downregulate multiple disease-driving proteins in the PI3K-AKT and RAS-MEK pathways and key resistance proteins. We plan to initially focus on patients with breast cancer and NSCLC, tumor types potentially having more than one oncogenic driver downregulated by zotatifin. We are currently evaluating zotatifin in combination with fulvestrant and abemaciclib in a Phase 2a open-label expansion cohort in patients with ER+ breast cancer. In light of the favorable safety results observed to date, we have also resumed dose escalation of zotatifin in combination with fulvestrant in patients with ER+ breast cancer to determine if a higher dose of zotatifin can be utilized in future clinical studies. Our goal is to progress zotatifin through registrational trials to provide a novel treatment to patients not sufficiently benefitting from existing therapies.
- ***Efficiently assess zotatifin's utility as an antiviral in the treatment of COVID-19 patients and pursue additional development as appropriate.*** We have completed a Phase 1b double-blind, randomized dose escalation trial of zotatifin in non-hospitalized patients with mild to moderate COVID-19 in approximately 36 patients evaluating three different doses of zotatifin. In this trial, zotatifin was found to be safe and well-tolerated, and demonstrated favorable trends in several assessments of viral clearance compared to placebo. While we believe the data generated from this trial warrant progression of the COVID program into later-stage development, we are focused on developing our assets in oncology and do not currently plan to pursue further development in COVID unless we secure a non-dilutive source of funding.
- ***Selectively evaluate opportunities to maximize the potential of our programs in collaboration with leading biopharmaceutical companies.*** We retain worldwide rights to tomivosertib and zotatifin and

plan to build the capabilities to effectively commercialize and market these product candidates for the treatment of cancer in North America, if approved. We plan to selectively evaluate potential opportunities on a program-by-program basis with biopharmaceutical companies whose research, development, and/or geographic capabilities complement our own with the goal to help mitigate clinical and commercial risk and/or maximize global commercial potential, including with respect to tomivosertib and zotatifin in markets outside of North America. For example, in December 2019, we entered into our research collaboration and license agreement with Pfizer for the development of our eIF4E program.

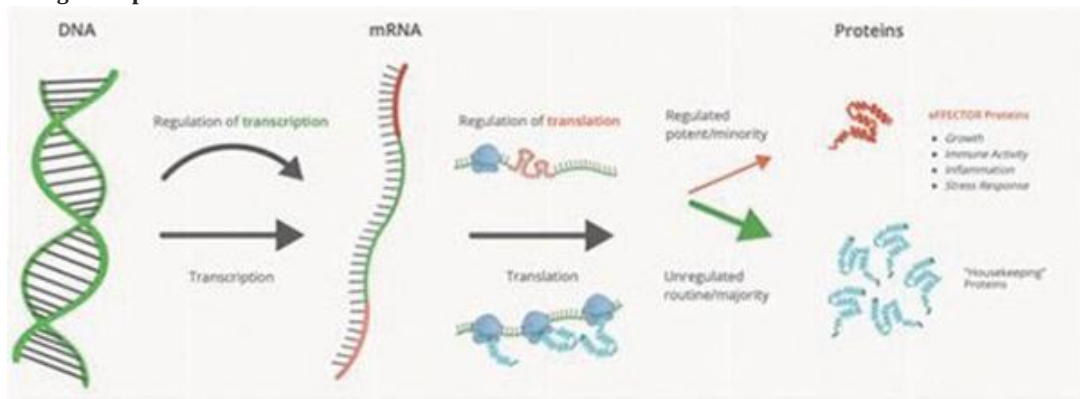
- **Maintain our corporate culture as we continue to grow our business.** We believe that our environment of scientific and intellectual integrity, combined with a focus on respect, collaboration and a commitment to patients will be essential for our continued success. We plan to continue to foster this culture as we progress our pipeline through clinical development.

Our Company Origin and Team

We founded our company in 2012 based on pioneering research in the laboratories of Drs. Davide Ruggero and Kevin Shokat, and subsequently licensed proprietary applications of translational profiling technology from UCSF. Our scientific founders and management team comprise industry veterans who have played important roles in the discovery and development of marketed small molecule drugs, monoclonal antibody therapeutics and cell therapy in oncology and other disease areas, including Adcetris, Avastin, Cabometyx, Cellcept, Cotellic, Inlyta, Tecentriq, Toradol and Viracept.

Role of Translational Regulations and the eIF4F Complex in Cancer

Figure 2: The process of gene expression.



The information embodied in the human genome directs cellular behavior through a process known as gene expression, whereby the instructions encoded in RNA are used to direct protein synthesis. Two critical steps in gene expression are transcription and translation (see figure 2 above). Transcription is the copying of DNA sequences into mRNA, whereas translation is the subsequent utilization of mRNA sequences to direct protein synthesis. Ever since a unidirectional flow of information from DNA to RNA to protein was named the central dogma of molecular biology by Francis Crick 60 more than years ago, biologists have focused on transcription as the primary point of regulation in gene expression. More recently, we and our scientific founders have demonstrated that translation serves as a critical regulatory step for overproduction of a small fraction of proteins in a cell and is amenable to drug development. Translational regulation typically controls the expression of functionally related proteins that can have profound effects on cellular physiology, including response to extracellular and intracellular signals that drive cellular growth and division and immune cell function. Disruption of the translational regulation of these effector proteins' expression can drive the initiation and advancement of many diseases.

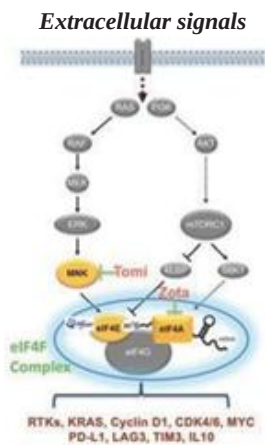
In cancer, the tightly controlled translation of certain mRNA frequently becomes dysregulated, via aberrant activation of the eIF4F complex, leading to the production of cancer-causing proteins and thus malignancy characterized by uncontrolled growth, immune evasion and metastasis. We believe our therapeutic approach can

restore the translational control of processes that tumors have hijacked for their benefit, while preserving normal cell function. Translationally regulated processes occur in tumor cells and T cells and are important for the survival and growth of tumors, including evasion of the body's immune system. By acting in tumor cells and/or T cells, our product candidates can regulate production of many proteins that drive cancer progression and thus have the potential to combine the benefits of multiple targeted therapies and/or immunotherapies in a single therapeutic agent.

We have discovered that multiple processes responsible for attenuating an immune response, including upregulating checkpoint proteins and downregulating antigen presenting proteins, are controlled through translational regulation. The ability to attenuate an immune response is important in healthy tissue in order to maintain a balanced, non-self-destructive tenor following immune activation, but can also enable tumors to escape immune detection and destruction. By reprogramming T cells and blocking the translation of factors that allow tumors to escape immune mediated destruction, we believe we can release a patient's immune system to more efficiently attack tumors.

The eIF4F complex is a central junction where two of the most frequently mutated signaling pathways in cancer, the PI3K-AKT and RAS-MEK pathways, converge and represents a central node responsible for the translation of select mRNA into proteins that are frequent culprits in key disease-driving processes (see figure 3 below). Furthermore, continuous activation of MNK and the eIF4F complex in T cells leads to exhaustion and dysfunction. Our proprietary selective translation regulation technology platform has demonstrated that certain disease states, such as cancer, result in substantial upregulation of MNK and the eIF4F complex, which collectively activate production of multiple oncoproteins that drive tumor growth and proliferation, as well as immunosuppressive proteins that cause exhaustion and dysfunction in T cells. These disease-driving proteins are controlled by key translation regulation factors, including our three targets: MNK, eIF4A and eIF4E. MNK is a kinase that plays an important role in signaling and survival and regulate genes known to reduce, or downregulate, tumor immune response. MNK is the terminal kinase that phosphorylates eIF4E, a key component of the complex responsible for translation initiation, while eIF4A is responsible for unwinding mRNA structures prior to translation. We have discovered that MNK, eIF4A and eIF4E each selectively regulate the translation of a largely unique subset of mRNA providing the opportunity to impact distinct facets of tumor biology and disease subsets with each target in our portfolio.

Figure 3: eFFECTOR's targets are located at a key node between oncogenic signaling pathways and the proteins they produce.



We see a high potential for improved therapeutic outcomes by targeting key translation regulators in the eIF4F complex to treat cancer. We believe targeting these translational regulators to treat cancer will allow our product candidates to have a broader therapeutic impact on tumors relative to programs directed at inhibiting activity of a single translated protein. By regulating the expression of sets of functionally related proteins that drive both tumor growth as well as the body's response to the tumor, our product candidates are designed to generate effects on both tumor and immune cells that we believe can address many of the limitations of current targeted or immunotherapies.

Our Development Programs

We are developing a portfolio of selective small molecule STRIs targeting the eIF4F complex that we believe have the potential to overcome some of the limitations of current targeted or immunotherapies in a number of significant cancer types for which current treatments are limited or unavailable.

Lead Product Candidate: Tomivosertib, a Potent and Highly Selective MNK Inhibitor

Tomivosertib Overview

Tomivosertib is an oral small molecule MNK inhibitor in development for the treatment of patients with solid tumors in combination with anti PD-(L)1 therapy. MNK activates the eIF4F complex and controls the production of multiple immune-suppressive factors in T cells including PD-1, PD-L1, TIM3, LAG3 and IL-10. Through inhibition of MNK, tomivosertib is designed to reprogram T cells to delay exhaustion and dysfunction, providing a greater ability to combat tumor cells. In our completed Phase 2a CPI-A clinical trial evaluating tomivosertib in combination with anti PD-(L)1 therapy, in 17 patients with NSCLC tomivosertib demonstrated the ability to substantially extend the mPFS in patients that were previously not responding to their anti PD-(L)1 therapies. In addition, as of study completion in September 2020, two of those 17 patients (12%) have confirmed PRs, one of which went on to achieve a confirmed CR, with a third showing 28% tumor regression. Tomivosertib was generally well tolerated in this clinical trial. Based on these results, in the second quarter of 2021 we initiated patient enrollment in KICKSTART, a double-blind, randomized, placebo-controlled Phase 2b trial of tomivosertib combined with pembrolizumab, in patients with metastatic NSCLC. We anticipate reporting topline data from the KICKSTART trial in the second half of 2023.

Market Opportunity

Lung cancer is the second most common cancer (excluding skin cancer) in the United States, and the leading cause of cancer death. The National Cancer Institute estimates over 237,000 new cases of lung cancer occurred in 2022. NSCLC is the most common subtype of lung cancer, accounting for 82% of all lung cancer diagnoses. Currently, approximately 75% of patients with NSCLC have tumors that lack a specific actionable mutation that is potentially conducive to approved mutation-specific targeted-therapies, but these patients may be eligible for anti PD-(L)1 as their frontline treatment for metastatic NSCLC. In 2022, the worldwide market value for anti PD-(L)1 therapies was greater than \$35 billion, of which nearly half accounted for the treatment of patients with metastatic NSCLC. While checkpoint inhibitor treatment is very effective in patients for a variety of cancers, these agents are generally not curative, and a large majority of patients ultimately progress on their checkpoint inhibitor therapy, emphasizing the need for novel frontline combination treatments that may increase the proportion of patients that experience long term durable benefit, and delay progression in other patients. There are an estimated approximately 27,000 U.S. patients with metastatic NSCLC that have PD-L1 expression $\geq 50\%$, which we estimate represents a \$4 billion market opportunity in the United States. We also believe tomivosertib can be used to treat patients with PD-L1 expression levels 1-49%, which we estimate to represent another \$5 billion dollar market opportunity in the United States.

We believe that the PD-L1 $\geq 50\%$ setting offers a substantial market opportunity in the United States and globally, and that there are many opportunities to expand the development of tomivosertib including other checkpoint responsive cancers, such as bladder cancer, renal cell carcinoma or MSI-H cancers.

Overview on Invention of Tomivosertib—A Highly Selective Inhibitor of MNK

We conducted an extensive medicinal chemistry effort incorporating structure-based drug design and identified tomivosertib as our lead product candidate. Tomivosertib has demonstrated highly potent and selective MNK inhibition, with a half-maximal inhibitory concentration (“IC₅₀”), of one to two nanomolar (one billionth of a mole per liter) against each of the MNK isoforms, MNK1 and MNK2 in enzyme assays and inhibits the kinase through a reversible, ATP-competitive mechanism of action. Treatment of tumor cell lines with tomivosertib led to a dose-dependent reduction in eIF4E phosphorylation at serine 209 (IC₅₀ = 1.4 to 21.5 nM), consistent with previous

findings that phosphorylation of this site is solely dependent upon MNK. Additionally, when tested in vitro against an enzyme panel of 414 kinases, tomivosertib was shown to be a highly selective inhibitor of MNK, with a potency against MNK approximately 100-fold greater than its potency against two of the profiled kinases, CLK4 and DRAK1, and more than 1000-fold greater than its potency against the remaining 412 kinase targets tested.

Tomivosertib is designed to inhibit MNK and thus block phosphorylation of eIF4E and activation of the eIF4F complex downstream of MAPK signaling in T cells, and to selectively regulate protein translation of select mRNAs. We performed a comprehensive and quantitative measurement of the effect of tomivosertib inhibition on the translation of expressed mRNA in multiple tumor cell lines and immune cell types. In this study, MNK was shown to play an important role in regulating anti-tumor immune response by controlling the expression of key known immune checkpoint proteins and cytokines that create an immunosuppressive tumor microenvironment, which together limit immune cell function.

We also tested tomivosertib in multiple in vivo tumor models, including syngeneic mouse models and genetically engineered mouse models of cancer conducted in immunocompetent mice, as well as multiple xenograft models comprising human tumor cells implanted in mice whose immune systems have been compromised in order to permit growth of human cells. Through this battery of in vivo preclinical tests, we have demonstrated that tomivosertib treatment as a single agent triggered a broad anti-tumor immune response in immunocompetent mouse models, including induction of anti-tumor immunity that persisted after tomivosertib dosing is stopped.

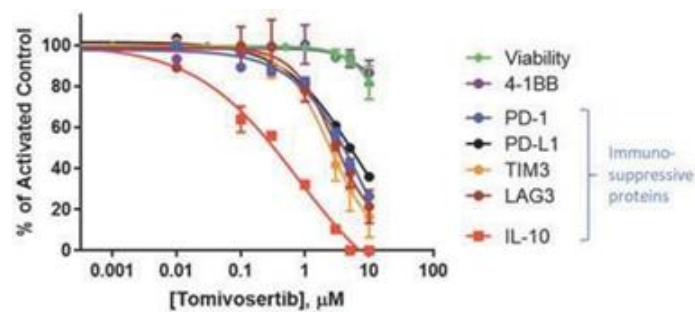
Tomivosertib Mechanism of Action: Stimulating the Immune System to Enhance Tumor Killing

Our preclinical and clinical data collected to date suggest combining tomivosertib with an anti PD-(L)1 inhibitor can overcome mechanisms of resistance to checkpoint inhibitors, resulting in enhanced sensitivity to checkpoint inhibitors. Our preclinical studies have shown that suppressing MNK broadly enhanced T cell effector response both in vivo and in vitro. Through its mechanism designed to reprogram T cells by blocking a pivotal intracellular signaling pathway, tomivosertib has been shown to:

- enhance tumor cell killing;
- downregulate several key checkpoint inhibitory proteins, including PD-1, PD-L1, TIM3 and LAG3;
- decrease production of immunosuppressive IL-10, while maintaining immune-stimulatory interferon gamma; and
- increase T cell central memory pool.

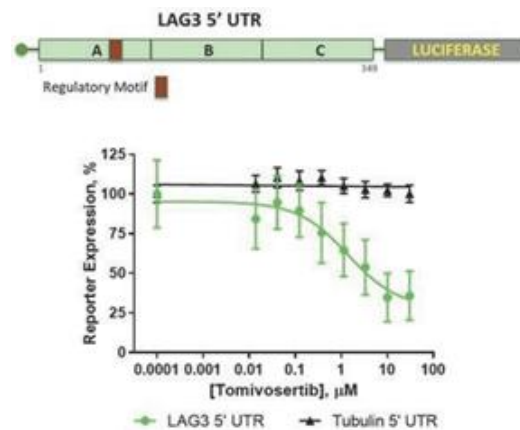
In preclinical studies, tomivosertib at clinically relevant concentrations has been shown to downregulate multiple immunosuppressive proteins simultaneously, including PD-1, PD-L1, TIM3, LAG3 and IL-10, as shown in figure 4 below. Specifically, incubating increasing concentration of tomivosertib with activated primary human T cells showed dose-dependent suppression of multiple checkpoints associated with T cell exhaustion, reaching statistical significance ($p < 0.05$) in the 0.1 to 1.0 μM range, coupled with maintenance of T cell viability and activation marker 4-1BB, an immune-stimulatory protein. Collectively, these experiments suggest that tomivosertib selectively reprogrammed T cells resulting in robust effector target killing activity by suppressing exhaustion/ dysfunction properties.

Figure 4: Tomivosertib downregulates multiple checkpoint proteins and immunosuppressive IL-10.



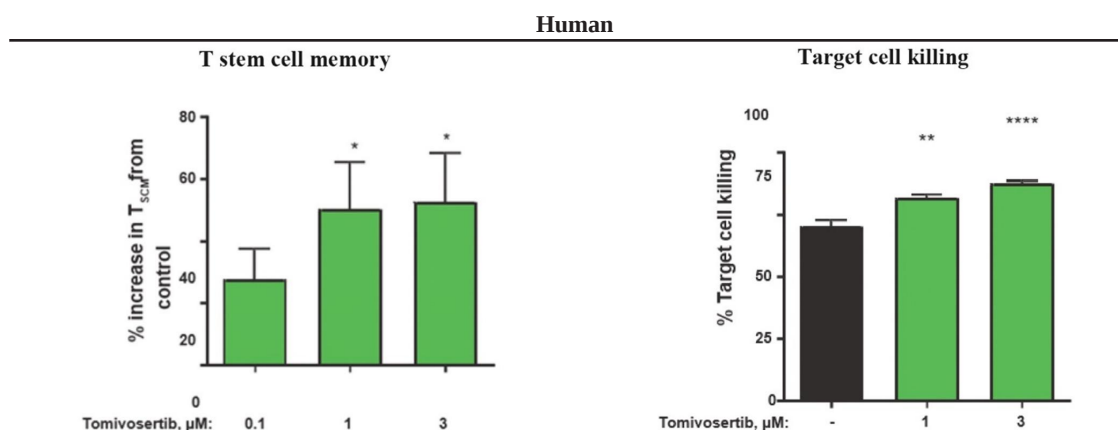
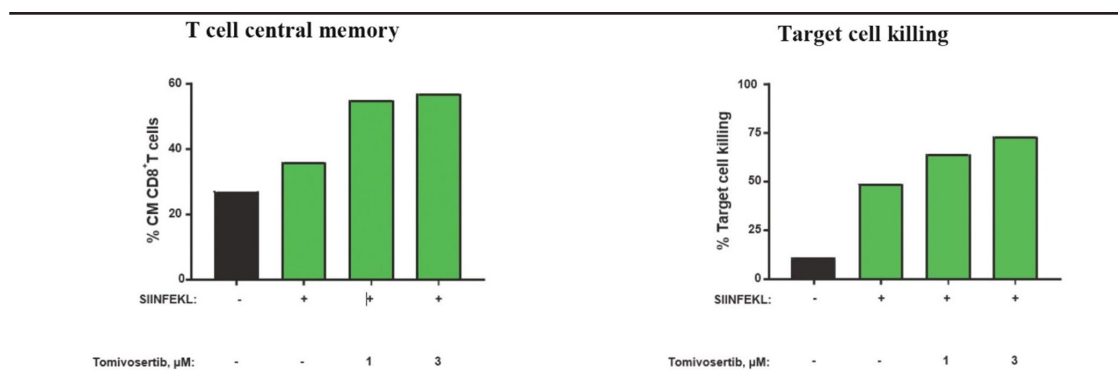
To explore the molecular mechanism of downregulation, we conducted a study placing sequences of the LAG3 5' UTR in a luciferase reporter assay and assessing for luciferase expression in T cells in the presence of increasing tomivosertib, which showed luciferase protein levels decrease as a function of tomivosertib concentration, reaching statistical significance ($p < 0.05$) in the 10 μM and above range (see figure 5 below). Similar results were obtained using the 5'-UTR of PD-L1. When the 5'-UTR of tubulin, a control protein not involved in immunosuppression, was used to drive luciferase expression, tomivosertib had no effect.

Figure 5: Tomivosertib downregulates production of protein from luciferase, a reporter gene, placed downstream of the LAG3 5' UTR.



To understand the impact of tomivosertib on T cell function, we utilized populations of mouse or human T cells engineered to recognize SIINFEKL, a peptide derived from ovalbumin, or the human protein CD19, respectively, as shown in figure 6 below. In mouse, stimulation of splenocytes comprised of the engineered T cells in the presence of increasing concentration of tomivosertib resulted in increased T cell central memory, as defined by cells with high expression of two markers CD44 and CD62L, and increased killing of target cells bearing the ovalbumin peptide. Likewise, stimulation of human engineered T cells targeting CD19 in the presence of increasing concentration of tomivosertib resulted in an increased pool of stem cell memory T cells, as defined by human surface markers CD45RA+CD27+ and increased killing of target cells expressing CD19.

Figure 6: Tomivosertib increases central memory and stem cell memory T cell pools and enhances target cell killing.



* $p < 0.05$; ** $p < 0.01$; **** $p < 0.001$

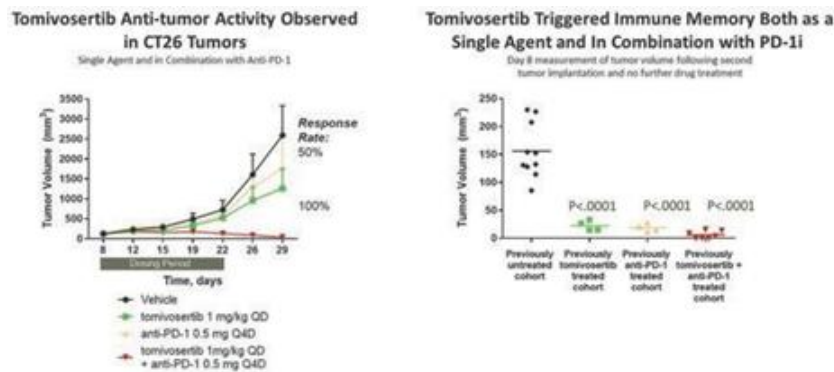
Thus, treatment with tomivosertib has been shown to suppress production of multiple proteins and factors that lead to T cell exhaustion and dysfunction, increase the pool of memory T cells, and increase the killing of target cells by T cells.

Tomivosertib Has Been Shown to Trigger Immune Memory as a Single Agent and Enhanced antiPD-1 Activity in Preclinical Models

To demonstrate that the immune-enhancing properties of tomivosertib can lead to anti-tumor activity, we conducted a preclinical study in mice with intact immune systems and implanted them with syngeneic tumor CT26. These tumor-bearing mice were subsequently dosed with either tomivosertib, a mouse version of antiPD-1 antibody, or the combination of the two drugs (see figure 7 below). All dosing was conducted for 2 weeks. These experiments showed administration of either single agent tomivosertib or antiPD-1 therapy resulted in tumor reduction in about 50% relative to control untreated mice, whereas the combination of both resulted in full regression of the tumor in all mice treated. To demonstrate the role of immune memory, mice in each cohort that showed tumor regression were re-challenged with additional CT-26 tumor cells injected in the contralateral flank and in the absence of any further drug treatment. The results showed these mice, including those pretreated with single agent tomivosertib, and the combination of tomivosertib plus anti PD-L1, were able to reject subsequent tumor challenge, indicating enhancement of immune memory which was able to prevent growth of the newly implanted tumors. Further pharmacodynamic biomarkers in the CT26 models showed that tomivosertib treatment also resulted in enhanced intratumor ratio of effector CD8⁺, cytotoxic T cells, to FOXP3⁺, immunosuppressive regulatory T cells, and resulted in lowering immunosuppressive M2 macrophages within the tumor. Collectively, these data demonstrate that tomivosertib potentiated the immune system and resulted in durable inhibition of tumor growth. A recent

publication by independent investigators at McGill University also showed that blocking MNK resulted in robust immune activation and tumor regressions across several mice models of melanoma (JCI, 2021) by further activating T cells and other immune cells.

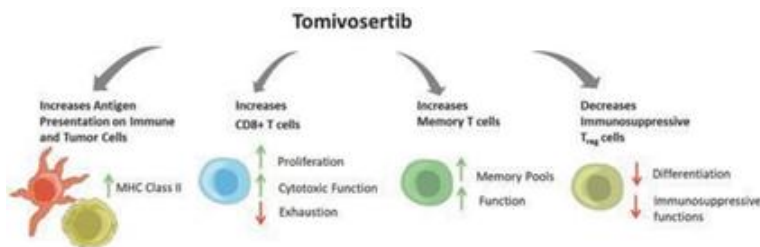
Figure 7: Preclinical studies show that tomivosertib plus an anti-PD-1 inhibitor resulted in regressions in all animals and persisting immune memory upon a tumor rechallenge even as a single agent.



Tomivosertib Acts on Multiple Cell Types That Drive Immune Response

Our data as well as recent data from McGill University suggest that blocking MNK on multiple immune cell types broadly engages the immune system to kill cancer cells (see figure 8 below). These mechanisms that drive immune activity include: (1) downregulating multiple checkpoint proteins and immunosuppressive cytokines on T cells; (2) increasing antigen presentation on dendritic cells; (3) increasing cytotoxic function of CD8+T cells and blocking T cell exhaustion/dysfunction; and (4) expanding T cell memory pools. Collectively, these effects may complement checkpoint inhibitors by increasing tumor recognition, restoring immune response, improving durability of response and preserving immune persistence.

Figure 8: Tomivosertib designed to act on multiple cell types that drive immune response.



Based on these findings, we believe tomivosertib has the potential to improve current immunological treatments for cancer by extending the benefit that patients experience with checkpoint inhibitors and restoring benefit to patients who have stopped responding to checkpoint inhibitors.

Phase 1 Dose Escalation Trial in Cancer Patients and Food Effect Study in Healthy Volunteers

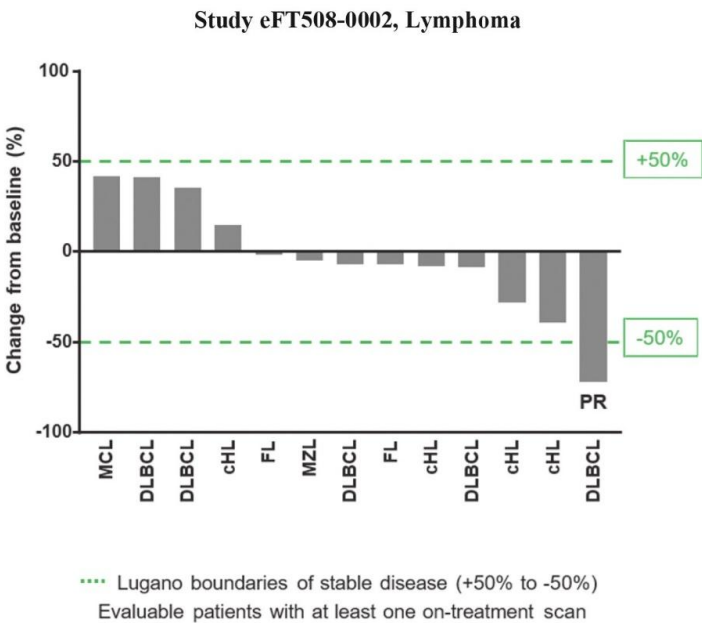
We conducted two independent Phase 1 dose escalation clinical trials in solid tumors and lymphoma, respectively, to assess the safety, pharmacokinetics, pharmacodynamics and tumor control of tomivosertib. The primary endpoint of each trial was to establish MTD and determine a recommended Phase 2 dose (“RP2D”).

In our solid tumor Phase 1 dose escalation trial, we enrolled patients with any metastatic solid tumor who had progressed on standard of care therapies. From this trial we established the RP2D as 200 mg twice daily (“BID”), in

a capsule formulation taken while fasted, and we subsequently conducted our Phase 2a CPI-A study using this dosing regimen. We also found that tomivosertib monotherapy treatment was generally well-tolerated in this patient population. The most frequent treatment-emergent AEs were nausea, vomiting, fatigue, constipation, dyspepsia and tremor. At doses that exceeded the RP2D, there was a higher incidence and severity of these AEs. The overall pharmacokinetic exposure showed increase as a function of dose with a half-life of approximately 12 hours, supporting a BID regimen.

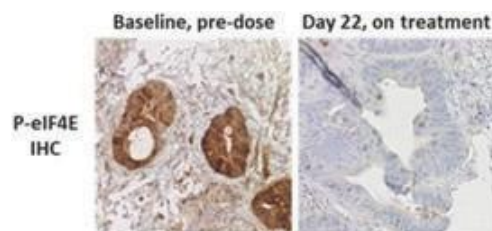
In our lymphoma Phase 1 dose escalation trial, we enrolled patients with B cell malignancies, predominantly patients with lymphoma, who had progressed on standard of care therapies. This trial initially tested safety in two dose levels, 300 mg or 450 mg once daily (“QD”) and 200 mg BID or 300 mg BID, followed by limited expansion at the RP2D, 200 mg BID capsule. In this study, we established the MTD as 200 mg BID capsules taken fasted. The most common AEs experienced by patients in the RP2D expansion cohort were nausea, vomiting, hypercalcemia, and fatigue. One patient who received the capsule formulation at 200 mg BID achieved a confirmed PR, or a confirmed decrease in tumor size by at least 50%, per the Lugano criteria for lymphoma, determined from a scan after treatment as compared to the immediately prior scan (see figure 9 below). This patient had previously experienced a radiographic progression on R-CHOP (chemotherapy combination regimen of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) and autologous stem cell transplant. Eight patients experienced stable disease, meaning their tumor assessments remained within the established boundaries for lymphoma of +/- 50% from baseline with no appearance of new lesions, with several of those patients demonstrating initial decreased tumor volume. Of 19 patients enrolled, 13 were radiographically evaluable with at least one on-treatment scan. Their overall best response is shown in Figure 9 below.

Figure 9: Phase 1 dose escalation trial included multiple patients with tumor regressions.



In addition, the pharmacodynamics in both peripheral blood mononuclear cells as well as in pre- and on-treatment tumor biopsies showed that phospho-eIF4E, a marker of MNK inhibition, was effectively inhibited at the RP2D. At the RP2D, we observed 90 to 100% inhibition of the MNK target as measured by phospho-eIF4E immunohistochemistry (“IHC”) from pre- and on-treatment biopsies samples (see figure 10 below).

Figure 10: Marker of MNK activation is down regulated in tumors as shown from a patient's biopsy samples



We also completed two healthy volunteer food effect studies in healthy volunteers in order to evaluate the pharmacokinetic distribution of tomivosertib under either fasted or fed conditions. These were single-dose crossover studies evaluating drug exposure in the same patients at either of two different doses of tomivosertib, 100 mg or 200 mg, each taken with or without food. The results of these studies determined that food increased blood exposure concentration of tomivosertib by approximately two-fold, demonstrating that exposure of tomivosertib at 100 mg taken with food is comparable to 200 mg taken without food. To facilitate patient convenience moving forward, the RP2D for tomivosertib will be 100 mg BID taken with food starting within our Phase 2b KICKSTART trial.

Phase 2a Trial of Tomivosertib in Combination with Checkpoint Inhibitors

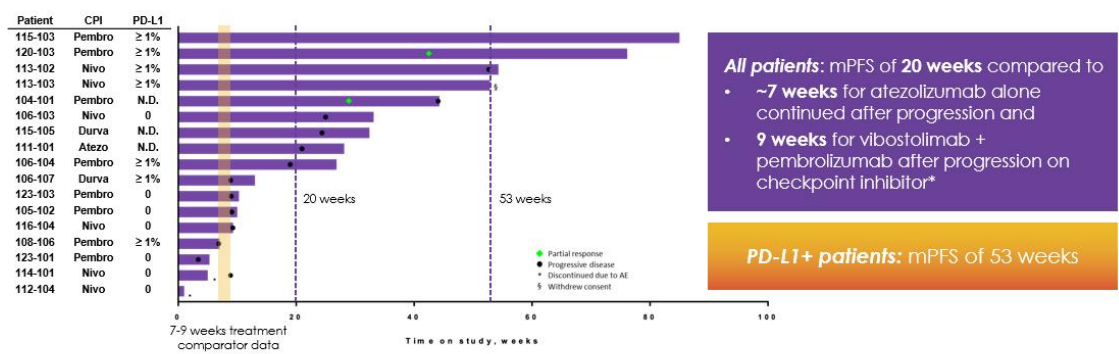
We conducted a Phase 2a CPI-A trial which evaluated tomivosertib in subjects who had initiated anti PD- (L)1 monotherapy and were not responding, that is had either developed progressive disease (“PD”), per RECIST criteria on their therapy, or a greater than 20% increase in target tumor size, or had undergone ≥ 12 weeks of anti PD-(L)1 therapy with no evidence of a PR or CR. We enrolled a total of 39 patients in this trial with diverse tumor types and any prior anti PD-(L)1 therapy approved by the FDA for the indication it was prescribed. Among these, 17 patients had a primary cancer type of NSCLC with advancing metastatic disease, on their anti PD-(L)1 therapy, including 16 of 17 who met the RECIST criteria for PD, prior to the addition of tomivosertib. Per our protocol, subjects continued their anti PD-(L)1 therapy according to their package insert, without a break in treatment schedule, and then initiated tomivosertib at 200 mg BID taken fasted 7 days prior to their next scheduled anti PD-(L)1 therapy. The primary objectives of this trial were to evaluate safety and antitumor activity, as measured by PFS and ORR. Overall, treatment with tomivosertib in combination with anti PD-(L)1 therapy was generally well tolerated. The AEs that occurred were generally consistent with the AE profiles of tomivosertib and anti PD-(L)1 therapy each as monotherapies. The most common AEs were nausea, fatigue, tremor, vomiting, and increased aspartate aminotransferase and alanine aminotransferase, which are two metabolic enzymes whose levels in blood are tracked as a measure of liver function. These AEs were generally grade 1 or 2 in severity.

In the Phase 2a study, 87% (34 of 39) of subjects experienced an adverse event potentially related to tomivosertib. The most common adverse events occurring in $>20\%$ of subjects and related to tomivosertib included: nausea, experienced by 16 (41.0%) subjects; tremor experienced by 15 (38.5%) subjects; fatigue experienced by 11 (28.2%) subjects, and vomiting experienced by 9 (23.1%) subjects. In the Phase 2a study, 28% of study subjects experienced a Grade 3 adverse event potentially related to tomivosertib. No specific Grade >3 adverse events potentially related to tomivosertib were experienced. The following Grade 3 adverse events potentially related to tomivosertib were experienced by two patients: alanine aminotransferase increase, blood creatinine phosphokinase (a metabolic enzyme whose levels in blood are assessed as a potential indicator of drug effects on muscle tissue) increase, and rash.

Of the total 39 patients enrolled, three (7.7%) patients had confirmed PRs, or decreases in tumor assessments of greater than or equal to 30% per RECIST 1.1 criteria. Of the patients with confirmed PRs, two had NSCLC and one had renal cell carcinoma. In addition, there was only one patient enrolled with gastric cancer and that patient had a 66% reduction of their target lesion upon addition of tomivosertib. One of five patients (20%) who enrolled with renal cell carcinoma had a confirmed PR. In the 17 patients with NSCLC, tomivosertib substantially extended the mPFS in patients that were previously progressing on their anti PD-(L)1 therapies. In addition, as of study completion in September 2020, two of those 17 NSCLC patients (12%) had confirmed PRs, one of which went on to achieve a confirmed CR after study completion, with a third showing 28% tumor regression. The patients with NSCLC generally had multiple treatments prior to coming on to study, with a median of two prior therapies, and 16

of the 17 (94%) NSCLC patients had RECIST progression on PD-(L)1 immediately prior to the addition of tomivosertib, and the other patient had a 13% increase in tumor size that was not classified as a RECIST progression. The mPFS in the 17 NSCLC patients was 20 weeks (see figure 11 below). Further, the mPFS in patients known to have PD-L1 expression level greater than 1% ("PD-L1>1%"), suggestive of an immune-responsive tumor, was 53 weeks. From our database, patients were either characterized as PD-L1=0, PD-L1>1% or PD-L1 unknown. As a comparison, in the Phase 3 OAK trial, which led to the FDA approval of atezolizumab, an inhibitor of PD-L1, in second line plus treatment of NSCLC patients, the average benefit of patients (n =168) treated beyond initial RECIST progression with continued treatment with atezolizumab was approximately 7 weeks. Thus, the benefit observed after the addition of tomivosertib in patients with NSCLC was nearly three-times greater relative to a historical comparator. Additionally, when vibostolimab, an agent directed against TIGIT, another immunosuppressive checkpoint protein, was added to pembrolizumab in patients who had progressed on pembrolizumab, a mPFS of 9 weeks was observed. However, because tomivosertib was not studied in head-to-head clinical trials with these agents, such data may not be directly comparable due to differences in study protocols, conditions and patient populations.

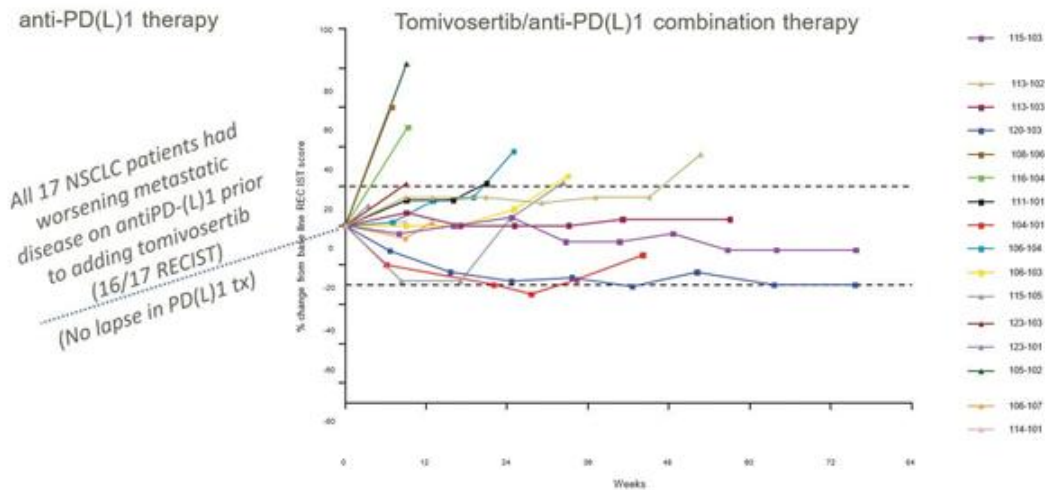
Figure 11. Swimmers plot showing length of time on tomivosertib plus anti PD-(L)1 combination therapy in NSCLC.



*FOR ILLUSTRATIVE PURPOSES ONLY: Data for atezolizumab from Treatment Beyond Progression (TBP) cohort in OAK trial. Data for vibostolimab+pembrolizumab from trial NCT02964013. Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across trials.

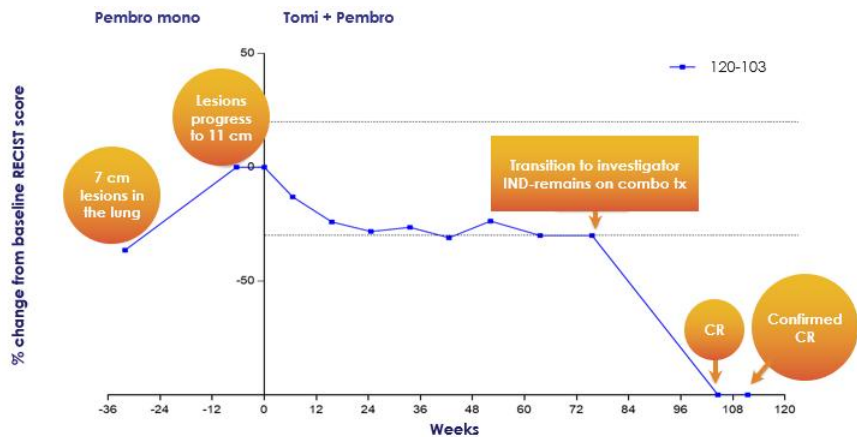
An important aspect of tomivosertib's activity in the P2a trial is its demonstrated ability to change the trajectory of tumor growth in patients that were already progressing on their anti PD-(L)1 therapy prior to the addition of tomivosertib. As shown in figure 12 below, most patients either stabilized or had their target tumor lesions regress upon the addition of tomivosertib, and 9 of the 17 (53%) patients experienced an extension of their PFS for at least 6 months which is generally believed to be clinically meaningful.

Figure 12: Spider plot showing trajectory of target tumor lesions after tomivosertib added to anti-PD(L)1 monotherapy.



As diagrammed in figure 13 below, one of our patients with NSCLC experienced a confirmed PR through approximately 80 weeks on our P2a trial before the trial was closed. This patient continued treatment with the combination of tomivosertib and pembrolizumab under an investigator sponsored compassionate use protocol after our trial ended, and subsequently experienced a confirmed CR, meaning a complete response confirmed on two scans, after a total of approximately 24 months on the combination therapy. This patient was PD-L1>50%.

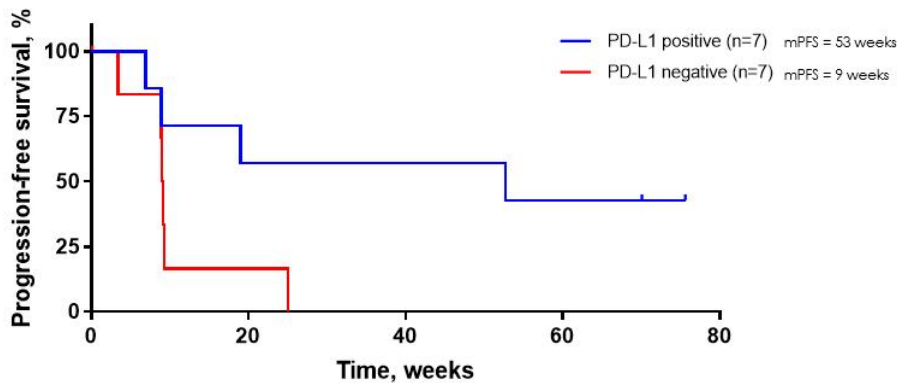
Figure 13: Tumor trajectory of patient who experienced a confirmed complete response with the combination of tomivosertib and pembrolizumab after two years on the combination therapy.



In our Phase 2a trial, patients known to have tumors that express biomarker PD-L1 showed a preferential treatment response relative to those patients known to have tumors that exhibited no PD-L1 expression. To assess the impact of PD-L1 status, a known marker for sensitivity to anti PD-(L)1 therapy in NSCLC, on the benefit of adding tomivosertib, we conducted a post hoc Kaplan Meier (KM) analysis of PFS in patients positive for PD-L1 compared to patients negative for this marker. PD-L1 status was available for 14 of the 17 patients. The KM analysis showed that PD-L1-positive patients had a three times lower hazard ratio, or risk of progressing, after addition of

tomivosertib compared to PD-L1-negative patients (see figure 14 below). We believe this correlation is consistent with tomivosertib’s mechanism of reversing T cell exhaustion and re-invigorating the immune system, and we are excluding PD-L1 negative patients from our Phase 2b KICKSTART trial. In contrast to the impact of PD-L1 status on tomivosertib treatment, in the treatment beyond progression cohort of the OAK study of atezolizumab monotherapy, PD-L1 status was not correlated with response, suggesting that exclusion of PD-L1 negative patients may differentially enhance response in the tomivosertib plus pembrolizumab arm compared to the placebo plus pembrolizumab arm in our Phase 2b KICKSTART trial.

Figure 14: Kaplan Meier curves showing the difference between PD-L1 positive and PD-L1 negative patients in our P2a trial.



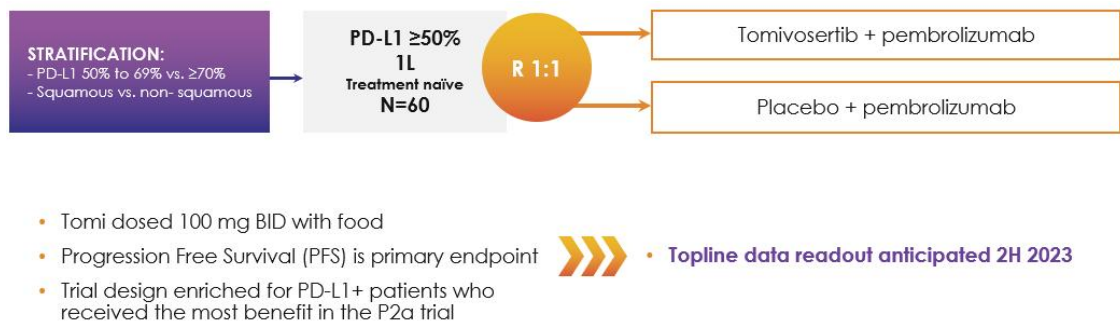
KICKSTART—A Randomized Phase 2b Trial Evaluating PD-L1≥50%

We are currently enrolling patients with metastatic NSCLC in KICKSTART, a randomized, double-blind, placebo-controlled Phase 2b clinical trial, as illustrated in figure 15 below. We are conducting this trial to evaluate the efficacy and safety of the addition of tomivosertib to frontline pembrolizumab treatment in NSCLC patients with PD-L1≥50%. In the KICKSTART trial, patients without prior treatment for metastatic NSCLC, including no prior anti PD-(L)1 treatment, will be randomized 1:1 to receive tomivosertib plus pembrolizumab or placebo plus pembrolizumab. Previously, we were also enrolling into a front-line extension cohort, treating patients who had progressed on pembrolizumab monotherapy as well as a maintenance cohort, treating patients with PD-L1>1% who initiated frontline therapy with pembrolizumab combined with platinum-based chemotherapy doublet, immediately after completing the platinum-based phase (4-6 cycles) of their frontline treatment without disease progression. We discontinued enrollment into the front-line extension cohort in part based on our belief that frontline treatment with a single immunotherapy agent such as pembrolizumab will diminish in the future, coupled with the fact that enrollment into this cohort was slower than anticipated. Enrollment was slower than anticipated, in part due to physician reluctance to expose patients after initial progression to a control group with continued treatment with pembrolizumab monotherapy, and in part due to the impact of COVID-19 on clinical site operations. In addition, we discontinued enrollment into the maintenance cohort due to slower than anticipated enrollment resulting from staffing issues across clinical sites, competition from other trials and patient reluctance to enroll in a clinical trial immediately after completing chemotherapy.

Enrollment challenges have persisted in the PD-L1≥50% cohort, and we recently updated our anticipated topline data readout to the second half of 2023. We believe that factors contributing to slower enrollment include the impact of COVID-19 on site operations and a greater than anticipated use of chemotherapy in combination with pembrolizumab as frontline therapy, especially at certain sites that may not always assess PD-L1 status prior to initiating therapy. We have taken several steps to mitigate these factors, including increasing our recruiting and patient identification activities, optimizing the number of sites and continuing emphasis on the importance of PD-L1 testing to select optimal frontline therapy, especially for patients with PD-L1 ≥50% who may be spared the challenges of chemotherapy. We believe these efforts, combined with our patient and physician outreach activities, will enhance enrollment.

We plan to enroll approximately 60 patients in the KICKSTART trial and the primary endpoint is PFS. In addition, OS and ORR will be assessed as secondary endpoints. If we obtain positive results from this Phase 2b clinical trial, we plan to follow this trial with subsequent Phase 3 registration trials.

Figure 15: Schematic of ongoing KICKSTART P2b trial in NSCLC frontline treatment indication.



SU2C Breast Cancer Trial

Tomivosertib has also been tested in a single-arm Phase 2a clinical trial in patients with metastatic breast cancer in combination with chemotherapy in a study led by Dr. Nahum Sonenberg of McGill University. We supplied tomivosertib capsules for this trial and all other costs were fully funded through a grant from Stand Up to Cancer (SU2C) Canada. The group initially planned to enroll up to 40 patients with metastatic breast cancer for whom approved and available therapies were not effective in controlling the cancer. Tomivosertib was administered in combination with paclitaxel or nab-paclitaxel. The primary objectives of this trial were to assess safety and tolerability of tomivosertib as monotherapy and in combination with paclitaxel, and to assess pharmacodynamic effects as an indication of biological activity of tomivosertib treatment. The group elected to enroll only 19 patients, which the investigators believe will be sufficient to report positive pharmacodynamic data.

Additional Exploratory Tomivosertib Trials in Solid Tumors

Tomivosertib was evaluated in several additional Phase 2a trials prior to our CPI-A and KICKSTART trials. In 2019, we completed a combination trial with avelumab, an inhibitor of PD-L1, in patients with microsatellite stable colorectal cancer (“MSS CRC”), through a clinical trial collaboration and supply agreement with Pfizer and Merck KGaA. MSS CRC is generally not responsive to immunologic agents. We enrolled 55 patients in this trial including an initial 10 patients in the dose escalation portion of tomivosertib combined with the standard of care dose of avelumab, 15 patients who initially received tomivosertib as monotherapy and were allowed an option to crossover to a combination of tomivosertib and avelumab, and 30 patients who received the combination of tomivosertib and avelumab. Tomivosertib was generally well tolerated in combination with avelumab at 200 mg BID, taken fasted, as the RP2D. We observed one confirmed PR and 25% of the patients remained on study for >12 weeks in this typically immune-refractory patient population. However, based on tomivosertib’s mechanism of action, we elected to focus future development of tomivosertib on more immune-responsive cancers. Prior to this trial, we enrolled 16 patients in a monotherapy trial treating castration resistant prostate cancer (“CRPC”). We observed no PRs or CRs in this CRPC trial and seven of the 16 (44%) patients experienced SD. We stopped this trial due to limited activity and to focus on further development in combination with checkpoint inhibitors.

Zotatifin—A Potent and Selective eIF4A mRNA Helicase Inhibitor

Zotatifin Overview

Our second product candidate in clinical development, zotatifin, is a small molecule inhibitor of eIF4A, a subunit of the eIF4F complex that regulates translation of cell proliferation proteins which can be oncogenic drivers

in cancer. eIF4A is a helicase responsible for unwinding complex mRNA secondary structures found in the 5' UTR of select mRNA, allowing efficient ribosome binding and subsequent translation of mRNA into important proteins. Zotatfin is designed to downregulate multiple oncoproteins, several of which are up-regulated as part of well-characterized feed-back pathways causing resistance to specific targeted therapies. Our preclinical experiments show zotatfin has the potential to both work as a single agent or in combination with several targeted therapies to prevent resistance, including in important indications such as several breast cancer tumor types and KRAS mutant NSCLC. We are currently evaluating zotatfin in a Phase 1/2 clinical trial in patients with solid tumors. We are currently evaluating patients in multiple open-label expansion cohorts in biomarker-positive patients with tumors driven by multiple proteins shown in our preclinical studies to be downregulated by zotatfin. To date, we've reported initial data from four cohorts including patients with ER+ breast cancer, which demonstrated that zotatfin appeared to be safe, well tolerated and showed signals of activity, including partial responses in heavily pretreated ER+ breast cancer patients. We anticipate reporting additional data from one of the ER+ breast cancer cohorts which was expanded from seven to 18 patients in the first half of 2023. In addition, based on the safety results and target engagement data generated to date, we've resumed dose escalation. Data from the dose escalation portion of the trial is anticipated in the second half of 2023.

Market Opportunity

The National Cancer Institute estimates that in the United States over 287,000 new cases of invasive breast cancer and over 237,000 new cases of lung cancer occurred in 2022. ER+ breast cancer represents approximately 60% or more of all breast cancers and NSCLC is the most common subtype of lung cancer, accounting for 82% of all lung cancer diagnoses. KRAS mutant lung cancer is estimated to represent about 25% of NSCLC. In metastatic ER+ breast cancer, patients are currently typically treated with inhibitors of estrogen receptor ("ER") and CDK4/6, but most patients eventually progress. Thus, there is a need for improved therapies. In KRAS mutant lung cancer, targeting KRAS G12C mutation subtype with selective inhibitor, two agents have received approval by the FDA, however, resistance is emerging and this agent is not effective against other KRAS mutation subtypes such as G12A, G12D or G12V.

We are currently focusing development of zotatfin in ER+ metastatic breast cancer. Based on our preclinical studies, we believe that a combination of zotatfin with an ER inhibitor, such as fulvestrant, may be able to treat patients with ER+ breast cancer, representing about 42,000 patients annually in the U.S. Fulvestrant is generic and marketed by several companies including AstraZeneca who markets it under the brand name Faslodex for the treatment of breast cancer. Furthermore, we believe a triple combination of zotatfin with fulvestrant and a CDK4/6 inhibitor may provide even greater activity. Currently marketed CDK4/6 inhibitors include abemaciclib (Verzenio), palbociclib (Ibrance) and ribociclib (KISQALI). We also believe that zotatfin could be active in other subsets of breast cancer, including FGFR+ and HER2+ subgroups. FGFR2 and HER2 are RTKs, important proteins driving cancer. Inhibitors of multiple RTKs are available on the market today such as inhibitors of HER2, EGFR and FGFR. However, challenges remain with emergent resistance to individual RTK inhibitors through either mutation or upregulated production of RTKs and/or downstream effector proteins. Based on preclinical data, zotatfin has single agent activity against certain ER+ breast cancers that also have mutations in either HER2 or FGFR, which we estimate combined total approximately 17,000 patients.

In NSCLC, we plan to develop zotatfin KRAS mutant NSCLC as either a single agent or in combination with targeted agents such as those inhibiting KRAS G12C. KRAS activating mutations occur in approximately 25% of patients with NSCLC and there are limited drugs available to treat these patients. There are multiple activating mutation subtypes of KRAS, including G12A, G12C, G12D and G12V, and we estimate there are 28,000 KRAS mutant NSCLC patients in the U.S.

Overview of Invention of Zotatfin—Persistent Chemistry Effort Incorporating a Natural Product as a Design Element

The discovery process that led to the identification of zotatfin as a clinical candidate began with a core pharmacophore found in silvestrol and rocaglamide A ("Roc A"), two natural products that have shown interesting biological activities but lack certain drug-like properties. We undertook a sophisticated and comprehensive computational analysis of available information, including a crystal structure of Roc A bound to eIF4A and RNA. Additionally, we used mutational analysis to identify critical amino acids in eIF4A required for binding, and structure-activity relationships amongst our early program compounds, to identify a preferred orientation of certain

substituents on the core pharmacophore. These insights enabled an efficient process whereby we limited synthesis and testing to compounds with a high chance of retaining strong affinity for eIF4A. This allowed us to focus our resources on a persistent discovery plan conferring drug-like properties to mature program compounds.

Zotatifin Mechanism of Action: Downregulating Multiple Disease-Driving Proteins in One Pill

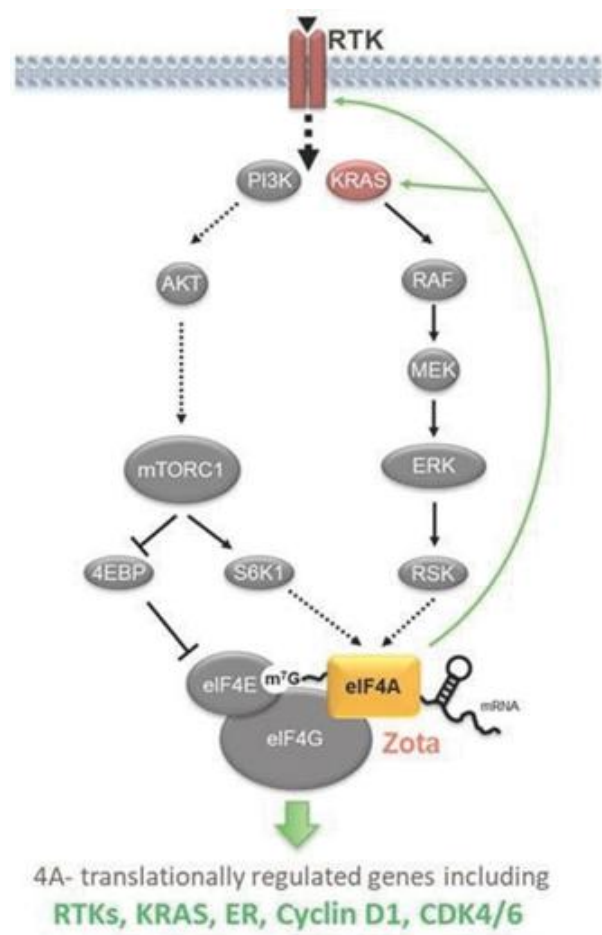
eIF4A is a catalytic subunit of the eIF4F complex that regulates translation of cell proliferation proteins which can be oncogenic drivers in cancer. eIF4A is a helicase and is responsible for unwinding complex secondary structures found in the 5' UTR of select mRNA. This unwinding is a regulatory control step that leads to efficient production of important proteins that enable normal cells to respond to growth signals, and which are upregulated in tumor cells.

As shown in figure 16 below, eIF4A is located at a central node at the intersection where two important cell growth and proliferation pathways, the PI3K-AKT and RAS-MEK pathways, converge to activate the translation of select messenger mRNA into proteins that are frequent culprits in key disease-driving processes. eIF4A regulates production of multiple growth-dependent proteins involved in cell growth, proliferation and survival. Many of these proteins are oncogenic drivers and often upregulated in cancer. Proteins in tumor cells that are controlled by eIF4A include:

- (1) multiple oncoproteins for which targeted therapies such as ER, HER2, FGFR and KRAS G12C are approved by the FDA;
- (2) oncoproteins for which there are currently no targeted therapies available, such as MYC and Cyclin D1; and
- (3) certain proteins that are often upregulated in response to targeted therapies as a resistance mechanism, such as Cyclin D1, CDK4/6, RTKs and KRAS.

Several of these oncoproteins can function in concert within a vertical signaling pathway to drive tumor growth, proliferation and survival in cancer, including certain breast cancers and NSCLC. Simultaneously inhibiting more than one oncoprotein in a vertical signaling pathway and/or set of cooperating pathways has become recognized as a generalizable way to approach cancer therapy. Because zotatifin simultaneously regulates multiple oncoproteins in the same vertical signaling pathways, as well as set of cooperating pathways, this may potentially lead to single agent activity. In addition, by combining with another targeted therapy acting within the same pathway, zotatifin has the potential to augment inhibition of multiple oncogenic drivers to deepen or broaden the response to zotatifin and complementary agents. Resistance to these targeted therapies can occur via upregulation of both the protein which is being targeted as well as other pathway proteins also regulated by eIF4A.

Figure 16: eIF4A is a key node that is activated by multiple RTKs and KRAS and controls production of many cancer driving proteins.



As illustrated in figure 17 below, we discovered that most proteins inhibited by zotatifin have common distinct translation initiation regulatory elements in the 5' UTR of the mRNA that are recognized by zotatifin. These common regulatory elements are found in the mRNA of multiple key oncoproteins that drive cancer. In addition, many of these proteins are over-expressed in response to targeted therapies, leading to drug resistance. Importantly, our preclinical data showed that zotatifin inhibition in physiologic concentrations in vitro only impacted translation of approximately 5% of mRNAs in a cell, indicating that global protein synthesis is unaffected at these concentrations. Further, because these translation initiation regulatory elements are located in the mRNA prior to and independent from the coding sequences that dictate the amino acids included in protein synthesis, their inhibition is independent of protein mutation variants. For example, in preclinical studies, zotatifin inhibited production of KRAS across multiple activating mutation subtypes such as G12C, G12V and G12D due to their common translation initiation regulatory elements.

Figure 17: Zotatfin is selective for proteins that drive tumor growth and resistance.

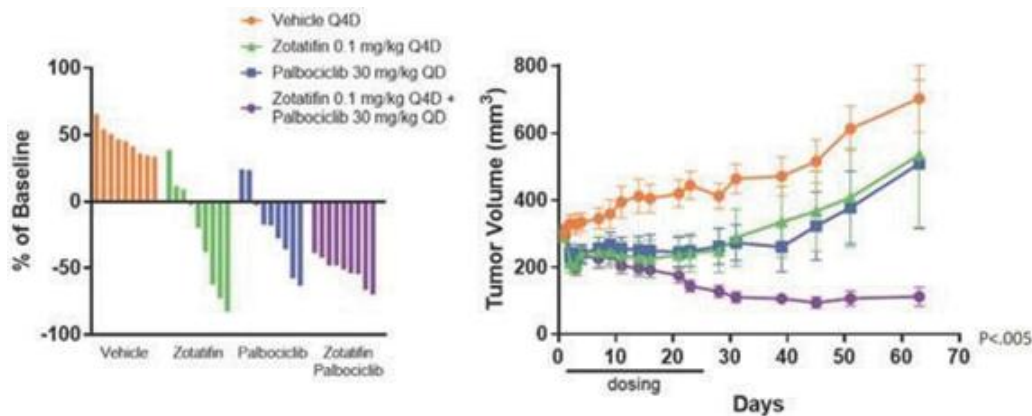


Preclinical Studies with Zotatfin

Preclinical experiments showed that zotatifin was most active in models with either two or more select oncogenic drivers that are directly downregulated by zotatifin. In addition, preclinical models have also demonstrated zotatifin’s tumor growth inhibition activity in combination with drugs that target specific protein in the same vertical pathways, such as inhibitors of HER2, FGFR, AKT or PI3K, or in combination with drugs against targets that are activated by these pathways such as ER and CDK4/6. There are no currently available drugs that directly target Cyclin D1 or MYC and we believe zotatifin may be an attractive drug candidate in cancers driven by these proteins.

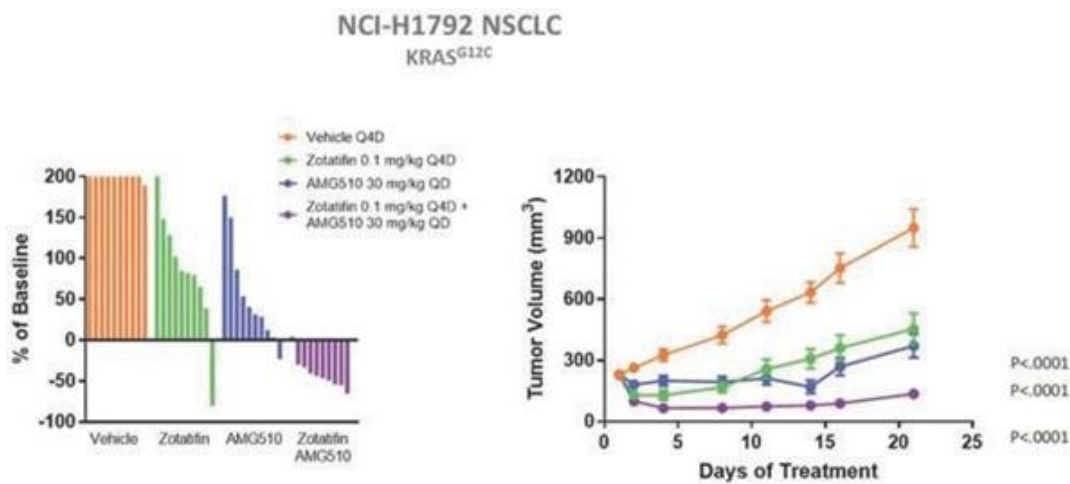
We believe the potential of zotatifin to downregulate multiple disease-driving proteins involved in specific breast cancer tumor types, including ER, Cyclin D1, CDK4/6 FGFR, and HER2, may provide an important treatment option for patients with these tumor types. In our preclinical studies, zotatifin demonstrated efficacy in several mice models of breast cancers. For example, in the MDA-MB-361, ER+HER2+PIK3CA mutant, model of breast cancer, treatment with either zotatifin or palbociclib, an inhibitor of CDK4/6, resulted in comparable efficacy. Interestingly, co-treatment with both zotatifin and palbociclib together showed strong combination activity with tumor regressions persisting for more than 40 days after dosing with the combination had stopped (see figure 18 below). In multiple preclinical models, zotatifin downregulates production of Cyclin D1. Upregulation of free Cyclin D1 has been shown to promote resistance to CDK4/6 inhibition and, therefore, we believe a combination of zotatifin with a CDK4/6 inhibitor has the potential to be a promising treatment option for patients with ER+ metastatic breast cancer.

Figure 18: Zotatfin demonstrates single agent activity comparable to palbociclib and compelling tumor regression in combination with palbociclib in a preclinical model of breast cancer.



Across a panel of approximately 100 cell lines evaluated, zotatifin treatment resulted in apoptosis in many lines harboring activating KRAS mutation. Furthermore, in cell proliferation and apoptosis assays, zotatifin showed strong activity in combination with a KRAS G12C inhibitor produced by Amgen, known as AMG510 or sotorasib, which recently received regulatory approval. We believe that zotatifin has the potential to overcome mechanisms of resistance to inhibitors of KRAS G12C by downregulating Cyclin D1 and certain RTKs, as well as inhibiting de novo KRAS protein production. Our preclinical studies showed that in models of NCI-H1792 KRAS G12C mutant NSCLC, zotatifin had similar tumor growth inhibition activity as AMG510. This preclinical data also showed that the combination of zotatifin and AMG510 led to tumor regressions in almost all animals tested (see figure 19 below). In preclinical models of KRAS mutant tumors, zotatifin downregulated KRAS, Cyclin D1 and several RTKs. Upregulation of these proteins has been shown to promote resistance to KRAS inhibition and, therefore, we believe a combination of zotatifin with a KRAS inhibitor has the potential to be a promising treatment option for patients with KRASG12C NSCLC.

Figure 19: Zotatifin demonstrates single agent activity comparable to KRAS G12C inhibitor, AMG510, and compelling tumor regression in combination with AMG510 in a preclinical model of KRASG12C NSCLC.



Phase 1/2 Clinical Trial Observations and Plans

We are evaluating zotatifin in a Phase 1/2 clinical trial in patients with certain solid tumors. We completed the initially planned dose escalation portion of this trial and are currently evaluating patients in multiple open-label expansion cohorts in patients with solid tumors driven by multiple proteins shown in our preclinical studies to be downregulated by zotatifin. The primary objectives of the Phase 1 portion of the trial included assessing safety and selecting a RP2D of zotatifin administered intravenously (“IV”). In the initial Phase 1 dose-escalation portion of the trial, we enrolled 37 patients at doses ranging from 0.005 mg/kg IV weekly to 0.1 mg/kg IV weekly including modified regimens of two weeks on treatment followed by one week off treatment. During dose escalation we observed three DLTs, including one DLT of grade 2 thrombocytopenia that prevented the completion of continued therapy throughout the DLT window observed in the 0.035 mg/kg IV weekly cohort and two DLTs observed in the 0.1 mg/kg IV weekly administered two weeks on and one week off cohort. One patient experienced a DLT of grade 3 anemia and another patient experienced a DLT of grade 3 gastrointestinal bleed in the setting of grade 2 thrombocytopenia. Based on this data, we concluded that the 0.1 mg/ kg dose exceeded the MTD. Overall AEs across all dose levels included predominantly Grade 1 and Grade 2 nausea, vomiting and anemia. Zotatifin exhibited dose-proportional pharmacokinetic exposure and had a relatively long half-life of approximately four days. At doses of 0.035 mg/kg and above, zotatifin has achieved exposures in blood in humans that correspond to levels resulting in preclinical activity in mice studies.

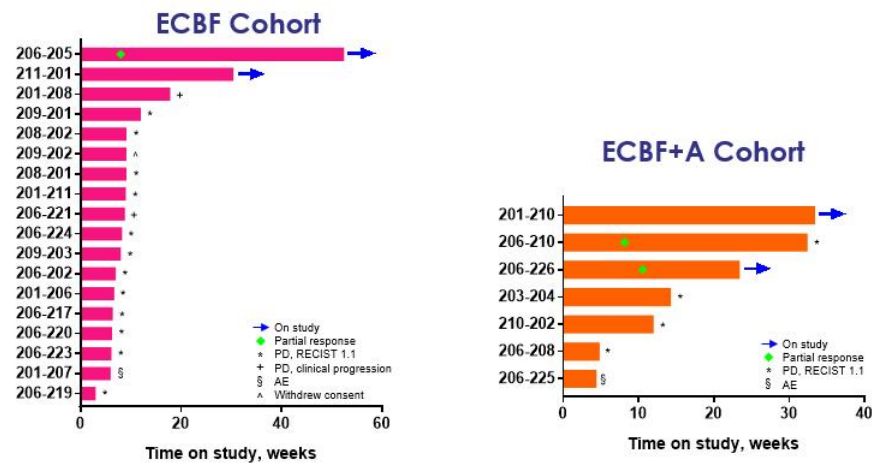
In June 2021, based on an evaluation of data from the Phase 1 dose escalation portion of our Phase 1/2 clinical trial of zotatifin, we selected 0.07 mg/kg given on Day 1 and Day 8 of a 21-day cycle, a dose and schedule at which we observed no DLTs, as the RP2D.

We initiated clinical evaluation of zotatifin in Phase 2a indication-specific expansion cohorts. The primary objectives of the Phase 2a cohorts are to further characterize safety and to identify initial signals of efficacy in biomarker-specific patient populations. We initiated four expansion cohorts, three in mBC and one in NSCLC. Specifically, we initiated cohorts evaluating zotatifin as a monotherapy treatment in ER+/FGFR+ mBC, as a combination with fulvestrant, an FDA-approved inhibitor of ER, in ER+ mBC, as a combination with fulvestrant and abemaciclib, an FDA-approved inhibitor of CDK4/6, in ER+/HER2- mBC, and as a combination with sotorasib, an FDA approved KRAS inhibitor, in KRAS G12C NSCLC. Each of our Phase 2a expansion cohorts were structured as a Simon's Two Stage design in which seven patients would be enrolled in the first stage of the trial and assessed for activity prior to advancing to the second stage of the trial.

In June 2022, we reported interim data from four of the ongoing Phase 2a expansion cohorts. As of the March 4, 2022 cutoff date, the interim results showed that zotatifin was generally well tolerated at the .07 kg/mg dose and treatment emergent adverse events ("TEAEs") related to zotatifin were mostly mild, readily managed and reversible, and included fatigue, anemia, diarrhea, vomiting and nausea. In the 25 patients that had received the recommended Phase 2 dose, none exhibited zotatifin-related Grade 3, 4 or 5 TEAEs. In the ER+ breast cancer cohort evaluating zotatifin and fulvestrant (ECBF cohort), we reported one out of seven partial responses and three out of seven patients with stable disease, which allowed for expansion from seven total patients to 18 patients. In the ER+/FGFR amplified breast cancer cohort evaluating zotatifin as a monotherapy, one out of seven patients had stable disease, which was not sufficient to expand the size of the cohort. In the KRAS G12C NSCLC cohort evaluating zotatifin in combination with sotorasib, one patient had been enrolled at the interim data cutoff date and reported stable disease. In the ER+ breast cancer cohort evaluating zotatifin, fulvestrant and abemaciclib (ECBF+A cohort), two patients had been enrolled at the interim data cutoff date with one reported partial response.

In January 2023, we reported updated interim data for the ECBF and ECBF+A cohorts. As of the December 15, 2022 cutoff date, zotatifin continued to be generally well tolerated with four Grade 3+ TEAE in the ECBF cohort (n=18) and four Grade 3+ TEAE in the ECBF+A cohort (n=7). One partial response and one patient with prolonged stable disease was reported in the ECBF cohort and two partial responses and one patient with prolonged stable disease was reported in the ECBF+A cohort. (See figure 20) Topline data for the remaining 11 patients in the ECBF+A cohort is anticipated to be available in the first half of 2023. In addition, based on the safety profile established and target engagement data generated to date, we announced that we resumed dose escalation. Data from the dose escalation portion of the trial is anticipated in the second half of 2023. We also announced that we would defer initiation of a previously planned cohort of Cyclin D1 amplified ER+ breast cancer patients and would pause enrollment in the KRAS G12C lung cancer cohort until completion of dose escalation.

Figure 20: Swimmers plots showing length of time on zotatifin plus fulvestrant (ECBF cohort) and fulvestrant and abemaciclib (ECBF+A cohort).



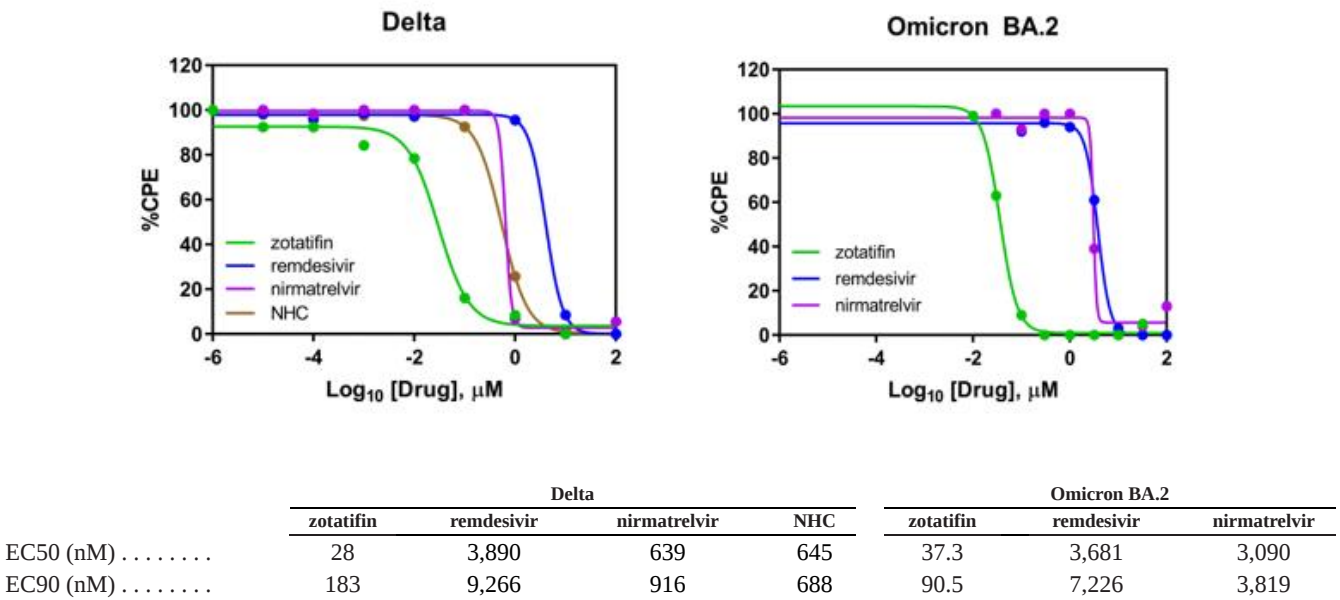
*Preliminary results from ongoing trial prior to database lock. Data cutoff December 15, 2022.

If zotatifin continues to demonstrate an adequate safety profile and sufficient signals of activity, we plan to continue clinical development of zotatifin, potentially as a combination in a randomized trial against a relevant comparator control group, or potentially in a single arm monotherapy trial following demonstration of an appropriate ORR in the Phase 2a expansion cohort.

Zotatifin as an antiviral agent for COVID-19

Zotatifin is designed to inhibit eIF4A-dependent translation of select mRNA into proteins. eIF4A is required to unwind the complex secondary structures within the 5' UTR of coronaviruses, including COVID-19, and other RNA viruses, to translate viral RNA and replicate. Zotatifin was evaluated as one of 69 compounds for in vitro antiviral activity against SARS CoV-2, the virus that causes COVID-19, by independent groups at Mount Sinai Hospital in New York and Institut Pasteur in Paris. Results from that study, published in Nature in April 2020, showed that zotatifin was one of the most active antiviral agents against SARS-CoV-2 among all the compounds tested. In subsequent studies using normal human bronchoepithelial cells, zotatifin demonstrated potent inhibition of SARS-CoV-2 as well as other coronaviruses including MERS-CoV. In addition, zotatifin was recently tested against numerous COVID isolates and other coronaviruses and was 10-100 times more potent than several agents authorized by the FDA for treatment of COVID, based on concentrations required to achieve comparable reductions in virus yield and protection from virus-induced cytopathic effects in cell-based assays. (see graphs in figure 21 below).

Figure 21: Zotatfin inhibits the replication of other SARS-CoV-2 variants with increased potency over other antivirals.



We have conducted a Phase 1b clinical trial of zotatfin as a potential host-directed anti-viral therapy in patients with mild to moderate COVID-19, in collaboration with QBI at UCSF, which held a \$5 million cooperative agreement sponsored by the Defensive Advanced Research Projects Agency. We have also used the funding to support the initiation of certain drug manufacturing activities and further development of a subcutaneous formulation for more convenient administration. We have recently completed a Phase 1b trial in patients with mild to moderate COVID-19. The trial is a double-blind, randomized dose escalation trial of zotatfin in non-hospitalized patients with mild to moderate COVID-19 in 36 patients evaluating three different doses of zotatfin. In this trial, zotatfin was found to be safe and well-tolerated, and demonstrated favorable trends in several assessments of viral clearance compared to placebo (see graphs in figures 22 and 23 below). This trial began utilizing the same IV formulation currently being used in cancer trials but switched to a newly developed sub-cutaneous formulation for the last 34 patients enrolled. Pharmacokinetics results show a profile of drug concentrations in blood over time virtually identical to the IV formulation, indicating the more convenient sub-cutaneous formulation could be used in future COVID or cancer trials. We have exhausted the full \$5.0 million of allowable costs under our agreement with UCSF as of December 31, 2022.

Figure 22: Viral load kinetics: absolute change over time (mean + SEM) in combined cohorts

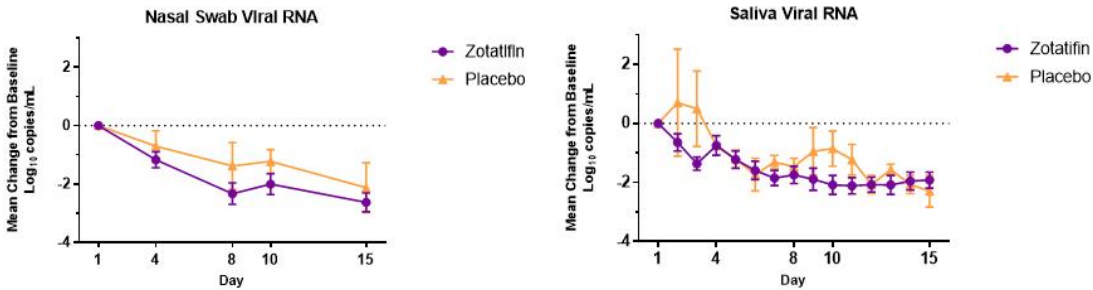
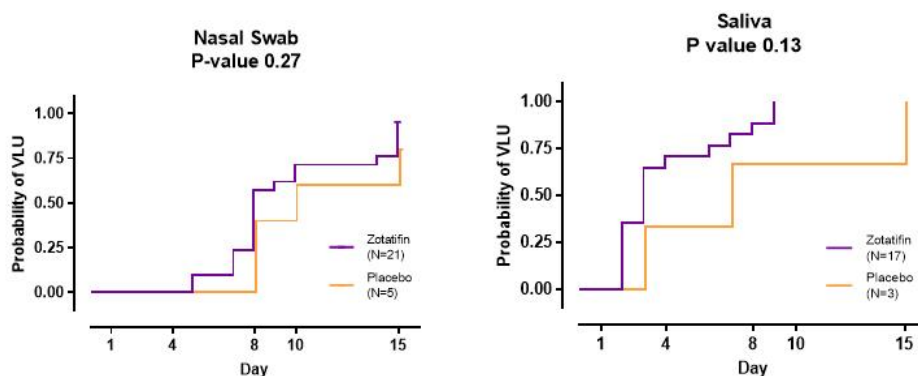


Figure 23: Nasal swab and saliva: time to viral load undetectability (VLU) in combined cohorts



eIF4E—Global Partnership with Pfizer

In December 2019, we entered into the Pfizer Agreement pursuant to which we granted Pfizer a global license to our earliest stage program, inhibitors of eIF4E. eIF4E is an oncogene and historically intractable target whose expression is increased, or upregulated, in a variety of human cancers and is linked to poor prognosis and resistance to certain therapies. eIF4E integrates signals from multiple important onco-genes and tumor suppressor proteins, including BRAF, MYC, mTOR, PI3K, AKT and PTEN, and selectively regulates the translation of a set of target mRNA largely distinct from those regulated by MNK and eIF4A. This may expand the potential patient population that may benefit from selective translation regulation therapy. In conjunction with Pfizer, we selected our lead development candidate to progress into IND-enabling studies that are ongoing. Pfizer is responsible for further development of this program, including submission of an IND and initiating a Phase 1 dose escalation clinical trial. See “—Pfizer Research Collaboration and License Agreement for Inhibitors of eIF4E” below for a description of the Pfizer Agreement.

Research conducted by Dr. Davide Ruggero and published in July 2015 in *Cell*, has demonstrated a small set of mRNA are sensitive to reduced levels of eIF4E. The eIF4E-sensitive mRNA encode proteins involved in oncogenic transformation, tumor growth stimulation, and inhibition of apoptotic pathways, suggesting eIF4E is an attractive target for cancer therapy. In addition, we believe tumors that overexpress eIF4E, including head and neck squamous cell carcinoma, lymphoma and breast cancer, represent significant clinical opportunities.

Because the natural ligand for eIF4E is a highly charged entity, termed the 5' cap, it has been historically difficult to identify product candidates to inhibit this protein within cells. Using our proprietary structure-based and fragment-based drug design expertise we have invented several small molecule inhibitors of eIF4E that bind to the same site as, and compete with, the 5' cap. In conjunction with Pfizer, we selected a lead product candidate which in preclinical models was shown to be a potent and selective inhibitor of eIF4E. This candidate has demonstrated activity in tumor cell assays and has demonstrated substantial in vivo anti-tumor activity.

We are continuing to collaborate with Pfizer regarding the design and analysis of preclinical studies that Pfizer is conducting and supporting the development activities related to Pfizer's fully funded activities of the worldwide development of our eIF4E inhibitors. We will continue to evaluate the development progress of the lead product candidate inhibitor of eIF4E, and consider building the sales and marketing infrastructure, as needed, to support the exercise of our option to co-promote and profit share in the United States as the data evolves.

Our Proprietary Translation Regulation Technology Platform

We discovered our product candidates using our proprietary selective translation regulation technology platform. Our platform includes our ribosomal profiling technology combined with state-of-the-art chemistry design strategies. Our ribosomal profiling technology enables comprehensive and quantitative measurement of the density

of ribosomes on expressed mRNA in the cell which predicts the rate of translation and, therefore, enables identification of targets that are upregulated in tumors and whose production is sensitive to selective inhibition by our product candidates. Information as to which mRNA's translation can be inhibited by our product candidates is an important part of our process to select tumor types and patient populations for clinical studies. Ribosomes are the macromolecular machines responsible for synthesizing proteins based on instructions contained in mRNA. This profiling has allowed us to assess the efficiency of mRNA's translation in cells or in tissues, distinguishes between transcriptional and translational regulation of gene expression, and identifies therapeutic targets, biomarkers and contexts of drug sensitivity or resistance. By measuring translational efficiency in various normal and diseased states we have been able to determine which proteins are subject to translational regulation and, importantly, which proteins are upregulated in various disease states. We incorporated and enhanced the original technology licensed from UCSF and industrialized it for use in our internal drug discovery and development efforts. The application of this technology has generated a proprietary understanding of genes that are translationally dysregulated in multiple tumor types and allowed us to identify specific points of therapeutic intervention.

To develop our product candidates, we conducted a focused approach to medicinal chemistry incorporating both fragment-based and structure-based design techniques. We also applied our specialized expertise regarding atomic interactions that offer potential for potent, highly specific drug target interactions. Our approach in identifying selective and potent inhibitors of our drug targets was based, in part, on balancing physical chemical properties with high binding affinity. We combined these drug design capabilities with external synthetic chemistry efforts to enhance our ability to identify potent and selective lead product candidates in an efficient and effective manner.

Manufacturing

We do not own or operate, and currently have no plans to establish any manufacturing facilities. We currently rely, and expect to continue to rely, on third-party manufacturers to produce sufficient quantities of our product candidates and their component raw materials for use in our preclinical development and clinical trials and in relation to any future commercialization of our product candidates. Our third-party manufacturers are responsible for obtaining the raw materials necessary to manufacture our product candidates, and we believe that these raw materials are readily available from more than one source. Additional third-party manufacturers are and will be used to fill, label, package and distribute investigational drug products. This approach allows us to maintain a more efficient infrastructure while enabling us to focus our expertise on developing our products. Although we believe we have multiple potential sources for the manufacture of our product candidates and the related raw materials, we currently rely on single manufacturers, including Curia Global (formerly AMRI), Catalent, and Corden, for different aspects of tomivosertib and zotatifin.

Commercialization Plan

We currently have no sales, marketing or commercial product distribution capabilities and have no experience as a company in commercializing products. We intend to build our own commercialization organization and capabilities over time to market any approved products in North America. We believe that this commercial organization can be modest in size and targeted to a relatively small number of oncologists specializing in our target markets. Outside of North America, we may establish collaborations with pharmaceutical companies to leverage their commercialization capabilities to maximize the potential of our product candidates.

As our product candidates progress through stages of development, our commercial plans may change. Clinical data, the size of the development programs, the size of our target markets, the size of a commercial infrastructure and manufacturing needs may all influence our U.S., European and rest of the world commercialization strategies.

Our Collaboration and License Agreements

Pfizer Research Collaboration and License Agreement for Inhibitors of eIF4E

In December 2019, we entered into the Pfizer Agreement, to research and develop small molecules that target eIF4E. Pursuant to the Pfizer Agreement, we granted Pfizer a worldwide, exclusive license, with a right to

sublicense, under certain of our patents, know-how, and materials to use, develop, manufacture, commercialize, and otherwise exploit compounds or products targeting eIF4E, for any and all indications. Pursuant to the Pfizer Agreement, Pfizer granted us an option to co-fund and co-promote a single such licensed product under a profit and loss share arrangement in the United States. The option can be exercised prior to a specified time before the first patient is expected to be enrolled in a clinical trial intended to support an NDA for marketing approval.

Under the Pfizer Agreement, eFFECTOR was responsible for initial research in collaboration with Pfizer, and Pfizer is responsible for all further development of this asset, including submission of an IND and conducting all clinical development and commercialization activities. Pfizer is obligated to use commercially reasonable efforts to develop and seek regulatory approval for a licensed product, and commercialize a licensed product where Pfizer has received regulatory approval, in the United States and certain other countries. In the event we exercise our co-funding and co-promotion option, a joint steering committee will oversee the development plan and budget of the co-developed product, and we will have the responsibility to conduct a portion of product marketing presentations to healthcare providers.

Pursuant to the Pfizer Agreement, we received an upfront, one-time, non-refundable, non-creditable payment of \$15 million dollars from Pfizer. Pfizer was obligated to reimburse us for costs incurred for research performed, up to a specified cap in the low double-digit millions. Upon the achievement of specified early development and regulatory milestones, Pfizer will be obligated to pay us up to \$80 million dollars in the aggregate. For other non-early stage development milestones Pfizer's payment obligations to us depend upon whether we have exercised our co-funding and co-promotion option: 1) if we do not exercise our option, non-early stage development payments may total up to \$165 million dollars in aggregate, and 2) if we do exercise our option, non-early stage development payments may total up to \$70 million dollars in aggregate. Upon the achievement of specified sales milestones, Pfizer is also obligated to make tiered milestone payments of up to \$235 million dollars in aggregate. On a product-by-product basis, Pfizer will also be required to pay us high single-digit percentage royalties on annual net sales of each licensed product. If we exercise our co-promotion and co-funding option, royalty payments will exclude sales in the United States and we will share with Pfizer profits from sale of the relevant licensed product in the United States.

Unless earlier terminated, the Pfizer Agreement will continue in effect until the expiration of all Pfizer payment obligations. Except in the U.S. if we exercise our co-funding and co-promotion option, following expiration of the obligation to pay royalties for any licensed product in a given country and payment of all amounts due, Pfizer's license to such licensed product in such country will become fully paid-up, perpetual, irrevocable and royalty-free. Pfizer may terminate the Pfizer Agreement for convenience upon written notice. Either party may terminate the Pfizer Agreement if an undisputed material breach by the other party is not cured within a defined period of time, or upon notice for insolvency-related events of the other party that are not discharged within a defined time period.

Exclusive License Agreement with UCSF

In May 2013, we entered into an agreement with UCSF which provides us an exclusive license to UCSF's patent rights in certain inventions ("UCSF Translational Profiling Patent Rights") relating to translational profiling laboratory techniques initially developed at UCSF, including certain patent rights we co-own with UCSF. Under the agreement we are permitted to research, develop, make and sell products that we discover and develop utilizing the UCSF Translational Profiling Patent Rights, which we refer to as licensed products, and use certain licensed processes utilizing the UCSF Translational Profiling Patent Rights and to sublicense such licensed products and processes. Our exclusivity is subject to certain retained research rights of UCSF and is subject to the rights of the U.S. government, if any, as set forth in 35 U.S.C. §§ 200-212. Pursuant to this law, the U.S. government may have acquired a nonexclusive, nontransferable, paid-up license to practice or have practiced for or on behalf of the U.S. government the inventions described in the UCSF Translational Profiling Patent Rights throughout the world. We have the first right to pursue patent infringement claims of potential commercial significance with respect to the licensed UCSF Translational Profiling Patent Rights, subject to certain conditions.

Under the agreement, we are required to use commercially reasonable efforts to meet certain specified development, regulatory and commercial milestones related to the licensed products within specified time periods. In consideration of the rights granted to us under the agreement, we made a one-time license issue fee cash payment to UCSF of \$50,000. In July 2021, we entered into an amendment to the license agreement to confirm the impact of

the merger on the license agreement, pursuant to which, upon the closing of the merger, we paid UCSF a one-time cash payment of approximately \$1.0 million. We are also required to make cash milestone payments to UCSF upon the completion of certain clinical and regulatory milestones for the licensed products.

To date, we have made cash milestone payments to UCSF in an aggregate amount of \$40,000. The aggregate remaining potential milestone payments are approximately \$375,000. Additionally, we have agreed to pay UCSF a royalty of less than one percent on net sales of each of the first two licensed products sold by us or our affiliates, subject to a minimum annual royalty payment of \$15,000 (creditable against the royalty payment otherwise due for the year in which the minimum payment was made) and other adjustments in certain circumstances. Our royalty obligations continue for each licensed product or service until the expiration of the last licensed patent covering the applicable licensed product or service which will be February 2034, absent any patent term adjustment or extensions.

UCSF may terminate the agreement if we fail to perform or violate any material term of the agreement and fail to cure such nonperformance or violation within 60 days of notice from UCSF or in the event of our insolvency. We are currently in compliance with all material terms of the agreement.

We may terminate the agreement upon 60 days' written notice to UCSF and may terminate the UCSF Translational Profiling Patent Rights on a claim-by-claim, patent-by-patent and country-by-country basis by giving written notice to UCSF. Absent early termination, the agreement will continue until the expiration date of the longest-lived patent right included in the UCSF Translational Profiling Patent Rights. In May 2016, pursuant to the terms of the UCSF license agreement, we provided notice of our election to terminate our obligations to pay the patent prosecution costs with respect to patent application claiming methods of treating cancer by inhibiting PRPS-2, thereby relinquishing our rights in any future products that would infringe the relinquished claims were they ever to be issued. At the time we made this election, we were aware of no such products within eFFECTOR or UCSF.

Intellectual Property

We strive to protect and enhance the proprietary technology, inventions, and improvements that are commercially important to our business, including seeking, maintaining and defending patent rights, whether developed internally or licensed from third parties. We own the issued patents and patent applications relating to our lead product candidate tomivosertib. Our policy is to seek to protect our proprietary position by, among other methods, filing patent applications in the United States and in jurisdictions outside of the United States directed to our proprietary technology, inventions, improvements and product candidates that are important to the development and implementation of our business. We also rely on trade secrets and know-how relating to our proprietary technology and product candidates, continuing innovation, and in-licensing opportunities to develop, strengthen and maintain our proprietary position in the field of immuno-oncology and targeted therapy with eIF4A inhibitors. We also plan to rely on data exclusivity, market exclusivity, and patent term extensions when available. Our commercial success will depend in part on our ability (1) to obtain and maintain patent and other proprietary protection for our technology, inventions, and improvements; (2) to preserve the confidentiality of our trade secrets; (3) to obtain and maintain licenses to use intellectual property owned by third parties; (4) to defend and enforce our proprietary rights, including any patents that we may own in the future; and (5) to operate without infringing on the valid and enforceable patents and other proprietary rights of third parties.

As of February 1, 2023, our licensed, owned and co-owned patent portfolio is directed to MNK inhibitors (including tomivosertib), eIF4A mRNA helicase inhibitors (including zotatifin) and various applications of our proprietary selective translation regulation platform, as well as certain of our proprietary technology, inventions, improvements or other product candidates. We also possess and/or in-license substantial know-how and trade secrets relating to the development and commercialization of our product candidates, including related manufacturing processes and technology.

Specifically, our patent portfolio includes the following families:

- MNK Inhibitors—We have twelve U.S. patents and thirty-one foreign patents (Australia (2), Belize, Canada, Chile, China (3), Columbia, Europe (2), Hong Kong, South Korea, India, Israel (2), Japan (4), Mexico (2), Peru, Philippines, Russia (3), Singapore, South Africa and Taiwan (2)), as well as seven pending U.S. patent applications and forty-six pending foreign patent applications (Australia (2), Belize, Brazil (3), Canada (5), Chile, China (2), Europe (4), Hong Kong (3), India (5), Israel, Japan (2), South

Korea (3), Malaysia, Mexico, New Zealand (4), Peru, Philippines, Russia, Singapore (3), Taiwan and South Africa), with claims directed to: composition of matter claims directed to our lead product candidate, tomivosertib and composition of matter claims to other MNK inhibitors; methods of treating MNK-related indications; the use of MNK inhibitors in combination with other translation inhibitors; processes for making tomivosertib the use of MNK inhibitors in immunotherapy; and the use of MNK inhibitor biomarkers for detecting MNK-related indications and for treating MNK-related indications. Any patents that issue from these pending patent applications will expire between June 2035 and June 2040, absent any patent term adjustments or extensions. The existing U.S. and foreign patents will expire between June 2035 and May 2038, absent any patent term extensions. We own the patents and all the pending patent applications in this patent family.

- eIF4A Inhibitors—We have five U.S. patents and thirteen foreign patents (Australia (2), China, Columbia, Europe, Hong Kong, Israel, Japan (2), Mexico, Russia, South Africa and Taiwan), as well as three pending U.S. patent applications, and 25 pending foreign patent applications (Australia (2), Belize, Brazil (2), Canada (3), Chile, China (2), Europe (3), Hong Kong (2), India, Japan, South Korea (3), Malaysia, New Zealand, Peru, and Philippines) with claims directed to: composition of matter claims directed to our lead product candidate zotatifin and other eIF4A inhibitors, as well as methods for treating eIF4A-related diseases. Any patents that issue from these pending patent applications will expire between November 2036 and March 2041, absent any patent term adjustments or extensions. The existing U.S. and foreign patents will expire between February 2035 and May 2038, absent any patent term extensions. We own all the pending patent applications in this patent family.
- eIF4E Inhibitors—We have three U.S. patents, two foreign patents (Australia, Taiwan), two pending U.S. patent applications, one pending PCT application and thirteen pending foreign patent applications (Australia, Brazil, Canada, Chile, Europe (2), Indonesia, Israel, India, Japan, South Korea, New Zealand and Singapore) with claims directed to eIF4E inhibitors, as well as claims directed to methods for treating eIF4E-related diseases. Patents that have or will issue from these pending patent applications will expire between February 2035 and December 2041, absent any patent term adjustments or extensions. The existing U.S. patents will expire between February 2035 and June 2040, absent any patent term extensions. While we own the patents and pending patent applications in this patent family, Pfizer has exclusively licensed most eIF4E patents and patent applications.
- UCSF Translational Profiling Patent Rights—We have a patent in Europe and China licensed from UCSF with claims directed to the use of translational profiling in methods of treatment. The last to expire patent right that has issued or will issue from these licensed and co-owned pending patent applications will expire in February 2034, absent any patent term adjustments or extensions.

With respect to our product candidates and processes we intend to develop and commercialize in the normal course of business, we intend to pursue patent protection covering, when possible, compositions, methods of use, dosing and formulations. We may also pursue patent protection with respect to manufacturing and drug development processes and technologies.

Issued patents can provide protection for varying periods of time, depending upon the date of filing of the patent application, the date of patent issuance, and the legal term of patents in the countries in which they are obtained. In general, patents issued for applications filed in the United States can provide exclusionary rights for 20 years from the earliest effective filing date. In addition, in certain instances, the term of an issued U.S. patent that covers or claims an FDA approved product can be extended to recapture a portion of the term effectively lost as a result of the FDA regulatory review period, which is called patent term extension. The restoration period cannot be longer than five years and the total patent term, including the restoration period, must not exceed 14 years following FDA approval. The term of patents outside of the United States varies in accordance with the laws of the foreign jurisdiction, but typically is also 20 years from the earliest effective filing date. However, the actual protection afforded by a patent varies on a product-by-product basis, from country-to-country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country, and the validity and enforceability of the patent.

The patent positions of companies like ours are generally uncertain and involve complex legal and factual questions. No consistent policy regarding the scope of claims allowable in patents in the field of immuno-oncology has emerged in the United States. The relevant patent laws and their interpretation outside of the United States is also uncertain. Changes in either the patent laws or their interpretation in the United States and other countries may

diminish our ability to protect our technology or product candidates and enforce the patent rights that we license and could affect the value of such intellectual property. In particular, our ability to stop third parties from making, using, selling, offering to sell, or importing products that infringe our intellectual property will depend in part on our success in obtaining and enforcing patent claims that cover our technology, inventions, and improvements. With respect to both licensed and company-owned intellectual property, we cannot guarantee that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications we may file in the future, nor can we be sure that any patents that may be granted to us in the future will be commercially useful in protecting our products, the methods of use or manufacture of those products.

Moreover, even the issued patents that we license do not guarantee us the right to practice our technology in relation to the commercialization of our products. Patent and other intellectual property rights in the pharmaceutical and biotechnology space are evolving and involve many risks and uncertainties. For example, third parties may have blocking patents that could be used to prevent us from commercializing our product candidates and practicing our proprietary technology. The issued patents that we in-license and those that may issue in the future may be challenged, invalidated, or circumvented, which could limit our ability to stop competitors from marketing related products or could limit the term of patent protection that otherwise may exist for our product candidates. In addition, the scope of the rights granted under any issued patents may not provide us with protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may independently develop similar technologies that are outside the scope of the rights granted under any issued patents that we own or exclusively in-license. For these reasons, we may face competition with respect to our product candidates. Moreover, because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that, before any particular product candidate can be commercialized, any patent protection for such product may expire or remain in force for only a short period following commercialization, thereby reducing the commercial advantage the patent provides.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technology, knowledge, experience and scientific resources provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize will 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, technical, manufacturing, marketing, sales and supply resources or experience than we do. Accordingly, our competitors may be more successful than us in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining approval for treatments and achieving widespread market acceptance, rendering our treatments obsolete or non-competitive. Merger and acquisition activity in the biotechnology and biopharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. These companies also compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials and acquiring technologies complementary to, or necessary for, our programs. We also face competition from such companies in seeking any future potential collaborations to partner our product candidates. Our commercial opportunity could be substantially limited if our competitors develop and commercialize products that are more effective, safer, less toxic, more convenient or less expensive than our comparable products. The key competitive factors affecting the success of all of our product candidates, if approved, are likely to be their efficacy, safety, convenience, price, the level of generic and other competition and the availability of reimbursement from government and other third-party payors.

If any of our product candidates are approved in oncology indications such as NSCLC or breast cancer, they will compete with small molecule therapies, biologics, cell-based therapies and traditional chemotherapy, or a combination of any such methods. With respect to tomivosertib, we are aware of AUM Biosciences which is developing a MNK inhibitor, AUM001 in solid tumors. In addition, several novel combinations with FDA-approved PD-1 or PD-L1 inhibitors are being developed in NSCLC. These include, among others, anti-TIGIT and anti-LAG3 therapies from Bristol-Myers Squibb Co., Gilead Sciences, GSK plc, Merck & Co, Novartis AG and Roche. With respect to zotatifin, we are aware of PIC Therapeutics which is developing pre-clinical small molecules targeting the

eukaryotic translation initiation factors (eIFs). Moreover, there are currently several marketed drugs and product candidates in development for the treatment of ER+ breast cancer that may compete with zotatifin, including fulvestrant marketed by AstraZeneca plc, elacestrant marketed by Menarini, AKT inhibitors being developed by AstraZeneca plc and Roche, oral SERDS being developed by Arvinas, Inc., AstraZeneca plc, Eli Lilly and Co, Eisai Co., Ltd, Roche and Zentalis Pharmaceuticals, Inc., among others.

Government Regulation

Government authorities in the United States, at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, marketing and export and import of drug 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. A new drug must be approved by the FDA through the NDA process before it may be legally marketed in the United States. We, along with any third-party contractors, will be required to navigate the various preclinical, clinical and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval of our products and product candidates. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

U.S. Drug Development Process

In the United States, the FDA regulates drugs under the federal Food, Drug, and Cosmetic Act (“FDCA”) and its implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in accordance with FDA’s Good Laboratory Practice requirements and other applicable regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval by an independent Institutional Review Board (“IRB”) or ethics committee at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with Good Clinical Practices (“GCPs”) to establish the safety and efficacy of the proposed drug for its intended use;
- preparation of and submission to the FDA of an NDA after completion of all pivotal trials;
- 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 advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with current Good Manufacturing Practice (“cGMP”) requirements to assure that the facilities, methods and controls are adequate to preserve the drug’s identity, strength, quality and purity, and of selected clinical investigation sites to assess compliance with GCPs; and
- FDA review and approval of the NDA to permit commercial marketing of the product for particular indications for use in the United States.

The preclinical developmental stage generally involves laboratory evaluations of drug chemistry, formulation and stability, as well as studies to evaluate the molecule’s toxicity in animals, which support subsequent clinical testing. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. The sponsor must submit the results of the preclinical studies, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the

IND. Prior to beginning the first clinical trial with a product candidate in the United States, a sponsor must submit an IND to the FDA. An IND is a request for authorization from the FDA to administer an investigational new drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for clinical studies. The IND also includes results of animal and in vitro studies assessing the toxicology, pharmacokinetics, pharmacology, and pharmacodynamic characteristics of the product; chemistry, manufacturing, and controls information; and any available human data or literature to support the use of the investigational product. Some long-term preclinical testing, such as animal tests of effects on reproduction and carcinogenicity, may continue after the IND is submitted. An IND must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises safety concerns or questions about the proposed clinical trial. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. Clinical holds also may be imposed by the FDA at any time before or during studies due to safety concerns or non-compliance. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical study. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, dosing procedures, subject selection and exclusion criteria, the parameters to be used in monitoring subject safety and the effectiveness criteria to be evaluated. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development and for any subsequent protocol amendments. While the IND is active and before approval, progress reports summarizing the results of the clinical trials and nonclinical studies performed since the last progress report must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the same or similar drugs, findings from animal or in vitro testing suggesting a significant risk to humans, and any clinically important increased incidence of a serious suspected adverse reaction compared to that listed in the protocol or investigator brochure.

Furthermore, an independent IRB for each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and its informed consent form before the clinical trial begins at that site and must monitor the study until completed. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. Depending on its charter, this group may determine whether a trial may move forward at designated check points based on access to certain data from the trial. The FDA or the sponsor may suspend 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. There are also requirements governing the reporting of ongoing clinical studies and clinical study results to public registries.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- Phase 1: The product candidate is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness.
- Phase 2: The product candidate is administered to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.
- Phase 3: The product candidate is administered to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of the product's effectiveness for its intended use(s)

and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval.

In some cases, the FDA may require, or sponsors may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These so-called Phase 4 studies, may be conducted after initial marketing approval, and may be 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.

In addition, during the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase 2, and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and the FDA to reach agreement on the next phase of development. Sponsors typically use the meetings at the end of the Phase 2 trial to discuss Phase 2 clinical results and present plans for the pivotal Phase 3 clinical trials that they believe will support approval of the new drug.

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

U.S. Review and Approval Process

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, preclinical and other non-clinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. Data can come from company-sponsored clinical studies intended to test the safety and effectiveness of a use of the product, or from a number of alternative sources, including studies initiated by independent investigators. The submission of an NDA is subject to the payment of substantial user fees; a waiver of such fees may be obtained under certain limited circumstances. Additionally, no user fees are assessed on NDAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once filed, the FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant to assure and preserve the product's identity, strength, quality and purity. Under the Prescription Drug User Fee Act guidelines that are currently in effect, the FDA has a goal of ten months from the filing date to complete a standard review of an NDA for a drug that is a new molecular entity. This review typically takes twelve months from the date the NDA is submitted to FDA because the FDA has approximately two months to make a "filing" decision after it the application is submitted.

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

Before approving an NDA, the FDA will typically inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and

facilities are in compliance with cGMP and adequate to assure consistent production of the product within required specifications. Additionally, before approving a NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCPs.

After the FDA evaluates an NDA and conducts inspections of manufacturing facilities where the investigational product and/or its drug substance will be produced, the FDA may issue an approval letter or a Complete Response Letter (“CRL”). An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A CRL will describe all of the deficiencies that the FDA has identified in the NDA, except that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the CRL without first conducting required inspections and/or reviewing proposed labeling. In issuing the CRL, the FDA may recommend actions that the applicant might take to place the NDA in condition for approval, including requests for additional information or clarification. The FDA may delay or refuse approval of an NDA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product.

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the NDA with a Risk Evaluation and Mitigation Strategy (“REMS”) to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy to manage a known or potential serious risk associated with a medicine and to enable patients to have continued access to such medicines by managing their safe use, and 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. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. The FDA may also require one or more Phase 4 post-market studies and surveillance to further assess and monitor the product’s safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post-marketing studies.

In addition, the Pediatric Research Equity Act (“PREA”), requires a sponsor to conduct pediatric clinical trials for most drugs, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs and supplements must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must evaluate the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or FDA may request a deferral of pediatric clinical trials for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug is ready for approval for use in adults before pediatric clinical trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric clinical trials begin. The FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

Expedited Development and Review Programs

The FDA offers a number of expedited development and review programs for qualifying product candidates. For example, the Fast Track program is intended to expedite or facilitate the process for reviewing new products that are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast Track designation applies to the combination of the product candidate and the specific indication for which it is being studied. The sponsor of a Fast Track product candidate has opportunities for more frequent interactions with the applicable FDA review team during product development and, once an NDA is submitted, the application may be eligible for priority review. A fast track product candidate may also be eligible for rolling review, where the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

A product candidate intended to treat a serious or life-threatening disease or condition may also be eligible for Breakthrough Therapy designation to expedite its development and review. A product candidate can receive Breakthrough Therapy designation if preliminary clinical evidence indicates that the product candidate, alone or in combination with one or more other drugs or biologics, may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in

clinical development. The designation includes all of the Fast Track program features, as well as more intensive FDA interaction and guidance beginning as early as Phase 1 and an organizational commitment to expedite the development and review of the product candidate, including involvement of senior managers.

Any marketing application for a drug submitted to the FDA for approval, including a product candidate with a Fast Track designation and/or Breakthrough Therapy designation, may be eligible for other types of FDA programs intended to expedite the FDA review and approval process, such as priority review and accelerated approval. An NDA is eligible for priority review if the product candidate is designed to treat a serious or life-threatening disease or condition, and if approved, would provide a significant improvement in safety or effectiveness compared to available alternatives for such disease or condition. For new-molecular-entity NDAs, priority review designation means the FDA's goal is to take action on the marketing application within six months of the 60-day filing date.

Additionally, product candidates studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may receive accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on an intermediate clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of accelerated approval, the FDA will generally require the sponsor to perform adequate and well-controlled confirmatory clinical studies to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. Products receiving accelerated approval may be subject to expedited withdrawal procedures if, among other things, the sponsor fails to conduct the required confirmatory studies in a timely manner or if such studies fail to verify the predicted clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

Fast Track designation, Breakthrough Therapy designation, priority review, and accelerated approval do not change the standards for approval, but may expedite the development or approval process. Even if a product candidate qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Orphan drug designation and exclusivity

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug intended to treat a rare disease or condition, which is generally defined as a disease or condition with either (i) a patient population of fewer than 200,000 individuals in the United States, or (ii) a patient population greater than 200,000 individuals in the United States and when there is no reasonable expectation that the cost of developing and making available the drug in the United States will be recovered from sales in the United States for that drug. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA.

If a product that has orphan drug designation subsequently receives the first FDA approval for a particular active ingredient for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including a full NDA, to market the same drug for the same disease or condition for seven years from the date of such approval, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. Orphan drug exclusivity does not prevent the FDA from approving a different drug for the same disease or condition, or the same drug for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA application user fee. A designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or, as noted above, if a second applicant demonstrates that its product is clinically superior to the approved product with orphan exclusivity or the manufacturer of the approved product is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Post-approval Requirements

Drug products manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record-keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution, and advertising and promotion of the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual program fees for any marketed products. Drug manufacturers and their subcontractors 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, which impose certain procedural and documentation requirements upon us and our third-party manufacturers. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting requirements. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical 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, complete withdrawal of the product from the market or product recalls;
- fines, warning letters, or untitled letters;
- clinical holds on clinical studies;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs;
- mandated modification of promotional materials and labeling and the issuance of corrective information;
- the issuance of safety alerts, Dear Healthcare Provider letters, press releases and other communications containing warnings or other safety information about the product; or
- injunctions or the imposition of civil or criminal penalties.

The FDA closely regulates the marketing, labeling, advertising and promotion of drug products. A company can make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA 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. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe, in their independent professional medical judgment, legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products. However, companies may share truthful and not misleading information that is otherwise consistent with a product's FDA-approved labelling.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act (“PDMA”) which regulates the distribution of drugs and drug samples at the federal level and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

Marketing Exclusivity

Market exclusivity provisions authorized under the FDCA can delay the submission or the approval of certain marketing applications. The FDCA provides a five-year period of non-patent data exclusivity within the United States to the first applicant to obtain 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 or even accept for review an abbreviated new drug application (“ANDA”) or an NDA submitted under Section 505(b)(2), (“505(b)(2) NDA”), submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovative drug or for another indication, 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 to one of the patents listed with the FDA by the innovator NDA holder.

The FDCA also provides three years of marketing exclusivity for an 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 modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for drugs containing the active agent for the original indication or condition of use. Five-year and three-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 any preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Pediatric exclusivity is another type of marketing exclusivity available in the United States. Pediatric exclusivity provides for an additional six months of marketing exclusivity attached to another period of exclusivity if a sponsor conducts clinical trials in children in response to a written request from the FDA. The issuance of a written request does not require the sponsor to undertake the described clinical trials. In addition, orphan drug exclusivity, as described above, may offer a seven-year period of marketing exclusivity, except in certain circumstances.

Other Healthcare Laws and Regulations

Pharmaceutical companies like us are subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which they conduct their business. Such regulation may constrain the financial arrangements and relationships through which we research, develop, and ultimately, sell, market and distribute any products for which we obtain marketing approval. Such laws include, without limitation, federal and state anti-kickback, fraud and abuse, and false claims laws, such as the federal Anti-Kickback Statute and the federal Civil False Claims Act, and transparency laws and regulations addressing drug pricing and payments and other transfers of value made by pharmaceutical manufacturers to physicians and other healthcare providers, such as the federal Physician Payment Sunshine Act. Violations of any of such laws or any other governmental regulations that apply may result in significant penalties, including, without limitation, administrative, civil and criminal penalties, damages, fines, disgorgement, the curtailment or restructuring of operations, integrity oversight and reporting obligations to resolve allegations of noncompliance, exclusion from participation in federal and state healthcare programs, such as Medicare and Medicaid, and imprisonment.

Coverage, Pricing and Reimbursement

Sales of any approved pharmaceutical product depend, in part, on the extent to which such product will be covered by third-party payors, such as federal, state, and foreign government healthcare programs, commercial

insurance and managed healthcare organizations, as well as the level of reimbursement for such product by third-party payors. Decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. Third-party payors are increasingly reducing coverage and reimbursement for medical products, drugs and related pharmaceutical company services. In addition, the U.S. government, state legislatures and foreign governments have continued implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit sales of any product for which we may receive marketing approval in one or more jurisdictions. Decreases in third-party reimbursement for any product or a decision by a third-party payor not to cover a product could reduce physician usage and patient demand for the product and also have a material adverse effect on sales.

Moreover, as a condition of participating in, and having products covered under, certain U.S. federal healthcare programs, such as Medicare and Medicaid, we may become subject to federal laws and regulations that require pharmaceutical manufacturers to calculate and report certain price reporting metrics to the government, such as Medicaid Average Manufacturer Price (“AMP”) and Best Price, Medicare Average Sales Price, the 340B Ceiling Price, and Non-Federal AMP reported to the Department of Veteran Affairs, and with respect to Medicaid, pay statutory rebates on utilization of manufacturers’ products by Medicaid beneficiaries.

Compliance with such laws and regulations will require significant resources and may have a material adverse effect on our revenues.

Healthcare Reform

In addition, as previously mentioned, the primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medical products and services, implementing reductions in Medicare and other health care funding and applying new payment methodologies. For example, in the United States, in March 2010, the ACA was enacted, which substantially changed the way healthcare is financed by both governmental and private insurers, and significantly affected the pharmaceutical industry. The ACA contained a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement adjustments and changes to fraud and abuse laws. As another example, the 2021 Consolidated Appropriations Act signed into law on December 27, 2020 incorporated extensive health care provisions and amendments to existing laws, including a requirement that all manufacturers of drugs products covered under Medicare Part B report the product’s average sales price to the federal government beginning on January 1, 2022, subject to enforcement via civil money penalties.

Since its enactment, there have been executive, judicial and Congressional challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court’s ruling, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA.

Other legislative changes have been proposed and adopted since the ACA was enacted, including the American Rescue Plan Act of 2021, effective January 1, 2024, which would eliminate the statutory cap on rebate amounts owed by drug manufacturers under the Medicaid Drug Rebate Program (“MDRP”) which is currently capped at 100% of the AMP for a covered outpatient drug.

Moreover, there has been heightened governmental scrutiny over the manner in which 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 pharmaceutical products. Most recently, on August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law. Among other things, the IRA requires manufacturers of certain drugs to engage

in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025).

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In December 2020, the U.S. Supreme Court held unanimously that federal law does not preempt the states' ability to regulate pharmaceutical benefit managers ("PBMs") and other members of the health care and pharmaceutical supply chain, an important decision that is expected to lead to further and more aggressive efforts by states in this area.

It also possible that governmental action will be taken in response to the COVID-19 pandemic. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could impact the amounts that federal and state governments and other third-party payors will pay for healthcare products and services.

Data Privacy & Security

Numerous state, federal and foreign laws govern the collection, use, disclosure and protection of personal information. In the United States, numerous federal and state laws and regulations, including data breach notification laws, health information privacy and security laws and consumer protection laws and regulations govern the collection, use, disclosure, and protection of health-related and other personal information. In addition, certain foreign laws govern the privacy and security of personal data, including health-related data. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and/or criminal penalties and restrictions on data processing.

Human Capital

As of February 28, 2023, we had 15 full-time employees and no part-time employees. Of these employees, 3 hold Ph.D. or M.D. degrees and 8 are engaged in research and development. Our employees are not represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, and incentivizing our management team and our clinical, scientific and other employees and consultants. The principal purposes of our equity and cash incentive plans are to attract, retain and motivate personnel through the granting of stock-based and cash-based compensation awards, in order to align our interests and the interests of our stockholders with those of our employees and consultants.

Corporate Information

We were incorporated under the laws of the state of Delaware on October 2, 2020 under the name Locust Walk Acquisition Corp ("LWAC"). eFFECTOR Therapeutics, Inc. was incorporated under the laws of the state of Delaware on May 1, 2012. On August 25, 2021, we consummated a merger pursuant to which a wholly-owned subsidiary of Locust Walk Acquisition Corp. merged with and into eFFECTOR Therapeutics Operations, Inc. (formerly known as eFFECTOR Therapeutics, Inc.) ("Old eFFECTOR"), with eFFECTOR Therapeutics Operations, Inc. becoming our wholly-owned subsidiary (the "Business Combination"). Upon the closing of the merger, we changed our name to eFFECTOR Therapeutics, Inc. Our corporate headquarters are currently located at 142 North Cedros, Suite B, Solana Beach, California 92075, and our telephone number is (858) 925-8215.

Unless the context otherwise requires, all references in this section to "we," "our," "us" or "eFFECTOR" refer to the business of eFFECTOR Therapeutics, Inc. prior to the consummation of the Business Combination, which is our business following the consummation of the Business Combination.

Available Information

Our internet address is www.effector.com. Our investor relations website is located at <https://investors.effector.com/>. We make available free of charge on our investor relations website under “SEC Filings” our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, our directors’ and officers’ Section 16 reports and any amendments to those reports as soon as reasonably practicable after filing or furnishing such materials to the U.S. Securities and Exchange Commission (“SEC”). They are also available for free on the SEC’s website at www.sec.gov.

We use our investor relations website as a means of disclosing material non-public information and for complying with our disclosure obligations under Regulation FD. Investors should monitor such website, in addition to following our press releases, SEC filings and public conference calls and webcasts. Information relating to our corporate governance is also included on our investor relations website. The information in or accessible through the SEC and our website are not incorporated into, and are not considered part of, this filing.

Item 1A. Risk Factors.

You should carefully consider the following risk factors, together with the other information contained in this Annual Report, including our financial statements and the related notes and “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” before making an investment regarding our common stock or warrants. We cannot assure you that any of the events discussed in the risk factors below will not occur. These risks could have a material and adverse impact on our business, results of operations, financial condition and growth prospects. If that were to happen, the trading price of our common stock or warrants could decline. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations or financial condition. In this section, we first provide a summary of the principal risks and uncertainties we face and then provide a full set of risk factors and discuss them in greater detail.

Summary of Risk Factors

- We have a limited operating history, have incurred significant operating losses since our inception and expects to incur significant losses for the foreseeable future. We may never generate any revenue from product sales or become profitable or, if we achieve profitability, we may not be able to sustain such profitability.
- We will require substantial additional capital to finance our operations, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our product development, commercialization efforts or other operations.
- We depend heavily on the success of our product candidates tomivosertib and zotatifin, which are in Phase 2 clinical development. If we or our collaborators are unable to successfully develop, obtain regulatory approval for and commercialize our product candidates or experience significant delays in doing so, our business will be materially harmed.
- Our failure to meet the continued listing requirements of the Nasdaq Capital Market could result in a delisting of our common stock and Warrants.
- Clinical and preclinical development involves a lengthy and expensive process with an uncertain outcome, and the results of preclinical studies and early clinical trials are not necessarily predictive of future results. Any of our product candidates may not have favorable results in later clinical trials, if any, or receive regulatory approval on a timely basis, if at all.
- Any difficulties or delays in the commencement or completion, or termination or suspension, of our current or planned clinical trials could result in increased costs to us, delay or limit our ability to generate revenue and adversely affect our commercial prospects.
- We may find it difficult to enroll patients in our clinical trials. If we encounter difficulties enrolling subjects in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.
- We rely on third parties to conduct our clinical trials and preclinical studies. If these third parties do not successfully carry out their contractual duties, comply with applicable regulatory requirements or meet

expected deadlines, our development programs and our ability to seek or obtain regulatory approval for our product candidates or commercialize our products may be delayed.

- We face significant competition from entities that have developed or may develop product candidates for cancer, including companies developing novel treatments and technology platforms. If our competitors develop technologies or product candidates more rapidly than we do or their technologies are more effective, our business and ability to develop and successfully commercialize products may be adversely affected;
- Our business is subject to risks arising from COVID-19 and other epidemic diseases.
- Our success depends on our ability to protect our intellectual property and proprietary technologies.
- The market price of our common stock and warrants is likely to be highly volatile, and you may lose some or all of your investment.

Risks Related to Our Limited Operating History, Financial Position and Capital Requirements

We have a limited operating history, have incurred significant operating losses since our inception and expect to incur significant losses for the foreseeable future. We may never generate any revenue from product sales or become profitable, or, if we achieve profitability, we may not be able to sustain it.

We are a clinical-stage biopharmaceutical company with a limited operating history upon which you can evaluate our business and prospects. We commenced operations in 2012. To date, we have focused primarily on raising capital, identifying potential product candidates, establishing our intellectual property portfolio, conducting preclinical studies and clinical trials, establishing arrangements with third parties for the manufacture of our product candidates and related raw materials, and providing general and administrative support for these operations. Our approach to the discovery and development of product candidates based on our technology platform is unproven, and we do not know whether we will be able to develop or obtain regulatory approval for any products of commercial value. In addition, we only have two product candidates, tomivosertib and zotatifin, in clinical development. We have not yet demonstrated an ability to successfully complete pivotal clinical trials, obtain regulatory 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. Consequently, any predictions made about our future success or viability may not be as accurate as they could be if we had a history of successfully developing and commercializing pharmaceutical products.

Other than revenue generated under our Research Collaboration and License Agreement with Pfizer, Inc. (the “Pfizer Agreement”), we have incurred significant operating losses since our inception and expect to incur significant losses for the foreseeable future. We do not have any products approved for sale and have not generated any product revenue since inception. If we are unable to successfully develop and obtain requisite approval for our product candidates, we may never generate any revenue from product sales. Our net income was \$15.8 million for the year ended December 31, 2021, and our net loss was \$22.7 million for the year ended December 31, 2022. As of December 31, 2022, we had an accumulated deficit of \$143.6 million. Substantially all of our operating losses resulted from expenses incurred in connection with the research and development of our product candidates and development programs, and general and administrative costs associated with our operations. All of our product candidates will require substantial additional development time and resources before we would be able to apply for or receive regulatory approvals and begin generating revenue from product sales. We expect to incur losses for the foreseeable future, and we anticipate these losses will increase substantially as we continue our development of, seek regulatory approval for and potentially commercialize any approved product candidates.

To become and remain profitable, we must succeed in developing and eventually commercializing products that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing clinical trials and preclinical studies of our product candidates, obtaining regulatory approval for these product candidates, and manufacturing, marketing, and selling any products for which we may obtain regulatory approval. We are only in the preliminary stages of most of these activities. We may never succeed in these activities and, even if we do, may never generate revenue that is significant enough to achieve profitability. In addition, we have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the biopharmaceutical industry. Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable

to accurately predict the timing or amount of increased expenses or if we will be able to achieve profitability. Even 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 may have an adverse effect on the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product candidates or even continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

We will require substantial additional capital to finance our operations, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our development programs, commercialization efforts or other operations.

The development of pharmaceutical product candidates is capital-intensive. Our operations have consumed substantial amounts of cash since inception. We expect our expenses to increase in connection with our ongoing activities, particularly as we conduct our ongoing and planned clinical trials of, and seek regulatory approval for, tomivosertib and zotatifin. Additionally, although Pfizer is currently responsible for the development of our eIF4E program, if we exercise our option to co-fund and co-promote this program pursuant to the terms of the Pfizer Agreement, we will incur additional expenses. Furthermore, if we obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. Because the outcome of any clinical trial or preclinical study is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of our product candidates. Furthermore, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

Based upon our current operating plans, we believe that our existing cash, cash equivalents and short-term investments will enable us to fund our operations into the first quarter of 2024. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. Our operating plans and other demands on our cash resources may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings or other capital sources, including potential collaborations, licenses and other similar arrangements. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. Attempting to secure additional financing may divert our management from our day-to-day activities, which may adversely affect our ability to develop our product candidates.

In January 2022, we entered into an equity purchase agreement (the "Purchase Agreement") with Lincoln Park Capital Fund, LLC ("Lincoln Park") which provides for the sale to Lincoln Park up to \$50.0 million of shares of our common stock over the 36 month term of the Purchase Agreement, subject to certain conditions, of which we have sold \$3.1 million through December 31, 2022. However, as of the date of this report, we were unable to sell additional shares under the Purchase Agreement because our shares are trading at less than \$1.00 per share, which is the minimum price that we can sell shares to Lincoln Park.

In September 2022, we entered into our Controlled Equity Offering Sales Agreement ("Sales Agreement") with Cantor Fitzgerald & Co ("Cantor") pursuant to which we may, from time to time, sell shares of our common stock having an aggregate of up to \$15.0 million pursuant to our Form S-3 registration statement (the "ATM Offering Program"). During the year ended December 31, 2022, we sold an aggregate of 478,964 shares of common stock for aggregate gross proceeds of \$0.3 million. There can be no assurance that the Sales Agent will be successful in consummating future sales based on prevailing market conditions or in the quantities or at the prices that we deem appropriate. In addition, under current SEC regulations, as of the filing of this annual report on Form 10-K, our public float is less than \$75 million, and under SEC regulations for so long as our public float remains less than \$75 million, the amount we can raise through primary public offerings of securities in any twelve-month period using shelf registration statements is limited to an aggregate of one-third of our public float, which is referred to as the baby shelf rules. As of February 28, 2023, our public float was approximately \$17.2 million, based on 34,520,253 shares of outstanding common stock held by non-affiliates and at a price of \$0.4982 per share, which was the last reported sale price of our common stock on the Nasdaq Capital Market on February 28, 2023. As a result of our public float being below \$75 million, we will be limited by the baby shelf rules until such time as our public float

exceeds \$75 million, which means we only have the capacity to sell shares up to one-third of our public float under shelf registration statements in any twelve-month period.

Our future capital requirements will depend on many factors, including, but not limited to:

- the type, number, scope, progress, expansions, results, costs and timing of, our clinical trials and preclinical studies of our product candidates which we are pursuing or may choose to pursue in the future;
- the costs and timing of manufacturing for our product candidates, including commercial manufacturing if any product candidate is approved;
- the timing and amount of the milestone or other payments made to us under our collaboration with Pfizer and any future collaborations, including with other parties;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs of obtaining, maintaining and enforcing our patents and other intellectual property rights;
- our efforts to enhance operational systems, including enhanced internal controls over financial reporting;
- the costs associated with hiring additional personnel and consultants as our clinical and preclinical activities increase;
- the costs and timing of establishing or securing sales and marketing capabilities if any product candidate is approved;
- our ability to achieve sufficient market acceptance, coverage and adequate reimbursement from third-party payors and adequate market share and revenue for any approved products;
- patients' willingness to pay out-of-pocket for any approved products in the absence of coverage and/or adequate reimbursement from third-party payors;
- any delays and cost increases that result from the COVID-19 pandemic or future epidemic diseases;
- the terms and timing of establishing and maintaining collaborations, licenses and other similar arrangements; and
- costs associated with any products or technologies that we may in-license or acquire.

Conducting clinical trials and preclinical studies is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and commercialize our product candidates. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenue, if any, will be derived from sales of products that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

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

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through equity offerings, debt financings, or other capital sources, including potential additional collaborations, licenses and other similar arrangements. We do not have any committed external source of funds, other than potential sales under our ATM Offering Program or Lincoln Park Purchase Agreement. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Our loan and security agreement with Oxford Financial LLC (the "Oxford LSA") includes, and any future debt financing and preferred equity financing, if available, may involve agreements that include, covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital

expenditures or declaring dividends. Such restrictions could adversely impact our ability to conduct our operations and execute our business plan.

If we raise funds through additional collaborations, licenses and other similar arrangements, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us and/or that may reduce the value of our Common Stock. If we are unable to raise additional funds through equity or debt financings or other arrangements when needed or on terms acceptable to us, we would be required to delay, limit, reduce, or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

The terms of the Oxford LSA place restrictions on our operating and financial flexibility. If we raise additional capital through debt financing, the terms of any new debt could further restrict our ability to operate our business.

As of December 31, 2022, we have an outstanding term loan in the principal amount of \$20.0 million under our Oxford LSA. The Oxford LSA permitted us to draw down an additional \$10.0 million (the “Term B Loan”) upon achievement of certain clinical development milestones on or prior to June 30, 2023. As a result of the discontinuation of one of the cohorts in our KICKSTART trial, which was previously announced in January 2023, we do not expect to achieve one of the clinical development milestones by June 30, 2023 and therefore do not expect to have access to the additional \$10.0 million under the Term B Loan. The term loan is secured by a lien covering substantially all of our personal property, rights and assets, excluding intellectual property, which is subject to a negative pledge. The Oxford LSA contains customary affirmative and negative covenants and events of default applicable to us. The affirmative covenants include, among others, covenants requiring us to maintain governmental approvals, deliver certain financial reports, maintain insurance coverage and protect material intellectual property. The negative covenants include, among others, restrictions on transferring collateral, incurring additional indebtedness, engaging in mergers or acquisitions, paying cash dividends or making other distributions, making investments, creating liens, selling assets and making any payment on subordinated debt, in each case subject to certain exceptions. The restrictive covenants of the Oxford LSA could cause us to be unable to pursue business opportunities that we or our stockholders may consider beneficial. In addition, Oxford could declare a default upon the occurrence of any event that it interprets as a material adverse change as defined under the Oxford LSA. Due to our determination that there is substantial doubt as to our ability to continue as a going concern, we have determined that the assessment about whether a material adverse change may occur under the Oxford LSA is not within our control, increasing the risk that the loan could be considered to be in default. If we default under the Oxford LSA, Oxford may accelerate all of our repayment obligations and take control of our pledged assets, potentially requiring us to renegotiate our agreement on terms less favorable to us or to immediately cease operations. Further, if we are liquidated, Oxford’s right to repayment would be senior to the rights of the holders of our common stock to receive any proceeds from the liquidation. Any declaration by Oxford of an event of default could significantly harm our business and prospects and could cause the price of our common stock to decline. If we raise any additional debt financing, the terms of such additional debt could further restrict our operating and financial flexibility.

Our management, as of December 31, 2022, and our independent registered public accounting firm, in their report on our financial statements as of and for the fiscal year ended December 31, 2022, have concluded that there is substantial doubt as to our ability to continue as a going concern.

Our audited financial statements for the fiscal year ended December 31, 2022 were prepared assuming that we will continue as a going concern. The going concern basis of the presentation assumes that we will continue in operation for the foreseeable future and will be able to realize our assets and satisfy our liabilities in the normal course of business and do not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or amounts and classification of liabilities that may result from our inability to continue as a going concern. As of December 31, 2022, our management concluded that, based on expected operating losses and negative cash flows, there is substantial doubt about our ability to continue as a going concern for the twelve months after the date the financial statements were issued. Our ability to continue as a going concern is subject to our ability to raise additional capital through equity offerings or debt financings, including through potential future sales of common stock to Lincoln Park under the Purchase Agreement and sales pursuant to the ATM Offering Program. As of the date of this report, we were unable to sell additional shares under the Purchase Agreement because our shares are trading at less than \$1.00 per share, which is the minimum price that we can sell shares to Lincoln Park.

Additionally, we may receive additional milestone payments under the Pfizer Agreement. However, we may not be able to secure additional financing in a timely manner or on favorable terms, if at all, and may not receive any milestone payments. If we cannot continue as a going concern, we may have to liquidate our assets and may receive less than the value at which those assets are carried on our financial statements, and it is likely that our stockholders may lose some or all of their investment in us. If we seek additional financing to fund our business activities in the future and there remains substantial doubt about our ability to continue as a going concern, investors or other financing sources may be unwilling to provide additional funding on commercially reasonable terms or at all.

Risks Related to the Discovery, Development and Regulatory Approval of Our Product Candidates

We depend heavily on the success of tomivosertib and zotatifin, which are in Phase 2 clinical development. If we or our collaborators are unable to successfully develop, obtain regulatory approval for and commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.

We are early in our development efforts and have only two product candidates, tomivosertib and zotatifin, in clinical development. Our other development program focused on eIF4E inhibitors is still in the preclinical stage under our collaboration with Pfizer. Our ability to generate product revenue, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our product candidates. The success of our product candidates will depend on several factors, including the following:

- timely initiation and successful enrollment of participants in our clinical trials and timely completion of clinical trials and preclinical studies with favorable results;
- authorization to proceed with clinical trials of our product candidates under investigational new drug applications (“INDs”) by the U.S. Food and Drug Administration, (the “FDA”) or under similar regulatory submissions by comparable foreign regulatory authorities;
- the frequency, duration and severity of potential adverse events in clinical trials;
- whether we are required by the FDA or other comparable foreign regulatory authorities to conduct additional clinical trials or other studies beyond those planned to support the approval and commercialization of our product candidates;
- maintaining and establishing relationships with contract research organizations (“CROs”) and clinical sites for the clinical development of our product candidates both in the United States and internationally;
- our ability to demonstrate the safety and efficacy of our product candidates to the satisfaction of the FDA and comparable regulatory authorities;
- timely receipt of marketing approvals from applicable regulatory authorities, including new drug applications (“NDAs”) from the FDA and maintaining such approvals;
- our ability and the ability of third parties with whom we contract to manufacture adequate clinical and commercial supplies of our product candidates or any future product candidates, remain in good standing with regulatory authorities and develop, validate and maintain commercially viable manufacturing processes that are compliant with current good manufacturing practices (“cGMPs”);
- establishing sales, marketing and distribution capabilities and launching commercial sales of our products, if and when approved, whether alone or in collaboration with others;
- establishing and maintaining patent and trade secret protection or regulatory exclusivity for our product candidates;
- the willingness of physicians, operators of clinics and patients to utilize or adopt any of our product candidates over alternative or more conventional therapies, such as chemotherapy, to treat solid tumors;
- maintaining an acceptable safety profile of our products following approval, if any; and
- maintaining and growing an organization of people who can develop and commercialize our products and technology.

Many of the factors listed above are beyond our control and could cause us to experience significant delays or prevent us from obtaining regulatory approvals or commercializing our product candidates. If we or our collaborator are unable to develop, obtain regulatory approval for, or, if approved, successfully commercialize our product candidates, we may not be able to generate sufficient revenue to continue our business.

Our approach to the discovery and development of product candidates based on our technology platform is unproven, and we do not know whether we will be able to develop any products of commercial value, or if competing approaches will limit the commercial value of our product candidates.

The success of our business depends primarily upon our ability to identify, develop and commercialize our product candidates based on our proprietary selective translation regulation technology platform. Additionally, some of the disease-driving proteins that our product candidates are designed to downregulate are not adequately addressed by any approved therapies, which we believe is due to the location and complexity of these targets. While we believe we have observed favorable preclinical study and early clinical trial results related to product candidates based on our technology platform, we have not yet succeeded and may not succeed in demonstrating efficacy and safety for any product candidates in clinical trials or in obtaining marketing approvals from the FDA or other regulatory authorities or in commercializing such product candidates. Any product candidates based on our proprietary selective translation technology platform may be shown to have harmful side effects or may have other characteristics that may necessitate additional clinical testing, or make the product candidates unmarketable or unlikely to receive marketing approval. In particular, our novel approach of targeting the components of the eIF4F complex and its activating kinases, mitogen-activated protein kinases (“MAPK”) interacting kinases (“MNK”) to simultaneously downregulate multiple disease-driving proteins may have unexpected consequences, including adverse events that preclude successful development and approval of our product candidates. Further, because all of our current product candidates and development programs are focused on the eIF4F complex and MNK, adverse developments with respect to one of our product candidates or development programs may have a significant adverse impact on the actual or perceived likelihood of success and value of our other product candidates or development programs.

In addition, the biotechnology and biopharmaceutical industries are characterized by rapidly advancing technologies. Our future success will depend in part on our ability to maintain a competitive position with our scientific approach. If we fail to stay at the forefront of technological change in utilizing our approach to create and develop STRI product candidates, we may be unable to compete effectively. Our competitors may render our approach obsolete, or limit the commercial value of our product candidates by advances in existing technological approaches or the development of new or different approaches, potentially eliminating the advantages in our drug discovery process that we believe we derive from our approach. By contrast, adverse developments with respect to other companies that attempt to use a similar approach to our approach may adversely impact the actual or perceived value and potential of our product candidates. If any of these events occur, we may be forced to delay, modify, or abandon our development efforts for a program or programs, which would have a material adverse effect on our business and could potentially cause us to cease operations.

Clinical and preclinical development involves a lengthy and expensive process with an uncertain outcome, and the results of preclinical studies and early clinical trials are not necessarily predictive of future results. Any of our product candidates may not have favorable results in later clinical trials, if any, or receive regulatory approval on a timely basis, if at all.

Clinical and preclinical development is expensive and can take many years to complete, and its outcome is inherently uncertain. We cannot guarantee that any clinical trials or preclinical studies will be conducted as planned or completed on schedule, if at all, and failure can occur at any time during the preclinical study or clinical trial process, including due to factors that are beyond our control. Further, we may not be able to meet expected timeframes for data readouts for our clinical trials. Despite promising preclinical or clinical results, any product candidate can unexpectedly fail at any stage of preclinical or clinical development. The historical failure rate for product candidates in our industry is high. The results from preclinical studies or clinical trials of a product candidate or a competitor’s product candidate in the same class may not predict the results of later clinical trials of our product candidate, and interim, topline or preliminary results of a clinical trial are not necessarily indicative of final results. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy characteristics despite having progressed through preclinical studies and initial clinical trials. In particular, while we

have conducted certain preclinical studies and early clinical trials of tomivosertib, we do not know whether tomivosertib will perform in ongoing and future clinical trials as it has performed in these prior studies. It is not uncommon to observe results in clinical trials that are unexpected based on preclinical studies and early clinical trials, and many product candidates fail in clinical trials despite very promising early results. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving promising results in earlier studies.

For the foregoing reasons, we cannot be certain that our ongoing and planned clinical trials and preclinical studies will be successful. 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.

Any difficulties or delays in the commencement or completion, or any terminations or suspensions, of our current or planned clinical trials could result in increased costs to us, delay or limit our ability to generate revenue and adversely affect our commercial prospects.

In order to obtain FDA approval to market a new drug we must demonstrate the safety and efficacy of our product candidates in humans to the satisfaction of the FDA. To meet these requirements, we will have to conduct adequate and well-controlled clinical trials. Clinical testing is expensive, time-consuming and subject to uncertainty.

Before we or our collaborator can initiate clinical trials for a product candidate, we or they must submit the results of preclinical studies to the FDA or comparable foreign regulatory authorities along with other information, including information about product candidate chemistry, manufacturing and controls and proposed clinical trial protocol, as part of an IND or similar regulatory submission. The FDA or comparable foreign regulatory authorities may require us or our collaborators to conduct additional preclinical studies for any product candidate before it allows us to initiate clinical trials under any IND or similar regulatory submission, which may lead to delays and increase the costs of our preclinical development programs. Moreover, even if these trials begin, issues may arise that could cause regulatory authorities to suspend or terminate such clinical trials. Any delays in the commencement or completion of our ongoing and planned clinical trials for our current and any future product candidate could significantly affect our product development timelines and product development costs.

We do not know whether our planned trials will begin on time or be completed on schedule, if at all. The commencement, data readouts, and completion of clinical trials can be delayed for a number of reasons, including delays related to:

- inability to generate sufficient preclinical, toxicology, or other in vivo or in vitro data to support the initiation or continuation of a clinical trial;
- obtaining regulatory authorizations to commence a trial or reaching a consensus with regulatory authorities on trial design or implementation;
- any failure or delay in reaching an agreement with CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- delays in identifying, recruiting and training suitable clinical investigators;
- delays in obtaining approval from one or more institutional review boards (“IRBs”) or ethics committees at clinical trial sites;
- IRBs refusing to approve, suspending or terminating the trial at an investigational site, precluding enrollment of additional subjects, or withdrawing their approval of the trial;
- changes to the clinical trial protocol;
- clinical sites deviating from the trial protocol or dropping out of a trial;
- failure by us or our CROs to perform in accordance with good clinical practice (“GCP”) requirements or applicable regulatory guidelines in other countries;
- manufacturing sufficient quantities of product candidate or obtaining sufficient quantities of combination therapies for use in clinical trials;

- subjects failing to enroll or remain in our trials at the rate we expect, or failing to return for post-treatment follow-up, including subjects failing to remain in our trials due to movement restrictions, health reasons or otherwise resulting from the COVID-19 pandemic;
- patients choosing alternative treatments for the indications for which we are developing our product candidates, or participating in competing clinical trials;
- lack of adequate funding to continue the clinical trials or costs being greater than we anticipate;
- subjects experiencing severe or unexpected drug-related adverse effects;
- occurrence of serious adverse events in trials of the same class of agents conducted by other companies;
- imposition of a temporary or permanent clinical hold by regulatory authorities;
- selection of clinical endpoints that require prolonged periods of clinical observation or analysis of the resulting data;
- the costs of clinical trials of our product candidates being greater than we anticipate;
- transfer of manufacturing processes to larger-scale facilities operated by a contract manufacturing organization, (“CMO”) delays or failure by our CMOs or us to make any necessary changes to such manufacturing process, or failure of our CMOs to produce clinical trial materials in accordance with cGMPs regulations or other applicable requirements; and
- third parties being unwilling or unable to satisfy their contractual obligations to us in a timely manner.

Clinical trials must be conducted in accordance with the FDA and other applicable regulatory authorities’ legal requirements, regulations or guidelines, and are subject to oversight by these governmental agencies and Ethics Committees or IRBs at the medical institutions where the clinical trials are conducted. We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by a Data Safety Monitoring Board for such trial or by the FDA or comparable foreign regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or comparable foreign regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. In addition, changes in regulatory requirements and policies may occur, and we may need to amend clinical trial protocols to comply with these changes. Amendments may require us to resubmit our clinical trial protocols to IRBs for reexamination, which may impact the costs, timing or successful completion of a clinical trial.

Further, our conduct of clinical trials in foreign countries presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks, including war, relevant to such foreign countries.

In addition, many of the factors that cause, or lead to, the termination or suspension of, or a delay in the commencement or completion of, clinical trials may also ultimately lead to the denial of regulatory approval of a product candidate. We may make formulation or manufacturing changes to our product candidates, in which case we may need to conduct additional preclinical studies and/or clinical trials to show that the results obtained from such new formulations are consistent with previous results. Any delays to our clinical trials that occur as a result could shorten any period during which we may have the exclusive right to commercialize our product candidates and our competitors may be able to bring products to market before we do, and the commercial viability of our product candidates could be significantly reduced. Any of these occurrences may harm our business, financial condition and prospects significantly.

We may find it difficult to enroll patients in our clinical trials. If we encounter difficulties enrolling subjects in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to identify and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the United States. Subject enrollment, a significant factor in the timeline of clinical trials, is affected by many factors including the size and characteristics of the patient population, the proximity of patients to clinical sites, the eligibility and exclusion criteria for the trial, the design of the clinical trial, the risk that enrolled patients will not complete a clinical trial, our ability to recruit clinical trial investigators with the appropriate competencies and experience, our ability to obtain and maintain patient consents, patient referral practices of physicians, ability to monitor patients adequately during and after treatment, competing clinical trials and clinicians' and patients' perceptions as to the potential advantages and risks 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 as well as any product candidates under development.

We will be required to identify and enroll a sufficient number of subjects for each of our clinical trials. Potential subjects for any planned clinical trials may not be adequately diagnosed or identified with the diseases which we are targeting or may not meet the entry criteria for such trials. We also may encounter difficulties in identifying and enrolling patients with a stage of disease appropriate for our ongoing and planned clinical trials and monitoring such patients adequately during and after treatment. The large number of clinical trials concurrently seeking to enroll patients with NSCLC and breast cancers, as well as the other cancers we intend to evaluate, may result in delays or difficulties enrolling a sufficient number of patients, particularly patients that meet our specific enrollment criteria, and completing the trials on schedule, if at all. We may not be able to initiate or continue clinical trials if we are unable to locate a sufficient number of eligible subjects to participate in the clinical trials required by the FDA or comparable foreign regulatory authorities. In addition, the process of finding and diagnosing patients is and will likely continue to be costly. The timing of our clinical trials depends, in part, on the speed at which we can recruit patients to participate in our trials, as well as completion of required follow-up periods. The eligibility criteria of our clinical trials further limits the pool of available trial participants. If patients are unwilling to participate in our trials for any reason, including the existence of concurrent clinical trials for similar patient populations, the availability of approved therapies or as a result of the COVID-19 pandemic, or we otherwise have difficulty enrolling a sufficient number of patients, the timeline for recruiting subjects, conducting studies and obtaining regulatory approval of our product candidates may be delayed. For example, in January 2023, we announced enrollment challenges due to staffing issues and completion of other trials across clinical sites for both the frontline PD-L1>50% cohort and the PD-L1>1% maintenance cohort of our KICKSTART trial of tomivosertib in combination with patients with metastatic NSCLC. As a result, we have discontinued enrollment in the PD-L1>1% cohort and focused on enrollment in the PD-L1>50% cohort. We anticipate topline data from the PD-L1>50% cohort in the second half of 2023. While we have taken steps to mitigate the impact of these factors, there can be no assurance that these efforts will enhance enrollment. Additionally, because our clinical trials may enroll patients with advanced/metastatic cancers, the patients are typically in the late stages of their disease and may experience clinical disease progression independent from our product candidates, making them unevaluable for purposes of the clinical trial and requiring additional patient enrollment. Our inability to enroll a sufficient number of subjects for any of our future clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. In addition, we expect to rely on CROs and clinical trial sites to ensure proper and timely conduct of our future clinical trials, and while we have entered into agreements governing their services, we have limited influence over their actual performance. We cannot assure you that our assumptions used in determining expected clinical trial timelines are correct or that we will not experience delays in enrollment, which would result in the delay of completion of such trials beyond our expected timelines.

Use of our product candidates could be associated with side effects, adverse events or other properties or safety risks, which could delay or preclude approval, cause us to suspend or discontinue clinical trials, abandon a product candidate, limit the commercial profile of an approved label or result in other significant negative consequences that could severely harm our business, prospects, operating results and financial condition.

As is the case with oncology drugs generally, it is likely that there may be side effects and adverse events associated with use of our product candidates. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. Undesirable side effects caused by our product candidates when used alone or in combination with other approved drugs or investigational agents could cause us or

regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label, or lead to the delay or denial of regulatory approval by the FDA or comparable foreign regulatory authorities. The drug-related side effects could 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.

Moreover, if our product candidates are associated with undesirable side effects in clinical trials or have characteristics that are unexpected, we may elect to abandon their development or limit their 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, which may limit the commercial expectations for the product candidate if approved. We may also be required to modify our study plans based on findings in our ongoing clinical trials.

In our Phase 1 dose escalation trial of tomivosertib in solid tumor patients, using a capsule formulation, the most frequent treatment-related adverse events (“TRAEs”) were nausea, vomiting, fatigue, constipation, dyspepsia and tremor. At doses that exceeded our recommended Phase 2 dose (“RP2D”), we observed a higher incidence and severity of TRAEs. In our Phase 1 dose escalation trial of tomivosertib in lymphoma patients, the most common TRAEs experienced by patients in the RP2D expansion cohort were nausea, vomiting, hypercalcemia, and fatigue. In our Phase 2a trial of tomivosertib combined with anti-PD-(L)1 agents, the most common TRAEs were nausea, fatigue, tremor, vomiting, increased aspartate aminotransferase and increased alanine aminotransferase. These TRAEs were generally Grade 1 or 2 in severity, although alanine aminotransferase increase, blood creatine phosphokinase increase and rash were experienced as Grade 3 in two patients each.

In the completed Phase 1 dose escalation portion of our Phase 1/2 clinical trial of zotatifin in patients with solid tumors with certain mutations, we have observed three dose limiting toxicities (“DLTs”). The first DLT, observed in the 0.035mg/kg IV weekly cohort, was a Grade 2 thrombocytopenia that prevented the completion of continued therapy throughout the DLT window. The second and third DLTs were observed in the 0.1 mg/kg IV two weeks on and one week off cohort. Thus the 0.1 mg/kg dose exceeded the maximum tolerated dose (“MTD”). One patient experienced a DLT of Grade 3 anemia and another patient experienced a DLT of Grade 3 GI bleed in the setting of Grade 2 thrombocytopenia. Overall adverse events (“AEs”) across all dose levels included predominantly Grade 1 and Grade 2 nausea, vomiting and anemia.

We may be required to modify our development and clinical trial plans based on findings in our ongoing clinical trials. 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 or, in larger patient populations, failed to demonstrate statistically significant efficacy. In addition, regulatory authorities may draw different conclusions or require additional testing to further explore adverse safety findings.

It is possible that as we test our product candidates in larger, longer and more extensive clinical trials, including with different dosing regimens, or as the use of these product candidates becomes more widespread if they receive regulatory approval, illnesses, injuries, discomforts and other adverse events that were observed in earlier trials, as well as conditions that did not occur or went undetected in previous trials, may be reported by subjects. If such side effects become known later in development or upon approval, if any, such findings may harm our business, financial condition and prospects significantly. In addition, our ongoing and planned clinical trials of tomivosertib in combination with inhibitors of programmed cell death protein 1 (“PD-1”) and programmed cell death ligand 1 (“PD-L1”) (collectively, “Anti-PD-(L)1” therapy) may result in adverse events based on the combination therapy that may negatively impact the reported adverse event profile in such clinical trial. Anti-PD-(L)1 therapy has been shown to have adverse events, including immune-related adverse events on the liver and other organ systems, which may limit the maximum dose in our clinical trials or otherwise negatively impact our combination 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 candidates 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.

In addition, if one or more of our product candidates receives marketing approval, and we or others later identify undesirable side effects caused by any such product, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw, suspend or limit approvals of such product, or seek an injunction against its manufacture or distribution;
- we may be required to recall a product or change the way such product is administered to patients;
- regulatory authorities may require additional warnings on the label, such as a “black box” warning or a contraindication;
- we may be required to implement a Risk Evaluation and Mitigation Strategy (“REMS”) or create a medication guide outlining the risks of such side effects for distribution to patients;
- we may be required to change the way a product is distributed or administered, conduct additional clinical trials or change the labeling of a product or be required to conduct additional post-marketing studies or surveillance;
- we could be sued and held liable for harm caused to patients;
- sales of the product may decrease significantly or the product could become less competitive; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, results of operations and prospects.

As an organization, we have never completed pivotal clinical trials and may be unable to do so for any of our product candidates.

We will need to successfully complete our planned clinical trials and later-stage and pivotal clinical trials in order to obtain FDA or comparable foreign regulatory approval to market our product candidates. Carrying out later-stage clinical trials and the submission of a successful NDA is a complicated process. As an organization, we have not previously conducted any pivotal clinical trials, have limited experience in preparing and submitting marketing applications, and have not previously submitted an NDA or other comparable foreign regulatory submission for any product candidate. In addition, we have had limited interactions with the FDA and cannot be certain how many additional clinical trials of our product candidates will be required or how such trials should be designed. Consequently, we may be unable to successfully and efficiently execute and complete necessary clinical trials in a way that leads to regulatory submission and approval of our product candidates. We may require more time and incur greater costs than our competitors and may not succeed in obtaining regulatory approvals of product candidates that we develop. Failure to commence or complete, or delays in, our planned clinical trials, could prevent us from or delay us in submitting NDAs for and commercializing our product candidates.

We are developing our product candidates to be used in combination with additional therapies, which exposes us to additional risks.

We are developing tomivosertib for use in combination with one or more currently approved anti-PD-(L)1 therapies and zotatifin for use in combination with ER inhibitors, such as fulvestrant, HER2 inhibitors, Herceptin, KRAS G12C inhibitors and abemaciclib, a CDK4/6 inhibitor. Fulvestrant is generic and marketed by several companies including Astrazeneca who markets it under the brand name Faslodex for the treatment of breast cancer. Herceptin is owned and marketed by Genentech for the treatment of breast cancer and other cancers. Two KRAS G12C inhibitors have now been approved for the treatment of NSCLC. Abemaciclib is marketed by Eli Lilly and Company under the name Verzenio for the treatment of ER+/Her2-breast cancer. Therefore, even if tomivosertib or zotatifin were to receive marketing approval or be commercialized for use in combination, we would continue to bear the risks that the FDA or similar foreign regulatory authorities could revoke approval of the anti-PD-(L)1 therapy or the ER, HER2 or KRAS G12C inhibitors used in combination with tomivosertib or zotatifin, respectively, or that safety, efficacy, manufacturing or supply issues could arise with these combination therapies. Combination therapies are commonly used for the treatment of cancer, and we would be subject to similar risks if we develop other product candidates for use in combination with other classes of oncology therapies. Developing combination

therapies using approved anti-PD-(L)1 therapies, or ER, HER2 and KRAS G12C inhibitors, as we plan to do for tomivosertib and zotatifin, respectively, also exposes us to additional clinical and development-related risks, such as the requirement that we collect data to demonstrate the safety and efficacy of each active component of any combination regimen we may develop. In addition, we may also evaluate the combination of tomivosertib, zotatifin or other product candidates with one or more other cancer therapies that have not yet been approved for marketing by the FDA or similar foreign regulatory authorities. We may not be able to market and sell our product candidates for use in combination regimens with any such unapproved cancer therapies that do not ultimately obtain their own marketing approvals.

If the FDA or similar foreign regulatory authorities do not approve these other combination agents or revoke their approval of, or if safety, efficacy, manufacturing, or supply issues arise with the drugs we choose to evaluate in combination with our product candidates, we may be unable to obtain approval of or market tomivosertib, zotatifin or other product candidates for combination therapy regimens.

Additionally, the use of one or more combination agents in our clinical trials increases the costs of such clinical trials. Furthermore, 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 costs of combination therapies are 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 may expend our limited resources to pursue a particular product candidate and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on specific product candidates, and specific indications. As a result, we may forgo or delay pursuit of opportunities with other product candidates that could have had greater commercial potential. Specifically, we are developing product candidates that singularly target the eIF4F complex and its activating kinase, MNK, and we are prioritizing the development of our product candidates in indications that are sensitive to the inhibition of these targets. For example, after completion of a combination trial of tomivosertib and avelumab, a PD-L1 inhibitor, in patients with microsatellite stable colorectal cancer, which is generally not responsive to immunological agents, we elected to focus future development of tomivosertib on more immune-responsive cancers. Similarly, we stopped our clinical trial evaluating tomivosertib in patients with castrate-resistant prostate cancer to focus on the development of tomivosertib in combination with anti-PD-(L)1 therapies. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable product candidates. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaborations, licenses and other similar arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

Interim, topline and preliminary data from our clinical trials and preclinical studies 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, topline or preliminary data from our clinical trials and preclinical studies, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a full analyses of all data related to the particular trial. We also make assumptions, estimations, calculations and 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 interim, topline, or preliminary results that we report may differ from future results of the same trials, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline and preliminary 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, topline and preliminary data should be viewed with caution until the final data are available.

We may also disclose interim data from our 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. Adverse differences between interim, topline, or preliminary data and final data could significantly harm our business prospects.

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, the approvability or commercialization of the particular product candidate or product and our business in general. In addition, the information we choose to publicly disclose 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 the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular drug, product candidate or our business. If the interim, topline, 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, our business, operating results, prospects or financial condition may be harmed.

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

As product candidates progress through 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 safety, efficacy, yield and manufacturing batch size, minimize costs and achieve consistent quality and results. For example, our completed Phase 1b trial of zotatifin in patients with mild to moderate COVID-19 began utilizing the same IV formulation currently being used in cancer trials, but switched to a newly developed sub-cutaneous formulation for the last 34 patients enrolled. Pharmacokinetics results show a profile of drug concentrations in blood over time virtually identical to the IV formulation, suggesting the more convenient sub-cutaneous formulation could be used in future COVID or cancer trials. However, there can be no assurance that such changes will achieve our intended objectives. These changes and any future changes we may make to our product candidates may also cause such candidates to perform differently and affect the results of future clinical trials. Such changes or related unfavorable clinical trial results could delay initiation or completion of additional clinical trials, require the conduct of bridging studies or clinical trials or the repetition of one or more studies or clinical trials, increase development costs, delay or prevent potential marketing approval and jeopardize our ability to commercialize our product candidates, if approved, and generate revenue.

We may attempt to secure approval from the FDA or comparable foreign regulatory authorities through the use of accelerated approval pathways. If we are unable to obtain such approval, we may be required to conduct additional clinical trials beyond those that we contemplate, which could increase the expense of obtaining, and delay the receipt of, necessary marketing approvals. Even if we receive accelerated approval from the FDA, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA may seek to withdraw accelerated approval.

We may in the future seek accelerated approval for our one or more of our product candidates. Under the accelerated approval program, the FDA may grant accelerated approval to a product candidate designed to treat a serious or life-threatening condition that provides meaningful therapeutic benefit over available therapies upon a determination that the product candidate has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as irreversible morbidity or mortality. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. The accelerated approval pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage, but is a clinically important improvement from a patient and public health perspective. If granted, accelerated approval is usually contingent on the sponsor's agreement to conduct, in a diligent manner, additional confirmatory studies to verify and describe the drug's clinical benefit. If such post-approval studies fail to confirm the drug's clinical benefit or are not completed in a timely manner, the FDA may withdraw its approval of the drug on an expedited basis. In addition, in December 2022, the President signed an omnibus appropriations bill to fund the U.S. government through fiscal year 2023. Included in the omnibus appropriations bill is the Food and Drug Omnibus Reform Act of 2022, which among other

things, introduced reforms intended to expand the FDA's ability to regulate products receiving accelerated approval, including by increasing the FDA's oversight over the conduct of confirmatory trials; however, the ultimate impact of these reforms remains unclear.

Prior to seeking accelerated approval for any of our product candidates, we intend to seek feedback from the FDA and will otherwise evaluate our ability to seek and receive accelerated approval. There can be no assurance that after our evaluation of the feedback and other factors we will decide to pursue or submit an NDA for accelerated approval or any other form of expedited development, review or approval. Furthermore, if we decide to submit an application for accelerated approval or receive for our product candidates, there can be no assurance that such application will be accepted or that any expedited development, review or approval will be granted on a timely basis, or at all. The FDA or other comparable foreign regulatory authorities could also require us to conduct further studies prior to considering our application or granting approval of any type. A failure to obtain accelerated approval or any other form of expedited development, review or approval for our product candidate would result in a longer time period to commercialization of such product candidate, if any, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace.

Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire, retain or deploy 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, 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, statutory, regulatory and policy changes, the FDA's ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the FDA have fluctuated in recent years. In addition, government funding of other government agencies 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 or modifications to approved drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities.

Separately, in response to the COVID-19 pandemic, the FDA postponed most inspections of domestic and foreign manufacturing facilities at various points. Even though the FDA has since resumed standard inspection operations of domestic facilities where feasible, the FDA has continued to monitor and implement changes to its inspectional activities to ensure the safety of its employees and those of the firms it regulates as it adapts to the evolving COVID-19 pandemic, and any resurgence of the virus or emergence of new variants may lead to further inspectional delays. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

We may seek orphan drug designation for certain future product candidates, but we may be unable to obtain such designation or to obtain or maintain the benefits associated with orphan drug designation, including market exclusivity, which may cause our product revenue, if any, to be reduced.

We may seek orphan product designation for some of our product candidates; however, we may never receive such designations. Under the Orphan Drug Act, the FDA may designate a drug product as an orphan drug if it is intended to treat a rare disease or condition, defined as a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. Orphan drug designation must be requested before submitting an NDA. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and application fee waivers. After the FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA.

In addition, if a product receives the first FDA approval for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer is unable to assure sufficient product quantity for the orphan patient population. Exclusive marketing rights in the United States may also be unavailable if we or our collaborators seek approval for an indication broader than the orphan designated indication and may be lost if the FDA later determines that the request for designation was materially defective.

Even if we obtain orphan drug designation, we may not be the first to obtain marketing approval for any particular orphan indication due to the uncertainties associated with developing pharmaceutical products. Further, even if we obtain orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is safer, more effective, or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

If we are required by the FDA to obtain approval of a companion diagnostic test in connection with approval of any of our product candidates, and we do not obtain or face delays in obtaining FDA approval of a diagnostic test, we will not be able to commercialize such product candidate and our ability to generate revenue will be materially impaired.

If safe and effective use of any of our product candidates depends on an *in vitro* diagnostic that is not otherwise commercially available, then the FDA generally will require approval or clearance of that diagnostic, known as a companion diagnostic, at the same time that the FDA approves our product candidates, if at all. According to FDA guidance, if the FDA determines that a companion diagnostic test is essential to the safe and effective use of a novel therapeutic product or indication, the FDA generally will not approve the therapeutic product or new therapeutic product indication if the companion diagnostic is not also approved or cleared for that indication. If a satisfactory companion diagnostic is not commercially available, we may be required to develop or obtain one that would be subject to regulatory approval requirements. The process of obtaining or creating such diagnostics is time consuming and costly.

Companion diagnostics are developed in conjunction with clinical programs for the associated product and are subject to regulation as medical tests by the FDA and comparable regulatory authorities, and, to date, the FDA has generally required premarket approval of companion diagnostics for cancer therapies. The approval of a companion diagnostic as part of the therapeutic product's labeling limits the use of the therapeutic product to only those patients who express the specific genetic alteration that the companion diagnostic was developed to detect. If the FDA or a comparable regulatory authority requires approval of a companion diagnostic for any of our product candidates, whether before or after it obtains marketing approval, we, and/or future collaborators, may encounter difficulties in developing and obtaining approval for such product candidate. Any delay or failure by us or third-party collaborators to develop or obtain regulatory approval of a companion diagnostic could delay or prevent approval or continued marketing of such product candidate. We may also experience delays in developing a sustainable, reproducible and scalable manufacturing process for the companion diagnostic or in transferring that process to commercial partners or negotiating insurance reimbursement plans, all of which may prevent us from completing our clinical trials or commercializing our product candidate, if approved, on a timely or profitable basis, if at all.

Risks Related to Our Reliance on Third Parties

We rely on third parties to conduct our clinical trials and preclinical studies. If these third parties do not successfully carry out their contractual duties, comply with applicable regulatory requirements or meet expected deadlines, our development programs and our ability to seek or obtain regulatory approval for or commercialize our product candidates may be delayed.

We are dependent on third parties to conduct our clinical trials and preclinical studies. Specifically, we have used and relied on, and intend to continue to use and rely on, medical institutions, clinical investigators, CROs and consultants to conduct our preclinical studies and clinical trials in accordance with our clinical protocols and

regulatory requirements. These CROs, investigators and other third parties play a significant role in the conduct and timing of these trials and subsequent collection and analysis of data. While we have and will have agreements governing the activities of our third-party contractors, we have limited influence over their actual performance. Nevertheless, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on our CROs and other third parties does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with GCP requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for all of our product 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 our CROs or trial sites fail to comply with applicable GCPs, the clinical data generated in our clinical trials 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. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

There is no guarantee that any of our CROs, investigators or other third parties will devote adequate time and resources to such trials or studies or perform as contractually required. If any of these third parties fail to meet expected deadlines, adhere to our clinical protocols or meet regulatory requirements, or otherwise performs in a substandard manner, our clinical trials may be extended, delayed or terminated. In addition, many of the third parties with whom we contract may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other development activities that could harm our competitive position. In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA concludes that the financial relationship may have affected the interpretation of the study, the integrity of the data generated at the applicable clinical trial site may be questioned and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection by the FDA of any NDA we submit. Any such delay or rejection could prevent us from commercializing our product candidates.

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 terminate, we may not be able to enter into arrangements with alternative third parties on commercially reasonable terms or at all. Switching or adding additional CROs, investigators and other third parties involves additional cost and requires our management's 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 our desired clinical development timelines. Though we carefully manage our relationships with our CROs, investigators and other third parties, 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 rely on third parties for the manufacture of our product candidates for clinical and preclinical development and expect to continue to do so for the foreseeable future. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not own or operate manufacturing facilities and have no plans to develop our own clinical or commercial- scale manufacturing capabilities. We rely, and expect to continue to rely, on third parties for the manufacture of our product candidates and related raw materials for clinical and preclinical development, as well as for commercial manufacture if any of our product candidates receive marketing approval. The facilities used by third-party manufacturers to manufacture our product candidates must be approved by the FDA and any comparable foreign regulatory authority pursuant to inspections that will be conducted after we submit an NDA to the FDA or any comparable submission to a foreign regulatory authority. We do not control the manufacturing process of, and are completely dependent on, third-party manufacturers for compliance with cGMP requirements for manufacture of products. If these third-party manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or any comparable foreign regulatory authority,

they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, we have no control over the ability of third-party manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or any 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 regulatory 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 clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products.

Our or a third party's failure to execute on our manufacturing requirements on commercially reasonable terms and in compliance with cGMP or other regulatory requirements could adversely affect our business in a number of ways, including:

- an inability to initiate clinical trials of our product candidates under development;
- delay in submitting regulatory applications, or receiving marketing approvals, for our product candidates;
- additional inspections by regulatory authorities of third-party manufacturing facilities or our manufacturing facilities;
- requirements to cease development or to recall batches of our product candidates; and
- in the event of approval to market and commercialize our product candidates, an inability to meet commercial demands for our product candidates or any other future product candidates.

In addition, we do not have any long-term commitments or supply agreements with our third-party manufacturers. We may be unable to establish any supply agreements with our third-party manufacturers or to do so on acceptable terms, which increases the risk of timely obtaining sufficient quantities of our product candidates or such quantities at an acceptable cost. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- failure of third-party manufacturers to comply with regulatory requirements and maintain quality assurance;
- breach of the manufacturing agreement by the third party;
- failure to manufacture our product according to our specifications;
- failure to manufacture our product according to our schedule or at all;
- misappropriation of our proprietary information, including our trade secrets and know-how; and
- termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

Our product candidates and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us, in particular due to the high potency of zotatifin. Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval, and any related remedial measures may be costly or time-consuming to implement. We do not currently have arrangements in place for redundant supply or a second source for all required raw materials used in the manufacture of our product candidates. If our existing or future third-party manufacturers cannot perform as agreed, we may be required to replace such manufacturers and we may be unable to replace them on a timely basis or at all. In particular, any replacement of our manufacturers could require significant effort and expertise because there may be a limited number of qualified replacements. In some cases, the technical skills or technology required to manufacture our product candidates may be unique or proprietary to the original manufacturer and we may have difficulty transferring such skills or technology to another third-party and a feasible alternative may not exist. In addition, certain of our product candidates and our own proprietary methods have never been produced or implemented outside of our company, and we may therefore experience delays to our development

programs if and when we attempt to establish new third-party manufacturing arrangements for these product candidates or methods.

Our current and anticipated future dependence upon others for the manufacture of our product candidates or products may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis.

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Because we currently rely on third parties to manufacture our product candidates and to perform quality testing, and because we collaborate with various organizations and academic institutions for the advancement of certain of our development programs, we must, at times, share our proprietary technology and confidential information, including trade secrets, with them. We seek to protect our proprietary technology, in part, by entering into confidentiality agreements and, if applicable, material transfer agreements, collaborative research agreements, consulting agreements or other similar agreements with our collaborators, advisors, employees and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information. 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 and despite our efforts to protect our trade secrets, a competitor's discovery of our proprietary technology and confidential information or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business, financial condition, results of operations and prospects.

We are dependent on the Pfizer Agreement for the discovery, development and commercialization of small molecule inhibitors of eIF4E. Pfizer may unilaterally terminate the agreement for convenience, which could materially and adversely affect our business.

In December 2019, we entered into the Pfizer Agreement for our earliest stage program, inhibitors of eIF4E, and Pfizer is currently conducting IND-enabling studies for this program. Under the Pfizer Agreement, we were responsible for initial research in collaboration with Pfizer, and Pfizer is responsible for all further development of our eIF4E development program, including submission of an IND and conducting all clinical development and commercialization activities. Pfizer primarily controls the development activities, pursuant to the terms of the Pfizer Agreement, and our lack of control over such activities could result in delays or other difficulties in the development and commercialization of our eIF4E program. Any dispute with Pfizer may result in the delay or termination of the development or commercialization of this program, and may result in costly litigation that diverts our management's attention and resources away from our day-to-day activities and which may adversely affect our business, financial condition, results of operation and prospects.

In addition, Pfizer can terminate the Pfizer Agreement (including for convenience), and in the event Pfizer terminates the Pfizer Agreement, we would no longer be eligible to receive any development funding, milestone payments, royalty payments and other benefits under the agreement. In addition, any decision by Pfizer to terminate the Pfizer agreement may negatively impact public perception of our product candidates, which could adversely affect the market price of our Common Stock. We cannot provide any assurance with respect to the success of the collaboration with Pfizer. Any of the foregoing events could have a materially adverse effect on our on our business, financial condition, results of operations and prospects.

We may seek to enter into additional collaborations, licenses and other similar arrangements and may not be successful in doing so, and even if we are, we may relinquish valuable rights and may not realize the benefits of such relationships.

We may seek to enter into additional collaborations, joint ventures, licenses and other similar arrangements for the development or commercialization of our product candidates, due to capital costs required to develop or commercialize the product candidate or manufacturing constraints. Such collaborative discovery efforts may not yield additional development or product candidates for our pipeline. We may not be successful in our efforts to

establish or maintain such collaborations for our product candidates because our research and development pipeline may be insufficient, our product candidates may be deemed to be at too early of a stage of development for collaborative effort or third parties may not view our product candidates as having the requisite potential to demonstrate safety and efficacy or significant commercial opportunity. In addition, we face significant competition in seeking appropriate strategic partners, and the negotiation process can be time-consuming and complex. We may have to relinquish valuable rights to our future revenue streams, research programs or product candidates, or grant licenses on terms that may not be favorable to us, as part of any such arrangement, and such arrangements may restrict us from entering into additional agreements with other potential collaborators. We cannot be certain that, following a collaboration, license or strategic transaction, we will achieve an economic benefit that justifies such transaction.

Even if we are successful in our efforts to establish such collaborations, the terms that we agree upon may not be favorable to us, and we may not be able to maintain such collaborations if, for example, the development or approval of a product candidate is delayed, the safety of a product candidate is questioned or the sales of an approved product candidate are unsatisfactory.

In addition, any potential future collaborations may be terminable by our strategic partners, and we may not be able to adequately protect our rights under these agreements. Furthermore, strategic partners may negotiate for certain rights to control decisions regarding the development and commercialization of our product candidates, if approved, and may not conduct those activities in the same manner as we do. Any termination of collaborations we enter into in the future, or any delay in entering into collaborations related to our product candidates, could delay the development and commercialization of our product candidates and reduce their competitiveness if they reach the market, which could have a material adverse effect on our business, financial condition and results of operations.

Risks Related to Commercialization of Our Product Candidates

Even if we receive regulatory approval for any product candidate, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense.

Any regulatory approvals that we or our existing or future collaborators may receive for our product candidates will require the submission of reports to regulatory authorities and surveillance to monitor the safety and efficacy of the product, may contain significant limitations related to use restrictions for specified age groups, warnings, precautions or contraindications, and may include burdensome post-approval study or risk management requirements. For example, the FDA may require a REMS as a condition of approval of our product candidates, which could include 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. In addition, if the FDA or a comparable foreign regulatory authority approves our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping for our products will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMP and GCP requirements for any clinical trials that we conduct post-approval. Manufacturers of approved products and their facilities are subject to continual review and periodic, unannounced inspections by the FDA and other regulatory authorities for compliance with cGMP regulations and standards. Later discovery of previously unknown problems with our products, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of our products, withdrawal of the product from the market or voluntary or mandatory product recalls;
- restrictions on product distribution or use, or requirements to conduct post-marketing studies or clinical trials;
- fines, restitutions, disgorgement of profits or revenue, warning letters, untitled letters or holds on clinical trials;
- refusal by the FDA 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 our products; and
- injunctions or the imposition of civil or criminal penalties.

The occurrence of any event or penalty described above may inhibit our ability to commercialize our products and generate revenue and could require us to expend significant time and resources in response and could generate negative publicity.

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. We also 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. 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 be subject to enforcement action and we may not achieve or sustain profitability.

The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses.

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

The commercial success of our product candidates, if approved, will depend upon the degree of market acceptance of such product candidates by physicians, patients, healthcare payors and others in the medical community.

Our product candidates, if approved, may not be commercially successful. Even if any of our product candidates receive regulatory approval, they may not gain market acceptance among physicians, patients, healthcare payors or the medical community. The commercial success of any of our current or future product candidates will depend significantly on the broad adoption and use of the resulting product by physicians and patients for approved indications. The degree of market acceptance of our products will depend on a number of factors, including:

- demonstration of clinical efficacy and safety compared to other more-established products;
- the indications for which our product candidates are approved;
- the limitation of our targeted patient population and other limitations or warnings contained in any FDA-approved labeling;
- acceptance of a new drug for the relevant indication by healthcare providers and their patients;
- the pricing and cost-effectiveness of our products, as well as the cost of treatment with our products in relation to alternative treatments and therapies;
- our ability to obtain and maintain sufficient third-party coverage and adequate reimbursement from government healthcare programs, including Medicare and Medicaid, private health insurers and other third-party payors;
- the willingness of patients to pay all, or a portion of, out-of-pocket costs associated with our products in the absence of sufficient third-party coverage and adequate reimbursement;

- any restrictions on the use of our products, and the prevalence and severity of any adverse effects;
- potential product liability claims;
- the timing of market introduction of our products as well as competitive drugs;
- the effectiveness of our or any of our current or potential future collaborators' sales and marketing strategies; and
- unfavorable publicity relating to the product.

If any product candidate is approved but does not achieve an adequate level of acceptance by physicians, hospitals, healthcare payors or patients, we may not generate sufficient revenue from that product and may not become or remain profitable. Our efforts to educate the medical community and third-party payors regarding the benefits of our products may require significant resources and may never be successful.

The successful commercialization of our product candidates, if approved, will depend in part on the extent to which governmental authorities and health insurers establish coverage, adequate reimbursement levels and favorable pricing policies. Failure to obtain or maintain coverage and adequate reimbursement for our products could limit our ability to market those products and decrease our ability to generate revenue.

The availability of coverage and the adequacy of reimbursement by governmental healthcare programs such as Medicare and Medicaid, private health insurers and other third-party payors are essential for most patients to be able to afford prescription medications such as our product candidates, if approved. Our ability to achieve coverage and acceptable levels of reimbursement for our products by third-party payors will have an effect on our ability to successfully commercialize those products. Accordingly, we will need to successfully implement a coverage and reimbursement strategy for any approved product candidate. Even if we obtain coverage for a given product by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may impact physician utilization. We cannot be sure that coverage and reimbursement in the United States, the European Union or elsewhere will be available for any product that we may develop, and any reimbursement that may become available may be decreased or eliminated in the future.

Third-party payors increasingly are challenging prices charged for biopharmaceutical products and services, and many third-party payors may refuse to provide coverage and reimbursement for particular drugs when an equivalent generic drug or a less expensive therapy is available. It is possible that a third-party payor may consider our products as substitutable and only offer to reimburse patients for the less expensive product. Even if we are successful in demonstrating improved efficacy or improved convenience of administration with our products, pricing of existing drugs may limit the amount we will be able to charge for our products. These payors may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are too low to enable us to realize an appropriate return on our investment in product development. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our products and may not be able to obtain a satisfactory financial return on products that we may develop.

There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved products and products added to existing therapies as combinations. In the United States, third-party payors, including private and governmental payors, such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs will be covered. Some third-party payors may require pre-approval of coverage for new or innovative devices or drug therapies before they will reimburse healthcare providers who use such therapies. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our products.

Obtaining and maintaining reimbursement status is time-consuming, costly and uncertain. The Medicare and Medicaid programs increasingly are used as models for how private payors and other governmental payors develop their coverage and reimbursement policies for drugs. However, no uniform policy for coverage and reimbursement for products exists among third-party payors in the United States. Therefore, coverage and reimbursement for

products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases at short notice, and we believe that changes in these rules and regulations are likely.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe and other countries has and will continue to put pressure on the pricing and usage of our products. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medical 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 products. 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.

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our products. We expect to experience pricing pressures in connection with the sale of any of our products due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products.

We face significant competition from entities that have developed or may develop product candidates for cancer, including companies developing novel treatments and technology platforms. If our competitors develop technologies or product candidates more rapidly than we do or their technologies are more effective, our business and our ability to develop and successfully commercialize products may be adversely affected.

The biotechnology and biopharmaceutical industries are characterized by rapid advancing technologies, intense competition and a strong emphasis on proprietary and novel products and product candidates. Our competitors have developed, are developing or may develop products, product candidates and processes competitive with our product candidates, including products that may also be proposed to be administered in combination with PD-(L)1 inhibitors. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. We believe that a significant number of products are currently under development, and may become commercially available in the future, for the treatment of indications for which we may attempt to develop product candidates. In particular, there is intense competition in the oncology field. Our competitors include larger and better-funded pharmaceutical, biopharmaceutical, biotechnological and therapeutics companies. Moreover, we may also compete with universities and other research institutions who may be active in oncology research and could be in direct competition with us. We also compete with these organizations to recruit management, scientists and clinical development personnel, which could negatively affect our level of expertise and our ability to execute our business plan. We will also face competition in establishing clinical trial sites, enrolling subjects for clinical trials and in identifying and in-licensing new product candidates. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

If any of our product candidates is approved in oncology indications such as NSCLC or breast cancer, they will compete with small molecule therapies, biologics, cell-based therapies and traditional chemotherapy. In addition to competing with other therapies targeting similar indications, there are numerous other companies and academic institutions focused on similar targets as our product candidates and/or different scientific approaches to treating the same indications. These companies include, among others, AUM Biosciences, Boehringer Ingelheim GmbH, Eli Lilly & Company, Exelixis, Novartis AG, and Selvita, Inc., with programs targeting MNK. Companies with FDA-approved PD-1 or PD-L1 inhibitors include AstraZeneca plc, Bristol-Myers Squibb Co., Merck & Co., Inc., Pfizer Inc./Merck KGaA, Regeneron Pharmaceuticals, Inc. and Roche Group/Genentech, Inc. In addition, a number of companies are actively testing checkpoint inhibitors in combination with novel immuno-modulatory

agents including antibody therapeutics, small molecule inhibitors, oncolytic viruses, cancer vaccines and cell-based therapies.

Many of our competitors have significantly greater financial, technical, manufacturing, marketing, sales and supply resources or experience than we do. If we successfully obtain approval for any product candidate, we will face competition based on many different factors, including the safety and effectiveness of our products, the ease with which our products can be administered and the extent to which patients accept relatively new routes of administration, the timing and scope of regulatory approvals for these products, the availability and cost of manufacturing, marketing and sales capabilities, price, reimbursement coverage and patent position. Competing products could present superior treatment alternatives, including by being more effective, safer, more convenient, less expensive or marketed and sold more effectively than any products we may develop. Competitive products approaches may make any products we develop obsolete or noncompetitive before we recover the expense of developing and commercializing our product candidates. If we are unable to compete effectively, our opportunity to generate revenue from the sale of our products we may develop, if approved, could be adversely affected.

The market opportunities for our product candidates may be limited to patients who are ineligible for or have failed prior treatments and may be small or different from our estimates.

Cancer therapies are defined by lines of therapy as well as by treatment-naïve or previously-treated status patients. Often the initial approval for a new therapy is in later lines and subsequent approval in an earlier line may not be feasible. When cancer is detected early enough, first line therapy is sometimes adequate to cure the cancer or prolong life without a cure. Whenever first line therapy, including targeted therapy, immunotherapy, chemotherapy, hormone therapy, surgery or a combination of these, proves unsuccessful, second line therapy may be administered. Second line therapies often consist of additional chemotherapy, radiation, antibody drugs, tumor targeted small molecules or a combination of these. Third line therapies can include bone marrow transplantation, antibody and small molecule targeted therapies, more invasive forms of surgery and new technologies. In markets with approved therapies, there is no guarantee that our product candidates, even if approved, would be approved for second line or first line therapy. This could limit our potential market opportunity. In addition, we may have to conduct additional clinical trials prior to gaining approval for second line or first line therapy.

Our projections of both the number of people who have the cancers we are targeting, as well as the subset of people with these cancers in a position to receive later stage therapy and who have the potential to benefit from treatment with our product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including the scientific literature, publicly available clinical molecular reports, patient foundations or market research, and may prove to be incorrect. Further, new trials or information may change the estimated incidence or prevalence of these cancers. The number of patients in the United States and other major markets and elsewhere may turn out to be lower than expected, patients may not be otherwise amenable to treatment with our products or new patients may become increasingly difficult to identify or gain access to, all of which would adversely affect our results of operations and our business. Further, even if we obtain significant market share for our product candidates, because some of our potential target populations are very small, we may not achieve profitability in the future.

We currently have no marketing and sales organization and have no experience as a company in commercializing products, and we may have to invest significant resources to develop these capabilities. If we are unable to establish marketing and sales capabilities or enter into agreements with third parties to market and sell our products, we may not be able to generate product revenue.

We have no internal sales, marketing or distribution capabilities, nor have we commercialized a product. If any of our product candidates ultimately receives regulatory approval, we must build a marketing and sales organization with technical expertise and supporting distribution capabilities to commercialize each such product in major markets, which will be expensive and time-consuming, or collaborate 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 have no prior experience as a company in the marketing, sale and distribution of biopharmaceutical products and there are significant risks involved in building and managing a sales organization, including our ability to hire, retain and incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing and distribution

capabilities would adversely impact the commercialization of these products. We may not be able to enter into collaborations or hire consultants or external service providers to assist us in sales, marketing and distribution functions on acceptable financial terms, or at all. In addition, our product revenue and our profitability, if any, may be lower if we rely on third parties for these functions than if we were to market, sell and distribute any products that we develop ourselves. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we are not successful in commercializing our products, either on our own or through arrangements with one or more third parties, we may not be able to generate any future product revenue and we would incur significant additional losses.

Our future growth may depend, in part, on our ability to operate in foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties.

Our future growth may depend, in part, on our ability to develop and commercialize our product candidates in foreign markets. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from applicable regulatory authorities in foreign markets, and we may never receive such regulatory approvals for any of our product candidates. To obtain separate regulatory approval in many other countries we must comply with numerous and varying regulatory requirements regarding safety and efficacy and governing, among other things, clinical trials, commercial sales, pricing and distribution of our product candidates. If we obtain regulatory approval of our product candidates and ultimately commercialize our products in foreign markets, we would be subject to additional risks and uncertainties, including:

- different regulatory requirements for approval of drugs in foreign countries;
- reduced protection for intellectual property rights;
- the existence of additional third-party patent rights of potential relevance to our business;
- unexpected changes in tariffs, trade barriers and 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 currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- foreign reimbursement, pricing and insurance regimes;
- workforce uncertainty in countries where labor unrest is common;
- 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, or natural disasters including earthquakes, typhoons, floods and fires.

Risks Related to Our Business Operations and Industry

Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations or any guidance we may provide.

Our quarterly and annual operating results may fluctuate significantly, which makes it difficult for us to predict our future operating results. These fluctuations may occur due to a variety of factors, many of which are outside of our control, including, but not limited to:

- the timing and cost of, and level of investment in, research, development, regulatory approval and commercialization activities relating to our product candidates, which may change from time to time;

- the timing and success or failure of preclinical studies or clinical trials for our product candidates or competing product candidates, or any other change in the competitive landscape of our industry, including consolidation among our competitors or partners;
- the success of our existing collaboration with Pfizer and any potential additional collaboration, licensing or similar arrangements;
- coverage and reimbursement policies with respect to our product candidates, if approved, and potential future drugs that compete with our products;
- the cost of manufacturing our product candidates, which may vary depending on the quantity of production and the terms of our agreements with third-party manufacturers;
- expenditures that we will or may incur to acquire, develop or commercialize additional product candidates and technologies or other assets;
- the level of demand for any approved products, which may vary significantly and be difficult to predict; and
- future accounting pronouncements or changes in our accounting policies;

The cumulative effects of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. Investors should not rely on our past results as an indication of our future performance.

This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our revenue or operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated revenue or earnings guidance we may provide.

Our success is dependent on our ability to attract and retain highly qualified management and other clinical and scientific personnel.

Our success depends in part on our continued ability to attract, retain, manage, and motivate highly qualified management, clinical, and scientific personnel, and we face significant competition for experienced personnel. We are highly dependent upon our senior management, as well as our senior scientists and other members of our management team. The loss of services of any of these individuals could delay or prevent the successful development of our product pipeline, initiation, or completion of our clinical trials and preclinical studies or the commercialization of our product candidates. Although we have executed employment agreements or offer letters with each member of our senior management team, these agreements are terminable at will with or without notice and, therefore, we may not be able to retain their services as expected. We do not currently maintain “key person” life insurance on the lives of our executives or any of our employees. This lack of insurance means that we may not have adequate compensation for the loss of the services of these individuals.

We will need to expand and effectively manage our managerial, operational, financial, and other resources in order to successfully pursue our clinical development and commercialization efforts. We may not be successful in maintaining our unique company culture and continuing to attract or retain qualified management, clinical, and scientific personnel in the future due to the intense competition for qualified personnel among biopharmaceutical, biotechnology, and other businesses, particularly in the San Diego area. Our industry has experienced a high rate of turnover of management personnel in recent years. If we are not able to attract, integrate, retain, and motivate necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital, and our ability to implement our business strategy.

We may encounter difficulties in managing our growth and expanding our operations successfully.

As of December 31, 2022, we had 14 full-time employees. As we continue development and pursue the potential commercialization of our product candidates, as well as function as a public company, we will need to

expand our financial, development, regulatory, manufacturing, marketing and sales capabilities or contract with third parties to provide these capabilities for us. As our operations expand, we expect that we will need to manage additional relationships with various strategic partners, suppliers and other third parties. Our future financial performance and our ability to develop and commercialize our product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively.

Our relationships with prescribers, purchasers, third-party payors and patients will be subject to applicable anti-kickback, fraud and abuse and other health care laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers expose us to broadly applicable foreign, federal and state fraud and abuse and other healthcare and privacy laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute any products for which we obtain marketing approval. Such laws include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or providing any remuneration (including any kickback, bribe or certain rebates), directly or indirectly, overtly or covertly, in cash or in kind, in return for, either the referral of an individual or the purchase, lease, or order, or arranging for or recommending the purchase, lease, or order 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 Medicare and Medicaid. A person or entity does not need to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it in order to have committed a violation;
- the federal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making or causing to be made a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act;
- the federal Health Insurance Portability and Accountability Act of 1996, which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to the Centers for Medicare & Medicaid Services ("CMS"), information related to payments and other "transfers of value" made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other non-physician practitioners (physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, anesthesiology assistants and certified nurse-midwives) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; some state laws require biotechnology companies to comply with the biotechnology industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require certain biotechnology companies to report information related to payments and other transfers of value to

physicians and other healthcare providers or marketing expenditures; some state laws that require biotechnology companies to report information on the pricing of certain drug products; and some state and local laws require the registration of pharmaceutical sales representatives.

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

Recently enacted legislation, future legislation and healthcare reform measures may increase the difficulty and cost for us to obtain marketing approval for and commercialize our product candidates and may affect the prices we may set.

In the United States and some foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system, including cost-containment measures that may reduce or limit coverage and reimbursement for newly approved drugs and affect our ability to profitably sell any product candidates for which we obtain marketing approval. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare.

For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, each as amended (collectively known as the “ACA”), was enacted in the United States. Among the provisions of the ACA of importance to our potential product candidates, the ACA established an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents; extended manufacturers’ Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations; expanded eligibility criteria for Medicaid programs; expanded the entities eligible for discounts under the Public Health Service pharmaceutical pricing program; increased the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program; created a new Medicare Part D coverage gap discount program; established a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in and conduct comparative clinical effectiveness research, along with funding for such research; and established a Center for Medicare and Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending.

Since its enactment, there have been executive, judicial and Congressional challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court’s decision, President Biden issued an executive order to initiate a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace from February 15, 2021 through August 15, 2021. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. On August 2, 2011, the Budget Control Act of 2011 was signed into law, which, among other things, resulted in reductions to Medicare payments to providers, which went into effect on April 1, 2013 and, due to subsequent legislative

amendments to the statute, will remain in effect through 2032, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022, unless additional Congressional action is taken. In addition, on January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Further, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs. Such scrutiny has resulted in several recent congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. For example, on March 11, 2021, the American Rescue Plan Act of 2021 was signed into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024. Most recently, on August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025).

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition and prospects. In December 2020, the U.S. Supreme Court held unanimously that federal law does not preempt the states' ability to regulate pharmaceutical benefit managers, ("PBMs") and other members of the health care and pharmaceutical supply chain, an important decision that is expected to lead to further and more aggressive efforts by states in this area. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our product candidates, if approved, or put pressure on our product pricing, which could negatively affect our business, results of operations, financial condition and prospects.

We expect that the ACA, these new laws and other healthcare reform measures that may be adopted in the future may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. 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.

Actual or perceived failures to comply with applicable data protection, privacy and security laws, regulations, standards and other requirements could adversely affect our business, results of operations, and financial condition.

The global data protection landscape is rapidly evolving, and we are or may become subject to numerous state, federal and foreign laws, requirements and regulations governing the collection, use, disclosure, retention, and security of personal information. Implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, and we cannot yet determine the impact future laws, regulations, standards, or perception of their requirements may have on our business. This evolution may create uncertainty in our business, affect our ability to operate in certain jurisdictions or to collect, store, transfer use and share personal information, necessitate the acceptance of more onerous obligations in our contracts, result in liability or impose additional costs on us. Each of these laws is subject to varying interpretations by courts and government agencies, creating complex compliance issues. If we fail to comply with applicable laws and regulations we may face government investigations and/or enforcement actions, fines, civil or criminal penalties, private litigation or adverse publicity that could adversely affect our business, financial condition and results of operation. For example, we may be subject to criminal penalties if we knowingly obtain or disclose individually identifiable health information from a covered entity in a

manner that is not authorized or permitted by the Health Insurance Portability and Accountability Act, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, and regulations implemented thereunder or applicable state laws.

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

We face an inherent risk of product liability as a result of the clinical trials of our product candidates and will face an even greater risk if we commercialize our product candidates. For example, we may be sued if our product candidates allegedly cause injury or are found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. In addition, we may be subject to liability based on the actions of our existing or future collaborators in connection with their development of product candidates. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product candidate, negligence, strict liability and a breach of warranties. Claims may be brought against us by clinical trial participants, patients or others using, administering or selling products that may be approved in the future. Claims could also be asserted under state consumer protection acts.

If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit or cease the commercialization of our products. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our products;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- costs to defend the related litigation;
- a diversion of our management's time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- significant negative financial impact;
- the inability to commercialize our product candidates; and
- a decline in our stock price.

We currently hold approximately \$5 million in product liability insurance coverage in the aggregate, with no per occurrence limit. We may need to increase our insurance coverage as we expand our clinical trials or if we commence commercialization of our product candidates. Insurance coverage is increasingly expensive. Our inability to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of our product candidates. Although we will maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies will also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

Our insurance policies are expensive and only protect us from some business risks, which will leave us exposed to significant uninsured liabilities.

We do not carry insurance for all categories of risk that our business may encounter. Some of the policies we currently maintain include property, general liability, employment benefits liability, business automobile, workers' compensation, products liability, malicious invasion of our electronic systems, clinical trials, and directors' and officers' employment practices and fiduciary liability insurance. We do not know, however, if we will be able to

maintain insurance with adequate levels of coverage. No assurance can be given that an insurance carrier will not seek to cancel or deny coverage after a claim has occurred. Any significant uninsured liability may require us to pay substantial amounts, which would adversely affect our financial position and results of operations.

We and any of our current or future collaborators will be required to report to regulatory authorities if any of our approved products cause or contribute to adverse medical events, and any failure to do so would result in sanctions that would materially harm our business.

If we or any of our current or potential future collaborators are successful in commercializing our products, the FDA and foreign regulatory authorities would require that we and such collaborators report certain information about adverse medical events if those products may have caused or contributed to those adverse events. The timing of our obligation to report would be triggered by the date we become aware of the adverse event as well as the nature of the event. We and any of our potential future collaborators or CROs may fail to report adverse events within the prescribed timeframe. If we or any of current or potential future collaborators or CROs fail to comply with such reporting obligations, the FDA or a foreign regulatory authority could take action, including criminal prosecution, the imposition of civil monetary penalties, seizure of our products or delay in approval or clearance of future products.

Our business and operations may suffer in the event of information technology system failures, cyberattacks or deficiencies in our cybersecurity.

In the ordinary course of business, we collect, store, transmit and otherwise process large amounts of data including, without limitation, proprietary business information and personal information. Despite the implementation of security measures, our information technology systems (including infrastructure) and those of our current and any future CROs and other contractors, consultants, third-party service providers and collaborators are vulnerable to attack, damage, and interruption from computer viruses, cybersecurity threats (such as denial-of-service attacks, ransomware, supply chain attacks, cyberattacks or cyber intrusions over the Internet, hacking, phishing and other social engineering attacks), unauthorized access or use, natural disasters, terrorism, war and telecommunication and electrical failures. Our systems are also subject to compromise from internal threats, such as theft, misuse, unauthorized access or other improper or accidental actions by employees, vendors and other third parties with otherwise legitimate access to our systems. Third parties may also attempt to fraudulently induce our employees and contractors into disclosing sensitive information such as usernames, passwords or other information, or otherwise compromise the security of our electronic systems, networks, and/or physical facilities in order to gain access to our data. Additionally, due to the COVID-19 pandemic, our employees are temporarily working remotely, which may pose additional data security risks.

Given the unpredictability of the timing, nature and scope of information technology disruptions, there can be no assurance that any security procedures and controls that we or our third-party partners and service providers have implemented will be sufficient to prevent cyberattacks from occurring. The latency of a compromise is often measured in months, but could be years, and we may not be able to detect a compromise in a timely manner. New techniques may not be identified until they are launched against a target, and we may be unable to anticipate these techniques or detect an incident, assess its severity or impact, react or appropriately respond in a timely manner or implement adequate preventative measures, resulting in potential data loss or other damage to our information technology systems. Even if identified, we may be unable to adequately investigate or remediate incidents or breaches due to attackers increasingly using tools and techniques that are designed to circumvent controls, to avoid detection, and to remove or obfuscate forensic evidence.

While we do not believe that we have experienced any significant system failure, accident or security breach to date, if a security breach were to occur and cause interruptions in our operations or result in the unauthorized disclosure of or access to personally identifiable information or individually identifiable health information (potentially violating certain privacy laws), it could result in a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other similar disruptions. Some of the federal, state and foreign government requirements include obligations of companies to notify individuals of security breaches involving particular personally identifiable information, which could result from breaches experienced by us or by our vendors, contractors, or organizations with which we have formed strategic relationships. Any security breach or other incident, whether actual or perceived, could impact our reputation, cause us to incur significant costs, including legal expenses, harm customer confidence, hurt our expansion into new markets, cause us to incur

remediation costs, or cause us to lose existing customers. For example, the loss of clinical trial data from clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. We also rely on third parties to manufacture our product candidates, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any actual or perceived disruption or security breach affects our systems (or those of our third-party collaborators, service providers, contractors or consultants) or were to result in a loss of or accidental, unlawful or unauthorized access to, use of, release of, or other processing of personally identifiable information, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, the further development and commercialization of our product candidates could be delayed, and we could be subject to significant fines, penalties or liabilities for any noncompliance with certain privacy and security laws. We maintain cyber liability insurance; however, this insurance may not be sufficient to cover the financial, legal, business or reputational losses that may result from an interruption or breach of our systems.

Our business is subject to risks arising from COVID-19 and other epidemic diseases.

The COVID-19 worldwide pandemic presented, and may continue to present, substantial public health and economic challenges by affecting our employees, patients, physicians and other healthcare providers, communities and business operations, as well as the U.S. and global economies and financial markets. To date, we have not experienced material disruptions in our business operations. However, there can be no assurance that COVID-19 and any future epidemic disease won't have an adverse impact on our business in the future. For example, a pandemic, including COVID-19 or other public health epidemic could: disrupt the supply chain and the manufacture or shipment of drug substances and finished drug products for our product candidates for use in our research, preclinical studies and clinical trials; delay, limit or prevent our employees and CROs from continuing research and development activities; impede our clinical trial initiation and recruitment and the ability of patients to continue in clinical trials, including the risk that participants enrolled in our clinical trials could contract COVID-19 or other epidemic disease while the clinical trial is ongoing, which could impact the results of the clinical trial, including by increasing the number of observed adverse events; impede testing, monitoring, data collection and analysis and other related activities; any of which could delay our preclinical studies and clinical trials and increase our development costs, and have a material adverse effect on our business, financial condition and results of operations. The COVID-19 pandemic and mitigation measures had, and may continue to have, and any future epidemic disease outbreak may have, an adverse impact on global economic conditions which could have an adverse effect on our business and financial condition, including impairing our ability to raise capital when needed. Further, to the extent the COVID-19 pandemic or any other outbreak of an epidemic disease adversely affects our business and financial results, it may also have the effect of heightening many of the other risks described in this section.

Our business could be affected by litigation, government investigations and enforcement actions.

We currently operate in a number of jurisdictions in a highly regulated industry and we could be subject to litigation, government investigation and enforcement actions on a variety of matters in the United States, or foreign jurisdictions, including, without limitation, intellectual property, regulatory, product liability, environmental, whistleblower, false claims, privacy, anti-kickback, anti-bribery, securities, commercial, employment and other claims and legal proceedings which may arise from conducting our business. Any determination that our operations or activities are not in compliance with existing laws or regulations could result in the imposition of fines, civil and criminal penalties, equitable remedies, including disgorgement, injunctive relief and/or other sanctions against us, and remediation of any such findings could have an adverse effect on our business operations.

Legal proceedings, government investigations and enforcement actions can be expensive and time-consuming. An adverse outcome resulting from any such proceeding, investigations or enforcement actions could result in significant damages awards, fines, penalties, exclusion from the federal healthcare programs, healthcare debarment, injunctive relief, product recalls, reputational damage and modifications of our business practices, which could have a material adverse effect on our business and results of operations.

Our employees and independent contractors, including principal investigators, CROs, consultants 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 and independent contractors, including principal investigators, CROs, consultants and vendors may engage in misconduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violate: (i) the laws and regulations of the FDA and other similar regulatory requirements, including those laws that require the reporting of true, complete and accurate information to such authorities, (ii) manufacturing standards, including cGMP requirements, (iii) federal and state data privacy, security, fraud and abuse and other healthcare laws and regulations in the United States and abroad or (iv) laws that require the true, complete and accurate reporting of financial information or data. Activities subject to these laws also involve the improper use or misrepresentation of information obtained in the course of clinical trials, the creation of fraudulent data in our preclinical studies or clinical trials or illegal misappropriation of drug product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third 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 be in compliance with such laws or regulations. In addition, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. 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 and financial results, including, without limitation, the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgements, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, imprisonment, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

We may engage in strategic transactions that could impact our liquidity, increase our expenses and present significant distractions to our management.

From time to time, we may consider strategic transactions, such as acquisitions of companies, asset purchases and out-licensing or in-licensing of intellectual property, products or technologies. Potential transactions that we may consider in the future include a variety of business arrangements, including spin-offs, strategic partnerships, joint ventures, restructurings, divestitures, business combinations and investments. Any future transactions could increase our near and long-term expenditures, result in potentially dilutive issuances of our equity securities, including our Common Stock, or the incurrence of debt, contingent liabilities, amortization expenses or acquired in-process research and development expenses, any of which could affect our financial condition, liquidity and results of operations. Future acquisitions may also require us to obtain additional financing, which may not be available on favorable terms or at all. These transactions may never be successful and may require significant time and attention of our management. In addition, the integration of any business that we may acquire in the future may disrupt our existing business and may be a complex, risky and costly endeavor for which we may never realize the full benefits of the acquisition. Accordingly, although there can be no assurance that we will undertake or successfully complete any additional transactions of the nature described above, any additional transactions that we do complete could have a material adverse effect on our business, results of operations, financial condition and prospects.

Our ability to use net operating loss carryforwards and other tax attributes may be limited in connection with this offering or other ownership changes.

We have incurred substantial losses during our history, do not expect to become profitable in the near future and may never achieve profitability. To the extent we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire (although federal net operating loss (“NOL”) carryforwards generated in taxable years beginning after December 31, 2017 will not be subject to expiration). As of December 31, 2022, we had federal and California NOL carryforwards of approximately \$181.6 million and \$92.8 million, respectively, and federal and California research and development credit carryforwards of approximately \$9.6 million, inclusive of the federal orphan drug tax credit carryforward, and \$4.3 million, respectively.

Under Section 382 of the Code, our federal NOL carryforwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership of our company. 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 over their lowest ownership percentage within a rolling three-year period. Similar rules may apply under state tax laws. We have not yet formally determined the amount of the cumulative change in our ownership, or any resulting limitations on our ability to utilize our NOL carryforwards and other tax attributes. However, we believe our ability to utilize our NOL carryforwards and other tax attributes to offset future taxable income or tax liabilities is likely to be limited as a result of ownership changes. In addition, our NOL carryforwards are subject to review and possible adjustment by the IRS and state tax authorities. Moreover, federal NOL carryforwards generated in taxable years beginning after December 31, 2017 may generally only be used to offset 80% of taxable income in taxable years beginning after December 31, 2020. If we earn taxable income, these limitations could result in increased future income tax liability to us and our future cash flows could be adversely affected. We have recorded a full valuation allowance related to our NOL carryforwards and other deferred tax assets due to the uncertainty of the ultimate realization of the future benefits of those assets.

Risks Related to Our Intellectual Property

Our success depends on our ability to protect our intellectual property and our proprietary technologies.

Our commercial success depends in part on our ability to obtain and maintain patent protection and trade secret protection for our product candidates, proprietary technologies and their uses as well as our ability to operate without infringing upon the proprietary rights of others. We generally seek to protect our proprietary position by filing patent applications in the United States and abroad related to our product candidates, proprietary technologies and their uses that are important to our business. Our patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until patents issue from such applications, and then only to the extent the issued claims cover the technology. There can be no assurance that our patent applications or those of our licensor will result in additional patents being issued or that issued patents will afford sufficient protection against competitors with similar technology, nor can there be any assurance that the patents issued will not be infringed, designed around or invalidated by third parties. 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. The degree of future protection for our proprietary rights is uncertain. Only limited protection may be available and may not adequately protect our rights or permit us to gain or keep any competitive advantage. If the scope of any patent protection we obtain is not sufficiently broad, or if we or our licensors lose any of the patent protection we license, our ability to prevent our competitors would be adversely affected. This failure to properly protect the intellectual property rights relating to our product candidates could have a material adverse effect on our financial condition and results of operations. Although we own issued patents in the United States directed to tomivosertib and zotatifin, we cannot be certain that the claims in our other U.S. pending patent applications, corresponding international patent applications and patent applications in certain foreign territories directed to tomivosertib and zotatifin, or any of our patent applications directed to our other product candidates, will be considered patentable by the United States Patent and Trademark Office (the "USPTO") courts in the United States or by the patent offices and courts in foreign countries, nor can we be certain that the claims in our issued patents will not be found invalid or unenforceable if challenged.

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

- 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;
- patent applications may not result in any patents being issued;
- patents that may be issued or in-licensed 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 whom have made significant investments in competing technologies, may seek or may have already obtained

patents that will limit, interfere with or eliminate our ability to make, use and sell our potential 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 disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and
- countries other than the United States may have patent laws less favorable to patentees than those upheld by U.S. courts, allowing foreign competitors a better opportunity to create, develop and market competing product candidates.

The patent prosecution process is also expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner or in all jurisdictions where protection may be commercially advantageous. 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, in some circumstances, including under our license agreement with UCSF, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, directed to technology that we license from third parties. We may also require the cooperation of our licensor in order to enforce the licensed patent rights, and such cooperation may not be provided. Therefore, these 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 our licensor 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.

Furthermore, our owned and in-licensed patent rights may be subject to a reservation of rights by one or more third parties. For example, the research resulting in the patent rights under our license agreement with UCSF was funded in part by the U.S. government. As a result, the government may have certain rights, or march-in rights, to such patent rights and technology. When new technologies are developed with government funding, the government generally obtains certain rights in any resulting patents, including a non-exclusive license authorizing the government to use the invention for non-commercial purposes. These rights may permit the government to disclose our confidential information to third parties and to exercise march-in rights to use or allow third parties to use our licensed technology. The government can exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the government-funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations, or to give preference to U.S. industry. In addition, our rights in such inventions may be subject to certain requirements to manufacture products embodying such inventions in the United States. Any exercise by the government of such rights could harm our competitive position, business, financial condition, results of operations and prospects.

In addition, although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, CROs, third-party manufacturers, consultants, advisors and other third parties, any of these parties may breach such agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection.

Moreover, the patent position of biopharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents, if issued, or the patent rights that we license from others, may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical products, or limit the duration of the patent protection of our products and product candidates. 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 intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Our commercial success depends significantly on our ability to operate without infringing the patents and other proprietary rights of third parties. Claims by third parties that we infringe their proprietary rights may result in liability for damages or prevent or delay our developmental and commercialization efforts.

Our commercial success depends in part on avoiding infringement of the patents and proprietary rights of third parties. Other entities may have or obtain patents or proprietary rights that could limit our ability to make, use, sell, offer for sale or import our product candidates and products that may be approved in the future, or impair our competitive position. 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, oppositions, reexaminations, inter partes review proceedings and post-grant review (“PGR”) proceedings before the USPTO and/or corresponding foreign patent offices. Numerous third-party U.S. and foreign issued patents and pending patent applications exist in the fields in which we are developing product candidates. 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 product candidates.

As the biotechnology 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. Because patent applications are maintained as confidential for a certain period of time, until the relevant application is published we may be unaware of third-party patents that may be infringed by commercialization of any of our product candidates, and we cannot be certain that we were the first to file a patent application related to a product candidate or technology. Moreover, because patent applications can take many years to issue, there may be currently-pending patent applications that may later result in issued patents that our product candidates may infringe. In addition, identification of third-party patent rights that may be relevant to our technology 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. There is also no assurance that there is not prior art of which we are aware, but which we do not believe is relevant to our business, which may, nonetheless, ultimately be found to limit our ability to make, use, sell, offer for sale or import our products that may be approved in the future, or impair our competitive position. Any claims of patent infringement asserted by third parties would be time consuming and could:

- result in costly litigation;
- divert the time and attention of our technical personnel and management;
- cause development delays;
- prevent us from commercializing any of our product candidates until the asserted patent expires or is held finally invalid or not infringed in a court of law;
- require us to develop non-infringing technology, which may not be possible on a cost-effective basis;
- subject us to significant liability to third parties; or
- require us to enter into royalty or licensing agreements, which may not be available on commercially reasonable terms, or at all.

Although no third party has asserted a claim of patent infringement against us as of the date of this Annual Report, others may hold proprietary rights that could prevent our product candidates from being marketed. Any patent-related legal action against us claiming damages and seeking to enjoin commercial activities relating to our product candidates or processes could subject us to potential liability for damages, including treble damages if we were determined to willfully infringe, and require us to obtain a license to manufacture or market our 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. We cannot predict whether we would prevail in any such actions or that any license required under any of these patents would be made available on commercially acceptable terms, if at all. Moreover, even if we or our future strategic partners were able to obtain a license, the rights may be nonexclusive, which could result in our competitors gaining access to the same intellectual property. In addition, we cannot be certain that we could redesign our product candidates or processes to avoid infringement, if necessary. Accordingly, an adverse determination in a judicial or administrative proceeding, or the failure to obtain necessary licenses, could prevent us from developing and commercializing our product candidates, which could harm our business, financial condition and operating results. In addition, intellectual property litigation,

regardless of its outcome, may cause negative publicity and could prohibit us from marketing or otherwise commercializing our product candidates and technology.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensor, which could be expensive, time consuming, and unsuccessful. Further, our issued patents could be found invalid or unenforceable if challenged in court.

Competitors may infringe our intellectual property rights or those of our licensor. To prevent infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in a patent infringement proceeding, a court may decide that a patent we own or in-license is not valid, is unenforceable and/or is not infringed. If we or any of our current or future collaborators were to initiate legal proceedings against a third party to enforce a patent directed at one of our product candidates, the defendant could counterclaim that our patent is invalid and/or unenforceable in whole or in part. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could include an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. Third parties may also raise similar claims before the USPTO, even outside the context of litigation.

The outcome following legal assertions of invalidity and unenforceability is unpredictable, and prior art could render our patents or those of our licensors invalid or could prevent a patent from issuing from one or more of our pending patent applications. There is no assurance that all potentially relevant prior art relating to our patents and patent applications has been found. There is also no assurance that there is not prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim in our patents and patent applications, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. Furthermore, even if our patents are unchallenged, they may not adequately protect our intellectual property, provide exclusivity for our product candidates, prevent others from designing around our claims or provide us with a competitive advantage. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on such product candidate. 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. Such a loss of patent protection would have a material adverse impact on our business.

The outcome following legal assertions of invalidity and unenforceability is unpredictable, and prior art could render our patents or those of our licensors invalid. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on such product candidate. Such a loss of patent protection would have a material adverse impact on our business.

Interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation, interference or derivation proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties or enter into development or manufacturing partnerships that would help us bring our product candidates to market.

Even if resolved in our favor, litigation or other legal proceedings relating to our intellectual property rights may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our Common Stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation

or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace.

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 a material adverse effect on the price of our Common Stock.

In addition, the issuance of a patent does not give us the right to practice the patented invention. Third parties may have blocking patents that could prevent us from marketing our own patented product and practicing our own patented technology. Our ability to enforce our patent rights also depends on our ability to detect infringement. It may be difficult to detect infringers who do not advertise the components or methods that are used in connection with their products and services. Moreover, it may be difficult or impossible to obtain evidence of infringement in a competitor's or potential competitor's product or service. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded if we were to prevail may not be commercially meaningful.

Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

On September 16, 2011, the Leahy-Smith America Invents Act (the "Leahy-Smith Act"), was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. In particular, under the Leahy-Smith Act, the United States transitioned in March 2013 to a "first inventor to file" system in which the first inventor to file a patent application will be entitled to the patent. Third parties are allowed to submit prior art before the issuance of a patent by the USPTO, and may become involved in post-grant proceedings including post grant review, derivation, reexamination, inter partes review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope or enforceability of, or invalidate, our patent rights, which could adversely affect our competitive position.

Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Thus, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our future patent applications or those of our current and future licensors and the enforcement or defense of our future issued patents or those of our current and future licensors, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

In 2012, the European Patent Package, or EU Patent Package, regulations were passed with the goal of providing a single pan-European Unitary Patent and a new European Unified Patent Court, or UPC, for litigation involving European patents. Implementation of the EU Patent Package will likely occur in the first half of 2023. Under the UPC, all European patents, including those issued prior to ratification of the European Patent Package, will by default automatically fall under the jurisdiction of the UPC. The UPC will provide our competitors with a new forum to centrally revoke our European patents, and allow for the possibility of a competitor to obtain pan-European injunctions. It will be several years before we will understand the scope of patent rights that will be recognized and the strength of patent remedies that will be provided by the UPC. As the UPC is a new court system, there is no precedent for the court, increasing the uncertainty of any litigation before the UPC. Under the EU Patent Package as currently proposed, we will have the right to opt our patents out of the UPC over the first seven years of the court's existence, but doing so may preclude us from realizing the benefits of the new unified court. Moreover, the decision whether to opt-out of Unitary Patent status will require coordinating with co-applicants, if any, adding complexity to any such decision.

If we fail to comply with any of our obligations under our existing license agreement or any future license agreements, or disputes arise with respect to those agreements, it could have a negative impact on our business and our intellectual property rights.

We are party to a license agreement with UCSF that imposes, and we may enter into additional licensing arrangements with third parties that may impose, diligence, development and commercialization timelines, milestone payment, royalty, insurance and other obligations on us. Our rights to use the licensed intellectual property are subject to the continuation of and our compliance with the terms of these agreements. Disputes may arise regarding our rights to intellectual property licensed to us from a third party, including but not limited to:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the ownership of inventions and know-how resulting from the creation or use of intellectual property by us, alone or with our licensors and collaborators;
- the scope and duration of our payment obligations;
- our rights upon termination of such agreement; and
- the scope and duration of exclusivity obligations of each party to the agreement.

If disputes over intellectual property and other rights that we have licensed or acquired from third parties prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates. If we fail to comply with our obligations under current or future licensing agreements, these agreements may be terminated or the scope of our rights under them may be reduced and we might be unable to develop, manufacture or market any product that is licensed under these agreements.

We may be subject to claims that we have wrongfully hired an employee from a competitor or that we or our employees have wrongfully used or disclosed alleged confidential information or trade secrets of their former employers.

As is common in the pharmaceutical industry, in addition to our employees, we engage the services of consultants to assist us in the development of our product candidates. Many of these consultants, and many of our employees, were previously employed at, or may have previously provided or may be currently providing consulting services to, other pharmaceutical companies including our competitors or potential competitors. We may become subject to claims that we, our employees or a consultant inadvertently or otherwise used or disclosed trade secrets or other information proprietary to their former employers or their former or current clients. 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, which could adversely affect our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to our management team.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We may also be subject to claims that former employees, collaborators or other third parties have an ownership interest in our patents or other intellectual property. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and distraction to management and other employees. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

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

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products, including biosimilars. 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 owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

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 product candidates.

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 patent application in the United States and abroad that is relevant to or necessary for the commercialization of our current and future products and product candidates in any jurisdiction. 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 patent application may be incorrect, which may negatively impact our ability to market our products. We may incorrectly determine that our products or product candidates are not covered by a third-party patent or may incorrectly predict whether a third party's pending patent 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. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

If we do not obtain patent term extension for our product candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of FDA marketing approval of our 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 ("Hatch-Waxman Amendments"). The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended. Similar patent term restoration provisions to compensate for commercialization delay caused by regulatory review are also available in certain foreign jurisdictions, such as in Europe under Supplemental Protection Certificate (SPC). However, 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 obtain patent term extension or restoration or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced,

possibly materially. Further, if this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case.

If our 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.

Our registered or unregistered trademarks or trade names may be challenged, infringed, circumvented or 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 in other foreign jurisdictions. 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. Moreover, any name we have proposed to use with our product candidate in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. Similar requirements exist in Europe. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA or an equivalent administrative body in a foreign jurisdiction objects to any of our proposed proprietary product names, we may be required to expend significant additional resources in an effort to identify a suitable substitute 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.

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 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 registered 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. Our efforts to enforce or protect our proprietary rights related to trademarks, 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.

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

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve a high degree of technological and legal complexity. Therefore, obtaining and enforcing biopharmaceutical patents is costly, time consuming and inherently uncertain. Changes in either the patent laws or in the interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property. We cannot predict the breadth of claims that may be allowed or enforced in our patents or in third-party patents. In addition, Congress or other foreign legislative bodies may pass patent reform legislation that is unfavorable to us. For example, 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 decisions by the U.S. Congress, the U.S. federal courts, the USPTO, or similar authorities in foreign jurisdictions, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents we might obtain in the future.

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

Although we own issued patents directed to tomivosertib and zotatifin in the United States and pending patent applications directed to tomivosertib, zotatifin, and other product candidates in the United States and other countries, filing, prosecuting and defending patents on tomivosertib, zotatifin and our other product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. 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. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. In addition, some jurisdictions, such as Europe, Japan and China, may have a higher standard for patentability than in the United States, including, for example, the requirement of claims having literal support in the original patent filing and the limitation on using supporting data that is not in the original patent filing. Under those heightened patentability requirements, we may not be able to obtain sufficient patent protection in certain jurisdictions even though the same or similar patent protection can be secured in the United States and other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but enforcement is not as strong as that in the United States. These products may compete with our product candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

In addition, geo-political actions in the United States and in foreign countries could increase the uncertainties and costs surrounding the prosecution or maintenance of our patent applications or those of any current or future licensors and the maintenance, enforcement or defense of our issued patents or those of any current or future licensors. For example, the United States and foreign government actions related to Russia's conflict in Ukraine may limit or prevent filing, prosecution, and maintenance of patent applications in Russia. Government actions may also prevent maintenance of issued patents in Russia. These actions could result in abandonment or lapse of our patents or patent applications, resulting in partial or complete loss of patent rights in Russia. If such an event were to occur, it could have a material adverse effect on our business. In addition, a decree was adopted by the Russian government in March 2022, allowing Russian companies and individuals to exploit inventions owned by patentees from the United States without consent or compensation. Consequently, we would not be able to prevent third parties from practicing our inventions in Russia or from selling or importing products made using our inventions in and into Russia. Accordingly, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of many foreign countries do not favor the enforcement of patents and other intellectual property protection, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. Many countries also 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 are 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.

Intellectual property litigation may lead to unfavorable publicity that harms our reputation and causes the market price of our common shares to decline.

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 market price of our common shares 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.

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

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to the USPTO and various foreign patent offices at various points over the lifetime of our patents and/or applications. We have systems in place to remind us to pay these fees, and we rely on our outside patent annuity service to pay these fees when due. Additionally, the USPTO and various foreign patent offices require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with rules applicable to the particular jurisdiction. However, 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. If such an event were to occur, it could have a material adverse effect on our business.

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. For example:

- others may be able to develop products that are similar to our product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed;
- we or our licensors or current or future collaborators might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed;
- we or our licensors or current or future collaborators might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own or have exclusively licensed may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities 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; and
- the patents of others may have an adverse effect on our business.

Should any of these events occur, they could significantly harm our business, 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, we rely on the protection of our trade secrets, including unpatented know-how, technology and other proprietary information to maintain our competitive position. Although we have taken steps to protect our

trade secrets and unpatented know-how, including entering into confidentiality agreements with third parties, and confidential information and inventions agreements with employees, consultants and advisors. Despite these efforts, we cannot provide any assurances that all such agreements have been duly executed, and any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. Moreover, third parties may still obtain this information or may come upon this or similar information independently, and we would have no right to prevent them from using that technology or information to compete with us. We may need to share our proprietary information, including trade secrets, with our current and future business 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. If any of these events occurs or if we otherwise lose protection for our trade secrets, the value of this information may be greatly reduced and our competitive position would be harmed. If we do not apply for patent protection prior to such publication or if we cannot otherwise maintain the confidentiality of our proprietary technology and other confidential information, then our ability to obtain patent protection or to protect our trade secret information may be jeopardized.

Our licensees may breach the terms and conditions under their intellectual property license agreements with us and we may not be successful in enforcing their compliance with these agreements.

We license patents, know-how and proprietary technology rights for certain product candidates to third parties in return for upfront, milestone, royalty, and other considerations. Our licensees may not be able to achieve approval of the licensed products in the countries for which they hold product rights and they may not diligently commercialize such licensed products if and when the licensed product is approved. Under such scenarios, we will not receive royalties or will receive diminished royalties. Our licensees may take actions or fail to take actions that result in safety issues with the licensed product in their licensed territory, and such safety issues could negatively impact the licensed product in countries outside of the licensed territory, whether due to reputational harm or standing to the licensed product or to our name, or by direct regulatory action by authorities outside of the licensed territory. Our licensees may violate certain laws and regulations in the licensed territory, including with respect to safety, patient and data privacy, antitrust, and bribery and corruption, and as a result of such violations may incur substantial fines, criminal investigation and liability, or cause a regulatory authority to remove the licensed product from the marketplace. If any of these events were to occur, we may not receive the financial consideration that we expected from our assignees or licensees, and we could potentially be named and implicated in any of their violations and our assignees or licensees may not indemnify us for relevant damages and liabilities. In the event of a breach of an agreement by our assignees or licensees, we may not be able to successfully enforce the terms and conditions of such agreements in court or via agreed upon dispute resolution mechanisms, and even if we were to prevail in any such dispute, the remedies may not be adequate to compensate us for the losses.

Patent protection and patent prosecution for any future product candidates may be dependent on third parties.

We may rely on third parties to file and prosecute patent applications and maintain patents and otherwise protect the licensed intellectual property under certain current and future license agreements. Under such arrangements, we may not have primary control over these activities for certain of licensed patents or patent applications and other intellectual property rights. We cannot be certain that such activities by third parties have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents or other intellectual property rights. In addition, our current and future licensors may not be fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, which could compromise such patent rights. We may in the future enter into license agreements where the licensors may have the right to control enforcement of our licensed patents or defense of any claims asserting the invalidity of these patents and even if we are permitted to pursue such enforcement or defense, we will require the cooperation of our licensors. We cannot be certain that our licensors will allocate sufficient resources or prioritize their or our enforcement of such patents or defense of such claims to protect our interests in the licensed patents. Even if we are not a party to these legal actions, an adverse outcome could harm our business because it might prevent us from continuing to license intellectual property that we may need to operate our business. If any of our licensors or any of our future licensors or current or future collaborators fail to appropriately prosecute and maintain patent protection for patents covering

any future product candidates, our ability to develop and commercialize those product candidates may be adversely affected and we may not be able to prevent competitors from making, using and selling competing products.

In addition, even where we have the right to control prosecution of patent applications or enforcement of patents we have acquired or licensed 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 such activities. Third parties may retain certain rights to the technology that they license to 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 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 or licensed technologies, or if we lose our rights to critical in-licensed technology, we may be unable to successfully develop, out-license, market and sell our products, which could prevent or delay new product introductions. Our business strategy depends on the successful development of licensed and acquired technologies 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 candidate.

We may not be successful in obtaining or maintaining necessary rights to any future product candidates through acquisitions and in-licenses.

Because our development programs may in the future require the use of proprietary rights held by other 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. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify as necessary for any future product candidates. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment. If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of that program and our business and financial condition could suffer.

Risks Related to Our Common Stock and Warrants

The market price of our common stock and warrants has been, and is likely to continue to be highly volatile, and you may lose some or all of your investment.

The market price of our common stock and warrants has been, and is likely to continue to be highly volatile and may be subject to wide fluctuations in response to a variety of factors, including the following:

- the inability to maintain the listing of our shares of common stock and warrants on Nasdaq;
- changes in applicable laws or regulations;
- timely initiation and successful enrollment of participants in our clinical trials, and completion of clinical trials and preclinical studies with favorable and timely results;
- unexpected adverse side effects or inadequate efficacy of our product candidates that may limit their development, regulatory approval and/or commercialization, or may result in recalls or product liability claims;
- innovations, clinical trial results, product approvals and other developments regarding our competitors;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures or capital commitments;

- manufacturing, supply or distribution delays or shortages;
- any changes to our relationship with any manufacturers, suppliers, collaborators or other strategic partners;
- achievement of expected product sales and profitability;
- variations in our financial results or those of companies that are perceived to be similar to us;
- trading volume of our common stock;
- an inability to obtain additional funding;
- sales of our stock by insiders and stockholders;
- additions or departures of key personnel; and
- risks related to the organic and inorganic growth of our business and the timing of expected business milestones; and
- the impact of the COVID-19 pandemic or other pandemic diseases on our business.

In addition, the stock markets have experienced extreme price and volume fluctuations that affected and continue to affect the market prices of equity securities of many companies. These fluctuations have often been unrelated or disproportionate to the operating performance of those companies. Broad market and industry factors, as well as general economic, political, regulatory and market conditions, may negatively affect the market price of our common stock and warrants, regardless of our actual operating performance.

Volatility in our share price could subject us to securities class action litigation.

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 biotechnology and biopharmaceutical 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.

Our failure to meet the continued listing requirements of the Nasdaq Capital Market could result in a delisting of our common stock and warrants.

If we fail to satisfy the continued listing requirements of the Nasdaq Capital Market, such as the minimum closing bid price, stockholders' equity or round lot holders requirements or the corporate governance requirements, Nasdaq may take steps to delist our common stock and/or warrants. On August 29, 2022, we received a letter from the Nasdaq Stock Market staff indicating that, for the last thirty consecutive business days, the bid price for our common stock had closed below the minimum \$1.00 per share requirement for continued listing on the Nasdaq Capital Market under Nasdaq Listing Rule 5550(a)(2).

In accordance with Nasdaq Listing Rule 5810(c)(3)(A), we were provided an initial period of 180 calendar days, or until February 27, 2023, to regain compliance. The Nasdaq letter had no immediate effect on the listing or trading of our common stock and warrants and such securities continue to trade on the Nasdaq Capital Market.

We did not regain compliance with Nasdaq listing rules by February 27, 2023, but Nasdaq provided an additional 180 calendar day compliance period. On February 28, 2023, we received notification from the Nasdaq Stock Market staff that we had been granted an additional 180 calendar days, or until August 28, 2023 (as the first trading day following such period), to regain compliance with the bid price requirement.

In order to regain compliance, the bid price of our common stock must close at a price of at least \$1.00 per share for a minimum of 10 consecutive trading days within the 180 day grace period. If we fail to regain compliance, our common stock will be subject to delisting. Such a delisting would likely have a negative effect on the price of our common stock and warrants and would impair your ability to sell or purchase our securities when you wish to do so. Such a delisting could also result in a limited amount of news and analyst coverage for the company; and a decreased ability for us to issue additional securities or obtain additional financing in the future. In the event of a delisting, we can provide no assurance that any action taken by us to restore compliance with listing

requirements would allow our securities to become listed again, stabilize the market price or improve the liquidity of our securities, or prevent future non-compliance with Nasdaq's listing requirements.

If securities or industry analysts do not publish research or reports about us, or publish negative reports, our stock price and trading volume could decline.

The trading market for our common stock and warrants depends, in part, on the research and reports that securities or industry analysts publish about us. We do not have any control over these analysts. If our financial performance fails to meet analyst estimates or one or more of the analysts who cover us downgrade our common stock or warrants or change their opinion, the trading price of our common stock and warrants would likely decline. If one or more of these analysts cease coverage of us or fail to regularly publish reports on us, it could lose visibility in the financial markets, which could cause the trading price or trading volume of our common stock and warrants to decline.

Because we do not anticipate paying any cash dividends in the foreseeable future, capital appreciation, if any, would be your sole source of gain.

We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. As a result, capital appreciation, if any, of our shares of common stock would be your sole source of gain on an investment in such shares for the foreseeable future.

Our executive officers, directors and principal stockholders, if they choose to act together, will continue to have the ability to significantly influence all matters submitted to stockholders for approval.

As of December 31, 2022, our executive officers, directors and greater than 5% stockholders, in the aggregate, owned approximately 58% of our outstanding common stock. As a result, such persons, acting together, have the ability to significantly influence all matters submitted to our board of directors or stockholders for approval, including the appointment of our management, the election and removal of directors and approval of any significant transaction, as well as our management and business affairs. This concentration of ownership may have the effect of delaying, deferring or preventing a change in control, impeding a merger, consolidation, takeover or other business combination involving us, or discouraging a potential acquiror from making a tender offer or otherwise attempting to obtain control of our business, even if such a transaction would benefit other stockholders.

Provisions in our certificate of incorporation and under Delaware law could discourage a takeover that stockholders may consider favorable and may lead to entrenchment of management.

Our certificate of incorporation and bylaws contain provisions that could significantly reduce the value of our shares to a potential acquiror or delay or prevent changes in control or changes in our management without the consent of our Board. The provisions in our charter documents include the following:

- a classified board of directors with three-year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our Board;
- no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;
- the exclusive right of our Board, unless the Board grants such right to the stockholders, to elect a director to fill a vacancy created by the expansion of the Board or the resignation, death or removal of a director, which prevents stockholders from being able to fill vacancies on our Board;
- the required approval of at least 66-2/3% of the shares entitled to vote to remove a director for cause, and the prohibition on removal of directors without cause;
- the ability of our Board to authorize the issuance of shares of preferred stock and to determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquiror;
- the ability of our Board to alter our bylaws without obtaining stockholder approval;

- the required approval of at least 66-2/3% of the shares entitled to vote to adopt, amend or repeal our bylaws or repeal the provisions of our certificate of incorporation regarding the election and removal of directors;
- a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;
- an exclusive forum provision providing that the Court of Chancery of the State of Delaware will be the exclusive forum for certain actions and proceedings;
- the requirement that a special meeting of stockholders may be called only by the Board, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and
- advance notice procedures that stockholders must comply with in order to nominate candidates to our Board or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquiror from conducting a solicitation of proxies to elect the acquiror's own slate of directors or otherwise attempting to obtain control of us.

We also are subject to the anti-takeover provisions contained in Section 203 of the Delaware General Corporation Law. Under Section 203, a corporation may not, in general, engage in a business combination with any holder of 15% or more of its capital stock unless the holder has held the stock for three years or, among other exceptions, the Board has approved the transaction.

Our certificate of incorporation provides that the Court of Chancery of the State of Delaware will be the exclusive forum for substantially all disputes between us and our stockholders and that the federal district courts shall be the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees or the underwriters or any offering giving rise to such claim.

Our certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a breach of fiduciary duty, any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our certificate of incorporation or our bylaws, or any action asserting a claim against us that is governed by the internal affairs doctrine. Furthermore, our certificate of incorporation also provides that unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States shall be the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act, including all causes of action asserted against any defendant named in such complaint. Notwithstanding the foregoing, this forum selection provision does not apply to suits brought to enforce any liability or duty created by the Exchange Act or any other claim for which the federal district courts of the United States have exclusive jurisdiction. For the avoidance of doubt, this provision is intended to benefit and may be enforced by us, our officers and directors, the underwriters to any offering giving rise to such complaint, and any other professional entity whose profession gives authority to a statement made by that person or entity and who has prepared or certified any part of the documents underlying the offering. These choice of forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and other employees and result in increased costs for investors to bring a claim. By agreeing to this provision, however, stockholders will not be deemed to have waived our compliance with the federal securities laws and the rules and regulations thereunder. Furthermore, the enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that a court could find these types of provisions to be inapplicable or unenforceable. If a court were to find the choice of forum provisions in our certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business and financial condition.

We are an emerging growth company and smaller reporting company, and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies and smaller reporting companies will make our shares less attractive to investors.

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act (the “JOBS Act”). 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 exemption from compliance with the auditor attestation requirements under Section 404 of the Sarbanes-Oxley Act of 2002, reduced disclosure obligations regarding executive compensation and exemptions from the requirements of holding a nonbinding advisory vote 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 the initial public offering (December 31, 2026), (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 means the market value of shares of our Common Stock that are held by non-affiliates exceeds \$700 million as of the prior June 30th, and (2) the date on which we have issued more than \$1.0 billion in non-convertible debt during the prior three-year period.

In addition, under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have elected to use this extended transition period for complying with new or revised accounting standards and, therefore, we will not be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

We are also a smaller reporting company as defined in the Exchange Act. 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 exemption from compliance with the auditor attestation requirements of Section 404 and reduced disclosure obligations regarding executive compensation in this Annual Report and our periodic reports and proxy statements. We are able to take advantage of these scaled disclosures for so long as our voting and non-voting common stock held by non-affiliates is less than \$250.0 million measured on the last business day of our second fiscal quarter, or our annual revenue is less than \$100.0 million during the most recently completed fiscal year and our voting and non-voting common stock held by non-affiliates is less than \$700.0 million measured on the last business day of our second fiscal quarter.

We cannot predict if investors will find its common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for the common stock and our market price may be more volatile.

If you exercise your public warrants on a “cashless basis,” you will receive fewer shares of common stock from such exercise than if you were to exercise such warrants for cash.

There are circumstances in which the exercise of the public warrants may be required or permitted to be made on a cashless basis. If our common stock is at any time of any exercise of a warrant not listed on a national securities exchange such that it satisfies the definition of a “covered security” under Section 18(b)(1) of the Securities Act, we may, at our option, require holders of public warrants who exercise their warrants to do so on a cashless basis in accordance with Section 3(a)(9) of the Securities Act and, in the event we so elect, we will not be required to file or maintain in effect a registration statement, and in the event we do not so elect, we will use our best efforts to register or qualify the shares under applicable blue sky laws to the extent an exemption is not available. Third, if we call the public warrants for redemption, our management will have the option to require all holders that wish to exercise warrants to do so on a cashless basis. In the event of an exercise on a cashless basis, a holder would pay the warrant exercise price by surrendering the warrants for that number of shares of common stock equal to the quotient obtained by dividing (x) the product of the number of shares of common stock underlying the warrants, multiplied by the difference between the exercise price of the warrants and the “fair market value” (as defined in the next sentence) by (y) the fair market value. The “fair market value” is the average reported last sale price of the common stock for the 10 trading days ending on the third trading day prior to the date on which the notice of exercise is received by the warrant agent or on which the notice of redemption is sent to the holders of warrants, as applicable. As a result, you would receive fewer shares of common stock from such exercise than if you were to exercise such warrants for cash.

We may amend the terms of the public warrants in a manner that may be adverse to holders with the approval by the holders of at least 65% of the then outstanding public warrants.

Our warrants were issued in registered form under a warrant agreement between Continental Stock Transfer & Trust Company, as warrant agent, and us. The warrant agreement provides that the terms of the warrants may be amended without the consent of any holder to cure any ambiguity or correct any defective provision, but requires the approval by the holders of at least 65% of the then outstanding public warrants to make any change that adversely affects the interests of the registered holders of public warrants. Accordingly, we may amend the terms of the public warrants in a manner adverse to a holder if holders of at least 65% of the then outstanding public warrants approve of such amendment. Although our ability to amend the terms of the public warrants with the consent of at least 65% of the then outstanding public warrants is unlimited, examples of such amendments could be amendments to, among other things, increase the exercise price of the warrants, convert the warrants into cash or stock, shorten the exercise period or decrease the number of shares of our common stock purchasable upon exercise of a warrant.

We may redeem your unexpired public warrants prior to their exercise at a time that is disadvantageous to you, thereby making public warrants worthless.

We have the ability to redeem outstanding public warrants at any time after they become exercisable and prior to their expiration, at \$0.01 per warrant, provided that the last reported sales price (or the closing bid price of our common stock in the event the shares of our common stock are not traded on any specific trading day) of the common stock equals or exceeds \$18.00 per share (as adjusted for stock splits, stock dividends, reorganizations and the like) for any 20 trading days within a 30 trading-day period ending on the third trading day prior to the date we send proper notice of such redemption, provided that on the date we give notice of redemption and during the entire period thereafter until the time we redeem the public warrants, we have an effective registration statement under the Securities Act covering the shares of common stock issuable upon exercise of the public warrants and a current prospectus relating to them is available. If and when the public warrants become redeemable by us, we may exercise our redemption right even if we are unable to register or qualify the underlying securities for sale under all applicable state securities laws. Redemption of the outstanding public warrants could force you: (i) to exercise public warrants and pay the exercise price therefor at a time when it may be disadvantageous for you to do so, (ii) to sell public warrants at the then-current market price when you might otherwise wish to hold public warrants or (iii) to accept the nominal redemption price which, at the time the outstanding public warrants are called for redemption, is likely to be substantially less than the market value of your public warrants.

General Risks Factors

We incur significant costs as a result of operating as a public company, and our management is required to devote substantial time to new compliance initiatives.

As a public company, we incur significant legal, accounting and other expenses that we did not incur as a private company. We are subject to the reporting requirements of the Exchange Act, which will require, among other things, that we file with the SEC annual, quarterly and current reports with respect to our business and financial condition. In addition, Sarbanes-Oxley, as well as rules subsequently adopted by the SEC and Nasdaq to implement provisions of Sarbanes-Oxley, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. Further, pursuant to the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010, the SEC has adopted additional rules and regulations in these areas, such as mandatory “say on pay” voting requirements that will apply to us when we cease to be an emerging growth company. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

We expect the rules and regulations applicable to public companies to substantially increase our legal and financial compliance costs and to make some activities more time consuming and costly. If these requirements divert the attention of our management and personnel from other business concerns, they could have a material adverse effect on our business, financial condition and results of operations. The increased costs will decrease our net income or increase our net loss, and may require us to reduce costs in other areas of our business or increase the

prices of our products or services. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to incur substantial costs to maintain the same or similar coverage. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our Board, our Board committees or as executive officers.

If we fail to maintain proper and effective internal control over financial reporting, our ability to produce accurate and timely financial statements could be impaired, investors may lose confidence in our financial reporting and the trading price of our Common Stock may decline.

Pursuant to Section 404 of Sarbanes-Oxley, our management is required to report upon the effectiveness of our internal control over financial reporting. When we lose our status as an “emerging growth company” and reach an accelerated filer threshold, our independent registered public accounting firm will be required to attest to the effectiveness of our internal control over financial reporting. The rules governing the standards that must be met for our management to assess our internal control over financial reporting are complex and require significant documentation, testing and possible remediation. To comply with the requirements of being a reporting company under the Exchange Act, we may need to upgrade our information technology systems; implement additional financial and management controls, reporting systems and procedures; and hire additional accounting and finance staff. If we or, if required, our auditors are unable to conclude that our internal control over financial reporting is effective, investors may lose confidence in our financial reporting and the trading price of our Common Stock may decline.

We are subject to U.S. and certain foreign export and import controls, sanctions, embargoes, anti-corruption laws and anti-money laundering laws and regulations. We could face criminal liability and other serious consequences for violations, which could harm our business.

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, and various economic and trade sanctions regulations administered by the U.S. Treasury Department’s Office of Foreign Assets Controls, and anti-corruption and anti-money laundering laws and regulations, including the U.S. Foreign Corrupt Practices Act of 1977, as amended, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, CROs, contractors and other collaborators and partners from authorizing, promising, offering, providing, soliciting or receiving, directly or indirectly, improper payments or anything else of value to or from recipients in the public or private sector. We may engage third parties for clinical trials outside of the United States, to sell our products abroad once we enter a commercialization phase, and/or to obtain necessary permits, licenses, patent registrations and other regulatory approvals. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, CROs, contractors and other collaborators and partners, even if we do not explicitly authorize or have actual knowledge of such activities. We are also subject to other U.S. laws and regulations governing export controls, as well as economic sanctions and embargoes on certain countries and persons.

Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm and other consequences.

Furthermore, U.S. export control laws and economic sanctions prohibit the provision of certain products and services to countries, governments, and persons targeted by U.S. sanctions. U.S. sanctions that have been or may be imposed as a result of military conflicts in other countries may impact our ability to continue activities at future clinical trial sites within regions covered by such sanctions. If we fail to comply with export and import regulations and such economic sanctions, penalties could be imposed, including fines and/or denial of certain export privileges. These export and import controls and economic sanctions could also adversely affect our supply chain.

We and any of our third-party manufacturers or suppliers may use potent chemical agents and hazardous materials, and any claims relating to improper handling, storage or disposal of these materials could be time consuming or costly.

We and any of our third-party manufacturers or suppliers and current or potential future collaborators will use biological materials, potent chemical agents and may use hazardous materials, including chemicals and biological agents and compounds that could be dangerous to human health and safety of the environment. Our operations and the operations of our third-party manufacturers and suppliers also produce hazardous waste products. Federal, state and local laws and regulations govern the use, generation, manufacture, storage, handling and disposal of these materials and wastes. Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our product development efforts. In addition, we cannot eliminate the risk of accidental injury or contamination from these materials or wastes. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. In the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended. Although we maintain workers' compensation insurance for certain costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for toxic tort claims that may be asserted against us in connection with our storage or disposal of biologic, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations, which have tended to become more stringent over time. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions or liabilities, which could materially adversely affect our business, financial condition, results of operations and prospects.

Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.

Our operations could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, war, terrorism, medical epidemics and other natural or manmade disasters or business interruptions, for which we are predominantly self-insured. We rely on third-party manufacturers to produce our product candidates. Our ability to obtain clinical supplies of our product candidates could be disrupted if the operations of these suppliers were affected by a man-made or natural disaster or other business interruption. In addition, our corporate headquarters is located in Solana Beach, California near major earthquake faults and fire zones, and the ultimate impact on us of being located near major earthquake faults and fire zones and being consolidated in a certain geographical area is unknown. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses.

Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and stock price.

From time to time, the global credit and financial markets have experienced extreme volatility and disruptions, including severely diminished liquidity and credit availability, rising interest and inflation rates, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. There can be no assurance that future deterioration in credit and financial markets and confidence in economic conditions will not occur. Our general business strategy may be adversely affected by any such economic downturn, volatile business environment or continued unpredictable and unstable market conditions. The financial markets and the global economy may also be adversely affected by the current or anticipated impact of military conflict, including the ongoing conflict between Russia and Ukraine, terrorism or other geopolitical events. Sanctions imposed by the United States and other countries in response to such conflicts, including the one in Ukraine, may also adversely impact the financial markets and the global economy, and any economic countermeasures by the affected countries or others could exacerbate market and economic instability. If the current equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a

material adverse effect on our growth strategy, financial performance and stock price and could require us to delay or abandon clinical development plans. In addition, there is a risk that one or more of our current service providers, manufacturers and other partners may not survive an economic downturn, which could directly affect our ability to attain our operating goals on schedule and on budget.

Changes in U.S. tax law may materially adversely affect our financial condition, results of operations and cash flows.

New income, sales, use or other tax laws, statutes, rules, regulations or ordinances could be enacted at any time, or interpreted, changed, modified or applied adversely to us, any of which could adversely affect our business operations and financial performance. In particular, the U.S. government may enact significant changes to the taxation of business entities including, among others, an increase in the corporate income tax rate and the imposition of minimum taxes or surtaxes on certain types of income. The likelihood of these changes being enacted or implemented is unclear. We are currently unable to predict whether such changes will occur. If such changes are enacted or implemented, we are currently unable to predict the ultimate impact on our business. We urge our investors to consult with their legal and tax advisors with respect to any changes in tax law and the potential tax consequences of investing in our common stock.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our corporate headquarters consists of an 1,800 square foot facility located in Solana Beach, California. The lease for our headquarters expires on October 31, 2024, with an option to extend the term for one additional three-year period. We believe that our existing facilities are adequate for our near-term needs. We believe that suitable additional or alternative space would be available if required in the future on commercially reasonable terms.

Item 3. Legal Proceedings.

We are not currently a party to any material legal proceedings. However, from time to time, we may become involved in legal proceedings or be subject to claims arising in the ordinary course of our business. Regardless of outcome, such proceedings or claims can have an adverse impact on us because of defense and settlement costs, diversion of resources and other factors, and there can be no assurances that favorable outcomes will be obtained.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

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

Market Information

Our common stock and warrants have been publicly traded on the Nasdaq Capital Market under the symbols “EFTR” and "EFTRW," respectively, since the completion of our Business Combination with Locust Walk Acquisition Corp. on August 25, 2021.

Holders of Common Stock

As of February 28, 2023, there were approximately 128 holders of record of our common stock. This number was derived from our shareholder records and does not include beneficial owners of our common stock whose shares are held in the name of various dealers, clearing agencies, banks, brokers and other fiduciaries.

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 after considering our financial condition, results of operations, capital requirements, business prospects and other factors the Board deems relevant, and subject to the restrictions contained in any future financing instruments. In addition, our loan and security agreement with Oxford Finance LLC governing our indebtedness contains restrictions on our ability to declare and pay cash dividends on our capital stock.

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.

Performance Graph

Not applicable.

Recent Sales of Unregistered Securities and Use of Proceeds

None.

Issuer Repurchases of Equity Securities

None.

Item 6. [Reserved]

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

The following discussion and analysis should be read in conjunction with our audited consolidated financial statements as of and for the years ended December 31, 2022 and 2021 included elsewhere in this Annual Report. This discussion and analysis contains forward-looking statements based upon our current beliefs, plans and expectations that involve risks, uncertainties and assumptions. Our actual results may differ materially from those anticipated 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 pioneering the development of a new class of oncology drugs we refer to as STRIs. Translation is the process in cells whereby the synthesis of proteins is directed by information contained in genetic sequences. We utilized our proprietary selective translation regulation technology platform to internally discover a portfolio of small molecule STRI product candidates. Our product candidates target the eIF4F complex and its activating kinase, mitogen-activated protein interacting kinase ("MNK"). The eIF4F complex is a central node where two of the most frequently mutated signaling pathways in cancer, the PI3K-AKT and RAS-MEK pathways, converge to activate the translation of select mRNA into proteins that are frequent culprits in key disease-driving processes. Inhibition of any one of these targets simultaneously downregulates multiple disease-driving proteins before they are synthesized. Each of our product candidates is designed to act on a single protein that drives the expression of a network of multiple functionally related proteins, including oncoproteins, which are proteins whose aberrant function can cause cancer, immunosuppressive proteins in T cells and proteins known to drive drug resistance that together control tumor growth, survival and immune evasion.

Our lead product candidate, tomivosertib, is an oral small-molecule inhibitor of MNK that we are developing in combination with inhibitors of anti-PD-(L)1 therapy, for the treatment of patients with solid tumors. In the second quarter of 2021, we initiated dosing in KICKSTART, our randomized Phase 2b clinical trial evaluating tomivosertib in combination with pembrolizumab in patients with metastatic non-small cell lung cancer ("NSCLC") with PD-L1 expression level greater than or equal to 50% ("PD-L1 \geq 50%"). Pembrolizumab is owned and marketed by Merck for frontline NSCLC and several other indications. We anticipate reporting topline data from the KICKSTART trial in the second half of 2023. Our second product candidate, zotatifin, is an inhibitor of eIF4A, a component of the eIF4F complex, and is currently being evaluated in a Phase 1/2 clinical trial in patients with certain solid tumors. We have completed the initial dose escalation portion of this trial and are currently evaluating zotatifin in combination with fulvestrant and abemaciclib in a Phase 2a open-label expansion cohort in patients with ER+ breast cancer. In light of the favorable safety results observed to date in the Phase 1/2 clinical trial, we have also resumed dose escalation of zotatifin in combination with fulvestrant in patients with ER+ breast cancer to determine if a higher dose of zotatifin can be utilized in future clinical studies. To date, we've reported initial data from four cohorts including patients with ER+ breast cancer, which demonstrated that zotatifin appeared to be safe, well tolerated and showed signals of activity, including partial responses in heavily pretreated ER+ breast cancer patients. We anticipate reporting additional data from one of the ER+ breast cancer cohorts which was expanded from seven to 18 patients in the first half of 2023. In addition, based on the safety profile established and target engagement data generated to date, we've resumed dose escalation. Data from the dose escalation portion of the trial is anticipated in the second half of 2023. We have also completed a Phase 1b clinical trial evaluating zotatifin as an antiviral agent against SARS-CoV-2. The study was a double-blind, randomized, placebo-controlled trial evaluating the safety and antiviral activity of a single dose of zotatifin. In this trial, zotatifin was found to be safe and well-tolerated, and demonstrated favorable trends in several assessments of viral clearance compared to placebo. We have entered into a global collaboration and license agreement with Pfizer for our earliest stage program, inhibitors of eIF4E, and Pfizer is currently conducting investigational new drug application ("IND") enabling studies for this program.

Since our inception in 2012 we have devoted substantially all of our resources to raising capital, identifying potential product candidates, establishing our intellectual property portfolio, conducting preclinical studies and clinical trials, establishing arrangements with third parties for the manufacture of our product candidates and related raw materials, and providing general and administrative support for these operations. We do not have any products approved for sale and have not generated any revenue from product sales. As of December 31, 2022, we have raised a total of \$302.4 million to fund our operations, comprised of aggregate gross proceeds of \$150.0 million from the sale and issuance of convertible preferred stock, gross proceeds of \$67.0 million from the issuance of common stock

in connection with the Business Combination in August 2021, \$42.0 million in collaboration revenue under our research collaboration and license agreement with Pfizer ("Pfizer Agreement"), \$35.0 million from loans under credit facilities, \$3.1 million gross proceeds from the sale of common stock under the equity purchase agreement ("Purchase Agreement") with Lincoln Park Capital Fund, LLC ("Lincoln Park"), \$5.0 million in grant revenue under the Research Subaward Agreement with The Regents of the University of California, on behalf of its San Francisco campus ("UCSF"), and \$0.3 million in gross proceeds from the sale of common stock under our Controlled Equity Offering Sales Agreement ("Sales Agreement") with Cantor Fitzgerald & Co ("Cantor") ("ATM Offering Program"). Other than with respect to the net income generated as a result of revenue under the Pfizer Agreement generated in 2020 and the net income generated in 2021 as a result of the change in valuation of the earn-out liability in 2021, we have incurred significant operating losses since our inception. Our net loss for the year ended December 31, 2022 was \$22.7 million and our net income for the year ended December 31, 2021 was \$15.8 million. As of December 31, 2022, we had an accumulated deficit of \$143.6 million. Substantially all of our operating losses resulted from expenses incurred in connection with the research and development of our product candidates and development programs, and general and administrative costs associated with our operations.

We expect to continue to incur significant expenses and losses for at least the next several years. We anticipate our expenses will increase substantially as we continue our development of, seek regulatory approval for and potentially commercialize any approved product candidates, hire additional personnel, protect our intellectual property and incur additional costs associated with being a public company. Our net losses may fluctuate significantly from quarter-to-quarter and year-to-year, depending on the timing of our clinical trials and preclinical studies and our expenditures on other research and development activities. As of December 31, 2022, we had \$26.3 million in cash, cash equivalents and short-term investments. To fund further operations, we will need to raise additional capital. Our current capital resources will not be sufficient for us to complete the clinical development of any of our product candidates or, if applicable, to prepare for commercializing any product candidate which may receive approval from the FDA or comparable foreign regulatory authority. Accordingly, we expect to finance our cash needs through a combination of equity offerings, debt financings, or other capital sources, including potential additional collaborations, licenses, and other similar arrangements. Adequate funding may not be available to us on acceptable terms, if at all. Our failure to raise capital or enter into such other arrangements when needed would have a negative impact on our financial condition and could force us to delay, limit, reduce, or terminate our research and development programs or other operations, or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Business Combination Transaction

On August 25, 2021, we completed the Business Combination pursuant to an Agreement and Plan of Merger dated May 26, 2021, among LWAC, LWAC Merger Sub Inc., and Old eFFECTOR (the "Merger Agreement"). Upon closing of the Business Combination, the combined company was renamed eFFECTOR Therapeutics, Inc. ("eFFECTOR").

Pursuant to the terms of the Merger Agreement, our shareholders exchanged their interests in LWAC and Old eFFECTOR for shares of common stock of eFFECTOR. In addition, awards under our existing equity incentive plans, including the 2013 Plan, continue in full force and effect on the same terms and conditions as were previously applicable to such awards, subject to adjustments to the exercise price and number of shares of common stock issuable upon exercise based on the final exchange ratio calculated in accordance with the Merger Agreement.

Gross proceeds from this transaction totaled approximately \$67.0 million, which included funds held in LWAC's trust and operating accounts and the completion of a concurrent PIPE Financing in which certain investors agreed to subscribe for and purchased an aggregate of \$60.7 million of common stock of eFFECTOR. The shareholders of LWAC approved the transaction on August 24, 2021. The transaction was previously approved by the boards of directors of both LWAC and Old eFFECTOR.

The transaction was accounted for as a "reverse recapitalization" in accordance with U.S. generally accepted accounting principles ("GAAP"). Under the reverse recapitalization model, the Business Combination was treated as Old eFFECTOR issuing equity for the net assets of LWAC, with no goodwill or intangible assets recorded. Under this method of accounting, LWAC was treated as the "acquired" company for financial reporting purposes. This determination is primarily based on the fact that subsequent to the Business Combination, eFFECTOR stockholders have a majority of the voting power of the combined company, comprise all of the ongoing operations of the combined entity, comprise a majority of the governing body of the combined company, and eFFECTOR senior

management comprise all of the senior management of the combined company. Reported results from operations included herein prior to the Business Combination are those of Old eFFECTOR. The shares and corresponding capital amounts, options and related per share amounts, and loss per share related to Old eFFECTOR's outstanding convertible preferred stock and common stock prior to the Business Combination have been retroactively restated to reflect the exchange ratio established in the Merger Agreement (1.00 share of Old eFFECTOR for 0.09657 shares of eFFECTOR) (the "Exchange Ratio").

The Combined Company's cash on hand after giving effect to these transactions, together with Old eFFECTOR's existing cash and cash equivalents will be used to fund the research and development of our development programs and for working capital and general corporate purposes. We may also use a portion of the remaining net proceeds and our existing cash and cash equivalents to in-license, acquire or invest in complementary businesses, technologies, products or assets. However, we have no current commitments or obligations to do so.

Financial Operations Overview

Revenue

We currently have no products approved for sale, and all revenue generated has been from the Pfizer Agreement along with grant revenue. In the future, we may generate additional revenue from collaboration, grant or license agreements we have entered into, or may enter into, with respect to our product candidates, as well as product sales from any approved product. Our ability to generate product revenues will depend on the successful development and eventual commercialization of our product candidates. If we fail to complete the development of our product candidates in a timely manner or to obtain regulatory approval for our product candidates, our ability to generate future revenue and our results of operations and financial position would be materially adversely affected.

Pfizer Agreement

In December 2019, we entered into the Pfizer Agreement, to research and develop small molecules that target eIF4E. Pursuant to the Pfizer Agreement, we granted Pfizer a worldwide, exclusive license, with a right to sublicense, under certain of our patents, know-how, and materials to use, develop, manufacture, commercialize, and otherwise exploit compounds or products targeting eIF4E, for any and all indications. Under the agreement, we were responsible for initial research in collaboration with Pfizer, and Pfizer is responsible for all further development of this development program, including submission of an IND and conducting all clinical development and commercialization activities.

Pursuant to the Pfizer Agreement, we received an upfront, one-time, non-refundable, non-creditable payment of \$15 million dollars from Pfizer. Pfizer was obligated to reimburse us for costs incurred for research performed, up to a specified cap in the low double-digit millions. Upon the achievement of specified development, regulatory and sales milestones, Pfizer will be obligated to pay us up to \$480 million dollars in the aggregate, as well as to pay us high single-digit percentage royalties on annual net sales of each licensed product. See "Business — Our Collaboration and License Agreements" included within this Annual Report on Form 10-K, for additional information about this agreement, including with respect to potential payments to us thereunder.

DARPA Subaward Agreement

In April 2021, we entered into a Research Subaward Agreement with UCSF (the "Subaward Agreement"), whereby up to \$5.0 million in allowable costs were reimbursable for clinical and manufacturing activities related to zotatifin for the treatment of COVID-19. Under the terms of Subaward Agreement, we were obligated to provide financial and technical reports to UCSF on a periodic basis. We have exhausted the full \$5.0 million of allowable costs under the Subaward Agreement as of December 31, 2022.

Operating Expenses

Research and Development Expenses

Research and development expenses primarily consist of costs associated with the preclinical and clinical development of our product candidates. Our research and development expenses include:

- external costs, including:
 - expenses incurred under arrangements with third parties, such as CROs and consultants and advisors that perform biology, chemistry, toxicology, clinical and regulatory functions;
 - costs related to acquiring and manufacturing preclinical and clinical trial materials, including continued testing such as process validation and stability of drug product;
 - costs related to toxicology testing and other research and preclinical studies; and
 - costs related to compliance with regulatory requirements and license fees.
- internal costs, including:
 - salaries and related overhead expenses, which include stock-based compensation and benefits, for personnel in research and development functions; and
 - facilities, depreciation, insurance and other expenses related to research and development.

We expense research and development costs as incurred. We account for nonrefundable advance payments for goods and services that will be used in future research and development activities as expenses when the service has been performed or when the goods have been received. We track external expenses on a development program and other program specific basis. However, we do not track internal costs on a program specific basis because these costs primarily relate to personnel and facilities, which are deployed across multiple programs under development.

The following table summarizes our research and development expenses for the periods indicated (in thousands).

	Year Ended December 31,	
	2022	2021
External development program expenses:		
tomivosertib (eFT508)	\$ 8,918	\$ 6,478
zotatifin (eFT226)	6,695	4,799
eIF4E	8	88
Unallocated internal research and development expenses:		
Personnel related	5,390	5,653
Other	2,302	2,938
Total research and development expenses	<u>\$ 23,313</u>	<u>\$ 19,956</u>

We expect our research and development expenses to increase substantially for the foreseeable future as we continue the development of our product candidates, particularly as we move into later stages of clinical development which typically cost more. The process of conducting clinical trials and preclinical studies necessary to obtain regulatory approval is costly and time-consuming. We may never succeed in achieving marketing approval for any of our product candidates. At this time, we cannot reasonably estimate the nature, timing or costs of the efforts that will be necessary to complete the remainder of the development of any of our product candidates or the period, if any, in which material net cash inflows from these product candidates may commence. We anticipate we will make determinations as to which product candidates and programs to pursue and how much funding to direct to each product candidate and program on an ongoing basis in response to clinical and preclinical results, regulatory developments, ongoing assessments as to each product candidate's and program's commercial potential, and our ability to enter into collaborations, to the extent we determine the resources or expertise of a collaborator would be beneficial for a given product candidate or program.

Our development costs may vary significantly based on factors such as:

- per patient trial costs;

- the number and scope of trials required for approval and preclinical and IND-enabling studies;
- the number of sites included in the trials;
- the length of time required to enroll suitable patients;
- the number of doses that patients receive;
- the number of patients that participate in the trials;
- the drop-out or discontinuation rates of patients;
- the duration of patient follow-up;
- the extent of reimbursement for the costs of approved therapies used in our combination trials;
- potential additional safety monitoring or other studies requested by regulatory agencies;
- the number and complexity of procedures, analyses and tests performed during the trial;
- the phase of development of the product candidate;
- the impact of any interruptions to our operations or to those of the third parties with whom we work due to the COVID-19 pandemic or any future epidemics;
- the efficacy and safety profile of the product candidate; and
- the extent to which we establish additional collaboration, license or other arrangements.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation and benefits, and consulting fees for finance, accounting, and other administrative functions. Other costs include legal fees relating to patent and corporate matters, insurance, and facility costs not otherwise included in research and development expenses.

We expect our general and administrative expenses will increase substantially for the foreseeable future as we advance our product candidates through clinical development. We also will incur additional expenses as a result of operating as a public company, including expenses related to compliance with the rules and regulations of the SEC and the Nasdaq listing rules, additional insurance expenses, investor relations activities and other administrative and professional services. In addition, if we obtain regulatory approval for any of our product candidates, we expect to incur expenses associated with building a sales and marketing team if we choose to commercialize such product candidates on our own.

Other Income (Expense)

Interest Income

Interest income consists of interest earned on our cash equivalents and short-term investments.

Interest Expense

Interest expense consists of interest on our outstanding debt facilities. We entered into a debt facility with Oxford Financial LLC ("Oxford") in March 2021. Interest expense recorded in 2022 consisted of amounts attributable to the Oxford term loan, and interest expense recorded in 2021 consisted of amounts attributable to our then outstanding term loans with Silicon Valley Bank ("SVB"), as well as the Oxford term loan.

Loss of Debt Extinguishment

In March 2021, we repaid the SVB term loans using the proceeds from the Oxford term loan. We recorded a loss on debt extinguishment in the amount of \$0.5 million in connection with the transaction, which includes the unamortized debt discount and final payment associated with outstanding SVB term loans at the time of extinguishment along with the \$0.1 million prepayment fee.

Other Income (Expense)

We issued preferred stock warrants in connection with our SVB and Oxford debt facilities and assumed private placement warrants in connection with the Business Combination transaction that are required to be accounted for as liabilities and remeasured to fair value at each reporting date, with changes in the fair value reported as a component of other income (expense).

In January 2022, we entered into the Purchase Agreement with Lincoln Park and recorded other expense in connection with commitment shares of common stock issued to Lincoln Park in the transaction.

Change in Fair Value of Earn-Out Liability

We determined that the contingent obligation to issue Earn-Out Shares to existing Old eFFECTOR shareholders is not indexed to our stock under Accounting Standards Codification ("ASC") 815-40 and are therefore required to be accounted for as liabilities and remeasured at fair value each reporting period, with changes in fair value reported as a component of other income (expense).

Results of Operations

Comparison of the Years Ended December 31, 2022 and 2021

The following table sets forth our results of operations for the years ended December 31, 2022 and 2021 (in thousands):

	Year Ended December 31,		Change
	2022	2021	
Grant revenue	3,553	1,430	2,123
Operating expenses:			
Research and development	23,313	19,956	3,357
General and administrative	12,643	13,371	(728)
Total operating expenses	35,956	33,327	2,629
Loss from operations	(32,403)	(31,897)	(506)
Other income (expense), net	9,738	47,695	(37,957)
Net income (loss)	<u>\$ (22,665)</u>	<u>\$ 15,798</u>	<u>\$ (38,463)</u>

Grant Revenue

Grant revenue was \$3.6 million and \$1.4 million for the years ended December 31, 2022 and 2021, respectively. The increase in grant revenue was due to the timing of the initial grant in April 2021 along with increased development activities associated with the development of zotatifin for the treatment of COVID-19 in the year ended December 31, 2022.

Research and Development Expenses

Research and development expenses were \$23.3 million and \$20.0 million for the years ended December 31, 2022 and 2021, respectively. The increase in research and development expenses of \$3.3 million was primarily due to a \$2.4 million increase for the tomivosertib program due to increased costs associated with the KICKSTART trial, and a \$1.9 million increase for the zotatifin program due to increased costs associated with the COVID-19 and oncology trials, along with increased costs related to drug product manufacturing. Further, there was a \$0.4 million increase in consultant costs in 2022 as compared to 2021. These costs were partially offset by a \$1.0 million decrease in license fees due to a one-time payment made to UCSF in connection with the completion of the Business Combination in 2021, a \$0.3 million decrease in employee expenses for stock-based compensation expense associated with the earn-out liability in 2022 as compared to 2021, and a \$0.1 million decrease in expenses related to the eIF4E program.

General and Administrative Expenses

General and administrative expenses were \$12.6 million and \$13.4 million for the years ended December 31, 2022 and 2021, respectively. The decrease in general and administrative expenses during this period of \$0.8 million was primarily due to a \$2.2 million decrease in personnel-related costs for stock-based compensation expense associated with the earn-out liability in 2022 as compared to 2021 and decreases in patent and corporate legal costs of \$0.5 million during 2022 as compared to the same period in 2021. These decreases were partially offset by an increase of \$1.6 million in costs primarily related to insurance costs, and a \$0.3 million increase in consultant costs in 2022 compared to the same period in 2021.

Other Income (Expense)

Other income was \$9.7 million and \$47.7 million for the years ended December 31, 2022 and 2021, respectively. The decrease in other income of \$38.0 million was mostly due to the difference in the change in fair value of the earn-out liability and warrant liability during 2022 along with \$1.2 million in other expense recorded in 2022 primarily related to the equity purchase agreement with Lincoln Park, partially offset by the loss on debt extinguishment of \$0.5 million recorded in 2021.

Liquidity and Capital Resources

Sources of Liquidity

From our inception through December 31, 2022, we have raised a total of \$302.4 million to fund our operations, comprised of aggregate gross proceeds of \$150.0 million from the sale and issuance of convertible preferred stock, gross proceeds of \$67.0 million from the issuance of common stock in connection with the Business Combination in August 2021, \$42.0 million in collaboration revenue under our research collaboration and license agreement with Pfizer, \$35.0 million from loans under credit facilities, \$3.1 million in gross proceeds from the sale of common stock to Lincoln Park under the equity purchase agreement (\$46.9 million remaining available for sale under the equity purchase agreement as of December 31, 2022), \$5.0 million in grant revenue under the Research Subaward Agreement with UCSF, and \$0.3 million in gross proceeds from the sale of common stock under the ATM Offering Program.

Prior to the Business Combination, our operations were funded primarily from the issuance of convertible preferred stock and common stock. Upon the closing of the Business Combination in August 2021, we received net proceeds totaling approximately \$52.9 million.

Our cash and cash equivalents and short-term investments totaled \$26.3 million as of December 31, 2022. Until required for use in our business, we typically invest our cash in investments that are highly liquid, readily convertible to cash with original maturities of 1 year or less at the date of purchase. We attempt to minimize the risks related to our cash and cash equivalents and investments by maintaining balances in accounts only with accredited financial institutions and, consequently, we do not believe we are subject to unusual credit risk beyond the normal credit risk associated with ordinary commercial banking relationships.

Oxford Loan Facility

In March 2021, we entered into a Loan and Security Agreement (“Oxford LSA”) with Oxford, pursuant to which we may borrow up to \$30.0 million, issuable in two separate tranches of \$20.0 million (“Term A Loan”) and \$10.0 million (“Term B Loan”), collectively referred to as the Oxford Loans. The Term A Loan became available at the effective date of the Oxford LSA and \$12.5 million of the proceeds were used to pay off the outstanding SVB Term Loans. The remaining net proceeds from the Term A Loan of \$7.4 million, after taking into effect specified issuance and legal fees designated within the distribution letter, were distributed in March 2021. The Term A Loan had an interest-only period that commenced upon the borrowing with interest due and payable upon the first day of each month. The interest-only period initially was planned to end May 1, 2023, provided that upon the funding of the Term B Loan the end date would be extended to May 1, 2024.

On February 22, 2022, we entered into an amendment to the Oxford LSA whereby the interest only period for the Term A Loans will end on March 1, 2024, instead of May 1, 2023. In connection with the amendment, the maturity of the Term A Loans was extended from March 18, 2026 to February 1, 2027. The principal payments due

under the Oxford Loans, and the related accrued final payment, have been classified as current liabilities as of December 31, 2022, due to our assessment that the material adverse change clause under the Oxford Loans is not within our control. We have not been notified of an event of default by the lender as of the date of this report.

The Term B Loan would become available upon achievement of certain clinical development milestones, and remain available until the earlier of (i) June 30, 2023, (ii) forty-five days after the occurrence of such clinical development milestone, and (iii) the occurrence of an event of default. As a result of the discontinuation of one of the cohorts in our KICKSTART trial, which was previously announced in January 2023, we do not expect to achieve the clinical development milestones by June 30, 2023 and therefore do not expect to have access to the additional \$10.0 million under the Term B Loan.

We are required to make a final payment equal to 5.5% of each funded tranche at maturity, which has been recorded as a debt discount and is being amortized over the term of the debt arrangements. In connection with the Oxford LSA, we issued warrants to purchase a total of 37,575 shares of Series C Preferred Stock at an exercise price of \$5.33 per share. The warrants were automatically cashless exercised on August 25, 2021, in connection with the completion of the Business Combination, for 17,575 shares of common stock.

DARPA Subaward Agreement

In April 2021, we entered into a Subaward Agreement with UCSF, whereby up to \$5.0 million in allowable costs were reimbursable for clinical and manufacturing activities related to zotatifin for the treatment of COVID-19. Under the terms of Research Subaward Agreement, we are obligated to provide financial and technical reports to UCSF on a periodic basis. The Subaward Agreement can be terminated by either party upon written notice and also in the event that DARPA suspends or terminates its cooperative agreement with UCSF. The initial award period for the Subaward Agreement ended in December 2021 and in April 2022 we received an extension of the award period to December 2022, with the same maximum \$5.0 million reimbursement amount. We have exhausted the full \$5.0 million of allowable costs under the Subaward Agreement as of December 31, 2022.

Equity Purchase Agreement with Lincoln Park

On January 24, 2022, we entered into the Purchase Agreement with Lincoln Park which provides for the sale to Lincoln Park up to \$50.0 million of shares of our common stock over the thirty-six (36) month term of the Purchase Agreement, subject to certain conditions. In connection with the Purchase Agreement, Lincoln Park made an initial purchase of \$3.0 million of shares of common stock, which equated to 557,610 shares of common stock, and we issued 142,939 shares of common stock to Lincoln Park as a commitment fee in connection with entering into the Purchase Agreement. As of December 31, 2022, we had issued an additional 30,000 shares at an average price per share of \$1.74 under the Purchase Agreement for gross proceeds of \$52 thousand. As of the date of this report, we were unable to sell additional shares under the Purchase Agreement because our shares are trading at less than \$1.00 per share, which is the minimum price that we can sell shares to Lincoln Park. No assurance can be given that we will sell any additional shares of common stock under the Purchase Agreement, or, if we do, as to the price or amount of shares of common stock that we sell or the dates when such sales will take place. See Note 9 to our consolidated financial statements contained elsewhere in this Form 10-K for information concerning the Purchase Agreement.

At-the-Market Offering Program with Cantor

In September 2022, we entered into the Sales Agreement with Cantor, under which we may, from time to time, sell shares of our common stock having an aggregate offering price of up to \$15.0 million (the "ATM Offering Program"). Sales of the shares of common stock will be made at prevailing market prices at the time of sale, or as otherwise agreed with Cantor. We will pay a commission to Cantor of 3.0% of the gross proceeds of any shares of common stock sold under the Sales Agreement. During the year ended December 31, 2022, we sold an aggregate of 478,964 shares of common stock at a weighted-average price of \$0.60 per share for gross proceeds of approximately \$0.3 million under the ATM Offering Program. We incurred offering costs in connection with the ATM Offering Program, including commissions, of approximately \$0.2 million during the year ended December 31, 2022.

In addition, under current SEC regulations, as of the filing of this report, our public float is less than \$75 million, and under SEC regulations for so long as our public float remains less than \$75 million, the amount we can raise through primary public offerings of securities in any twelve-month period using shelf registration statements is

limited to an aggregate of one-third of our public float, which is referred to as the baby shelf rules. As of February 28, 2023, our public float was approximately \$17.2 million, based on 34,520,253 shares of outstanding common stock held by non-affiliates and at a price of \$0.4982 per share, which was the last reported sale price of our common stock on the Nasdaq Capital Market on February 28, 2023. As a result of our public float being below \$75 million, we will be limited by the baby shelf rules until such time as our public float exceeds \$75 million, which means we only have the capacity to sell shares up to one-third of our public float under shelf registration statements in any twelve-month period. We will remain constrained by the baby shelf rules under our Form S-3 shelf registration statement until such time as our public float exceeds \$75 million, at which time, the number of securities we may sell under a Form S-3 registration statement will no longer be limited by the baby shelf rules.

Funding Requirements

As of December 31, 2022, we had \$26.3 million in cash and cash equivalents and short-term investments, which we estimate is sufficient to fund operations into the first quarter of 2024. However, we have prepared cash flow forecasts which indicate that based on our expected operating cash flows, without taking into account future projected cash inflows, there is substantial doubt about our ability to continue as a going concern within twelve months after the date that the financial statements for the year ended December 31, 2022, are issued. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we expect. Furthermore, our operating plans may change and we may need additional funds sooner than planned. Additionally, the process of testing product candidates in clinical trials is costly, and the timing of progress in these trials is uncertain. Our future capital requirements are difficult to forecast and will depend on many factors, including but not limited to:

- the type, number, scope, progress, expansions, results of and timing of clinical trials and preclinical studies of our product candidates which we are pursuing or may choose to pursue in the future;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs of obtaining, maintaining and enforcing our patents and other intellectual property rights;
- the costs and timing of manufacturing for our product candidates, including commercial manufacturing if any product candidate is approved;
- our efforts to enhance operational systems and hire additional personnel to satisfy our obligations as a public company, including enhanced internal controls over financial reporting;
- the costs associated with hiring additional personnel and consultants as our clinical and preclinical activities increase;
- the costs and timing of establishing or securing sales and marketing capabilities if any product candidate is approved;
- our ability to achieve sufficient market acceptance, coverage and adequate reimbursement from third-party payors and adequate market share and revenue for any approved products;
- any delays and cost increases that result from the COVID-19 pandemic or future epidemic diseases;
- the terms and timing of establishing and maintaining additional collaborations, licenses and other similar arrangements; and
- the costs associated with any products or technologies that we may in-license or acquire.

We have no other committed sources of capital, other than potential future sales under the Purchase Agreement with Lincoln Park and the ATM Offering Program with Cantor. Until we can generate a sufficient amount of product revenue to finance our cash requirements, if ever, we expect to finance our future cash needs primarily through equity offerings, debt financings or other capital sources, including potential additional collaborations, licenses and other similar arrangements. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be or could be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing, if available, may involve agreements that include covenants

limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through other collaborations or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our research and development programs or other operations, or grant rights to develop and market product candidates to third parties that we would otherwise prefer to develop and market ourselves.

Public Warrants and Private Placement Warrants

LWAC issued public warrants and private placement warrants (collectively, the "Warrants") in its initial public offering in January 2021. The Warrants became exercisable beginning on January 12, 2022, which was 12 months from the closing of LWAC's initial public offering. Warrants may only be exercised for a whole number of shares. No fractional shares will be issued upon exercise of the warrants. Each whole warrant entitles the holder to purchase one share of common stock at an exercise price of \$11.50 per share.

We will use commercially reasonable efforts to maintain the effectiveness of our registration statement and a current prospectus relating to those common shares issuable upon exercise of the warrants until the warrants expire or are redeemed, as specified in the Warrant Agreement, dated January 7, 2021, between the Company and Continental Stock Transfer & Trust Company (the "Warrant Agreement"). If the common stock at the time of any exercise of a warrant is not listed on a national securities exchange, we may, at our option, require holders of the warrants who exercise their warrants to do so on a "cashless basis." We are not required to file or maintain in effect a registration statement. In no event will the Company be required to net cash settle any warrant.

As the Warrants are now exercisable, we may redeem the outstanding warrants in whole and not in part at a price of \$0.01 per warrant upon a minimum of 30 days' prior written notice of redemption, and, if and only if the last sale price of our common stock equals or exceeds \$18.00 per share for any 20 trading days within a 30-trading day period ending three business days before the Company sends the notice of redemption to the Warrant holders.

The private placement warrants are identical to the public warrants except that, so long as they are held by the Locust Walk Sponsor, LLC (the "Sponsor") or its permitted transferees: (i) they will not be redeemable by the Company; (ii) they may be exercised by the holders on a cashless basis; and (iii) they are subject to registration rights.

The Warrants will expire on August 25, 2026, which is five years after the completion of the Business Combination, or earlier upon redemption or liquidation.

Cash Flows

The following table sets forth a summary of the net cash flow activity for each of the periods indicated (in thousands):

	Year Ended December 31,	
	2022	2021
Net cash provided by (used in):		
Operating activities	\$ (25,899)	\$ (24,888)
Investing activities	(17,860)	565
Financing activities	2,765	58,809
Net increase (decrease) in cash	\$ (40,994)	\$ 34,486

Operating Activities

During the year ended December 31, 2022, net cash used in operating activities was \$25.9 million, which resulted from a net loss of \$22.7 million adjusted for changes in operating assets and liabilities and non-cash charges. Non-cash charges and other adjustments included \$12.1 million from a gain recorded from the change in fair value of the earn-out liability, \$5.3 million in stock-based compensation, \$1.2 million other expense recorded in connection with the Purchase Agreement with Lincoln Park, \$0.6 million from a gain recorded from change in fair value of liability-classified warrants and \$0.3 million in non-cash interest expense. Changes in operating assets and

liabilities included a \$1.8 million decrease in prepaid expenses and other assets related to the amortization of prepaid public company insurance policies and a reduction in prepaid research and development balances, and a \$1.0 million increase in accounts payable.

During the year ended December 31, 2021, net cash used in operating activities was \$24.9 million, which resulted from net income of \$15.8 million adjusted for changes in operating assets and liabilities and non-cash charges. Non-cash charges included \$48.9 million from a gain recorded from the change in fair value of the earn-out liability, \$1.0 million from a gain recorded from change in fair value of liability-classified warrants, \$0.5 million from a loss recorded on debt extinguishment, \$8.7 million in stock-based compensation and \$0.3 million in non-cash interest expense. Changes in operating assets and liabilities included a \$2.2 million increase in prepaid expenses and other assets and other non-current assets related to the payment of public company insurance policies and a \$1.8 million increase in accrued expenses primarily related to legal and public company accounting fees, along with the accrued bonus.

Investing Activities

During the year ended December 31, 2022, net cash used in investing activities was \$17.9 million as a result of the purchases of short-term investments, partially offset by maturities during the period.

During the year ended December 31, 2021, net cash provided by investing activities was \$0.6 million as a result of proceeds received in connection with the sale of laboratory equipment.

Financing Activities

During the year ended December 31, 2022, net cash provided by financing activities was \$2.8 million, which was the result of net proceeds from the issuance of common stock to Lincoln Park under the Purchase Agreement and net proceeds from the issuance of common stock under the ATM Offering Program during the period.

During the year ended December 31, 2021, net cash provided by financing activities was \$58.8 million, which was the result of net proceeds of \$19.8 million from the issuance of the Oxford Term A Loans, partially offset by the \$13.9 million repayment of the previously outstanding SVB Term A and Term B Loans, and net proceeds of \$52.9 million as a result of the completion of the Business Combination during the period.

Critical Accounting Policies and Estimates

The SEC defines critical accounting policies as those that are, in management's view, important to the portrayal of our financial condition and results of operations and demanding of management's judgment. 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 GAAP. The preparation of these consolidated financial statements required estimates and judgments that affect the reported amounts of assets, liabilities, and expenses and the disclosure of contingent assets and liabilities in the consolidated financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to accrued expenses and share-based compensation. We base our estimates on historical experience, known trends and events, and various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully described in Note 2 to our consolidated financial statements appearing elsewhere in this Annual Report, we believe that the following accounting policies are the most critical for fully understanding and evaluating our financial condition and results of operations.

Clinical Trial Accruals and Preclinical Studies

We record expenses resulting from our obligations under contracts with vendors and consultants, CROs and clinical sites in connection with conducting clinical trials and preclinical studies. 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 clinical trial and preclinical study expenses in our consolidated 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 clinical

trial or preclinical study as measured by the timing of various aspects of the clinical trial, preclinical study, or related activities. We determine accrual estimates through review of the underlying contracts along with preparation of financial models taking into account correspondence with clinical and other key personnel and third-party service providers as to the progress of the clinical trials, preclinical studies, or other services being conducted. During the course of a clinical trial or preclinical study, we adjust our rate of expense recognition if actual results differ from our estimates. To date, there have been no material differences from our estimates to the amount incurred. However, due to the nature of estimates, we cannot assure you that we will not make changes to our estimates in the future as we become aware of additional information about the status or conduct of our clinical trials, preclinical studies or other research activities.

Public Warrants and Private Placement Warrants

Upon completion of the Business Combination, we assumed public warrants and private placement warrants that were issued by LWAC in connection with their initial public offering in January 2021 whereby holders of the public warrants and private placement warrants are entitled to acquire common stock of the Company. We have concluded that the public warrants are equity-classified. Since the settlement value of the private placement warrants is dependent, in part, on who holds the warrants at the time of settlement, they are not considered indexed to the Company's stock and are therefore recorded as liabilities. Warrants classified as liabilities are recorded at their estimated fair value on the date of issuance and are revalued at each subsequent balance sheet date, with fair value changes recognized in other income (expense), net in the accompanying consolidated statements of operations and comprehensive income (loss). We estimate the fair value of these warrants using the Black-Scholes option pricing model. Fluctuations in our stock price have the most significant impact on the value derived from the pricing model.

Earn-Out Shares

In accordance with the Merger Agreement, 5,000,000 shares are contingently issuable to Old eFFECTOR stockholders and option holders upon the occurrence of the Triggering Event, defined within the Merger Agreement as the date on which the common stock price equals or exceeds \$20.00 over at least 20 trading days out of 30 consecutive trading day period for the two-year period following the close date of the Business Combination. The estimated fair value of the Earn-Out Shares was determined using a Monte Carlo simulation valuation model using a distribution of potential outcomes on a monthly basis over the earn-out period using the most reliable information available.

We have determined that the contingent obligation to issue Earn-Out Shares to existing Old eFFECTOR shareholders is not indexed to the Company's stock under ASC 815-40 and therefore equity treatment is precluded. The Triggering Event that determines the issuance of the Earn-Out Shares includes terms that are not solely indexed to our common stock, and as such, liability classification is required. Equity-linked instruments classified as liabilities are recorded at their estimated fair value on the date of issuance and are revalued at each subsequent balance sheet date, with fair value changes recognized in other income (expense), net in the accompanying consolidated statements of operations and comprehensive income (loss).

We have determined that the contingent obligation to issue Earn-Out Shares to existing Old eFFECTOR option holders falls within the scope of ASC 718, Share-based Compensation, because the option holders are required to continue providing service until the occurrence of the Triggering Event. The fair value of the option holder Earn-Out Shares is recorded as share-based compensation over the derived service period of the Monte Carlo simulation valuation model, recognized in research and development and general and administrative expense in the accompanying consolidated statements of operations and comprehensive income (loss). Fluctuations in our stock price have the most significant impact on the value derived from the valuation model.

Emerging growth company and smaller reporting company status

Following the Business Combination, we qualify as an emerging growth company under the JOBS Act. As such, we can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to avail ourselves of this exemption from new or revised accounting standards and, therefore, our consolidated financial statements may not be comparable to companies that comply with new or revised accounting pronouncements as of public company

effective dates. We also intend to rely on other exemptions provided by the JOBS Act, including without limitation, not being required to comply with the auditor attestation requirements of Section 404(b) of Sarbanes-Oxley.

We will remain an emerging growth company until the earliest of (i) December 31, 2026; (ii) the last day of the fiscal year in which we have total annual gross revenue of at least \$1.235 billion; (iii) the last day of the fiscal year in which we are deemed to be a “large accelerated filer” as defined in Rule 12b-2 under the Exchange Act, which would occur if the market value of our common stock held by non-affiliates exceeded \$700.0 million as of the last business day of the second fiscal quarter of such year; or (iv) the date on which we have issued more than \$1.0 billion in nonconvertible debt securities during the prior three-year period.

We are also a smaller reporting company as defined in the Exchange Act. We may continue to be a smaller reporting company even after we are no longer an emerging growth company. We may take advantage of certain of the scaled disclosures available to smaller reporting companies and will be able to take advantage of these scaled disclosures for so long as our voting and non-voting common stock held by non-affiliates is less than \$250.0 million measured on the last business day of our second fiscal quarter, or our annual revenue is less than \$100.0 million during the most recently completed fiscal year and our voting and non voting common stock held by non-affiliates is less than \$700.0 million measured on the last business day of our second fiscal quarter.

Recent Accounting Pronouncements

See Note 2 to our consolidated financial statements contained elsewhere in this Annual Report for information concerning recent accounting pronouncements.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

Interest rate risk

The market risk inherent in our financial instruments and in our financial position represents the potential loss arising from adverse changes in interest rates. As of December 31, 2022, we had \$8.7 million in cash and cash equivalents, consisting of non-interest operating accounts and interest-bearing money market funds. As of December 31, 2022, we had \$17.6 million in short-term investments, consisting of U.S. Treasury securities. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. Due to the short-term, low-risk profile of our money market funds and short-term investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our cash equivalents.

Our Oxford Term A Loan carries a variable interest rate equal to the greater of (i) 7.7% and (ii) the sum of the prime rate plus 4.45%. The impact of a 100 basis point change in market interest rate would not have a material impact on our financial condition and/or results of operations.

Foreign currency exchange risk

Our reporting and functional currency is the U.S. dollar. We currently do not have significant exposure to foreign currencies as we hold no foreign exchange contracts, option contracts, or other foreign hedging arrangements. Our operations may be subject to fluctuations in foreign currency exchange rates in the future.

Effects of inflation

Inflation generally affects us by increasing our costs of labor and research and development. We believe inflation has not had a material effect on our results of operations during the periods presented.

Item 8. Consolidated Financial Statements and Supplementary Data.

The consolidated financial statements required pursuant to this item are included in Item 15 of this Annual Report and are presented beginning on page F-1.

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.***Conclusion Regarding the Effectiveness of Disclosure Controls and Procedures***

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed by us in our reports that we file or submit pursuant to the Exchange Act, is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow for timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and management is required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Under the supervision and with participation of our management, including our Chief Executive Officer and our Chief Financial Officer, we carried out an evaluation of the effectiveness of our disclosure controls and procedures (as such term is defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) as of the end of the period covered by this report. Based on this evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that our disclosure controls and procedures were effective at a reasonable level of assurance as of December 31, 2022.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with GAAP. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions or that the degree of compliance with the policies or procedures may deteriorate.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2022 based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in its 2013 Internal Control — Integrated Framework. Based on this assessment, our management has concluded that our internal control over financial reporting was effective as of December 31, 2022.

Attestation Report of the Registered Public Accounting Firm

This Annual Report does not include an attestation report of our registered public accounting firm due to an exemption provided 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 during the quarter ended December 31, 2022 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

Item 10. Directors, Executive Officers and Corporate Governance.**Management and Board of Directors**

The following sets forth certain information, as of February 15, 2023, concerning the persons who serve as our executive officers and members of our Board.

Name	Age	Position
Executive Officers		
Stephen T. Worland, Ph.D.	65	President, Chief Executive Officer and Director
Michael Byrnes	46	Chief Financial Officer
Douglas Warner, M.D.	51	Chief Medical Officer
Non-Employee Directors		
Brian M. Gallagher, Jr., Ph.D. (1)(3)	53	Chair
Elizabeth P. Bhatt (3)	55	Director
Chris Ehrlich (1)(2)	52	Director
Kristen Harrington-Smith (2)(3)	50	Director
Barbara Klencke, M.D. (2)	65	Director
John W. Smither (1)(3)	70	Director

- (1) Member of the Audit Committee.
- (2) Member of the Compensation Committee
- (3) Member of the Nominating and Corporate Governance Committee

Executive Officers

Stephen T. Worland, Ph.D. has served as our President and Chief Executive Officer and as a member of the Old eFFECTOR board of directors since our inception in May 2012, and has served on the Board since August 2021. Previously, Dr. Worland served as Chief Executive Officer and as a member of the board of directors of Anadys Pharmaceuticals, Inc. from August 2007 until its acquisition by Roche Holding AG in 2011. Prior to his appointment as Chief Executive Officer of Anadys Pharmaceuticals, Dr. Worland served as its Chief Scientific Officer and President, Pharmaceuticals. Prior to Anadys Pharmaceuticals, Inc., Dr. Worland was Vice President and Head of Antiviral Research at Pfizer Inc. and Vice President at Warner Lambert Co., where he was responsible for worldwide anti-infectives strategy. Dr. Worland has served as a director of Tracon Pharmaceuticals, Inc. since February 2015 and as a director of Blackstone Medicines since April 2017. Dr. Worland was an NIH postdoctoral fellow in molecular biology at Harvard University and completed a Ph.D. in Chemistry at the University of California, Berkeley. He received his B.S. with Highest Honors in Biological Chemistry from the University of Michigan. Dr. Worland's extensive knowledge of our business, as well as his extensive experience in the biotechnology and pharmaceutical industries contributed to our Board's conclusion that he should serve as a director of our company.

Michael Byrnes has served as our Chief Financial Officer since December 2020. Previously, Mr. Byrnes was Senior Vice President of Finance at Principia Biopharma, Inc. from January 2020 until its acquisition by Sanofi in September 2020. Prior to that, Mr. Byrnes served as Chief Financial Officer of Alkahest, Inc. from May 2018 to January 2020 and Chief Financial Officer of Ocera Therapeutics, Inc., from December 2014 until its acquisition by Mallinckrodt Pharmaceuticals in December 2017. Mr. Byrnes served as Corporate Controller of Maxygen, Inc. from March 2010 to December 2014 and prior to that, held finance positions of increasing responsibility from 2000 to 2010 with NeurogesX, Inc., Lipid Sciences, Inc. and ADAC Laboratories, Inc., a Philips Medical Systems company. Mr. Byrnes received his B.S.C. in Finance from Santa Clara University and an M.B.A. from California State University, Hayward.

Douglas Warner M.D. has served as our Chief Medical Officer since August 2022. Previously, Dr. Warner held roles of increasing responsibility over 18 years at Amgen where he oversaw extensive clinical development

programs in multiple indications across oncology and general medicine. In his most recent position, Executive Medical Director, Group Product Area Lead, Dr. Warner provided development guidance and oversight over a broad portfolio of solid tumor immune-oncology and pathway inhibitor development programs that ranged from Phase 1 to marketed products. Prior to this position, Dr. Warner was the Global Development Lead for several products including Vectibix®, XGEVA®, and Prolia®. In this role, Dr. Warner led evidence generation and oversaw the design, execution, and analysis of studies across the phases of development, including large global Phase 3 trials, and was the clinical development leader for major regulatory filings worldwide. Dr. Warner is co-author on numerous peer-reviewed articles including those in *The Lancet*, *The Lancet Oncology*, and *The Journal of Clinical Oncology*. He received his B.A. from the University of Pennsylvania, his M.D. from the Duke University School of Medicine, and his M.B.A. from the UCLA Anderson School of Management.

Non-Employee Directors

Brian M. Gallagher, Jr., Ph.D. served on Old eFFECTOR's board of directors since 2020, and as chair of its board since 2020 and has served as chair of the Board since August 2021. Currently, Dr. Gallagher is Managing Partner and Co-founder of Trekk Venture Partners, an early stage biotech focused venture firm. Dr. Gallagher previously served as a Partner at Abingworth LLP from 2018 to 2022. Previously, from 2010 to 2018, Dr. Gallagher was a Partner at SR One, the venture capital arm of GlaxoSmithKline. He is currently on the board of directors of Slate Bio and was formerly a board director at Q32 Bio from 2020 to 2022, Abingworth Management Inc. from 2018 to 2022, and Nimbus Therapeutics from 2011 to 2018, River Vision (acquired by Horizon Pharma) from 2012 to 2017, Translate Bio (TBIO) from 2011 to 2019, Aileron Therapeutics (ALRN) from 2010 to 2018, Navitor Pharmaceuticals from 2014 to 2018, and CalciMedica from 2013 to 2018, and was a board observer at Constellation Pharmaceuticals (CNST) from 2010 to 2018 and Dicerna Pharmaceuticals (DRNA) from 2010 to 2014, and has served on the boards of other private and public companies. Prior to SR One, Dr. Gallagher was at Sirtris Pharmaceuticals where he was responsible for corporate development, operations and post-merger integration after the company's acquisition by GSK. Earlier in his career, Dr. Gallagher held key roles in operations and R&D at Alantors Pharmaceuticals (acquired by Amgen) and at Eisai. Dr. Gallagher holds a Ph.D. in organic chemistry from the University of Michigan and a BS in chemistry from the University of Massachusetts, where he was a Shapiro scholar. He is an inventor on over 25 patents and applications and is the senior author of a number of publications in prominent journals. He currently serves on the Investment Advisory Board for University of Michigan Biomedical Venture Fund, and the Advisory Boards for Michigan Drug Discovery and formerly NYU Medical School's Therapeutic Alliances. Dr. Gallagher's experience as a venture capitalist and service as a director of other biopharmaceutical companies contributed to our Board's conclusion that he should serve as a Chair of our company.

Elizabeth P. Bhatt served as an independent director of LWAC since January 2021 and continues to serve on the Board following the Business Combination. Since June 2022, Ms. Bhatt has served as Chief Operating Officer of Septerna, Inc. From September 2019 to May 2022, Ms. Bhatt served as the Chief Business and Strategy Officer of Applied Molecular Transport Inc. (NASDAQ: AMTI), a publicly traded clinical-stage biopharmaceutical company. Before that, Ms. Bhatt was at Achaogen, Inc., a biopharmaceutical company, where she served as Chief Operating Officer from July 2018 to June 2019 and Chief Business Officer from September 2017 to June 2019. In April 2019, Achaogen filed a petition for bankruptcy in federal court seeking protection under Chapter 11 of the Bankruptcy Code. Prior to Achaogen, Ms. Bhatt held various roles at Gilead Sciences, Inc. (NASDAQ: GILD), a publicly traded research based biopharmaceutical company, from July 2006 to September 2017, including Vice President, Corporate Development from January 2016 to September 2017 and Senior Director, Corporate Development from May 2011 to December 2015. Ms. Bhatt holds a B.A. in Chemistry from Pomona College, an M.S. in Biomedical Sciences from the University of California, San Diego and a M.B.A. from the Kellogg School of Management at Northwestern University. Ms. Bhatt's strong scientific background, experience in various technical roles within the biotechnology industry, as well as her experience evaluating, investing and overseeing biotechnology companies contributed to our Board's conclusion that she should serve as a director of our company.

Chris Ehrlich served as LWAC's Chief Executive Officer and Director from October 2020 to August 2021 and continues to serve on the Board following the Business Combination. Mr. Ehrlich has served as Chief Executive Officer of Phoenix Biotech Acquisition Corp. since October 2021. Mr. Ehrlich served in various roles at Locust Walk Partners starting in 2013, first as Senior Managing Director and Head of Locust Walk Partners' Global Biopharma team until 2021, and beginning in 2021 as Chief Executive Officer of Locust Walk Acquisition Corp. Prior to joining Locust Walk Partners in 2013, Mr. Ehrlich served as a Managing Director at InterWest Partners, a venture capital firm focused on healthcare and information technology, from 2000 to 2013. At InterWest, he served

on the boards of KAI Pharmaceuticals, a privately held pharmaceutical company (acquired by Amgen in 2012), Biomimetic Therapeutics, Inc., a biotechnology company (acquired by Wright Medical Technologies in 2013), Invuity, Inc., a medical technology company acquired by Stryker in 2018) and Xenon Pharmaceuticals, a biopharmaceutical company (NASDAQ:XENE). Prior to joining InterWest, Mr. Ehrlich was the Director of Licensing and Business Development at Purdue Pharma, a private pharmaceutical firm, where he was responsible for developing a biologic oncology franchise, including in-licensing key intellectual properties, establishing and managing collaborations with biotechnology companies and leading the commercial operations of Purdue BioPharma, a biotechnology company. Prior to joining Purdue BioPharma, Mr. Ehrlich worked in business development at Genentech, a biotechnology company, in venture capital at the U.S. Russia Investment Fund, and in biotechnology strategy development at L.E.K. Consulting. Since 2014, Mr. Ehrlich has served on the board of directors of Prostate Management Diagnostics, Inc., a diagnostics company, on the Advisory Board of the Peter Michael Foundation, a charity focused on prostate cancer where he has been a Senior Advisor since 2012, and on the Healthcare at Kellogg Advisory Board at Northwestern University since 2019. He received his undergraduate degree from Dartmouth College and a MBA from the Kellogg School of Management at Northwestern University. He is also a registered representative with FINRA, holding his Series 79, 63 and 24 licenses. Mr. Ehrlich's extensive experience in the biotechnology industry generally, as well as extensive experience in venture capital and business development, contributed to our Board's conclusion that he should serve as a director of our company.

Kristen Harrington-Smith has served on the Board since February 2022. Ms. Harrington-Smith has served as Senior Vice President and Chief Commercial Officer of ADC Therapeutics, a publicly traded biopharmaceutical company, since November 2022. Prior to joining ADC Therapeutics, Ms. Harrington-Smith served as Chief Commercial Officer at ImmunoGen where she helped the organization prepare for their first commercial launch. Prior to joining ImmunoGen, Ms. Harrington-Smith held roles of increasing responsibility at Novartis Pharmaceuticals starting in July 2000, most recently as U.S. Commercial Head of Hematology from 2020 to 2021 and as Vice President and Head of U.S. CAR-T from 2016 to 2020. She holds a BA from Williams College and an MBA from the Kenan-Flagler Business School at the University of North Carolina, Chapel Hill. Ms. Harrington-Smith's extensive commercial experience in the pharmaceutical industry contributed to our Board's conclusion that she should serve as a director of our company.

Barbara Klencke, M.D. has served on the Board since November 2021. Dr. Klencke has served as the Chief Medical and Chief Development Officer of Sierra Oncology Inc., a publicly traded clinical-stage biopharmaceutical company since 2015. Concurrently, she was an independent board member of Lexent Bio from 2017 until the company's acquisition by Foundation Medicine in 2020. From 2011 to 2015, Dr. Klencke served as SVP, Global Development, at Onyx Pharmaceuticals, which was acquired by Amgen Inc., in 2013. She also led a variety of both early- and late-stage oncology programs while at Genentech, Inc. from 2003 to 2011. She completed Internal Medicine and Hematology/Oncology training at the University of California, San Francisco and remained there as an Assistant Professor of Medicine in Oncology focusing on clinical research from 1995 to 2002. Dr. Klencke holds a B.S. from Indiana University and an M.D. from the University of California, Davis. Dr. Klencke's significant scientific expertise in biotechnology contributed to our Board's conclusion that she should serve as a director of our company.

John W. Smither served on Old eFFECTOR's board of directors from March 2018 and has served on the Board since August 2021. Mr. Smither most recently served as the chief financial officer of Arcutis Biotherapeutics, Inc. from May 2019 to March 2021 where he was responsible for all financial aspects including leading the Company's successful initial public offering and two follow-on financings. Previously, Mr. Smither was the chief financial officer at Sienna Biopharmaceutics from January 2016 to April 2017, and again from April 2018 to March 2019. He also served as the interim chief financial officer at Kite Pharma, a Gilead Company from November 2017 through April 2018, and was the chief financial officer of Unity Biotechnology. He also served as chief financial officer at Kythera Biopharmaceuticals, where he was responsible for all financial activities during early clinical stage through approval and launch, led private fundraising rounds, prepared the company for its successful initial public offering in October 2012, and oversaw its acquisition by Allergan for approximately \$2.1 billion. At Amgen, he held several financial positions of increasing responsibility, including vice president of finance and administration for Amgen's European operations in 28 countries, and also served as Executive Director, Corporate Accounting. In January 2023, Mr. Smither was appointed to the board of NewAmsterdam Pharma and is its chair of the audit committee, and since January 2022, Mr. Smither has served as member of the board of directors of Applied Molecular Transport Inc., and is its chair of the audit committee, and a member of the compensation committee. Additionally, from December 2013 to May 2020, Mr. Smither served as a member of the board of directors of

Achaogen, Inc., and was its chair of the audit committee, and a member of the compensation committee. Mr. Smither began his career at Ernst & Young, where he was audit partner and held certification as a Certified Public Accountant (inactive). He holds a B.S. in accounting, with honors, from California State University at Los Angeles. Mr. Smither's extensive experience as a chief financial officer contributed to our Board's conclusion that he should serve as a director of our company.

Family Relationships

There are no family relationships between our Board and any of our executive officers.

Board of Directors and Election of Directors

Director Independence

Nasdaq listing rules require that a majority of the board of directors of a company listed on Nasdaq be composed of "independent directors," which is defined generally as a person other than an officer or employee of the company or its subsidiaries or any other individual having a relationship, which, in the opinion of the company's board of directors, would interfere with the director's exercise of independent judgment in carrying out the responsibilities of a director. Our Board of Directors has determined that each of Mr. Ehrlich, Ms. Bhatt, Dr. Gallagher, Ms. Harrington-Smith, Dr. Klencke and Mr. Smither are an independent director under the Nasdaq listing rules and Rule 10A-3 of the Exchange Act. In making these determinations, our Board of Directors considered the current and prior relationships that each non-employee director has with us and all other facts and circumstances our Board of Directors deemed relevant in determining independence, including the beneficial ownership of our Common Stock by each non-employee director, and the transactions involving them described in the section titled "Certain Relationships and Related Transactions."

Classified Board of Directors

In accordance with the terms of our certificate of incorporation, our Board is divided into three classes with staggered, three-year terms. At each annual meeting of stockholders, the directors whose terms then expire will be eligible for reelection until the third annual meeting following reelection. Our directors are divided among the three classes as follows:

- the Class I directors are Ms. Harrington-Smith and Dr. Worland, and their terms will expire at our 2025 annual meeting of stockholders;
- the Class II directors are Mr. Ehrlich, Dr. Gallagher and Mr. Smither, and their terms will expire at our 2023 annual meeting of stockholders; and
- the Class III directors are Ms. Bhatt and Dr. Klencke, and their terms will expire at our 2024 annual meeting of stockholders.

Our certificate of incorporation provides that the authorized number of directors may be changed only by resolution of the Board. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class will consist of one-third of the directors. The division of our Board into three classes with staggered three-year terms may delay or prevent a change of our Board or a change in control of our company. Our directors may be removed only for cause by the affirmative vote of the holders of at least two-thirds of our outstanding voting stock then entitled to vote in an election of directors.

Board Leadership Structure

Our Board is currently chaired by Dr. Gallagher. Our Board recognizes that it is important to determine an optimal board leadership structure to ensure the independent oversight of management as the company continues to grow. We separate the roles of chief executive officer and chair of the Board in recognition of the differences between the two roles. The chief executive officer is responsible for setting the strategic direction for our company and the day-to-day leadership and performance of our company, while the chair of the Board provides guidance to the chief executive officer and presides over meetings of the full board of directors. We believe that this separation of responsibilities provides a balanced approach to managing the Board and overseeing our company.

Our Board has concluded that our current leadership structure is appropriate at this time. However, our Board will continue to periodically review our leadership structure and may make such changes in the future as it deems appropriate.

Role of Board in Risk Oversight Process

Our Board has responsibility for the oversight of our risk management processes and, either as a whole or through its committees, regularly discusses with management our major risk exposures, their potential impact on our business and the steps we take to manage them. The risk oversight process includes receiving regular reports from board committees and members of senior management to enable our Board to understand our risk identification, risk management and risk mitigation strategies with respect to areas of potential material risk, including operations, finance, legal, regulatory, strategic and reputational risk.

The audit committee reviews information regarding liquidity and operations, and oversees our management of financial risks. Periodically, the audit committee reviews our policies with respect to risk assessment, risk management, loss prevention and regulatory compliance. Oversight by the audit committee includes direct communication with our external auditors, and discussions with management regarding significant risk exposures and the actions management has taken to limit, monitor or control such exposures. The compensation and talent committee is responsible for assessing whether any of our compensation policies or programs has the potential to encourage excessive risk-taking. The nominating and corporate governance committee manages risks associated with the independence of the Board, corporate disclosure practices and potential conflicts of interest. While each committee is responsible for evaluating certain risks and overseeing the management of such risks, the entire board of directors is regularly informed through committee reports about such risks. Matters of significant strategic risk are considered by our Board as a whole.

Committees of the Board of Directors

The standing committees of our Board of Directors include an Audit Committee, a Compensation Committee, and a Nominating and Corporate Governance Committee, each of which operates under a charter that has been approved by our Board.

Audit Committee

The audit committee's main function is to oversee our accounting and financial reporting processes and the audits of our consolidated financial statements. This committee's responsibilities include, among other things:

- appointing our independent registered public accounting firm;
- evaluating the qualifications, independence and performance of our independent registered public accounting firm;
- approving the audit and non-audit services to be performed by our independent registered public accounting firm;
- reviewing the design, implementation, adequacy and effectiveness of our internal accounting controls and our critical accounting policies;
- discussing with management and the independent registered public accounting firm the results of our annual audit and the review of our quarterly unaudited consolidated financial statements;
- reviewing, overseeing and monitoring the integrity of our consolidated financial statements and our compliance with legal and regulatory requirements as they relate to financial statements or accounting matters;
- reviewing on a periodic basis, or as appropriate, any investment policy and recommending to our Board any changes to such investment policy;
- reviewing with management any earnings announcements and other public announcements regarding our results of operations;
- preparing the report that the SEC requires in our annual proxy statement;

- reviewing and approving any related party transactions and reviewing and monitoring compliance with our code of conduct and ethics; and
- reviewing and evaluating, at least annually, the performance of the audit committee and its members including compliance of the audit committee with its charter.

The members of our audit committee are Mr. Ehrlich, Dr. Gallagher and Mr. Smither. Mr. Smither serves as the chairperson of the committee. All members of our audit committee meet the requirements for financial literacy under the applicable rules and regulations of the SEC and Nasdaq. Our Board has determined that Mr. Smither is an “audit committee financial expert” as defined by applicable SEC rules and has the requisite financial sophistication as defined under the applicable Nasdaq listing standards. Our Board has determined each of Mr. Ehrlich, Dr. Gallagher and Mr. Smither is independent under the applicable rules of the SEC and Nasdaq.

Compensation Committee

Our compensation committee approves policies relating to compensation and benefits of our officers and employees. The compensation committee approves corporate goals and objectives relevant to the compensation of our Chief Executive Officer and other executive officers, evaluates the performance of these officers in light of those goals and objectives and approves the compensation of these officers based on such evaluations. The compensation committee also approves the issuance of stock options and other awards under our equity plans. The compensation committee will review and evaluate, at least annually, the performance of the compensation committee and its members, including compliance by the compensation committee with its charter.

The members of our compensation committee are Mr. Ehrlich, Ms. Harrington-Smith and Dr. Klencke. Mr. Ehrlich serves as the chairperson of the committee. Our Board has determined that each of Mr. Ehrlich, Ms. Harrington-Smith and Dr. Klencke is independent under the applicable Nasdaq listing standards and is a “non-employee director” as defined in Rule 16b-3 promulgated under the Exchange Act.

Nominating and Corporate Governance Committee

The nominating and corporate governance committee is responsible for assisting our Board in discharging the Board’s responsibilities regarding the identification of qualified candidates to become board members, the selection of nominees for election as directors at our annual meetings of stockholders (or special meetings of stockholders at which directors are to be elected), and the selection of candidates to fill any vacancies on our Board and any committees thereof. In addition, the nominating and corporate governance committee is responsible for overseeing our corporate governance policies, reporting and making recommendations to our Board concerning governance matters and oversight of the evaluation of our Board. The members of our nominating and corporate governance committee are Ms. Bhatt, Dr. Gallagher and Mr. Smither. Ms. Bhatt serves as the chairperson of the committee. Our Board has determined that each of Ms. Bhatt, Dr. Gallagher and Mr. Smither is independent under the applicable Nasdaq listing standards.

Compensation Committee Interlocks and Insider Participation

None of the members of our compensation committee has ever been one of our officers or employees. None of our executive officers currently serves, or has served, as a member of our Board or compensation committee of any entity that has one or more executive officers serving as a member of our Board or compensation committee.

Board Diversity

Our nominating and corporate governance committee is responsible for reviewing with our Board, on an annual basis, the appropriate characteristics, skills and experience required for the Board as a whole and its individual members. In evaluating the suitability of individual candidates (both new candidates and current members) for election or appointment, the nominating and corporate governance committee and the Board will take into account many factors, including the following:

- personal and professional integrity, ethics, and values;
- experience in corporate management, such as serving as an officer or former officer of a publicly-held company;

- experience as a board member or executive officer of another publicly-held company;
- strong finance experience;
- diversity of expertise and experience in substantive matters pertaining to our business relative to other board members;
- diversity of background and perspective, including, but not limited to, with respect to age, gender, race, place of residence, and specialized experience;
- experience relevant to our business industry and with relevant social policy concerns; and
- relevant academic expertise or other proficiency in an area of our business operations.

Our Board evaluates each individual in the context of the Board as a whole, with the objective of assembling a group that can best maximize the success of the business and represent stockholder interests through the exercise of sound judgment using its diversity of experience in these various areas.

Code of Conduct and Ethics

We have adopted a written code of business conduct and ethics that applies to our directors, officers, and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. Our code of business conduct and ethics is available under the Corporate Governance section of our website at www.effector.com. In addition, we intend to post on our website all disclosures that are required by law or the listing standards of Nasdaq concerning any amendments to, or waivers from, any provision of the code. The reference to our website address does not constitute incorporation by reference of the information contained at or available through our website. We have included our website address as an inactive textual reference only.

Item 11. Executive Compensation.

This section discusses the material components of the executive compensation program for our executive officers who are named in the “Summary Compensation Table” below. In 2022, our “named executive officers” and their positions were as follows:

- Stephen T. Worland, Ph.D., who serves as President and Chief Executive Officer;
- Michael Byrnes, who serves as Chief Financial Officer;
- Douglas Warner, M.D., who serves as Chief Medical Officer;
- Premal Patel, M.D., Ph.D., our former Chief Medical Officer (terminated April 1, 2022); and
- Alana McNulty, our former Chief Business Officer (terminated July 15, 2022).

This discussion may contain forward-looking statements that are based on our current plans, considerations, expectations and determinations regarding future compensation programs. Actual compensation programs that we adopt in the future may differ materially from the currently planned programs summarized in this discussion.

Summary Compensation Table

The following table presents summary information regarding the total compensation that was awarded to, earned by or paid to the named executive officers for services rendered during the years ended December 31, 2022 and December 31, 2021.

Name and principal position	Year	Salary (\$)	Bonus (\$) (1)	Option Awards \$(2)	Stock Awards (\$) (3)	Non-equity Incentive Plan Compensatio n \$(4)	All Other Compensatio n \$(5)	Total (\$)
Stephen T. Worland, Ph.D.	2022	566,500	—	2,987,797	—	254,295	34,460	3,843,052
President and Chief Executive Officer	2021	501,442	—	—	2,652,658	220,000	31,952	3,406,052
Michael Byrnes	2022	435,735	—	1,351,611	—	156,865	31,090	1,975,301
Chief Financial Officer	2021	390,865	—	—	687,217	134,400	29,172	1,241,654
Douglas Warner, M.D.	2022	179,135	50,000	407,562	—	64,356	10,909	711,962
Chief Medical Officer								
Premal Patel, M.D., Ph.D.	2022	164,270	—	700,198	—	—	71,347	935,815
Former Chief Medical Officer	2021	480,288	—	—	863,934	156,800	20,007	1,521,029
Alana McNulty	2022	255,921	—	860,749	—	—	494,864	1,611,534
Former Chief Business Officer	2021	383,814	—	—	1,168,270	128,000	30,264	1,710,348

- (1) Represents a \$50,000 one-time signing bonus for Dr. Warner in connection with his commencement of employment.
- (2) In accordance with SEC rules, this column reflects the aggregate grant-date fair value of the option awards granted during 2022 computed in accordance with ASC Topic 718 for stock-based compensation transactions. Assumptions used in the calculation of these amounts are included in Note 9 to our consolidated financial statements. 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.
- (3) In accordance with SEC rules, this column reflects the aggregate grant-date fair value computed in accordance with ASC Topic 718 for stock-based compensation transactions of the Earn-Out Shares that may be issuable to each named executive officer with respect to outstanding stock options held by the executive as of the consummation of the Business Combination if the Triggering Event occurs within the two years following the consummation of the Business Combination (the “Earn-Out Period”), subject to the executives’ continued services through the time of such Triggering Event. The Earn-Out Shares will also be earned and issuable in the event of a change in control during the Earn-Out Period that results in the holders of our common stock receiving a per-share price equal to or in excess of \$20.00. The Earn-Out Shares are described below under “—Equity-Based Incentive Awards.” We have determined that the contingent obligation to issue Earn-Out Shares to existing Old eFFECTOR option holders, including the named executive officers, falls within the scope of ASC Topic 718 for stock-based compensation transactions because the option holders are required to continue providing service until the occurrence of the Triggering Event. The fair value of the option holder Earn-Out Shares is recorded as share-based compensation over the derived service period of the Monte Carlo simulation valuation model using a distribution of potential outcomes on a monthly basis over the earn-out period using the most reliable information available. Assumptions used in the calculation of these amounts are included in Note 10 to our consolidated financial statements.
- (4) Amounts reflect bonuses awarded to our named executive officers by our Board in recognition of annual performance and paid in cash as further described below in “Bonus Compensation.”
- (5) For 2022, amounts reflect (i) \$30,400, \$6,792, \$24,062, \$30,400 and \$10,449 in health and welfare insurance premium payments for Dr. Worland, Dr. Patel, Ms. McNulty, Mr. Byrnes, and Dr. Warner, respectively, (ii) \$4,061, \$310, \$1,004, \$690 and \$460 in group term life premiums for Dr. Worland, Dr. Patel, Ms. McNulty, Mr. Byrnes and Dr. Warner, respectively, (iii) \$309,000 in severance paid to Ms. McNulty in connection with her termination of employment, (iv) \$18,000 in consulting payments paid

to Dr. Patel in connection with his consulting services following his termination of employment, and (v) \$46,245 and \$160,798 for Dr. Patel and Ms. McNulty, respectively, which represents the incremental grant date fair value recognized by us in accordance with ASC Topic 718 in connection with the modification of their stock options in connection with their termination of employment, as described below under “— Separation Arrangements with the Named Executive Officers.”

Narrative Disclosure to Compensation Tables

Base Salary

The compensation of the named executive officers is generally determined and approved at the beginning of each year or, if later, in connection with the commencement of employment of the executive, by our Board or the compensation committee. The following represent the base salaries which were effective for 2022 for the named executive officers.

Name	2022 Annual Base Salary (\$)
Stephen T. Worland, Ph.D.	566,500
Michael Byrnes	435,735
Douglas Warner, M.D.	450,000
Premal Patel, M.D., Ph.D.	504,700
Alana McNulty	412,000

Bonus Compensation

We consider annual cash incentive bonuses to be an important component of our total compensation program and to provide incentives necessary to retain executive officers. Each of the named executive officers is eligible to receive an annual performance-based cash bonus based on a specified target annual bonus award amount, expressed as a percentage of the named executive officer’s base salary. The following represent the target percentages of base salary for 2022 for the named executive officers:

Name	2022 Target Percentage
Stephen T. Worland, Ph.D.	50%
Michael Byrnes	40%
Douglas Warner, M.D. (2)	40%
Premal Patel, M.D., Ph.D. (1)	40%
Alana McNulty (1)	40%

- (1) The employment of Dr. Patel and Ms. McNulty terminated on April 1, 2022 and July 15, 2022, respectively, and they were not eligible for an annual bonus for 2022.
- (2) Dr. Warner's bonus payment was prorated based on his start date of August 8, 2022.

Each of our named executive officers received a target bonus increase at the time of the Business Combination, as described below under “Employment Arrangements with Named Executive Officers.”

Bonuses for any one year are usually determined and paid in the first quarter of the following year. For 2022, our Board reviewed our corporate goals and, following such review, determined to pay annual bonuses to the named executive officers at 90% of target based on its assessment of our progress during 2022 relative to such goals, which were based on clinical, financial, regulatory and corporate development objectives. The 2022 annual bonuses paid to our named executive officers are reflected in the Summary Compensation Table above.

Equity-Based Incentive Awards

Our equity-based incentive awards are designed to align our interests and the interests of our stockholders with those of our employees and consultants, including the named executive officers. The Board is responsible for approving equity grants.

Prior to the consummation of the Business Combination, Old eFFECTOR maintained the 2013 Equity Incentive Plan (the “2013 Plan”). Old eFFECTOR offered awards of stock options to purchase shares of its common stock to eligible service providers, including our named executive officers, pursuant to the 2013 Plan. In connection with the completion of the Business Combination and the adoption of the eFFECTOR Therapeutics, Inc. 2021 Incentive Award Plan (the “2021 Plan”), no further awards will be granted under the 2013 Plan.

All options are granted with an exercise price per share that is no less than the fair market value of our common stock on the date of grant of each award. Our stock option awards generally vest over a four-year period and may be subject to acceleration of vesting and exercisability under certain termination and change of control events, as described below under “Employment Arrangements with the Named Executive Officers.”

In connection with his commencement of employment on August 8, 2022, Dr. Warner received stock options to purchase 618,160 shares of our Common Stock. The stock options have an exercise price per share of \$0.8975, which was the closing price per share of our Common Stock on the date of grant. The stock options vest over four years following the date of grant, with 25% vesting on the first anniversary of the date of grant and the remainder vesting in equal monthly installments thereafter, subject to his continuous service with us through the applicable vesting dates. Dr. Warner’s employment agreement entitles him to accelerated vesting of all outstanding equity awards upon a qualifying termination in connection with or following a change in control of our company. For additional discussion, please see “—Employment Arrangements with our Named Executive Officers” below.

The other stock option awards granted to our other named executive officers during 2022 are described below in the “Outstanding Equity Awards at Fiscal Year End” table.

Executive Earn-Out Shares

In connection with the Business Combination, holders of stock options will be entitled to receive a pro rata share of up to 5,000,000 additional shares of Common Stock (the “Earn-Out Shares”), if, within a two-year period following the signing date of the Merger Agreement (the “Earn-Out Period”), the closing share price of our Common Stock equals or exceeds \$20.00 over at least 20 trading days within a 30-day trading period (the “Triggering Event”) and the holder continues to provide services through the time of such Triggering Event. The Earn-Out Shares will also be earned and issuable in the event of a change in control during the Earn-Out Period that results in the holders of our Common Stock receiving a per-share price equal to or in excess of \$20.00. The Outstanding Equity Awards at Fiscal Year-End table below shows the number of Earn-Out Shares each named executive officer is eligible to earn in respect of outstanding stock options owned as of the consummation of the Business Combination. Dr. Patel and Ms. McNulty forfeited their right to any Earn-Out Shares attributable to their underlying stock options upon their termination of employment or service with us.

Employment Arrangements with the Named Executive Officers

We are party to employment agreements with each of our named executive officers. The arrangements generally provide for at-will employment without any specific term and set forth the named executive officer’s initial base salary, bonus potential, eligibility for employee benefits and severance benefits upon a qualifying termination of employment, subject to such employee executing a separation agreement with us.

Employment Agreement with Dr. Worland

We have entered into an employment agreement with Dr. Worland, our President and Chief Executive Officer. Pursuant to his agreement, Mr. Byrnes is entitled to an annual base salary and a target annual incentive bonus, in each case as established from time to time by the compensation committee of our Board.

Pursuant to his employment agreement, if Dr. Worland’s employment is terminated by us without “cause” prior to a “change in control” or more than twelve months following a “change in control” (each as defined in his employment agreement), he will be entitled to: (1) continued payment of his base salary for a period of twelve months, and (2) payment of premiums for continued health benefits to him under COBRA for up to twelve months following his termination.

Pursuant to his employment agreement, if Dr. Worland’s employment is terminated by us without “cause” or by Dr. Worland with “good reason” upon or within twelve months following a “change in control,” he will be entitled to: (1) continued payment of his base salary for a period of eighteen months, (2) payment of premiums for

continued health benefits to him under COBRA for up to eighteen months following his termination, (3) payment of an amount equal to 150% of his current year target bonus, and (4) full acceleration of the vesting of all his outstanding equity awards.

Dr. Worland's benefits are conditioned, among other things, on him complying with his post-termination obligations under his agreement, including a one-year non-solicitation obligation, and timely signing a general release of claims in our favor.

Employment Agreement with Mr. Byrnes

We have entered into an employment agreement with Mr. Byrnes, our Chief Financial Officer. Pursuant to his agreement, Mr. Byrnes is entitled to an annual base salary and a target annual incentive bonus, in each case as established from time to time by the compensation committee of our Board.

Pursuant to his employment agreement, if Mr. Byrnes' employment is terminated by us without "cause" prior to a "change in control" or more than twelve months following a "change in control" (each as defined in his employment agreement), he will be entitled to: (1) continued payment of his base salary for a period of nine months, and (2) payment of premiums for continued health benefits to him under COBRA for up to nine months following his termination.

Pursuant to his employment agreement, if Mr. Byrnes' employment is terminated by us without "cause" or by Mr. Byrnes with "good reason" upon or within twelve months following a "change in control," he will be entitled to: (1) continued payment of his base salary for a period of twelve months, (2) payment of premiums for continued health benefits to him under COBRA for up to twelve months following his termination, (3) payment of an amount equal to his current year target bonus, and (4) full acceleration of the vesting of all his outstanding equity awards.

Mr. Byrnes' benefits are conditioned, among other things, on his complying with his post-termination obligations under his agreement, including a one-year non-solicitation obligation, and timely signing a general release of claims in our favor.

Employment Agreement with Dr. Warner

We have entered into an employment agreement with Dr. Warner, our Chief Medical Officer. Pursuant to his agreement, Dr. Warner is entitled to an annual base salary and a target annual incentive bonus, in each case as established from time to time by the compensation committee of our Board. Pursuant to his employment agreement, Dr. Warner received a one-time signing bonus in the amount of \$50,000, which bonus is subject to repayment by Dr. Warner if Dr. Warner is terminated by us for cause or he resigns for any reason, in each case prior to the first anniversary of his start date.

Pursuant to his employment agreement, if Dr. Warner's employment is terminated by us without "cause" prior to a "change in control" or more than twelve months following a "change in control" (each as defined in his employment agreement), he will be entitled to: (1) continued payment of his base salary for a period of twelve months, and (2) payment of premiums for continued health benefits to him under COBRA for up to twelve months following his termination.

Pursuant to his employment agreement, if Dr. Warner's employment is terminated by us without "cause" or by Dr. Warner with "good reason" upon or within twelve months following a "change in control," he will be entitled to: (1) continued payment of his base salary for a period of twelve months, (2) payment of premiums for continued health benefits to him under COBRA for up to twelve months following his termination, (3) payment of an amount equal to his current year target bonus, and (4) full acceleration of the vesting of all his outstanding equity awards.

Dr. Warner's benefits are conditioned, among other things, on his complying with his post-termination obligations under his agreement, including a one-year non-solicitation obligation, and timely signing a general release of claims in our favor.

Separation Arrangements with the Named Executive Officers

Separation Arrangements with Dr. Patel

On April 1, 2022, Premal Patel, M.D., Ph.D., our former Chief Medical Officer, resigned from the Company in order to pursue a new career opportunity. Dr. Patel continued to serve the company as a consultant to the company until Sept. 30, 2022. In connection with Dr. Patel's termination of employment with the Company, Dr. Patel executed a general release of claims (the "Release"), pursuant to which Dr. Patel's vested Company stock options were amended so that they will remain exercisable until April 1, 2023, and we agreed to continue to pay the employer portion of the healthcare coverage for Mr. Patel and his eligible dependents, in each case, until December 31, 2022. Pursuant to a Consulting Agreement (the "Consulting Agreement") entered into as of April 1, 2022, Dr. Patel received an hourly consulting fee of \$600, and continued vesting of his outstanding equity awards during the term of his consulting services.

Release Agreement with Alana McNulty

On July 15, 2022, Alana McNulty, our former Chief Business Officer, departed the Company. In connection with Ms. McNulty's departure, Ms. McNulty and the Company executed a general release of claims (the "Release Agreement"), pursuant to which Ms. McNulty received nine months base salary and continued healthcare coverage at Company expense, and her outstanding vested Company stock options will remain exercisable until July 15, 2024.

Outstanding Equity Awards at Fiscal Year-End

The following table sets forth certain information regarding equity awards granted to the named executive officers that remained outstanding as of December 31, 2022, in each case, as adjusted to reflect the conversion of such awards in connection with the Business Combination, as further described below.

Name and principal position	Grant Date	Option Awards (1)(2)				Stock Awards		
		Number of Securities Underlying Unexercised Options Exercisable (#)	Number of Securities Underlying Unexercised Options Unexercisable (#)	Option Exercise Price (\$)	Option Expiration Date	Equity Incentive Plan Awards: Number of Unearned Shares That Have Not Vested (#)	Equity Incentive Plan Awards: Market Value of Shares That Have Not Vested (\$)(3)	
Stephen T. Worland, Ph.D.	12/17/2013	33,799	—	0.52	12/17/2023	—	—	
	12/4/2014	217,284	—	0.73	12/4/2024	—	—	
	1/8/2016	619,018	—	1.14	1/8/2026	—	—	
	2/17/2016	144,856	—	1.14	2/17/2026	—	—	
	8/21/2017	289,712	—	1.66	8/21/2027	—	—	
	8/25/2021	—	—	—	—	198,224 (4)	85,236	
	1/20/2022	119,321	401,353	6.65	1/20/2032	—	—	
	6/20/2022	—	520,674	1.49	6/20/2032	—	—	
Michael Byrnes	12/10/2020	168,999	168,998	2.39	12/10/2030	—	—	
	8/25/2021	—	—	—	—	51,353 (4)	22,082	
	1/20/2022	53,978	181,563	6.65	1/20/2032	—	—	
	6/20/2022	—	235,541	1.49	6/20/2032	—	—	
Douglas Warner, M.D.	8/8/2022	—	618,160	0.90	8/8/2032	—	—	
Premal Patel, M.D., Ph.D.	7/29/2020	230,160 (5)	—	2.08	4/1/2023	—	—	
Alana McNulty	1/20/2022	25,000 (5)	—	6.65	4/1/2023	—	—	
	12/4/2014	38,628 (6)	—	0.73	7/15/2024	—	—	
	10/9/2015	120,713 (6)	—	0.94	7/15/2024	—	—	
	1/8/2016	113,470 (6)	—	1.14	7/15/2024	—	—	
	2/17/2016	43,456 (6)	—	1.14	7/15/2024	—	—	
	8/21/2017	96,570 (6)	—	1.66	7/15/2024	—	—	
	6/6/2019	50,247 (6)	—	1.35	7/15/2024	—	—	
	4/13/2020	54,320 (6)	—	1.35	7/15/2024	—	—	
	1/20/2022	15,625 (6)	—	6.65	7/15/2024	—	—	

- (1) All of the outstanding equity awards are stock options granted under and subject to the terms of the 2013 Plan, described below under "—Incentive Award Plans." The vesting of each equity award is subject to the executive's continuous service with us through the applicable vesting dates. Each of our named executive officers' employment agreements entitles them to accelerated vesting of all outstanding equity awards upon a qualifying termination in connection with or following a change in control of our company. For additional discussion, please see "—Employment Arrangements with our Named Executive Officers" above.

- (2) Each option award vests over four years with 25% vesting on the first anniversary of the vesting commencement date and the remainder vesting in equal monthly installments thereafter, with the exception of the January 20, 2022 grants which vest in equal monthly installments for four years, and the June 20, 2022 grants which vests over two years with 50% vesting on the first anniversary of the vesting commencement date and the remainder vesting in equal monthly installments thereafter.
- (3) The market value was computed using \$0.43 per share, which is the closing price per share of our Common Stock on December 30, 2022, the last trading day of 2022.
- (4) Represents the Earn-Out Shares each named executive officer is eligible to receive with respect to outstanding stock options held by the executive as of the consummation of the Business Combination, if a Triggering Event occurs within the Earn-Out Period, and the executive continues to provide services through the time of such Triggering Event. The Earn-Out Shares will also be earned and issuable in the event of a change in control during the Earn-Out Period that results in the holders of our Common Stock receiving a per-share price equal to or in excess of \$20.00. The Earn-Out Shares are described above under “—Equity-Based Incentive Awards.”
- (5) In connection with Dr. Patel's termination, his outstanding vested stock options were amended to provide that they will remain exercisable until April 1, 2023.
- (6) In connection with Ms. McNulty's termination, her outstanding vested stock options were amended to provide that they will remain exercisable until July 15, 2024.

Other Elements of Compensation

Perquisites, Health and Welfare Benefits

The named executive officers are eligible to participate in our employee benefit plans, including our medical, dental, vision, group life, disability and accidental death and dismemberment insurance plans, in each case on the same basis as all of our other employees.

We generally do not provide perquisites or personal benefits to the named executive officers, except in limited circumstances. We do, however, pay the premiums for term life insurance and disability insurance for all of our employees, including the named executive officers. Our Board may elect to adopt qualified or non-qualified benefit plans in the future if it determines that doing so is in our best interests.

401(k) Plan

We provide a 401(k) plan that provides eligible U.S. employees with an opportunity to save for retirement on a tax advantaged basis. Eligible employees are able to defer eligible compensation up to certain Code limits, which are updated annually. The 401(k) plan is intended to be qualified under Section 401(a) of the Code, with the related trust intended to be tax exempt under Section 501(a) of the Code. As a tax-qualified retirement plan, contributions to the 401(k) plan are deductible by us when made, and contributions and earnings on those amounts are not generally taxable to the employees until withdrawn or distributed from the 401(k) plan. We believe that providing a vehicle for tax-deferred retirement savings through our 401(k) plan adds to the overall desirability of our executive compensation package and further incentivizes our employees, including our named executive officers, in accordance with our compensation policies.

Nonqualified Deferred Compensation

We do not maintain nonqualified defined contribution plans or other nonqualified deferred compensation plans. We may elect to provide our officers and other employees with non-qualified defined contribution or other nonqualified deferred compensation benefits in the future if it determines that doing so is in our best interests.

No Tax Gross Ups

We do not make gross-up payments to cover our named executive officers' personal income taxes that may pertain to any of the compensation or benefits paid or provided by us.

Director Compensation

The following table summarizes compensation received by our non-employee directors during the year ended December 31, 2022. Dr. Worland, our President and Chief Executive Officer, is also a member of our Board, but does not receive any additional compensation for his service as a director in addition to the compensation he received as an employee. Dr. Worland's compensation is described further above.

Name	Fees Earned or Paid in Cash \$(1)	Option Awards \$(2)	Stock Awards (\$)	All Other Compensation (\$)	Total (\$)
Brian Gallagher	81,500	23,361	—	—	104,861
John Smither	58,482	23,361	—	—	81,843
Jonathon Root (3)	6,679	—	—	—	6,679
Barbara Klencke	45,000	23,361	—	—	68,361
Chris Ehrlich	57,500	23,361	—	—	80,861
Elizabeth Bhatt	51,214	23,361	—	—	74,575
Kristen Harrington-Smith (4)	39,175	144,644	—	—	183,819

- (1) Reflects cash retainer fees earned by our non-employee directors in 2022.
- (2) In accordance with SEC rules, this column represents the aggregate grant-date fair value of option awards granted during 2022 computed in accordance with ASC Topic 718 for stock-based compensation transactions. Assumptions used in the calculation of these amounts are included in Note 9 to our consolidated financial statements. These amounts do not reflect the actual economic value that will be realized by the director upon the vesting of the stock options, the exercise of the stock options, or the sale of the common stock underlying such stock options. The table below shows the aggregate number of outstanding options held as of December 31, 2022 by each individual who served as a non-employee director during 2022.

Name	Number of Securities Underlying Options Outstanding at December 31, 2022
Brian Gallagher	60,000
John Smither (a)	84,142
Jonathon Root	—
Barbara Klencke	60,000
Chris Ehrlich	60,000
Elizabeth Bhatt	60,000
Kristen Harrington-Smith	53,333

- (a) As the only non-employee director who held options upon the consummation of the Business Combination, as of December 31, 2022, Mr. Smither is eligible to receive 3,668 Earn-Out Shares, subject to his continued service through the occurrence of the Triggering Event during the Earn-Out Period.
- (3) Mr. Root resigned as a member of our Board on February 15, 2022.
- (4) Ms. Harrington-Smith was appointed as a member of our Board on February 15, 2022.

Director Compensation Program

Our Board has approved a non-employee director compensation program (the “Director Compensation Program”). The Director Compensation Program provides for annual retainer fees and long-term equity awards for our non-employee directors.

The Director Compensation Program consists of the following components:

Cash Compensation

- Annual Base Board Fee: \$40,000
- Annual Chair Fees:
 - o Chair of the Board/Lead Independent Director: \$30,000
 - o Audit Committee: \$15,000
 - o Compensation Committee: \$10,000
 - o Nominating and Corporate Governance Committee: \$8,000
- Annual Committee Member Fees (non-Chair):
 - o Audit Committee: \$7,500
 - o Compensation Committee: \$5,000
 - o Nominating and Corporate Governance Committee: \$4,000

Annual cash fees will be paid in quarterly installments in arrears and will be pro-rated for any partial calendar quarter of service.

Equity Compensation

- Initial Awards: Each non-employee director who is initially elected or appointed to our Board following the effective date of the Director Compensation Program and those directors who were serving on our Board immediately following the consummation of the Business Combination shall be granted stock options to purchase 40,000 shares (each, an “Initial Award”). Each Initial Award will vest in equal monthly installments over three years beginning on the non-employee director’s appointment to the Board, subject to the non-employee director’s continued service through each such vesting date.
- Annual Awards: Each non-employee director who is serving on our Board as of the date of the annual meeting of our stockholders each calendar year beginning with calendar year 2022 shall be granted, on such annual meeting date, stock options to purchase 20,000 shares (each, an “Annual Award”). Each Annual Award will vest in full on the earlier to occur of (A) the first anniversary of the applicable grant date and (B) the date of the next annual meeting following the grant date, subject to the non-employee director’s continued service through the applicable vesting date.

On January 20, 2023, each non-employee member of the Board received an additional award of stock options to purchase 25,000 shares. These awards vest in equal monthly installments over the twelve months following the date of grant, subject to the non-employee director’s continued service through the applicable vesting date.

Non-employee directors elected for the first time within the six month period preceding an annual meeting or at an annual meeting will receive only an Initial Award and will not receive an Annual Award with respect to such annual meeting, unless otherwise determined by the Board in its discretion. In addition, each Initial Award and Annual Award, and the awards granted to our non-employee directors in January 2023, shall vest in full immediately prior to the occurrence of a Change in Control, as defined in the 2021 Plan, to the extent outstanding at such time.

Compensation under our Director Compensation Program will be subject to the annual limits on non-employee director compensation set forth in the 2021 Plan, as described above.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

Beneficial Ownership of Securities

The following table sets forth the beneficial ownership of Common Stock as of February 28, 2023 by:

- each person who is known to be the beneficial owner of more than 5% of shares of Common Stock;
- each of our current named executive officers and directors; and
- all current executive officers and directors as a group.

The beneficial ownership of Common Stock is based on 42,401,219 shares of Common Stock outstanding as of February 28, 2023.

Beneficial ownership is determined according to the rules of the SEC, which generally provide that a person has beneficial ownership of a security if he, she or it possesses sole or shared voting or investment power over that security, including options and warrants that are currently exercisable within 60 days of February 28, 2023.

Unless otherwise indicated, we believe that all persons named in the table below have sole voting and investment power with respect to the voting securities beneficially owned by them.

Name and Address of Beneficial Owner (1)	Number of Shares	% of Ownership
<i>5% Holders</i>		
Entities affiliated with SR One Capital (2)	6,822,114	16.1%
Abingworth Bioventures VI, L.P. (3)	4,829,891	11.4%
The Column Group II, L.P. (4)	4,309,329	10.2%
Entities affiliated with Altitude Life Sciences Ventures (5)	2,826,350	6.7%
New Emerging Medical Opportunities Fund III, L.P. (6)	2,382,644	5.6%
Entities affiliated with Pfizer Inc. (7)	2,243,850	5.3%
<i>Directors and Executive Officers</i>		
Stephen T. Worland, Ph.D. (8)	2,313,244	5.3%
Michael Byrnes (9)	335,905	*
Premal Patel, M.D., Ph.D. (10)	255,160	*
Alana McNulty (11)	581,797	1.4%
Douglas Warner, M.D. (12)	15,625	*
Mayank Gandhi, M.D. (13)	9,375	*
Elizabeth Bhatt (14)	31,269	*
Chris Ehrlich (15)	200,637	*
Brian Gallagher (16)	52,222	*
Kristen Harrington-Smith (17)	15,556	*
Barbara Klencke (18)	17,778	*
John Smither (19)	70,506	*
All directors and executive officers as a group (12 individuals) (20)	3,899,074	8.6%

* Less than one percent

- (1) Unless otherwise noted, the business address of each of those listed in the table above is 142 North Cedros Avenue, Suite B, Solana Beach, California 92075.
- (2) Based on information contained in Schedule 13G filed with the SEC on February 14, 2022 by SR One Capital Fund I Aggregator, LP ("SR One Capital Fund"), SR One Capital Partners I, LP ("SR One Capital Partners"), SR One Capital Management, LLC ("SR One Capital Management"), SR One Co-Invest I, LLC ("SR One Co-Invest"), SR One Co-Invest Manager I, LLC ("SR One Co-Invest Management") and Simeon George. Represents (i) 4,822,114 shares held by SR One Capital Fund and

(ii) 2,000,000 shares held by SR One Co-Invest. SR One Capital Partners is the general partner of SR One Capital Fund. SR One Co-Invest Manager is the managing member of SR One Co-Invest. SR One Capital Management is the general partner of SR One Capital Partners and the managing member of SR One Co-Invest Manager. Simeon George, M.D. is the managing member of SR One Capital Management. By virtue of such relationships, Dr. George, SR One Capital Partners, SR One Capital Management and SR One Co-Invest Manager may be deemed to have voting and investment power with respect to the shares held by SR One Capital Fund and/or SR One Co-Invest, as applicable, and as a result may be deemed to have beneficial ownership of such shares. Each of Dr. George, SR One Capital Partners, SR One Capital and SR One Co-Invest Manager disclaims beneficial ownership of the shares held by SR One Capital Fund and SR One Co-Invest, except to the extent of its or his pecuniary interest therein if any. The address for SR One Capital Fund I Aggregator, LP and SR One Co-Invest I, LLC is 985 Old Eagle School Road, Suite 511, Wayne, PA 19087.

- (3) Based on the information contained in the Schedule 13D/A filed with the SEC on August 11, 2022 by The Carlyle Group Inc. Includes (i) 4,822,114 shares of common stock held of record by Abingworth Bioventures VI LP and (ii) 7,777 shares of Common Stock underlying stock options exercisable within 60 days of August 1, 2022. The Carlyle Group Inc., which is a publicly traded entity listed on Nasdaq, is the sole shareholder of Carlyle Holdings I GP Inc., which is the sole member of Carlyle Holdings I GP Sub L.L.C., which is the general partner of Carlyle Holdings I L.P., which, with respect to the securities reported herein, is the managing member of CG Subsidiary Holdings L.L.C., which is the managing member of TC Group, L.L.C., which is the managing member of Carlyle Investment Management, L.L.C., which is the sole member of Carlyle Genesis UK LLC, which is the principal member of Abingworth LLP. Abingworth Bioventures VI LP has delegated to Abingworth LLP all investment and dispositive power over the securities held of record by Abingworth Bioventures VI LP. Accordingly, each of the foregoing entities may be deemed to share beneficial ownership of the securities held of record by Abingworth Bioventures VI LP, but each disclaims beneficial ownership of such securities. The address of each of Abingworth LLP and Abingworth Bioventures VI LP is 38 Jermyn Street, London, SW1Y 6DN, England, United Kingdom. The address of each of the other Reporting Persons is c/o The Carlyle Group, 1001 Pennsylvania Ave. NW, Suite 220 South, Washington, DC 20004-2505.
- (4) Based on information contained in Schedule 13D filed with the SEC on September 7, 2021 by The Column Group II, LP and The Column Group II GP, LP. Peter Svennilson and David Goeddel, Ph.D. are the managing partners of The Column Group II GP, LP, which is the general partner of The Column Group II, LP and may be deemed to have shared voting, investment and dispositive power with respect to these shares. Each individual managing partner disclaims beneficial ownership of these shares, except to the extent of their pecuniary interest in such shares. The principal address of The Column Group II, L.P. is 1 Letterman Drive, Bldg D, Suite DM-900, San Francisco, California 94158.
- (5) Based on the Company's records as of February 15, 2023. Represents 1,413,175 shares by Altitude Life Sciences Ventures Fund II, L.P. and 1,413,175 shares held by Altitude Life Sciences Ventures Side Fund II, L.P. David Maki is the managing member of Altitude Life Science Ventures II, LLC, which is the general partner of each of Altitude Life Science Ventures Fund II, L.P. and Altitude Life Science Ventures Side Fund II, L.P., and holds voting, investment and dispositive power with respect to these shares. The address for the Altitude Life Science Ventures is 1014 Market Street, Suite 200, Kirkland, WA 98074.
- (6) Based on the information contained in the Schedule 13G/A filed with the SEC on February 13, 2023 by New Emerging Medical Opportunities Fund III, L.P. and Sectoral GP III, L.P. Sectoral Asset Management Inc., in its capacity as investment adviser to New Emerging Medical Opportunities Fund III, L.P. (NEMO), has the sole right to dispose of or vote the NEMO shares and is the owner of the general partner (Sectoral GP III L.P.) of NEMO. Michael Sjöström and Jérôme Pfund are ultimate beneficial owners and senior executives of Sectoral Management Inc. Each of Sectoral Asset Management Inc., Mr. Sjöström and Mr. Pfund disclaims beneficial ownership of the NEMO shares except to the extent of its or his pecuniary interest therein. The mailing address for NEMO is c/o Sectoral Asset Management Inc. at 1010 Sherbrooke St. West, #1610, Montreal, QC Canada H3A 2R7.
- (7) Based on the information contained in Schedule 13G filed with the SEC on February 14, 2022 by Pfizer Inc., Pfizer Investment Ventures LLC, and Pfizer Ventures (US) LLC. Represents 1,878,808 shares held

by Pfizer Ventures Investments LLC (Pfizer Ventures) and 365,042 shares held by Pfizer Ventures (US) LLC (Pfizer US). Pfizer Ventures and Pfizer US are each a wholly-owned subsidiary of Pfizer Inc., a publicly traded company (Pfizer). By virtue of the relationship between Pfizer, Pfizer Ventures and Pfizer US, Pfizer may be deemed to have beneficial ownership of shares held by Pfizer Ventures and Pfizer US. Pfizer's address is 235 East 42nd Street, New York, New York 10017.

- (8) Represents 783,364 shares held by a family trust of Dr. Worland of which he is a trustee and 1,529,880 shares underlying options to purchase shares of Common Stock.
- (9) Includes 302,021 shares underlying options to purchase shares of Common Stock.
- (10) Represents 255,160 shares underlying options to purchase shares of Common Stock.
- (11) Includes 533,029 shares underlying options to purchase shares of Common Stock.
- (12) Represents 15,625 shares underlying options to purchase shares of Common Stock.
- (13) Represents 9,375 shares underlying options to purchase shares of Common Stock.
- (14) Represents 9,047 shares of Common Stock held directly by LWAC Sponsor and allocated to Ms. Bhatt by LWAC D&O LLC, a member of LWAC Sponsor, and 22,222 shares underlying options to purchase shares of Common Stock held by Ms. Bhatt.
- (15) Represents 142,168 shares of Common Stock held directly by LWAC Sponsor and allocated to Mr. Ehrlich by Locust Walk Partners LLC (LWP), a member of LWAC Sponsor, 1,034 shares of Common Stock held directly by LWAC Sponsor and allocated to Mr. Ehrlich's spouse by LWP, 35,213 shares of Common Stock held directly by Mr. Ehrlich, and 22,222 shares underlying options to purchase shares of Common Stock held by Mr. Ehrlich.
- (16) Includes 22,222 shares underlying options to purchase shares of Common Stock.
- (17) Represents 15,556 shares underlying options to purchase shares of Common Stock.
- (18) Represents 17,778 shares underlying options to purchase shares of Common Stock.
- (19) Includes 46,364 shares underlying options to purchase shares of Common Stock.
- (20) Represents 1,107,620 shares of Common stock and 2,791,454 options to purchase shares of Common Stock.

Securities Authorized for Issuance Under Equity Compensation Plans (as of December 31, 2022)

The following table provides information as of December 31, 2022 regarding compensation plans under which our equity securities are authorized for issuance:

Plan Category	Number Of Securities To Be Issued Upon Exercise Of Outstanding Options, Warrants and Rights	Weighted Average Exercise Price of Outstanding Options	Number Of Securities Remaining Available For Future Issuance Under Equity Compensation Plans
Equity compensation plans approved by stockholders (1)	8,848,284 (2)	\$ 2.73 (3)	4,886,293 (4)
Equity compensation plans not approved by stockholders	—	—	—
Total	8,848,284	\$ 2.73	4,886,293

- (1) Consists of the 2021 Plan, 2013 Plan and eFFECTOR Therapeutics, Inc. 2021 Employee Stock Purchase Plan (the "ESPP").

- (2) Represents 3,629,846 shares and 5,109,034 shares subject to outstanding stock options under the 2013 Plan and 2021 Plan, respectively. With respect to the ESPP, represents 1,200,842 shares available for issuance under such plan as of December 31, 2022 (all of which were eligible for issuance pursuant to the offering period in effect on such date).
- (3) Represents the weighted-average exercise price of outstanding options.
- (4) Includes 3,685,451 shares available for issuance under the 2021 Plan and 1,200,842 shares reserved for issuance under the ESPP as of December 31, 2022. We are no longer permitted to grant awards under the 2013 Plan. The maximum number of shares subject to purchase under our ESPP offering outstanding on December 31, 2022 is 1,200,842 shares.

The number of shares of our common stock available for issuance under the 2021 Plan will be annually increased on January 1 of each calendar year ending in 2031 by an amount equal to the lesser of (i) a number equal to 5% of the outstanding shares on the final day of the immediately preceding calendar year or (ii) such smaller number of shares as is determined by our Board. Effective as of January 1, 2023, the number of shares available for issuance under the 2021 Plan was increased by 2,099,519 shares, which is not reflected in the table above.

In addition, the number of shares of common stock available for issuance under the ESPP will be annually increased on January 1 of each calendar year ending in 2031 by an amount equal to the lesser of (a) a number equal to 1% of the shares of common stock outstanding on the final day of the immediately preceding calendar year or (b) such smaller number of shares as is determined by our Board. Effective as of January 1, 2023, the number of shares available for issuance under the ESPP was increased by 416,903 shares, which is not reflected in the table above.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The following is a summary of transactions entered since January 1, 2022 to which we have been a party in which the amount involved exceeded or will exceed \$120,000 (or, if less, 1% of the average of our total assets amounts as of December 31, 2022), and in which any of our directors, executive officers or, to our knowledge, beneficial owners 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 equity and other compensation, termination, change in control and other arrangements, which are described under “Executive and Director Compensation.” We also describe below certain other transactions with our directors, executive officers and stockholders.

Registration Rights Agreements

Certain directors and officers and entities that hold more than 5% of our Common Stock following the consummation of the Business Combination entered into the Amended and Restated Registration Rights Agreement, pursuant to which they are entitled to registration rights to require us to register the resale of any of our securities held by them. In addition, in connection with the Purchase Agreement with Lincoln Park, Lincoln Park entered into a registration rights agreement, pursuant to which they are entitled to registration rights to require us to register the resale of any of our securities held by them. For additional information regarding the registration rights agreements, see the “Description of Registered Securities” exhibit filed herewith.

Indemnification under the Certificate of Incorporation and Amended Bylaws; Indemnification Agreements

Our bylaws provide that we will indemnify our directors and officers to the fullest extent permitted by the DGCL, subject to certain exceptions contained in the bylaws. In addition, the certificate of incorporation provides that our directors will not be liable for monetary damages for breach of fiduciary duty.

We also entered into indemnification agreements with each of our executive officers and directors. The indemnification agreements provide the indemnitees with contractual rights to indemnification, and expense advancement and reimbursement, to the fullest extent permitted under the DGCL, subject to certain exceptions contained in those agreements. For additional information, see “Description of our Securities—Limitations on Liability and Indemnification of Officers and Directors.”

Related Person Transaction Policy

Our Board has adopted a written related person transaction policy, setting forth the policies and procedures for the review and approval or ratification of related-person transactions. This policy will cover, with certain exceptions set forth in Item 404 of Regulation S-K under the Securities Act, any transaction, arrangement or relationship, or any series of similar transactions, arrangements or relationships in which we were or are to be a participant, where the amount involved exceeds the lesser of \$120,000 or one percent of the average of our total assets at year-end for the last two completed fiscal years, and a related person had or will have a direct or indirect material interest, including, without limitation, purchases of goods or services by or from the related person or entities in which the related person has a material interest, indebtedness, guarantees of indebtedness and employment by us of a related person. In reviewing and approving any such transactions, our audit committee is tasked to consider all relevant facts and circumstances, including, but not limited to, whether the transaction is on terms comparable to those that could be obtained in an arm's length transaction and the extent of the related person's interest in the transaction.

Director Independence

See Item 10 of Part III of this Annual Report for information about our director independence which is incorporated by reference herein.

Item 14. Principal Accounting Fees and Services.

Independent Registered Public Accounting Firms Fees

Ernst & Young LLP ("E&Y") has served as eFFECTOR's independent registered public accounting firm since 2013.

The following table sets forth the aggregate fees and expenses billed to us by E&Y for fiscal years 2022 and 2021:

	2022	2021
Audit Fees (1)	763,800	1,064,550
Tax Fees (2)	33,990	80,941
All Other Fees	—	—
Total	797,790	1,145,491

- (1) Audit fees consist of fees for professional services rendered for the audit of our year-end consolidated financial statements and services that are normally provided by our independent registered public accounting firm in connection with regulatory filings, and other fees in connection with the Business Combination.
- (2) Tax fees consist of fees for tax consultation services for the Business Combination and professional services relating to tax compliance, tax planning, and tax advice.

Pre-Approval Policies and Procedures

Our audit committee has established a policy that all audit and permissible non-audit services provided by our independent registered public accounting firm will be pre-approved by the audit committee, and all such services were pre-approved in accordance with this policy during the fiscal year ended December 31, 2021. These services may include audit services, audit-related services, tax services and other services. The audit committee considers whether the provision of each non-audit service is compatible with maintaining the independence of our auditors. Pre-approval is detailed as to the particular service or category of services and is generally subject to a specific budget. Our independent registered public accounting firm and management are required to periodically report to the audit committee regarding the extent of services provided by the independent registered public accounting firm in accordance with this pre-approval, and the fees for the services performed to date.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

1. All consolidated financial statements.

The consolidated financial statements of eFFECTOR Therapeutics, Inc., together with the report thereon of Ernst & Young LLP, an independent registered public accounting firm, are included in this Annual Report beginning on page F-1.

2. Financial statement schedules.

All schedules have been omitted because the information required to be set forth therein is not applicable or is shown in the consolidated financial statements or notes thereto.

3. Exhibits

A list of exhibits is set forth on the Exhibit Index immediately preceding the signature page of this Annual Report and is incorporated herein by reference.

Item 16. Form 10-K Summary

None.

eFFECTOR Therapeutics, Inc.
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Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of eFFECTOR Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of eFFECTOR Therapeutics, Inc. (the Company) as of December 31, 2022 and 2021, the related consolidated statements of operations and comprehensive income (loss), convertible preferred stock and stockholders' equity (deficit) and cash flows for each of the two years in the period ended December 31, 2022, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2022, in conformity with U.S. generally accepted accounting principles.

The Company's Ability to Continue as a Going Concern

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has net losses in 2022 and negative cash flows from operating activities since its inception, and has stated that substantial doubt exists about the Company's ability to continue as a going concern. Management's evaluation of the events and conditions and management's plans regarding these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

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

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

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

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2013.

San Diego, California

March 8, 2023

PART I—FINANCIAL INFORMATION

Item 1. Financial Statements.

eFFECTOR THERAPEUTICS, INC.
Consolidated Balance Sheets
(in thousands, except share and par value data)

	December 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	\$ 8,708	\$ 49,702
Short-term investments	17,602	—
Prepaid expenses and other current assets	1,704	3,194
Total current assets	28,014	52,896
Property and equipment, net	241	91
Operating lease right-of-use assets	111	166
Other assets	711	903
Total assets	\$ 29,077	\$ 54,056
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	\$ 1,486	\$ 516
Accrued expenses	3,368	3,418
Current term loans, net	19,061	—
Accrued final payment on term loans, current	1,100	—
Lease liabilities, current portion	60	44
Total current liabilities	25,075	3,978
Earn-out liability	6	12,130
Non-current term loans, net	—	18,760
Accrued final payment on term loans, non-current	—	1,100
Non-current warrant liability	40	678
Non-current lease liabilities	60	126
Total liabilities	25,181	36,772
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, \$0.0001 par value; 100,000,000 and zero shares authorized at December 31, 2022 and December 31, 2021, respectively; zero shares issued and outstanding as of December 31, 2022 and December 31, 2021	—	—
Common stock, \$0.0001 par value; 1,000,000,000 shares authorized at December 31, 2022 and December 31, 2021; 41,990,383 shares issued and 41,690,383 shares issued and outstanding as of December 31, 2022; 40,689,975 shares issued and 40,389,975 shares issued and outstanding as of December 31, 2021	4	4
Additional paid-in capital	147,476	138,181
Accumulated other comprehensive loss	(18)	—
Accumulated deficit	(143,566)	(120,901)
Total stockholders' equity	3,896	17,284
Total liabilities and stockholders' equity	\$ 29,077	\$ 54,056

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

eFFECTOR THERAPEUTICS, INC.

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

	Year Ended December 31,	
	2022	2021
Grant revenue	\$ 3,553	\$ 1,430
Operating expenses:		
Research and development	23,313	19,956
General and administrative	12,643	13,371
Total operating expenses	35,956	33,327
Operating loss	(32,403)	(31,897)
Other income (expense)		
Interest income	439	6
Interest expense	(2,251)	(1,764)
Other income (expense), net	(574)	1,035
Change in fair value of earn-out liability	12,124	48,910
Loss on debt extinguishment	—	(492)
Total other income	9,738	47,695
Net income (loss)	\$ (22,665)	\$ 15,798
Comprehensive income (loss):		
Net income (loss)	(22,665)	15,798
Other comprehensive loss	(18)	—
Comprehensive income (loss):	\$ (22,683)	\$ 15,798
Net income (loss) per share attributable to common shareholders:		
Basic	\$ (0.55)	\$ 1.05
Diluted	\$ (0.55)	\$ 0.44
Weighted-average common shares outstanding:		
Basic	41,179,741	15,105,851
Diluted	41,179,741	36,004,063

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

eFFECTOR THERAPEUTICS, INC.
Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity
(in thousands, except share data)

	Series A Convertible Preferred Stock		Series B Convertible Preferred Stock		Series C Convertible Preferred Stock		Common Stock		Additional Paid-in	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Capital	Loss	Deficit	Equity
Balance at December 31, 2020	11,563,819	\$ 46,567	10,154,819	\$ 51,084	6,734,590	\$ 35,573	1,445,065	\$ —	\$ 4,454	\$ —	\$ (136,699)	\$ (132,245)
Recapitalization transaction, net of transaction costs	—	—	—	—	—	—	10,347,611	1	51,973	—	—	51,974
Conversion of preferred stock into common stock upon completion of the Business Combination	(11,563,819)	(46,567)	(10,154,819)	(51,084)	(6,734,590)	(35,573)	28,453,228	3	133,221	—	—	133,224
Contingently issuable Earn-Out Shares	—	—	—	—	—	—	—	—	(61,040)	—	—	(61,040)
Stock option exercises, net	—	—	—	—	—	—	93,542	—	56	—	—	56
Cashless exercise of warrants	—	—	—	—	—	—	50,529	—	857	—	—	857
Stock-based compensation expense	—	—	—	—	—	—	—	—	8,660	—	—	8,660
Net income	—	—	—	—	—	—	—	—	—	—	15,798	15,798
Balance at December 31, 2021	<u>—</u>	<u>\$ —</u>	<u>—</u>	<u>\$ —</u>	<u>—</u>	<u>\$ —</u>	<u>40,389,975</u>	<u>\$ 4</u>	<u>\$ 138,181</u>	<u>\$ —</u>	<u>\$ (120,901)</u>	<u>\$ 17,284</u>
Stock option exercises	—	—	—	—	—	—	4,828	—	3	—	—	3
Issuance of common stock, net of issuance costs	—	—	—	—	—	—	1,295,580	—	3,958	—	—	3,958
Stock-based compensation expense	—	—	—	—	—	—	—	—	5,334	—	—	5,334
Unrealized loss on short-term investments	—	—	—	—	—	—	—	—	—	(18)	—	(18)
Net loss	—	—	—	—	—	—	—	—	—	—	(22,665)	(22,665)
Balance at December 31, 2022	<u>—</u>	<u>\$ —</u>	<u>—</u>	<u>\$ —</u>	<u>—</u>	<u>\$ —</u>	<u>41,690,383</u>	<u>\$ 4</u>	<u>\$ 147,476</u>	<u>\$ (18)</u>	<u>\$ (143,566)</u>	<u>\$ 3,896</u>

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

eFFECTOR THERAPEUTICS, INC.

Consolidated Statements of Cash Flows
(in thousands)

	Year Ended December 31,	
	2022	2021
Operating activities:		
Net income (loss)	\$ (22,665)	\$ 15,798
Adjustments to reconcile net income (loss) to cash used in operating activities:		
Depreciation and amortization expense	53	24
Accretion of discount and amortization of premium on investments, net	(37)	—
Stock-based compensation	5,334	8,660
Loss on disposal of assets	1	—
Loss on debt extinguishment	—	492
Gain on change in fair value of warrant liability	(638)	(1,031)
Gain on change in fair value of earn-out liability	(12,124)	(48,910)
Other expense related to the equity purchase agreement	1,161	—
Non-cash interest expense	339	317
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	1,575	(1,270)
Other non-current assets	192	(903)
Accounts payable	958	155
Accrued expenses	(52)	1,791
Operating lease right-of-use assets and liabilities, net	4	(11)
Net cash used in operating activities	(25,899)	(24,888)
Investing activities:		
Proceeds from sale of fixed assets	—	607
Purchases of fixed assets	(192)	(42)
Maturities of short-term investments	34,750	—
Purchases of short-term investments	(52,418)	—
Net cash provided by (used in) investing activities	(17,860)	565
Financing activities:		
Payment of debt issuance costs	(37)	—
Proceeds from exercise of common stock options and warrants, net	3	56
Proceeds from issuance of common stock including ESPP, net of issuance costs	2,799	—
Issuance of term loans, net of issuance costs	—	19,835
Repayment of term loans	—	(13,940)
Proceeds from Business Combination, net of offering costs paid (see Note 3)	—	52,858
Net cash provided by financing activities	2,765	58,809
Net increase (decrease) in cash and cash equivalents	(40,994)	34,486
Cash and cash equivalents at beginning of period	49,702	15,216
Cash and cash equivalents at end of period	\$ 8,708	\$ 49,702
Supplemental disclosure of cash flow information:		
Interest paid	\$ 1,823	\$ 1,340
Operating lease liabilities arising from obtaining right-of-use assets	—	179
Supplemental disclosure of non-cash investing and financing activities:		
Issuance of commitment shares	862	—
Accrued issuance costs	2	—
Conversion of preferred stock into common stock	—	133,224
Cashless warrant exercise	—	857
Purchases of fixed assets included in accounts payable and accrued expenses	12	38

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

Notes to Consolidated Financial Statements

1. Organization and Basis of Presentation**Description of Business**

Locust Walk Acquisition Corp. ("LWAC") was initially formed on October 2, 2020 as a Delaware corporation formed for the purpose of effecting a merger, capital stock exchange, asset acquisition, stock purchase, reorganization or other similar business transaction with one or more operating businesses.

On May 26, 2021, LWAC entered into an Agreement and Plan of Merger (the "Merger Agreement") with Locust Walk Merger Sub, Inc., a Delaware corporation and a wholly owned subsidiary of LWAC ("Merger Sub"), and eFFECTOR Therapeutics, Inc., a Delaware corporation ("Old eFFECTOR").

Pursuant to the terms of the Merger Agreement, a business combination between LWAC and Old eFFECTOR was effected through the merger of the Merger Sub with and into Old eFFECTOR, with Old eFFECTOR becoming the surviving company and a wholly-owned subsidiary of LWAC with the name of eFFECTOR Therapeutics Operations, Inc. On August 25, 2021, and in connection with the closing of the business combination (the "Business Combination"), LWAC was renamed eFFECTOR Therapeutics, Inc. ("eFFECTOR" or the "Company"). All outstanding preferred shares of Old eFFECTOR converted into common shares of Old eFFECTOR on a 1:1 basis, which were then converted, along with all outstanding common shares of Old eFFECTOR, into common shares of the surviving eFFECTOR company through application of an exchange ratio of approximately 0.09657 (the "Exchange Ratio").

The Company is a clinical-stage biopharmaceutical company focused on pioneering the discovery and development of a new class of oncology drugs the Company refers to as selective translation regulator inhibitors ("STRIs"). The Company's principal operations are in the United States, with its headquarters in Solana Beach, California. The Company has devoted substantially all of its resources to raising capital, identifying potential product candidates, establishing its intellectual property portfolio, conducting preclinical studies and clinical trials, establishing arrangements with third parties for the manufacture of its product candidates and related raw materials, and providing general and administrative support for these operations. The Company has not generated revenues from its principal operations, other than from licensing and grant revenue, through December 31, 2022.

Basis of Presentation

The Company's consolidated financial statements are prepared in accordance with U.S. generally accepted accounting principles ("GAAP"). All intercompany balances and transactions have been eliminated in consolidation.

The Business Combination was accounted for as a reverse recapitalization in accordance with U.S. GAAP. Under this method of accounting, LWAC was treated as the "acquired" company and eFFECTOR is treated as the acquirer for financial reporting purposes.

Accordingly, for accounting purposes, the Business Combination was treated as the equivalent of Old eFFECTOR issuing stock for the net assets of LWAC, accompanied by a recapitalization. The net assets of LWAC are stated at historical cost, with no goodwill or other intangible assets recorded.

Old eFFECTOR was determined to be the accounting acquirer based on the following predominant factors:

- Old eFFECTOR's shareholders have a majority of the voting power of the combined company;
- the Board and Management are primarily composed of individuals associated with Old eFFECTOR; and
- Old eFFECTOR comprises all of the ongoing operations of the combined company.

The consolidated assets, liabilities and results of operations prior to the Business Combination are those of Old eFFECTOR.

Liquidity

The Company has a limited operating history and the sales and income potential of the Company's business and market are unproven. The accompanying consolidated financial statements have been prepared assuming the Company will continue as a going concern, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business, and do not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or amounts and classification of liabilities that may result from the outcome of this uncertainty.

Management is required to perform a two-step analysis over its ability to continue as a going concern. Management must first evaluate whether there are conditions and events that raise substantial doubt about the Company's ability to continue as a going

concern (step 1). If management concludes that substantial doubt is raised, management is also required to consider whether its plans alleviate that doubt (step 2).

The Company has experienced net losses and negative cash flows from operating activities since its inception, aside from the years ended December 31, 2021 and December 31, 2020 when net income was realized as a result of a gain in fair value recognized associated with the earn-out liability and non-recurring revenue in connection with the Research Collaboration and License Agreement with Pfizer, respectively. The Company has an accumulated deficit of \$143.6 million at December 31, 2022. For the year ended December 31, 2022, the Company used \$25.9 million in cash for operations. At December 31, 2022, the Company had cash and cash equivalents and short-term investments of \$26.3 million. The Company anticipates that its expenses will increase significantly in connection with its ongoing activities to support its research and development efforts, and it expects to incur substantial operating losses and negative cash flows from operations for the foreseeable future. Management has prepared cash flow forecasts which indicate that based on the Company's expected operating losses and negative cash flows, there is substantial doubt about the Company's ability to continue as a going concern within twelve months from the date that these financial statements for the year ended December 31, 2022 are issued. The principal payments due under the Oxford Loans (as defined below), and the related accrued final payment, have been classified as current liabilities as of December 31, 2022, due to the considerations discussed above and the assessment that the material adverse change clause under the Oxford Loans is not within the Company's control. The Company has not been notified of an event of default by the lender as of the date of issuance of these financial statements.

The Company's ability to continue as a going concern is dependent upon its ability to receive additional capital. Management intends to raise additional capital through equity offerings or other capital sources, including potential additional collaborations, licenses and other similar arrangements. Additionally, the Company may receive additional milestone payments from the Research Collaboration and License Agreement with Pfizer (described in Note 12), through the issuance of common stock under the equity purchase agreement with Lincoln Park Capital Fund, LLC (described in Note 9) or through the issuance of common stock under the at-the-market offering program (described in Note 9) with Cantor Fitzgerald & Co. However, the Company may not be able to secure additional financing in a timely manner or on favorable terms, if at all, and may not receive any milestone payments. Without additional capital, the Company may be forced to delay, scale back or eliminate some of its research and development activities, or other operations and potentially delay product development in an effort to provide sufficient funds to continue its operations, or may be required to pursue merger or acquisition strategies, all of which could adversely affect the holdings or the rights of its stockholders.

2. Summary of Significant Accounting Policies

Use of Estimates

The Company's consolidated financial statements are prepared in accordance with accounting principles generally accepted in the United States ("GAAP"). The preparation of the Company's consolidated financial statements requires it to make estimates and assumptions that impact the reported amounts of assets, liabilities and expenses and the disclosure of contingent liabilities in the Company's consolidated financial statements and accompanying notes. The most significant estimate in the Company's consolidated financial statements relates to its clinical trial expense accruals. Management evaluates its estimates on an ongoing basis. Although these estimates are based on the Company's historical experience, knowledge of current events and actions it may undertake in the future, actual results may ultimately materially differ from these estimates and assumptions.

Cash, Cash Equivalents and Short-term Investments

Cash and Cash Equivalents

The Company considers all highly liquid investments with insignificant interest rate risk and an original maturity of three months or less at the date of purchase to be cash equivalents. Cash and cash equivalents consist of money market funds with an original maturity of less than three months at the date of purchase.

Short-term Investments

Short-term investments consist of U.S. Treasury securities, classified as available-for-sale securities and have maturities of greater than three months but less than one year. The Company has classified all of its available-for-sale securities as current assets on the balance sheets because these are considered highly liquid securities and are available for use in current operations. The Company carries these securities at fair value, and reports unrealized gains and losses as a separate component of accumulated other comprehensive loss. Amortization and accretion of any purchase premiums or discounts is included in interest income in the consolidated statements of operations and comprehensive income (loss).

Fair Value of Financial Instruments

The carrying amounts of all cash equivalents, prepaid expenses and other assets, accounts payable and accrued liabilities are reasonable estimates of their fair value because of the short-term nature of these items. Based on the borrowing rates currently available to the Company for loans with similar terms, the Company believes the fair value of the term loans approximate their carrying value (see Note 7).

Concentration of Credit Risk and Other Risks and Uncertainties

Financial instruments, which potentially subject the Company to significant concentration of credit risk, consist primarily of cash and cash equivalents and short-term investments. The Company maintains deposits in a federally insured major financial institution in excess of federally insured limits. The Company has not experienced any losses in such accounts and management believes that the Company is not exposed to significant credit risk due to the financial position of the depository institution in which those deposits are held.

The Company is subject to a number of risks similar to other biopharmaceutical companies, including, but not limited to, the need to obtain adequate additional funding, possible failure of current or future preclinical studies or clinical trials, reliance on third parties or partners to conduct its clinical trials, the need to obtain regulatory and marketing approvals for its drug candidates or to rely on partners to do so, competitors developing new technological innovations, the need to successfully commercialize and gain market acceptance of its drug candidates, the right to develop and commercialize drug candidates pursuant to the terms and conditions of the licenses granted to the Company, protection of proprietary technology, the ability to make milestone, royalty or other payments due under any license or collaboration agreements, and the need to secure and maintain adequate manufacturing arrangements with third parties. If the Company does not successfully commercialize or partner any of its drug candidates, it will be unable to generate product revenue or achieve profitability.

Property and Equipment

Property and equipment are recorded at cost and depreciated or amortized using the straight-line method over the estimated useful lives of the assets (generally three to five years, or the remaining term of the lease for leasehold improvements, whichever is shorter) and generally consist of laboratory equipment, computer and office equipment, furniture and fixtures, and leasehold improvements. Repairs and maintenance costs are charged to expense as incurred.

Long-Lived Assets

The Company regularly reviews the carrying value and estimated lives of all of its long-lived assets, including property and equipment to determine whether indicators of impairment may exist which warrant adjustments to carrying values or estimated useful lives. Should an impairment exist, the impairment loss would be measured based on the excess over the carrying amount of the asset's fair value. The Company has not recognized any impairment losses from inception through December 31, 2022.

Leases

At the inception of a contractual arrangement, the Company determines whether the contract contains a lease by assessing whether there is an identified asset and whether the contract conveys the right to control the use of the identified asset in exchange for consideration over a period of time. If both criteria are met, the Company records the associated lease liability and corresponding right-of-use asset upon commencement of the lease using the implicit rate or a discount rate based on a credit-adjusted secured borrowing rate commensurate with the term of the lease. The Company additionally evaluates leases at their inception to determine if they are to be accounted for as an operating lease or a finance lease. A lease is accounted for as a finance lease if it meets one of the following five criteria: the lease has a purchase option that is reasonably certain of being exercised, the present value of the future cash flows is substantially all of the fair market value of the underlying asset, the lease term is for a significant portion of the remaining economic life of the underlying asset, the title to the underlying asset transfers at the end of the lease term, or if the underlying asset is of such a specialized nature that it is expected to have no alternative uses to the lessor at the end of the term. Leases that do not meet the finance lease criteria are accounted for as an operating lease. Operating lease assets represent a right to use an underlying asset for the lease term and operating lease liabilities represent an obligation to make lease payments arising from the lease. Operating lease liabilities with a term greater than one year and their corresponding right-of-use assets are recognized on the balance sheet at the commencement date of the lease based on the present value of lease payments over the expected lease term. Certain adjustments to the right-of-use asset may be required for items such as initial direct costs paid or incentives received. As the Company's leases do not typically provide an implicit rate, the Company utilizes the appropriate incremental borrowing rate, determined as the rate of interest that the Company would have to pay to borrow on a collateralized basis over a similar term and in a similar economic environment. Lease cost is recognized on a straight-line basis over the lease term and variable lease payments are recognized as operating expenses in the period in which the obligation for those payments is incurred. Variable lease payments primarily include common area maintenance, utilities, real estate taxes, insurance, and other operating costs that are passed on from the lessor in proportion to the

space leased by the Company. The Company has elected the practical expedient to not separate between lease and non-lease components.

Grant Revenue

The Company's grant revenues were derived from a grant with the Defense Advanced Research Projects Agency ("DARPA") through the University of California, San Francisco ("UCSF"). The Company recognizes DARPA grant revenue as reimbursable grant costs are incurred up to pre-approved award limits within the budget period. The costs associated with these reimbursements are reflected as a component of research and development expense in the accompanying consolidated statements of operations and comprehensive income (loss). Billings in excess of receipts are included as a receivable recorded within prepaid expenses and other current assets on the consolidated balance sheets.

Research and Development Costs

Research and development expenses primarily consist of costs associated with the preclinical and clinical development of the Company's product candidates. Research and development costs are expensed as incurred.

Clinical Trial Accruals and Preclinical Studies

The Company records expenses resulting from our obligations under contracts with vendors and consultants, CROs and clinical sites in connection with conducting clinical trials and preclinical studies. 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 clinical trial and preclinical study expenses in the 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 clinical trial or preclinical study as measured by the timing of various aspects of the clinical trial, preclinical study, or related activities. The Company determines accrual estimates based on the underlying contracts, correspondence with clinical and other key personnel and third-party service providers as to the progress of the clinical trials, preclinical studies, or other services being conducted, and amounts invoiced or paid to date. During the course of a clinical trial or preclinical study, the Company adjusts the rate of expense recognition if actual results differ from estimates.

Patent Costs

Costs related to filing and pursuing patent applications are recorded as general and administrative expense and expensed as incurred since recoverability of such expenditures is uncertain.

Revenue Recognition

The Company evaluates collaboration arrangements to determine whether units of account within the collaboration arrangement exhibit the characteristics of a vendor and customer relationship. For arrangements and units of account where a customer relationship exists, the Company applies the revenue recognition guidance. The Company recognizes revenue upon the transfer of promised goods or services to customers in an amount that reflects the consideration to which the Company expects to be entitled in exchange for those goods or services. To determine revenue recognition for contracts with customers the Company performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the Company satisfies the performance obligations. At contract inception, the Company assesses the goods or services promised within each contract and assesses whether each promised good or service is distinct and determines those that are performance obligations. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

If a license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenues from non-refundable, upfront fees allocated to the license when the license is transferred to the licensee and the licensee is able to use and benefit from the license. For licenses that are bundled with other performance obligations, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition on a prospective basis.

For research and development services performed under a collaboration agreement in which the performance obligation is satisfied over time, the Company measures the progress of the activities using an input method. The input methods used are based on the effort expended or costs incurred toward the satisfaction of the related performance obligation. The Company estimates the amount of effort expended, including the time the Company estimates it will take to complete the activities, or costs incurred in a given period, relative to the estimated total effort or costs to satisfy the performance obligation. This results in a percentage that is multiplied by the consideration allocated to the research and development services to determine the amount of revenue recognized

each period. This approach requires estimates and the use of significant judgement. If the estimates or judgements change over the course of the collaboration, they may affect the timing and amount of revenue recognized in the current and future periods.

Milestones

At the inception of each arrangement that includes milestone payments (variable consideration), the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the Company or the Company's collaboration partner's control, such as regulatory approvals, are generally not considered probable of being achieved until those approvals are received. The transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, the Company re-evaluates the probability of achievement of such milestones and any related constraint, and if necessary, adjusts the Company's estimate of the overall transaction price. Any such adjustments are allocated on a cumulative catch-up basis to satisfied and partially satisfied performance obligations, with the consideration allocated to an ongoing performance obligation being recognized over the period of performance.

Royalties

For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and for which the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any royalty revenue from any collaborative arrangement.

Income Taxes

The Company accounts for income taxes under the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the consolidated financial statements. Under this method, deferred tax assets and liabilities are determined on the basis of the differences between the consolidated financial statements and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. The effect of a change in tax rates on deferred tax assets and liabilities is recognized in income in the period that includes the enactment date.

The Company recognizes deferred tax assets to the extent that the Company believes these assets are more likely than not to be realized. In making such a determination, management considers all available positive and negative evidence, including future reversals of existing taxable temporary differences, projected future taxable income, tax-planning strategies, and results of recent operations. If management determines that the Company would be able to realize its deferred tax assets in the future in excess of their recorded amount, management would make an adjustment to the deferred tax asset valuation allowance, which would reduce the provision for income taxes.

As of December 31, 2022 and 2021, the Company maintained valuation allowances against its deferred tax assets as the Company concluded it had not met the "more likely than not" to be realized threshold. Changes in the valuation allowance when they are recognized in the provision for income taxes may result in a change in the estimated annual effective tax rate.

The Company records uncertain tax positions on the basis of a two-step process whereby (1) management determines whether it is more likely than not that the tax positions will be sustained on the basis of the technical merits of the position and (2) for those tax positions that meet the more likely than not recognition threshold, management recognizes the largest amount of tax benefit that is more than 50% likely to be realized upon ultimate settlement with the related tax authority. The Company recognizes interest and penalties related to unrecognized tax benefits within income tax expense. Any accrued interest and penalties are included within the related tax liability.

Comprehensive Loss

Comprehensive loss consists of net loss and unrealized gains or losses on available-for-sale investments. The Company presents comprehensive loss and its components as part of the consolidated statements of operations and comprehensive income (loss).

Segment Reporting

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision-maker in making decisions regarding resource allocation and assessing performance. The Company and its chief operating decision-maker view the Company's operations and manage its business in one operating segment.

Stock-Based Compensation Expense

Stock-based compensation expense represents the cost of the grant date fair value of employee stock option grants recognized over the requisite service period of the awards (usually the vesting period) on a straight-line basis. The Company estimates the fair value of stock option grants using the Black-Scholes option-pricing model. The Company accounts for stock options granted to non-employees using the fair value approach.

The Black-Scholes option-pricing model requires the use of subjective assumptions, including the risk-free interest rate, the expected stock price volatility, the expected term of stock options, and the expected dividend yield. 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 average of the contractual term of the stock option and its weighted-average vesting period. The fair value of the underlying common stock used within the Black-Scholes option-pricing model is based on the closing price of common stock on the date of grant.

Public and Private Placement Warrants

Upon completion of the Business Combination, the Company assumed public and private placement warrants that were issued by LWAC in connection with their initial public offering in January 2021 whereby holders of the public and private placement warrants are entitled to acquire common stock of the Company. The Company has concluded that the public warrants are equity-classified. Since the settlement value of the private placement warrants is dependent, in part, on who holds the warrants at the time of settlement, they are not considered indexed to the Company's stock and are therefore recorded as liabilities. Warrants classified as liabilities are recorded at their estimated fair value on the date of issuance and are revalued at each subsequent balance sheet date, with fair value changes recognized in other income (expense), net in the accompanying consolidated statements of operations and comprehensive income (loss). The Company estimates the fair value of these warrants using the Black-Scholes option pricing model.

Earn-out Shares

In accordance with the Merger Agreement, 5,000,000 shares ("Earn-Out Shares") are contingently issuable to Old eFFECTOR stockholders and option holders upon the occurrence of the Triggering Event (see Note 3), defined within the Merger Agreement as the date on which the common stock price equals or exceeds \$20.00 over at least 20 trading days out of a 30 consecutive trading day period during the two-year period following the close date of the Business Combination. The estimated fair value of the Earn-Out Shares was determined using a Monte Carlo simulation valuation model using a distribution of potential outcomes on a monthly basis over the earn-out period using the most reliable information available.

The Company has determined that the contingent obligation to issue Earn-Out Shares to existing Old eFFECTOR shareholders is not indexed to the Company's stock under ASC 815-40 and therefore equity treatment is precluded. The Triggering Event that determines the issuance of the Earn-Out Shares includes terms that are not solely indexed to our common stock, and as such liability classification is required. Equity-linked instruments classified as liabilities are recorded at their estimated fair value on the date of issuance and are revalued at each subsequent balance sheet date, with fair value changes recognized in other income (expense), net in the accompanying consolidated statements of operations and comprehensive income (loss).

The Company has determined that the contingent obligation to issue Earn-Out Shares to existing Old eFFECTOR option holders falls within the scope of ASC 718, Share-based Compensation, because the option holders are required to continue providing service until the occurrence of the Triggering Event. The fair value of the option holder Earn-Out Shares is recorded as share-based compensation over the derived service period of the Monte Carlo simulation valuation model, recognized in research and development and general and administrative expense in the consolidated statements of operations and comprehensive income (loss).

Recent Accounting Pronouncements

From time to time, new accounting pronouncements are issued by the Financial Accounting Standards Board ("FASB") or other standard setting bodies and adopted by the Company as of the specified effective date. Unless otherwise discussed, the Company believes, based on their preliminary assessment, that the impact of recently issued standards that are not yet effective will not have a material impact on their financial position or results of operations upon adoption.

In August 2020, the FASB issued ASU 2020-06, *Debt-Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging-Contracts in Entity's Own Equity (Subtopic 815-40)*, which addresses the complexity associated with applying generally accepted accounting principles for certain financial instruments with characteristics of liabilities and equity. The amendments in this ASU reduce the number of accounting models for convertible debt instruments and convertible preferred stock, as well as amend the guidance for the derivatives scope exception for contracts in an entity's own equity to reduce form-over-substance-based accounting conclusion. In addition, this ASU improves and amends the related earnings per share guidance. The amendments in this ASU are effective for the Company on January 1, 2024, including interim periods within those fiscal years. Early adoption is permitted, but no earlier than fiscal years beginning after December 15, 2020, including interim periods within those fiscal years. Adoption is either a modified retrospective method or a fully retrospective method of transition. The Company adopted this standard

as of January 1, 2022 under the modified retrospective transition method, and it did not have a material impact on the consolidated financial statements or the related disclosures.

Net Income (Loss) Per Share

The Company computes net income (loss) per share in accordance with the FASB guidance for Earnings Per Share, which established standards regarding the computation of earnings per share by companies that have issued securities other than common stock that contractually entitle the holder to participate in earnings and dividends. The guidance requires earnings available to common shareholders for the period, after deduction of preferred stock preferences, to be allocated between the common and preferred shareholders based on their respective rights to receive dividends. The Company is not required to present basic and diluted net income per share for securities other than common stock; therefore, the net income (loss) per share amounts only pertain to the Company's common stock.

Basic net income (loss) per share is calculated by dividing income (loss) allocable to common shareholders (net income after reduction for any required returns to preferred stock shareholders prior to paying dividends to the common shareholders, assuming current income for the period had been distributed) by the weighted-average number of common shares outstanding, during the period. The Company calculates diluted net income per share using the more dilutive of the 1) treasury stock method, if-converted method, or contingently issuable share method, as applicable, or 2) the two-class method.

Due to the Company recording net loss for the year ended December 31, 2022, and none of the outstanding securities being dilutive for this period, basic and diluted loss per share are the same for the year ended December 31, 2022.

The Company has used the treasury stock method to calculate diluted net income per share for the year ended December 31, 2021, as there were no participating securities as of December 31, 2021 (and there were no participating securities in the period of net income during 2021). Diluted net income per share for the year ended December 31, 2021 also reflects the assumed exercise of options outstanding during the period using the treasury stock method, to the extent dilutive. Warrants were included in the calculation of diluted net income per share for the year ended December 31, 2021 to the extent the warrants were dilutive.

The following table sets forth the computation of basic and diluted net income (loss) per share (in thousands, except share and per share data):

	For the Year Ended December 31,	
	2022	2021
Basic Net Income (Loss) per share		
Net income (loss)	\$ (22,665)	\$ 15,798
Weighted average common shares outstanding - basic	41,179,741	15,105,851
Net income (loss) per share - basic	<u>\$ (0.55)</u>	<u>\$ 1.05</u>
Diluted Net Income (Loss) per share		
Net income (loss) attributable to common shareholders	\$ (22,665)	\$ 15,798
Weighted average common shares outstanding - basic	41,179,741	15,105,851
Weighted average effect of dilutive securities:		
Convertible preferred stock	—	18,556,453
Stock options	—	2,341,759
Weighted average common shares outstanding - diluted	41,179,741	36,004,063
Net income (loss) per share - diluted	<u>\$ (0.55)</u>	<u>\$ 0.44</u>

Potentially dilutive securities as of December 31, 2022 and 2021 are as follows (in common stock equivalent shares):

	For the Year Ended December 31,	
	2022	2021
Public warrants	5,833,323	5,833,333
Private placement warrants	181,667	181,667
Earn-Out Shares	5,000,000	5,000,000
Unvested sponsor shares	300,000	300,000
Stock options outstanding	8,738,880	403,278
Total	<u>20,053,870</u>	<u>11,718,278</u>

3. Business Combination

As discussed in Note 1, on August 25, 2021, the Company completed the Business Combination pursuant to the Merger Agreement. Upon closing of the Business Combination, the combined company was renamed eFFECTOR Therapeutics, Inc.

As a result of the Business Combination, each share of Old eFFECTOR preferred stock and common stock was converted into the right to receive approximately 0.09657 shares of the Company's common stock for an aggregate of 30,021,762 shares of common stock issued in the Business Combination. Former holders of shares of Old eFFECTOR common stock (including shares received as a result of the conversion of Old eFFECTOR preferred stock and the exercise of Old eFFECTOR warrants) and former holders of options to purchase shares of Old eFFECTOR will also be entitled to receive their pro rata share of up to 5,000,000 Earn-Out Shares of common stock if, on or prior to August 26, 2023, the closing share price of shares of common stock equals or exceeds \$20.00 over at least 20 trading days within a 30-day trading period (the "Triggering Event") and, in respect of each former holder of Old eFFECTOR stock options, such holder continues to provide services to the Company or one of its subsidiaries at the time of such Triggering Event. The Earn-Out Shares will also be earned and issuable in the event of a change in control of the Company on or prior to August 26, 2023 that results in the holders of common stock receiving a per-share price equal to or in excess of \$20.00.

Pursuant to subscription agreements entered into in connection with the Merger Agreement (collectively, the "Subscription Agreements"), certain investors agreed to subscribe for an aggregate of 6,070,003 newly-issued shares of common stock at a purchase price of \$10.00 per share for an aggregate purchase price of \$60.7 million (the "PIPE Financing"). At the closing, we consummated the PIPE Financing. A total of 10,347,611 shares of common stock were issued in connection with the close of the Business Combination, inclusive of the PIPE Financing shares and shares held by LWAC sponsor and public investors.

In connection with the closing of the Business Combination, the LWAC sponsor received 4,056,250 shares of eFFECTOR common stock, of which 300,000 shares were subject to vesting if, on or prior to August 25, 2024, the price of shares of common stock equals or exceeds \$15.00 per share for a period of at least 20 trading days out of 30 consecutive trading days ending on the trading day immediately prior to the date of determination (the "Sponsor Shares"). The 300,000 sponsor shares subject to vesting meet the criteria for equity classification, but are not considered outstanding from an accounting perspective. These shares are considered issued but not outstanding as of December 31, 2022 and December 31, 2021, and have been excluded from outstanding shares in the calculation of income (loss) per share for the years ended December 31, 2022 and 2021.

After giving effect to the Business Combination, and the consummation of the PIPE Financing, there were 40,669,373 shares of common stock issued and 40,369,373 shares of common stock issued and outstanding. In connection with the closing of the Business Combination, options to purchase shares of Old eFFECTOR common stock were converted, at an exchange ratio of approximately 0.09657, into options to purchase an aggregate of 3,920,657 shares of common stock, with a weighted-average exercise price of \$1.56 per share.

Pursuant to the terms of the Merger Agreement, the Company's shareholders exchanged their interests in the Company for shares of common stock of eFFECTOR. In addition, awards under the Company's existing equity incentive plans, including the 2013 Plan, continue in full force and effect on the same terms and conditions as were previously applicable to such awards, subject to adjustments to the exercise price and number of shares of common stock issuable upon exercise based on the final exchange ratio of approximately 0.09657.

Gross proceeds from this transaction totaled approximately \$67.0 million, which included funds held in LWAC's trust and operating accounts and the completion of a concurrent sale of 6,070,003 shares of common stock at a purchase price of \$10.00 per share in the PIPE Financing. The transaction was accounted for as a "reverse recapitalization" in accordance with GAAP. Under the reverse recapitalization model, the Business Combination was treated as eFFECTOR issuing equity for the net assets of LWAC, with no goodwill or intangible assets recorded. Under this method of accounting, LWAC was treated as the "acquired" company for financial reporting purposes. This determination is primarily based on the fact that subsequent to the Business Combination, eFFECTOR stockholders have a majority of the voting power of the combined company, comprise all of the ongoing operations of the combined entity, comprise a majority of the governing body of the combined company, and eFFECTOR senior management comprise all of the senior management of the combined company.

In connection with the Business Combination, the Company raised \$52.9 million of net proceeds. This amount was comprised of \$6.3 million of cash held in LWAC's trust and operating accounts from its initial public offering and \$60.7 million of cash in connection with the PIPE Financing, less LWAC's transaction costs and underwriters' fees of \$11.1 million. Old eFFECTOR incurred \$3.0 million of transaction costs, consisting of banking, legal, and other professional fees which were recorded as a reduction to additional paid-in capital. In addition to the net proceeds disclosed above, the Company also assumed \$0.9 million of net liabilities of LWAC upon closing of the Business Combination.

The following summarizes the common stock outstanding following the consummation of the Business Combination, PIPE Financing and the automatic cashless exercise of Old eFFECTOR warrants:

	Shares	%
Old eFFECTOR Stockholders	30,021,762	74.4%
LWAC Stockholders	521,358	1.3%
LWAC Founders (1)	3,756,250	9.3%
PIPE Investors	6,070,003	15.0%
Total	<u>40,369,373</u>	<u>100.0%</u>

(1) Excludes 300,000 Sponsor Shares subject to vesting that are not considered outstanding from an accounting perspective.

4. Fair Value Measurements

The accounting guidance defines fair value, establishes a consistent framework for measuring fair value and expands disclosure for each major asset and liability category measured at fair value on either a recurring or nonrecurring basis. Fair value is defined as an 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 such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability. As a basis for considering such assumptions, the accounting guidance establishes a three-tier fair value hierarchy, which prioritizes the inputs used in measuring fair value as follows:

Level 1: Unadjusted quoted prices in active markets that are accessible at the measurement date for identical, unrestricted assets or liabilities.

Level 2: Quoted prices for similar assets and liabilities in active markets, quoted prices in markets that are not active, or inputs which are observable, either directly or indirectly, for substantially the full term of the asset or liability.

Level 3: Prices or valuation techniques that require inputs that are both significant to the fair value measurement and unobservable (i.e. supported by little or no market activity).

The Company's cash equivalents are classified using Level 1 inputs within the fair value hierarchy because they are valued using quoted market prices, broker or dealer quotations, or alternative pricing sources with reasonable levels of price transparency. None of the Company's non-financial assets or liabilities are recorded at fair value on a non-recurring basis. No transfers between levels have occurred during the periods presented.

The Company estimates the fair value of its warrant liabilities at the time of issuance and subsequent remeasurement using the Black-Scholes option pricing model at each reporting date, if required, based on the following inputs: the risk-free interest rates; the expected dividend rates; the remaining contractual life of the warrants; the fair value of the underlying stock; and the expected volatility of the price of the underlying stock. The estimates are based, in part, on subjective assumptions and could differ materially in the future. Changes to these assumptions as well as the fair value of the Company's stock on the reporting date can have a significant impact on the fair value of the warrant liability.

The following table summarizes the Company's assets and liabilities that require fair value measurements on a recurring basis and their respective input levels based on the fair value hierarchy as of December 31, 2022 and December 31, 2021 (in thousands):

	December 31, 2022	Fair Value Measurements Using		
		Quoted Prices in Active Markets for Identical Assets Level 1	Significant Other Observable Inputs Level 2	Significant Unobservable Inputs Level 3
Assets				
Cash equivalents:				
Money market funds	\$ 8,708	\$ 8,708	\$ —	\$ —
Short-term investments:				
U.S. Treasury securities	17,602	—	\$ 17,602	—
Total assets	<u>\$ 26,310</u>	<u>\$ 8,708</u>	<u>\$ 17,602</u>	<u>\$ —</u>
Liabilities				
Private placement warrant liability	\$ 40	\$ —	\$ —	\$ 40
Earn-out liability	6	—	—	6
Total liabilities	<u>\$ 46</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 46</u>

	December 31, 2021	Fair Value Measurements Using		
		Quoted Prices in Active Markets for Identical Assets Level 1	Significant Other Observable Inputs Level 2	Significant Unobservable Inputs Level 3
Assets				
Money market funds	\$ 49,702	\$ 49,702	\$ —	\$ —
Total assets	<u>\$ 49,702</u>	<u>\$ 49,702</u>	<u>\$ —</u>	<u>\$ —</u>
Liabilities				
Private placement warrant liability	\$ 678	\$ —	\$ —	\$ 678
Earn-out liability	12,130	—	—	12,130
Total liabilities	<u>\$ 12,808</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 12,808</u>

Cash Equivalents and Short-Term Investments

Financial assets measured at fair value on a recurring basis consist of the Company's cash equivalents and short-term investments. Cash equivalents consisted of money market funds and short-term investments consisted of U.S. Treasury securities. The Company obtains pricing information from its investment manager and generally determines the fair value of investment securities using standard observable inputs, including reported trades, broker/dealer quotes, and bids and/or offers.

Investments are classified as Level 1 within the fair value hierarchy if their quoted prices are available in active markets for identical securities. Investments in money market funds of \$8.7 million and \$49.7 million as of December 31, 2022 and December 31, 2021, respectively, were classified as Level 1 instruments and were included in cash and cash equivalents.

Investments in marketable securities are valued using Level 2 inputs. Level 2 securities are initially valued at the transaction price and subsequently valued and reported upon utilizing inputs other than quoted prices that are observable either directly or indirectly, such as quotes from third-party pricing vendors. Fair values determined by Level 2 inputs, which utilize data points that are observable such as quoted prices, interest rates and yield curves, require the exercise of judgment and use of estimates, that if changed, could significantly affect the Company's financial position and results of operations. The marketable securities of \$17.6 million as of December 31, 2022 were classified as Level 2 instruments, all of which are included in short-term investments. There were no marketable securities as of December 31, 2021. Accrued interest receivable related to short-term investments was \$27,000 as of December 31, 2022, and included as part of prepaid expenses and other current assets in the condensed balance sheets.

The following tables summarize the Company's short-term investments accounted for as available-for-sale securities as of December 31, 2022 (in thousands):

	Maturity (in years)	Amortized Cost	December 31, 2022		
			Unrealized Gains	Unrealized Losses	Estimated Fair Value
U.S. Treasury securities	1 year or less	\$ 17,620	\$ 1	\$ (19)	\$ 17,602
		\$ 17,620	\$ 1	\$ (19)	\$ 17,602

Preferred Stock Warrant Liability

The preferred stock warrant liability was measured at fair value, using a combination of observable and unobservable inputs. The change in fair value of preferred stock warrant liabilities were recorded in Other income (expense) on the statement of operations and comprehensive income (loss). All outstanding preferred stock warrants were cashless exercised as a result of the Business Combination on August 25, 2021 (See Note 8). The preferred stock warrants were remeasured to fair value on the date of cashless exercise based on the net shares issued and fair value of common stock on the settlement date, which was the close date of the Business Combination on August 25, 2021.

The following table presents activity for the preferred stock warrant liability measured at fair value using significant unobservable Level 3 inputs during the year ended December 31, 2021 (in thousands):

	Series C Preferred Stock Warrant Liability	
Balance at December 31, 2020	\$	433
Issuance of new warrants		271
Change in fair value		153
Warrant exercises		(857)
Balance at December 31, 2021	\$	—

Private Placement Warrant Liability

In connection with the Business Combination, the Company assumed the public and private placement warrants described in Note 2. The private placement warrants are precluded from equity treatment and are recorded as liabilities as they are not considered indexed to the Company's common stock. The private placement warrant liability is measured at fair value, using a combination of observable and unobservable inputs. The change in fair value of the private placement warrant liability is recorded in other income (expense) on the statement of operations and comprehensive income (loss). The following key assumptions were used in determining the fair value of the private placement warrant liability valued using the Black-Scholes option pricing model as of December 31, 2022 and December 31, 2021:

	December 31, 2022		December 31, 2021	
Common stock price	\$	0.43	\$	8.28
Expected volatility		125.0 %		65.0 %
Risk-free interest rate		4.2 %		1.3 %
Expected term (in years)		3.7		4.7
Expected dividend yield		—		—

The following table presents activity for the private placement warrant liability measured at fair value using significant unobservable Level 3 inputs during the year ended December 31, 2022 (in thousands):

	Private Placement Warrant Liability	
Private Placement Warrants liability - August 25, 2021 (closing date)	\$	1,862
Change in fair value - Closing Date through December 31, 2021		(1,184)
Balance at December 31, 2021		678
Change in fair value		(638)
Balance at December 31, 2022	\$	40

Earn-Out Liability

Former holders of shares of Old eFFECTOR common stock were allocated Earn-Out Shares in connection with the completion of the Business Combination with LWAC which are accounted for as liabilities. Please refer to Note 10 for additional details surrounding the valuation methodology for these Earn-Out Shares.

5. Property and Equipment, net

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

	December 31, 2022		December 31, 2021	
Lab equipment	\$	30	\$	30
Computer and office equipment		149		127
Furniture and fixtures		61		64
Leasehold improvements		188		—
Construction in process		29		74
		457		295
Less accumulated depreciation and amortization		(216)		(204)
	\$	241	\$	91

The Company recorded depreciation and amortization expense of \$53,000 and \$24,000 for the years ended December 31, 2022 and 2021, respectively.

6. Accrued Expenses

Accrued expenses consist of the following (in thousands):

	December 31, 2022	December 31, 2021
Employee compensation	\$ 1,385	\$ 1,343
Research and development	1,206	1,115
Professional and outside services	112	452
Interest	197	133
Income taxes payable	463	351
Other	5	24
	<u>\$ 3,368</u>	<u>\$ 3,418</u>

7. Term Loans

Oxford Term Loans

In March 2021, Old eFFECTOR entered into a Loan and Security Agreement ("Oxford LSA") with Oxford Finance LLC ("Oxford"), pursuant to which the Company may borrow up to \$30.0 million, issuable in two separate tranches of \$20.0 million ("Term A Loans") and \$10.0 million ("Term B Loans"), collectively referred to as the Oxford Loans. The Term A Loans became available to the Company at the effective date of the Oxford LSA on March 19, 2021 and \$12.5 million of the proceeds were used to pay off the outstanding SVB Term Loans. The remaining net proceeds from Term A Loans of \$7.4 million, after taking into effect specified issuance and legal fees designated within the distribution letter, were distributed to the Company in March 2021. The Company is required to make a final payment equal to 5.5% of each funded tranche at maturity, which has been recorded as a debt discount for the Term A Loans and is being amortized over the term of the debt arrangements. In connection with the Oxford LSA, the Company issued warrants to purchase a total of 37,575 shares of Series C Preferred Stock at an exercise price of \$5.33 per share. The warrants were automatically exercised on a cashless basis on August 25, 2021, in connection with the completion of the Business Combination, for 17,575 shares of common stock.

On February 22, 2022, the Company entered into an amendment to the Oxford LSA whereby the interest only period for the Term A Loans will end on March 1, 2024, instead of May 1, 2023. In connection with the amendment, the maturity of the Term A Loans was extended from March 18, 2026 to February 1, 2027. Additionally, Term B Loans would have become available to the Company after January 1, 2023 upon achievement of certain clinical development milestones, until the earlier of (i) June 30, 2023, (ii) 45 days after the achievement of certain clinical development milestones (the "Phase II Milestones"), and (iii) the occurrence of an event of default. As a result of the discontinuation of one of the cohorts in the KICKSTART trial, which was previously announced in January 2023, the Company does not expect to achieve the clinical development milestones by June 30, 2023 and therefore does not expect to have access to the additional \$10.0 million under the Term B Loans.

The Oxford Loans carry a variable interest rate equal to the greater of (i) 7.7% and (ii) the sum of the prime rate plus 4.45%. The Company has the option to prepay all, but not less than all, of the borrowed amounts, provided that the Company will be obligated to pay a prepayment fee equal to (i) 3.0% of the outstanding principal balance of the applicable Oxford Loans if prepayment is made prior to the first anniversary of the effective date of the Oxford LSA, (ii) 2.0% of the outstanding principal balance of the applicable Oxford Loans if prepayment is made after the first anniversary of the effective date of the Oxford LSA but before the second anniversary, and (iii) 1.0% of the outstanding principal balance of the applicable Oxford Loans if prepayment is made after the second anniversary of the effective date of the Oxford LSA but before the third anniversary. No prepayment fee will apply for a prepayment made after the third anniversary of the effective date of the Oxford LSA and prior to the maturity date.

The Company's obligations under the Oxford LSA are secured by a first priority security interest in substantially all of its current and future assets, other than its owned intellectual property. The Company is also obligated to comply with various other customary covenants, including restrictions on its ability to encumber intellectual property assets without consent.

The Company recorded a debt discount of \$1.6 million for the estimated fair value of warrants, debt issuance costs, and final payment to be made, which is being amortized to interest expense over the term of the loan using the effective-interest method. As of December 31, 2022, the Company had \$20.0 million of outstanding principal under the Term A Loans of which \$19.1 million is reflected on the balance sheet net of debt discounts. Interest expense, including amortization of debt discount related to the Oxford Term A Loans, totaled \$2.2 million for the year ended December 31, 2022. The Company is in compliance with all covenants under

the Oxford LSA as of December 31, 2022. The Term A Loans include customary events of default, including instances of a material adverse change in our operations, that may require prepayment of the outstanding Term A Loans. The principal payments due under the Oxford Loans, and the related accrued final payment, have been classified as current liabilities as of December 31, 2022, due to the considerations discussed in Liquidity section of Note 1. The Company has not been notified of an event of default by the lender as of the date of issuance of these financial statements.

Based on the outstanding principal amounts for the Company's Term A Loans, the following table sets forth by year the Company's required future principal payments as of December 31, 2022 (in thousands):

As of December 31, 2022		
2024	\$	5,555
2025		6,667
2026		6,667
2027		1,111
Required future principal payments	\$	20,000
Unamortized debt discount		(939)
Current term loans, net as of December 31, 2022	\$	<u>19,061</u>

SVB Term Loans

On August 31, 2018, Old eFFECTOR entered into a Loan and Security Agreement ("LSA") with Silicon Valley Bank ("SVB"), pursuant to which the Company borrowed \$15 million.

In March 2021, Old eFFECTOR repaid the SVB loan using the proceeds from Oxford Term A Loans (defined above). The outstanding principal balance of the SVB loan was \$11.5 million at the date of repayment. The Company paid the entire outstanding principal balance, along with a final payment in the amount of \$0.8 million (equal to 5.5% of the original aggregate principal amount), a prepayment fee of \$0.1 million (equal to 1% of the original aggregate principal amount), and \$37,000 of accrued interest. The Company recorded a loss on debt extinguishment in the amount of \$0.5 million in connection with the transaction, which has been recorded in Loss on debt extinguishment on the consolidated statement of operations and other comprehensive income (loss) for the period. The loss on debt extinguishment includes the unamortized debt discount and final payment associated with the SVB loan at the time of extinguishment along with the \$0.1 million prepayment fee.

8. Warrants

Preferred Stock Warrants

The Company accounted for its warrants to purchase shares of convertible preferred stock as a liability. The Company adjusted the liability for changes in fair value of these warrants up until the closing date of the Business Combination. Upon consummation of the Business Combination on August 25, 2021, the outstanding warrants were cashless exercised and 50,529 total net shares were issued.

Assumed Public Warrants and Private Placement Warrants

Following the consummation of the Business Combination, holders of the public warrants and private placement warrants are entitled to acquire common stock of the Company. The warrants became exercisable on January 12, 2022, which is 12 months from the closing of the LWAC's initial public offering. Each warrant entitles the registered holder to purchase one share of common stock at an exercise price of \$11.50 per share. The public warrants and private placement warrants will expire on August 25, 2026, which is five years after the completion of the Business Combination.

Once the public warrants and private placement warrants became exercisable, the Company has the right to redeem the outstanding warrants in whole and not in part at a price of \$0.01 per warrant upon a minimum of 30 days' prior written notice of redemption, if and only if the last sale price of the common stock equals or exceeds \$18.00 per share for any 20 trading days within a 30-trading day period ending on the third trading day prior to the date on which the Company sends the notice of redemption to the warrant holders.

The private placement warrants are identical to the public warrants except that, so long as they are held by the Sponsor or its permitted transferees: (i) they will not be redeemable by the Company; (ii) they may be exercised by the holders on a cashless basis; and (iii) they are subject to registration rights.

Private placement warrants are liability-classified (See Note 4) and the public warrants are equity-classified. The following table summarizes the number of outstanding public warrants and private placement warrants and the corresponding exercise price as of December 31, 2022 and December 31, 2021:

	December 31, 2022	December 31, 2021	Exercise Price	Expiration Date
Public warrants	5,833,323	5,833,333	\$ 11.50	August 24, 2026
Private placement warrants	181,667	181,667	\$ 11.50	August 24, 2026

During the year ended December 31, 2022, warrants to purchase ten shares of common stock were exercised for gross proceeds of less than \$1 thousand. No warrants were exercised in the year ended December 31, 2021.

9. Preferred Stock and Stockholders' Equity

Equity Purchase Agreement

On January 24, 2022, the Company entered into an equity purchase agreement (the "Purchase Agreement") and a registration rights agreement with Lincoln Park Capital Fund, LLC ("Lincoln Park" or "Investor") which provides for the sale to Lincoln Park up to \$50.0 million of shares (the "Purchase Shares") of the Company's common stock over the thirty-six (36) month term of the Purchase Agreement. In connection with the Purchase Agreement, Lincoln Park made an initial purchase of \$3.0 million of shares of common stock (the "Initial Purchase"), which equated to 557,610 shares of common stock, and the Company issued 142,939 shares of common stock to Lincoln Park as a commitment fee in connection with entering into the Purchase Agreement. The Company recognized \$0.8 million of other expense relating to the commitment fee share issuance. For the year ended December 31, 2022, an additional 30,000 shares of common stock were sold at an average price per share of \$1.74 for gross proceeds of \$52 thousand.

Under the Purchase Agreement, the Company has sole discretion, subject to certain conditions, on any business day selected by the Company to require Lincoln Park to purchase up to 30,000 shares of common stock (the "Regular Purchase Amount") at the Purchase Price (as defined below) per purchase notice (each such purchase, a "Regular Purchase"). The Regular Purchase Amount may be increased as follows: to up to 50,000 shares if the closing price is not below \$5.00, and up to 75,000 shares if the closing price is not below \$10.00. Lincoln Park's committed obligation under each Regular Purchase is capped at \$2,500,000, unless the Parties agree otherwise. The purchase price for Regular Purchases (the "Purchase Price") shall be equal to the lesser of: (i) the lowest sale price of the common shares during the Purchase Date, or (ii) the average of the three (3) lowest closing sale prices of the common shares during the ten (10) business days prior to the Purchase Date.

In addition to Regular Purchases and subject to certain conditions and limitations, the Company in its sole discretion may require Lincoln Park on each Purchase Date to purchase on the following business day up to the lesser of (i) three (3) times the number of shares purchased pursuant to such Regular Purchase or (ii) 25% of the trading volume on the Accelerated Purchase Date (the "Accelerated Purchase") (unless the Parties agree otherwise) at a purchase price equal to the lesser of 97% of (i) the closing sale price on the Accelerated Purchase Date, or (ii) the Accelerated Purchase Date's volume weighted average price (the "Accelerated Purchase Price"). The Company has the sole right to set a minimum price threshold for each Accelerated Purchase in the notice provided with respect to such Accelerated Purchase and under certain circumstances and in accordance with the Purchase Agreement the Company may direct multiple Accelerated Purchases in a day.

The aggregate number of shares that the Company can sell to Lincoln Park under the Purchase Agreement may not exceed 8,133,926 shares of the Common Shares (which is equal to approximately 19.99% of the shares of the Common Shares outstanding immediately prior to the execution of the Purchase Agreement) (the "Exchange Cap"), unless (i) shareholder approval is obtained to issue Purchase Shares above the Exchange Cap, in which the Exchange Cap will no longer apply, or (ii) the average price of all applicable sales of Common Shares to Lincoln Park under the Purchase Agreement equals or exceeds \$6.42 per share; provided that at no time may Lincoln Park (together with its affiliates) beneficially own more than 4.99% of the Company's issued and outstanding Common Shares.

The Purchase Agreement contains customary representations, warranties, covenants, closing conditions, indemnification and termination provisions. The Purchase Agreement may be terminated by the Company at any time, at its sole discretion, without any cost or penalty, by giving one business day notice to Lincoln Park. Further, Lincoln Park has covenanted not to engage in any direct or indirect short selling or hedging of the Common Shares. There are no limitations on the use of proceeds, financial or business covenants, restrictions on future financings (other than restrictions on the Company's ability to enter into a similar type of agreement or Equity Line of Credit during the Term, excluding an At-The-Market transaction with a registered broker-dealer), rights of first refusal, participation rights, penalties or liquidated damages in the Purchase Agreement.

At-the-Market Offering Program

In September 2022, the Company entered into a Controlled Equity Offering Sales Agreement (the "Sales Agreement") with Cantor Fitzgerald & Co (the "Agent", or "Cantor"), under which the Company may, from time to time, sell shares of the Company's common stock having an aggregate offering price of up to \$15.0 million in "at the market" offerings (the "ATM Offering Program") through Cantor. Sales of the shares of common stock will be made at prevailing market prices at the time of sale, or as otherwise agreed with Cantor. Cantor will receive a commission from the Company of 3.0% of the gross proceeds of any shares of common stock sold under the Sales Agreement. During the year ended December 31, 2022, the Company sold an aggregate of 478,964 shares of common stock at a weighted-average price of \$0.60 per share for gross proceeds of approximately \$0.3 million under the ATM Offering Program. Offering costs, including commissions, of approximately \$0.2 million were recorded as an offset to gross proceeds within additional paid-in capital.

Preferred Stock

Upon closing of the Business Combination transaction, pursuant to the terms of the Amended and Restated Certificate of Incorporation, 100,000,000 shares of preferred stock with a par value of \$0.0001 per share were authorized. eFFECTOR's board of directors has the authority, without further action by the stockholders to issue such shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each such series, and to fix the dividend, voting, and other rights, preferences and privileges of the shares. There were no issued and outstanding shares of preferred stock immediately after the closing of the Business Combination.

In connection with the closing of the Business Combination on August 25, 2021, all Old eFFECTOR convertible preferred stock was converted into common stock of eFFECTOR at an Exchange Ratio of 0.09657. 28,453,228 total shares of Old eFFECTOR convertible preferred stock (as adjusted for the Exchange Ratio), composed of 11,563,819 shares of Old eFFECTOR Series A convertible preferred stock, 10,154,819 shares of Old eFFECTOR Series B convertible preferred stock, and 6,734,590 shares of Old eFFECTOR Series C convertible preferred stock, were converted into 28,453,228 shares of eFFECTOR common stock.

Employee Stock Purchase Plan

The ESPP provides for six-month offering periods, and at the end of each offering period, employees are able to purchase shares at 85% of the lower of the fair market value of the Company's common stock on the first trading day of the offering period or on the last trading day of the offering period. An aggregate of 880,000 shares were initially reserved and available for issuance under the ESPP. The ESPP provides that the number of shares reserved and available for issuance under the plan will automatically increase each January 1, beginning on January 1, 2022, by 1.0% of the outstanding number of shares of common stock on the immediately preceding December 31, or such lesser amount as determined by our board of directors; provided that the total number of shares of common stock that become available for issuance under the ESPP will never exceed 15,000,000. If our capital structure changes because of a stock dividend, stock split or similar event, the number of shares that can be issued under the ESPP will be appropriately adjusted. As of December 31, 2022, 1,200,842 shares were reserved for future issuance under the ESPP. During the year ended December 31, 2022, 86,057 shares of common stock were issued under the ESPP.

2013 Equity Incentive Plan

Prior to the Business Combination, Old eFFECTOR maintained its 2013 Equity Incentive Plan (the "2013 Plan"), under which Old eFFECTOR granted incentive stock options, restricted stock awards, and other stock-based awards to employees, directors, and non-employee consultants. Upon the closing, the Company ceased granting awards under the 2013 Plan and, as described below, all awards under the 2013 Plan were converted into awards under the 2021 Plan with the same terms and conditions. As of August 25, 2021, prior to the Business Combination transaction, 3,920,657 Old eFFECTOR options remained outstanding under the 2013 Plan. As of December 31, 2022, the number of shares reserved under the 2013 Plan was 3,629,846. There were zero shares available for grant under the 2013 Plan as of December 31, 2022. In connection with the completion of the Business Combination and the adoption of the 2021 Plan, no further awards will be granted under the 2013 Plan.

2021 Equity Incentive Plan

In connection with the consummation of the Business Combination on August 25, 2021, the Board of Directors approved the adoption of the 2021 Equity Incentive Plan (the "2021 Plan"). As of December 31, 2022, 8,794,485 shares of common stock are authorized for issuance pursuant to awards under the 2021 Plan, inclusive of any shares of common stock subject to stock options, restricted stock awards or other awards that were assumed in the Business Combination. As of December 31, 2022, 5,598,409 options to purchase common shares have been awarded and 3,685,451 shares remain available for issuance under the 2021 Plan. The 2021 Plan permits the granting of incentive stock options, restricted stock awards, other stock-based award or other cash-based awards to employees, directors, and non-employee consultants.

Options granted under the 2021 Plan are exercisable at various dates as determined upon grant and will expire no more than ten years from their date of grant, or in the case of certain non-statutory options, ten years from the date of grant. The exercise price of each option shall be determined by the Board of Directors based on the Fair Market Value of the Company's stock on the date of the option grant, defined as the closing sales price of the Company's common stock. In the case of incentive stock options, the exercise price shall not be less than 100% of the Fair Market Value of the Company's common stock at the time the option is granted. For holders of more than 10% of the Company's total combined voting power of all classes of stock, incentive stock options may not be granted at less than 110% of the Fair Market Value of the Company's stock at the date of grant and for a term not to exceed five years.

A summary of the Company's stock option activity under the plans is as follows (in thousands, except share and per share amounts and years):

	Shares	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term	Aggregate Intrinsic Value
Outstanding at December 31, 2021	4,193,321	\$ 2.41	6.0	\$ 26,115
Granted	5,253,923	3.17	9.4	
Exercised	(4,828)	0.52	0.4	
Cancelled or forfeited	(703,536)	4.14	8.6	
Outstanding at December 31, 2022	8,738,880	\$ 2.73	7.4	\$ —
Vested and exercisable at December 31, 2022	4,354,101	\$ 2.40	5.4	\$ —

For the years ended December 31, 2022 and 2021, the total fair value of vested options was \$4.2 million and \$1.1 million, respectively. The intrinsic value of options exercised during the years ended December 31, 2022 and 2021 was zero and \$0.7 million, respectively.

The weighted-average grant date fair value of employee option grants during the years ended December 31, 2022 and 2021 was \$2.21 per share and \$4.75 per share, respectively. The weighted-average grant date fair value of non-employee option grants during the years ended December 31, 2022 and 2021 was \$2.30 per share and \$8.71 per share, respectively.

Stock-Based Compensation Expense

The Company recognized stock-based compensation expense specifically related to stock options of \$5.0 million and \$1.0 million for the years ended December 31, 2022 and 2021, respectively. The assumptions used in the Black-Scholes option pricing model to determine the fair value of the stock option grants were as follows:

	Year Ended December 31,	
	2022	2021
Risk-free interest rate	1.7% - 4.1%	0.7% - 1.3%
Expected volatility	82% - 86%	81% - 90%
Expected term (in years)	5.2 - 6.1	5.5 - 6.1
Expected dividend yield	0%	0%

Risk-free interest rate. The risk-free rate assumption is based on the U.S. Treasury instruments, the terms of which were consistent with the expected term of the Company's stock options.

Expected volatility. Due to the Company's limited operating history and lack of company-specific historical or implied volatility, the expected volatility assumption was determined by examining the historical volatilities of a group of industry peers whose share prices are publicly available.

Expected term. The expected term of stock options represents the weighted-average period the stock options are expected to be outstanding. The Company uses the simplified method for estimating the expected term as provided by the SEC. The simplified method calculates the expected term as the weighted average of the time-to-vesting and the contractual life of the options.

Expected dividend yield. The expected dividend assumption is based on the Company's history and expectation of dividend payouts. The Company has not paid and does not intend to pay dividends.

Forfeitures. The Company reduces stock-based compensation expense for actual forfeitures during the period in which they occur.

As of December 31, 2022, the unrecognized compensation cost related to outstanding employee options was \$7.3 million and is expected to be recognized as expense over approximately 2.4 years. Unrecognized compensation cost related to outstanding

nonemployee options was \$1.5 million as of December 31, 2022, and is expected to be recognized as expense over approximately 1.0 years.

Common Stock Reserved for Future Issuance

Common stock reserved for future issuance consists of the following as of December 31, 2022 and December 31, 2021:

	December 31, 2022	December 31, 2021
Stock options issued and outstanding	8,738,880	4,193,321
Public warrants issued and outstanding	5,833,323	5,833,333
Private placement warrants issued and outstanding	181,667	181,667
Earn-Out shares	5,000,000	5,000,000
Unvested sponsor shares	300,000	300,000
Authorized for future stock awards or option grants	3,685,451	6,201,340
Authorized for future issuances under the ESPP	1,200,842	880,000
Total	<u>24,940,163</u>	<u>22,589,661</u>

10. Earn-Out Shares

In accordance with the Merger Agreement, 5,000,000 Earn-Out Shares are contingently issuable to Old eFFECTOR stockholders and option holders upon the occurrence of the Triggering Event, defined within the Merger Agreement as the date on which the common stock price equals or exceeds \$20.00 over at least 20 trading days out of 30 consecutive trading day period for the two-year period following the close date of the Business Combination. As of December 31, 2022, the stockholders and option holders would be eligible to receive approximately 4,561,353 and 438,647 Earn-Out Shares, respectively. As of December 31, 2021, the stockholders and option holders would be eligible to receive approximately 4,426,889 and 573,111 Earn-Out Shares, respectively.

The fair value per share of the Earn-Out Shares was \$0.0014 and \$2.74, respectively as of December 31, 2022 and December 31, 2021. The fair value was determined using a Monte Carlo simulation valuation model using a distribution of potential outcomes on a monthly basis over the Earn-Out Period using the most reliable information available. Assumptions used in the valuation were as follows:

	December 31, 2022	December 31, 2021
Stock price	\$ 0.43	\$ 8.28
Expected volatility	115.0%	65.0%
Risk-free interest rate	4.8%	0.6%
Forecast period (in years)	0.6	1.6
Cost of equity	20.0%	20.0%

Old eFFECTOR Shareholders

The Company has determined that the contingent obligation to issue Earn-Out Shares to existing Old eFFECTOR shareholders is not indexed to the Company's stock under ASC 815-40 and therefore equity treatment is precluded. The Triggering Event that determines the issuance of the Earn-Out Shares includes terms that are not solely indexed to the common stock of the Company, and as such liability classification is required. As of the consummation date of the Business Combination, the estimated fair value of the shareholder Earn-Out Shares was approximately \$61.0 million and the Company will revalue the liability each reporting period with the changes in fair value being recorded to the consolidated statements of operations and comprehensive income (loss). For the years ended December 31, 2022 and 2021, there was a decrease in the earn-out liability of \$12.1 million and \$48.9 million, respectively, which was recorded as a gain on change in fair value within the consolidated statements of operations and comprehensive income (loss). In accordance with the Merger Agreement, Earn-Out Shares attributable to Old eFFECTOR option holders who discontinue providing service before the occurrence of the Triggering Event are reallocated to the remaining eligible stockholders and option holders.

The following table presents activity for the earn-out liability measured at fair value using significant unobservable Level 3 inputs at December 31, 2021 and December 31, 2022 (in thousands):

	Earn-out Liability
Earn-out liability - August 25, 2021 (Closing Date)	\$ 61,024
Incremental shares due to option holder forfeitures	16
Change in fair value - Closing Date through December 31, 2021	(48,910)
Earn-out liability - December 31, 2021	12,130
Change in fair value	(12,124)
Balance at December 31, 2022	\$ 6

Old eFFECTOR Option Holders

The contingent obligation to issue Earn-Out Shares to existing Old eFFECTOR option holders falls within the scope of ASC 718, Share-based Compensation, because the option holders are required to continue providing service until the occurrence of the Triggering Event. The fair value of the option holder Earn-Out Shares at the consummation date of the Business Combination was approximately \$7.9 million, which was recorded as share-based compensation over the derived service period of 0.36 years following the consummation of the Business Combination. For the years ended December 31, 2022 and 2021, there was approximately \$0.3 million and \$7.6 million recorded in share-based compensation related to the Earn-Out Shares, respectively, and the derived service period was completed as of March 31, 2022, with no additional share-based compensation expense to be recorded.

11. License Agreements

In May 2013, the Company entered into an agreement with the Regents of the University of California (“UCSF”) which provides the Company with an exclusive license to UCSF’s patent rights in certain inventions (the “UCSF Translational Profiling Patent Rights”) relating to translational profiling laboratory techniques initially developed at UCSF. Under the agreement, the Company is permitted to research, develop, make and sell products that it discovers and develops utilizing the UCSF Translational Profiling Patent Rights, which the Company refers to as licensed products, and use certain licensed processes utilizing the UCSF Translational Profiling Patent Rights and to sublicense such licensed products and processes.

In July 2021, the Company entered into an amendment to the license agreement to confirm the impact of the Business Combination on the license agreement, including clarifying that in connection with the closing of the Business Combination, the Company would pay UCSF a one-time cash payment of approximately \$1.0 million. The \$1.0 million payment was made to UCSF in August 2021 in connection with the close of the Business Combination. The Company is also required to make cash milestone payments to UCSF upon the completion of certain clinical and regulatory milestones for the licensed products. The aggregate remaining potential milestone payments are approximately \$375,000.

The Company paid an annual minimum royalty of \$15,000 to UCSF for each of the years ended December 31, 2022 and 2021. All license related fees were recorded as research and development expense.

12. Research Collaboration and License Agreement

In December 2019, the Company entered into a Research Collaboration and License Agreement (the “Pfizer Agreement”) with Pfizer to research and develop small molecules that target eIF4E.

Under the Pfizer Agreement, the Company was responsible for initial research in collaboration with Pfizer, and Pfizer is responsible for all further development of the program, including submission of an IND and conducting all clinical development and commercialization activities. Pfizer is obligated to use commercially reasonable efforts to develop and seek regulatory approval for a licensed product, and commercialize a licensed product where Pfizer has received regulatory approval, in the United States and certain other countries. In the event the Company exercises its co-funding and co-promotion option, a joint steering committee will oversee the development plan and budget of the co-developed product, and the Company will have the responsibility to conduct a portion of product marketing presentations to healthcare providers.

Pursuant to the Pfizer Agreement, the Company received an upfront, one-time, non-refundable, non-creditable payment of \$15 million from Pfizer. Pfizer was obligated to reimburse the Company for costs incurred for research performed, up to a specified cap in the low double-digit millions. Upon the achievement of specified early development and regulatory milestones, Pfizer will be obligated to pay the Company up to \$80 million in the aggregate. For other non-early stage development milestones Pfizer’s payment obligations to the Company depends upon whether the Company has exercised its co-funding and co-promotion option: 1) if it does not exercise the option, non-early stage development payments may total up to \$165 million in aggregate, and 2) if it does exercise the option, non-early stage development payments may total up to \$70 million in aggregate. Upon the achievement of specified sales milestones, Pfizer is also obligated to make tiered milestone payments of up to \$235 million in aggregate. On a product-by-product basis, Pfizer will also be required to pay the Company high single-digit percentage royalties on annual net sales of each licensed

product. If the Company exercises its co-promotion and co-funding option, royalty payments will exclude sales in the United States and the Company will share with Pfizer profits from sale of the relevant licensed product in the United States.

The initial transaction price of \$27.0 million was allocated to the two performance obligations on a relative standalone value basis, with \$25.6 million allocated to the license and \$1.4 million allocated to the research activities, which were completed in 2020. The value attributable to the license was recognized upon delivery of the license to Pfizer and the value attributable to the research activities was recognized pro-rata based on the actual costs incurred by the Company compared to the total estimated costs of the research activities from the time of execution to the end of the research program.

There was no revenue recorded in connection with this agreement for the years ended December 31, 2022 and 2021 because all development and sales milestones (variable consideration) were fully constrained.

13. DARPA Grant Revenue

In April 2021, the Company entered into a Research Subaward Agreement with UCSF (the "Subaward Agreement"), whereby up to \$5.0 million in allowable costs were reimbursable for clinical and manufacturing activities related to zotatifin for the treatment of COVID-19. Under the terms of the Subaward Agreement, the Company was obligated to provide financial and technical reports to UCSF on a periodic basis. The Subaward Agreement can be terminated by either party upon written notice and also in the event that DARPA suspends or terminates its cooperative agreement with UCSF. The initial award period for the Subaward Agreement ended in December 2021, and in April 2022 the Company received an extension of the award period to December 2022, with the same maximum \$5.0 million reimbursement amount. The Company recognized \$3.6 million and \$1.4 million of revenue under the Subaward Agreement in the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, the Company exhausted the full \$5.0 million of allowable reimbursable costs under the Subaward Agreement.

14. Commitments and Contingencies

Leases

In November 2020, the Company entered into a non-cancelable operating sublease for office space in San Diego, California, with a lease term through December 2021. Rent expense under this lease was \$0.1 million for the year ended December 31, 2021.

In September 2021, the Company entered a non-cancelable three-year lease for certain new office space in Solana Beach, California, with an option to renew for an additional three-year term. The initial term of the lease started on November 1, 2021, and is serving as the Company's new headquarters. Rent expense under this lease was \$0.1 million and \$16,400 for the years ended December 31, 2022 and 2021, respectively.

During each of the years ended December 31, 2022 and 2021, the Company paid \$0.1 million in lease payments. All lease payments were included in operating activities in the statements of cash flows.

The following table summarizes supplemental balance sheet information related to leases as of December 31, 2022 and December 31, 2021 (in thousands):

	December 31, 2022	December 31, 2021
Assets:		
Operating lease right-of-use assets	\$ 111	\$ 166
Total right-of-use assets	<u>111</u>	<u>166</u>
Liabilities		
Operating lease liabilities, current	60	44
Operating lease liabilities, non-current	60	126
Total operating lease liabilities	<u>\$ 120</u>	<u>\$ 170</u>

As of December 31, 2022, the future minimum annual lease payments under the existing operating leases were as follows (in thousands, except for weighted-average remaining lease term and weighted-average discount rate):

2023	67
2024	62
Total remaining lease payments	<u>129</u>
Less: imputed interest	(9)
Total operating lease liabilities	<u>120</u>
Less: current portion	(60)
Long-term operating lease liabilities	<u>\$ 60</u>
Weighted-average remaining lease term (in years)	1.8
Weighted-average discount rate	8%

15. Employee Benefits

The Company has a defined contribution 401(k) plan available to eligible employees. Under the terms of the plan, employees may make voluntary contributions as a percent of compensation, limited to the maximum amount allowable under federal tax regulations. The Company, at its discretion, may make certain contributions to the 401(k) plan. Through December 31, 2022, the Company made no matching contributions.

16. Income Taxes

There was no income tax expense recorded by the Company for the years ended December 31, 2022 and 2021. Significant components of the Company's net deferred tax assets are summarized as follows (in thousands):

	December 31, 2022	December 31, 2021
Deferred tax assets:		
Net operating loss carryforwards	\$ 42,243	\$ 36,898
Intangibles	189	3,565
Research and development capitalization	3,839	—
Accrued compensation	2,282	1,284
Credits	8,013	7,107
Fixed assets	10	6
Other, net	88	74
Right-of-use liability	25	36
Deferred tax assets	56,689	48,970
Deferred tax liabilities:		
Right-of-use asset	(23)	(35)
Deferred tax liabilities	(23)	(35)
Net deferred tax assets	56,666	48,935
Valuation allowance	(56,666)	(48,935)
Net deferred tax assets	\$ —	\$ —

A reconciliation of the income tax computed at the federal statutory tax rate to the expense (benefit) for income taxes for the years ended December 31, 2022 and 2021 is as follows (in thousands):

	December 31, 2022	December 31, 2021
Tax at statutory rate	\$ (4,760)	\$ 3,318
State income taxes, net of federal benefits	(2,076)	(1,853)
Change in valuation allowance	7,726	8,515
Uncertain tax positions	586	569
Gain on change in fair value of earn-out liability	(2,546)	(10,271)
Permanent differences and other	281	636
Transaction costs	244	—
Capitalized R&D	3,381	510
LWAC net operating loss	(1,370)	—
Credits	(1,466)	(1,424)
Income tax expense	\$ —	\$ —

Management assesses all available evidence to estimate if sufficient future taxable income will be generated to use the existing deferred tax assets. The Company has experienced net losses since inception (aside from the years ended December 31, 2021 and December 31, 2020 when net income was realized as a result of a gain in fair value recognized associated with the earn-out liability and non-recurring revenue in connection with the Research Collaboration and License Agreement with Pfizer, respectively), and the revenue and income potential of the Company's business and market are unproven. Due to the Company's continuing research and development activities, the Company expects to continue to incur net losses into the foreseeable future. As such, the Company cannot conclude that it is more likely than not that its deferred tax assets will be realized. A valuation allowance of \$56.7 million and \$48.9 million at December 31, 2022 and 2021, respectively, has been established to offset the deferred tax assets, as realization of such assets is uncertain.

Utilization of net operating loss ("NOL") and research and development ("R&D") credit carryforwards may be subject to a substantial annual limitation due to ownership change limitations that may have occurred or that could occur in the future, as required by Section 382 of the Internal Revenue Code of 1986, as amended (the "Code"), as well as similar state and foreign provisions. These ownership changes may limit the amount of NOL and R&D credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. In general, an "ownership change" as defined by Section 382 of the Code results from a transaction or series of transactions over a three-year period resulting in an ownership change of more than 50 percentage points of the outstanding stock of a company by certain stockholders. Since the Company's formation, the Company has raised capital through the issuance of capital stock on several occasions, which on its own or combined with the purchasing stockholders' subsequent disposition of those shares, may have resulted in such an ownership change, or could result in an ownership change in the future.

The Company completed a preliminary Code section 382 and 383 study from inception through December 31, 2020 and concluded that \$1.8 million of federal and California net operating losses and \$0.1 million of federal R&D credits will expire unused. The Company removed deferred tax assets for net operating loss of \$0.6 million and research credits of \$0.1 million from its deferred tax assets schedule and has recorded a corresponding decrease in the valuation allowance. The Company has not conducted the 382 study after December 31, 2020. When the study is completed, the Company will adjust its deferred tax assets accordingly. Due to the existence of a full valuation allowance any subsequent ownership changes will not impact the Company's effective tax rate.

The Company had federal and California NOL carryforwards of approximately \$181.6 million and \$92.8 million, respectively, portions of which begin to expire in 2034 and 2036, respectively. Federal NOLs of \$103.1 million carry forward indefinitely.

As of December 31, 2022, the Company had federal and California research and development ("R&D") tax credit carryforwards of approximately \$9.6 million, inclusive of the federal orphan drug tax credit carryforward, and \$4.3 million, respectively. The federal R&D tax credit carryforwards will begin to expire in 2034, unless previously utilized. The California R&D tax credit carryforwards are available indefinitely. As of December 31, 2022, the Company also had federal orphan drug tax credit carryforwards of \$2.2 million that will begin to expire in 2037.

The Inflation Reduction Act 2022 which incorporates a Corporate Alternative Minimum Tax (CAMT) was signed on August 16, 2022. The changes will affect for the tax years beginning after December 31, 2022. The new tax will require companies to compute two separate calculations for federal income tax purposes and pay the greater of the new minimum tax or their regular tax liability. The Company will be monitoring the impacts of the act to determine if this will have an impact for the Company for years beginning after December 31, 2022. The act is not expected to have a material impact for the Company.

The Company recognizes a tax benefit from an uncertain tax position when it is more likely than not that the position will be sustained upon examination, including resolutions of any related appeals or litigation processes, based on the technical merits. Income tax positions must meet a more likely than not recognition at the effective date to be recognized.

A reconciliation of the beginning and ending amount of unrecognized tax benefits for 2022 and 2021, excluding interest and penalties, is as follows (in thousands):

	December 31, 2022	December 31, 2021
Balance at beginning of the year	\$ 8,235	\$ 7,623
Additions/(reductions) for tax positions - prior year	—	—
Increase related to current year positions	625	612
Balance at the end of the year	<u>\$ 8,860</u>	<u>\$ 8,235</u>

For the year ended December 31, 2022, the Company recognized interest and penalties of approximately \$62,000 and \$50,000, respectively, which are recorded in accrued expenses on the consolidated balance sheets. Interest and penalties are captured within the interest expense and other income (expense) lines, respectively, on the consolidated statements of operations and comprehensive income (loss). For the year ended December 31, 2021, the Company did not recognize any interest or penalties.

The Company currently files income tax returns in California and with the U.S. Internal Revenue Service. The Company currently has no tax periods under examination by any jurisdiction. Due to the existence of net operating loss carryforwards, all tax periods from inception of the Company are open for examination by taxing authorities for all jurisdictions.

Included in the balance of unrecognized tax benefits at December 31, 2022 is \$7.4 million that, if recognized, would not impact the Company's income tax expense (benefit) or effective tax rate as long as our deferred tax asset remains subject to a full valuation allowance. The Company does not expect any significant increases or decreases to our unrecognized tax benefits within the next 12 months.

EXHIBIT INDEX

Exhibit Number	Description	Incorporated by Reference		
		Form	Exhibit	Filing Date
2.1†	Agreement and Plan of Merger dated as of May 26, 2021, by and among Locust Walk Acquisition Corp., Locust Walk Merger Sub, Inc. and eFFECTOR Therapeutics, Inc.	8-K	2.1	5/27/2021
3.1	Amended and Restated Certificate of Incorporation of eFFECTOR Therapeutics, Inc.	8-K	3.1	8/31/2021
3.2	Amended and Restated Bylaws of eFFECTOR Therapeutics, Inc.	8-K	3.2	8/31/2021
4.1	Specimen common stock certificate.	S-4/A	4.1	8/5/2021
4.2	Warrant Agreement, dated January 7, 2021, by and between Continental Stock Transfer & Trust Company and Locust Walk Acquisition Corp.	8-K	4.1	1/13/2021
4.3	Description of Registered Securities.	10-K	4.3	3/16/2022
10.1	Letter of Agreement, dated January 7, 2021, by and among Locust Walk Acquisition Corp. and certain security holders, officers and director of Locust Walk Acquisition Corp.	8-K	10.1	1/13/2021
10.2	Investment Management Trust Agreement, dated January 7, 2021, by and between Continental Stock Transfer & Trust Company and Locust Walk Acquisition Corp.	8-K	10.2	1/13/2021
10.3	Amended and Restated Registration Rights Agreement, dated August 25, 2021, by and among eFFECTOR Therapeutics, Inc., eFFECTOR Therapeutics Operations, Inc., Locust Walk Sponsor, LLC and certain stockholders.	8-K	10.3	8/31/2021
10.4	Unit Subscription Agreement, dated January 7, 2021, by and between Locust Walk Acquisition Corp. and Locust Walk Sponsor, LLC.	8-K	10.4	1/13/2021
10.5	Administrative Service Agreement, dated January 7, 2021, by and between Locust Walk Acquisition Corp. and Locust Walk Sponsor, LLC.	8-K	10.5	1/13/2021
10.6	Form of Indemnity Agreement of Locust Walk Acquisition Corp.	S-1	10.5	12/18/2020
10.7	Sponsor Support Agreement, dated May 26, 2021, by and among Locust Walk Acquisition Corp. and Locust Walk Sponsor, LLC.	8-K	10.1	5/27/2021
10.8	Sponsor Lock-up Agreement, dated May 26, 2021, by and between Locust Walk Sponsor, LLC. and Locust Walk Acquisition Corp.	8-K	10.2	5/27/2021
10.9	Form of Subscription Agreement, dated May 26, 2021, by and among Locust Walk Acquisition Corp. and certain subscribers.	8-K	10.3	5/27/2021
10.10+	eFFECTOR Therapeutics, Inc. 2021 Incentive Award Plan and Form of Stock Option Agreement thereunder.	8-K	10.10	8/31/2021
10.11+	eFFECTOR Therapeutics, Inc. 2021 Employee Stock Purchase Plan.	8-K	10.11	8/31/2021
10.12+	Form of Indemnification Agreement.	S-4/A	10.12	8/5/2021
10.13#	Exclusive License Agreement, dated May 9, 2013, by and between eFFECTOR and the Regents of the University of California.	S-4	10.13	6/14/2021
10.14#	Research Collaboration and License Agreement, dated December 20, 2019, by and between eFFECTOR and Pfizer Inc.	S-4	10.14	6/14/2021
10.15	Loan and Security Agreement, dated March 19, 2021, by and among eFFECTOR and Oxford Finance LLC and the other lenders party thereto.	S-4	10.15	6/14/2021
10.16	Sublease Agreement, dated August 24, 2020, by and between eFFECTOR and Cardiff Oncology, Inc.	S-4	10.16	6/14/2021
10.17+	eFFECTOR Therapeutics, Inc. 2013 Equity Incentive Plan, as amended, and form of option agreement thereunder.	8-K	10.17	8/31/2021
10.18+	eFFECTOR Therapeutics, Inc. Non-Employee Director Compensation Program.	8-K	10.18	8/31/2021

10.19+	Second Amended and Restated Employment Agreement by and between Stephen T. Worland, Ph.D. and eFFECTOR.	S-4	10.19	6/14/2021
10.20+	Amended and Restated Employment Agreement by and between Alana McNulty and eFFECTOR.	S-4	10.20	6/14/2021
10.21+	Amended and Restated Employment Agreement by and between Mike Byrnes and eFFECTOR.	S-4	10.21	6/14/2021
10.22+	Amended and Restated Employment Agreement by and between Premal Patel and eFFECTOR.	S-4	10.22	6/14/2021
10.23†+	General Release of Claims, effective as of April 8, 2022, by and between eFFECTOR and Premal Patel, M.D., Ph.D.	10-Q	10.2	8/9/2022
10.24†+	Consulting Agreement, dated April 1, 2022, by and between eFFECTOR and Premal Patel, M.D., Ph.D.	10-Q	10.3	8/9/2022
10.25†+	General Release of Claims, effective as of July 22, 2022, by and between eFFECTOR and Alana McNulty.	10-Q	10.4	8/9/2022
10.26#	Amendment to Exclusive License Agreement, dated July 12, 2021, by and between eFFECTOR and the Regents of the University of California.	S-4/A	10.23	7/19/2021
10.27	Purchase Agreement, dated January 24, 2022, between eFFECTOR and Lincoln Park Capital Fund, LLC.	8-K	10.1	1/24/2022
10.28	Registration Rights Agreement, dated January 24, 2022, between eFFECTOR and Lincoln Park Capital Fund, LLC.	8-K	10.2	1/24/2022
10.29	Joinder and First Amendment to Loan and Security Agreement, dated September 7, 2021, by and among eFFECTOR and Oxford Finance LLC.	8-K	10.1	2/24/2022
10.30	Second Amendment to Loan and Security Agreement, dated February 22, 2022, by and among eFFECTOR and Oxford Finance LLC.	8-K	10.2	2/24/2022
10.31	Third Amendment to Loan and Security Agreement, dated April 28, 2022, by and among eFFECTOR and Oxford Finance LLC.	10-Q	10.1	5/10/2022
10.32	Controlled Equity OfferingSM Sales Agreement Sale Agreement by and between eFFECTOR and Cantor Fitzgerald & Co., dated September 1, 2022.	S-3	1.2	9/1/2022
10.33+	Employment Agreement, effective as of August 8, 2022, by and between eFFECTOR and Douglas Warner.			*
10.34+	Employment Agreement, effective as of September 1, 2022, by and between eFFECTOR and Mayank Gandhi.			*
23.1	Consent of Independent Registered Public Accounting Firm			*
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.			*
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.			*
32.1**	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.			*
32.2**	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.			*
101.INS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document.			*
101.SCH	Inline XBRL Taxonomy Extension Schema Document			*
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document			*

101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document	*
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document	*
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document	*
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)	*

† Certain of the exhibits and schedules to this Exhibit have been omitted in accordance with Regulation S-K Item 601(a)(5). The Company agrees to furnish a copy of all omitted exhibits and schedules to the SEC upon its request.

+ Indicates a management contract or compensatory plan.

Portions of this Exhibit have been omitted in accordance with Regulation S-K Item 601(b)(10)(iv). The Registrant agrees to furnish an unredacted copy of this Exhibit to the SEC upon its request.

* Filed herewith.

** This certification is deemed not filed for purpose 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.

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.

eFFECTOR Therapeutics, Inc.

Date: March 8, 2023

By: /s/ Stephen Worland
Stephen Worland, Ph.D.
President and Chief Executive Officer

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 in the capacities and on the dates indicated.

Name	Title	Date
<u>/s/ Stephen Worland, Ph.D.</u> Stephen Worland, Ph.D.	President and Chief Executive Officer (Principal Executive Officer)	March 8, 2023
<u>/s/ Michael Byrnes</u> Michael Byrnes	Chief Financial Officer (Principal Financial and Accounting Officer)	March 8, 2023
<u>/s/ Brian M. Gallagher, Jr., Ph.D.</u> Brian M. Gallagher, Jr., Ph.D.	Director and Board Chair	March 8, 2023
<u>/s/ Elizabeth P. Bhatt</u> Elizabeth P. Bhatt	Director	March 8, 2023
<u>/s/ Chris Ehrlich</u> Chris Ehrlich	Director	March 8, 2023
<u>/s/ Kristen Harrington-Smith</u> Kristen Harrington-Smith	Director	March 8, 2023
<u>/s/ Barbara Klencke</u> Barbara Klencke	Director	March 8, 2023
<u>/s/ John W. Smither</u> John W. Smither	Director	March 8, 2023

EMPLOYMENT AGREEMENT

THIS EMPLOYMENT AGREEMENT (this “Agreement”) is entered into by and among eFFECTOR Therapeutics, Inc., a Delaware corporation (the “Company”) and Douglas Warner, M.D. (“Executive”), and shall be effective August 8, 2022 (the “Effective Date”).

WHEREAS, the Company and the Executive previously entered into that certain Offer Letter, dated July 1, 2022, (the “Offer Letter”), which sets forth the terms and conditions of the Executive’s employment with the Company; and

WHEREAS, the Company desires to employ Executive, and Executive desires to commence employment with the Company, on the terms and conditions set forth in this Agreement.

NOW, THEREFORE, in consideration of the mutual promises herein contained, the parties agree as follows:

1. Definitions. As used in this Agreement, the following terms shall have the following meanings:

(a) Board. “Board” means the Board of Directors of the Company.

(b) Cause. “Cause” means any of the following:

(i) the commission of an act of fraud, embezzlement or dishonesty by Executive, or the commission of some other illegal act by Executive (other than traffic violations or other offenses or violations outside of the course of Executive’s employment), that has a demonstrable material adverse impact on the Company or any successor or affiliate thereof;

(ii) a conviction of, or plea of “guilty” or “no contest” to, a felony by Executive;

(iii) any unauthorized use or disclosure by Executive of confidential information or trade secrets of the Company or any successor or affiliate thereof that has, or may reasonably be expected to have, a material adverse impact on any such entity;

(iv) Executive’s gross negligence, insubordination or material violation of any duty of loyalty to the Company or any successor or affiliate thereof, or any other demonstrable material misconduct on the part of Executive;

(v) Executive’s ongoing and repeated failure or refusal to perform or neglect of Executive’s duties as required by this Agreement or to comply with the instructions given to him or her by the Chief Executive Officer or the Board; or

(vi) Executive’s willful, material breach of any Company policy or any material provision of this Agreement;

provided, however, that, for the matters set forth in clauses (v) or (vi) above, “Cause” shall additionally mean Executive’s failure to cure such conduct to the reasonable satisfaction of the Board within thirty (30) days of written notice to Executive setting forth in reasonable detail the conduct resulting in such determination of “Cause” and the need for Executive to cure such matter. Prior to the determination “Cause” under this Section 1(b) has occurred, the Company shall provide the Executive an opportunity to be heard prior to the final decision to terminate the Executive’s employment hereunder for such “Cause” and make any decision that such “Cause” exists in good faith.

The foregoing definition shall not in any way preclude or restrict the right of the Company or any successor or affiliate thereof to discharge or dismiss Executive for any other acts or omissions, but such other acts or omissions shall not be deemed, for purposes of this Agreement, to constitute grounds for termination for Cause.

(c) Change in Control. “Change in Control” shall have the meaning given to such term in the eFFECTOR Therapeutics, Inc. 2021 Incentive Award Plan.

(d) Code. “Code” means the Internal Revenue Code of 1986, as amended from time to time, and the Treasury Regulations and other interpretive guidance issued thereunder.

(e) Good Reason. “Good Reason” means the occurrence of any of the following events or conditions without Executive’s written consent:

- (i) a material diminution in Executive’s authority, duties or responsibilities;
- (ii) a material diminution in Executive’s base compensation, unless such a reduction is imposed as part of a generalized reduction in the base salaries of senior management of the Company;
- (iii) a change to the geographic location at which Executive must perform his or her duties on a regular basis to a location that is more than fifty (50) miles from the Company’s then-current offices (excepting reasonable travel on the Company’s business); or
- (iv) a material breach by the Company or any successor or affiliate of its obligations to Executive under this Agreement.

Executive must provide written notice to the Company of the occurrence of any of the foregoing events or conditions without Executive’s written consent within thirty (30) days of the occurrence of such event. The Company or any successor or affiliate shall have a period of thirty (30) days to cure such event or condition after receipt of written notice of such event from Executive. The Executive’s Separation from Service by reason of resignation from employment with the Company for Good Reason must occur within ninety (90) days following the initial existence of the act or failure to act constituting Good Reason.

(f) Involuntary Termination. “Involuntary Termination” means (i) the Executive’s Separation from Service by reason of Executive’s discharge by the Company other than for Cause, or (ii) the Executive’s Separation from Service by reason of Executive’s resignation of employment with the Company for Good Reason. Executive’s Separation from Service by reason of Executive’s death or discharge by the Company following Executive’s disability shall not constitute an Involuntary Termination.

(g) Separation from Service. “Separation from Service,” with respect to the Executive, means the Executive’s “separation from service,” as defined in Treasury Regulation Section 1.409A-1(h).

(h) Stock Awards. “Stock Awards” means all stock options, restricted stock and such other awards granted pursuant to the Company’s stock option and equity incentive award plans or agreements and any shares of stock issued upon exercise thereof.

2. Services to Be Rendered.

(a) Duties and Responsibilities. Executive shall serve as Chief Medical Officer of the Company. In the performance of such duties, Executive shall report directly to the Chief Executive Officer. Executive hereby consents to serve as an officer and/or director of the Company or any subsidiary or affiliate thereof without any additional salary or compensation, if so requested by the Chief Executive Officer or the Board. Executive shall be employed by the Company on a full time basis. Executive’s primary place of work shall be the Company’s facility in San Diego, California, or such other location as may be designated by the Chief Executive Officer or the Board from time to time. Executive shall also render services at such other places within or outside the United States as the Chief Executive Officer or the Board may direct from time to time. Executive shall be subject to and comply with the policies and procedures generally applicable to senior executives of the Company to the extent the same are not inconsistent with any term of this Agreement.

(b) Exclusive Services. Executive shall at all times faithfully, industriously and to the best of his or her ability, experience and talent perform to the satisfaction of the Chief Executive Officer or the Board all of the duties that may be assigned to Executive hereunder and shall devote substantially all of his or her productive time and efforts to the performance of such duties. Subject to the terms of the Proprietary Information and Inventions Agreement referred to in Section 5(b), this shall not preclude Executive from devoting time to personal and family investments or serving on community and civic boards, or participating in industry associations, provided such activities do not interfere with his or her duties to the Company, as determined in good faith by the Chief Executive Officer or the Board. Executive agrees that he or she will not join any boards, other than community and civic boards (which do not interfere with his or her duties to the Company), without the prior approval of the Chief Executive Officer or the Board.

3. Compensation and Benefits. The Company shall pay or provide, as the case may be, to Executive the compensation and other benefits and rights set forth in this Section 3.

(a) Base Salary. As of the Effective Date, the Company shall pay to Executive a base salary of \$450,000 per year, payable in accordance with the Company’s usual payroll practices (and in any event no less frequently than monthly). Executive’s base salary shall be subject to review annually by and at the sole discretion of the Board or its designee.

(b) Annual Bonus. Executive shall participate in any bonus plan, program or arrangement that the Board or its designee may approve for the senior executives of the Company. Commencing with the calendar year in which the Effective Date occurs, Executive’s target bonus under the Company’s annual bonus plan shall be forty percent (40%) of Executive’s base salary (the “Target Bonus”). Notwithstanding anything to the contrary contained in this Agreement or any applicable bonus plan, program or arrangement, but except as provided in Section 4(d)(ii) Executive shall not be entitled to receive any such bonus, nor any portion thereof, if Executive is not employed on the day such bonus is paid.

(c) Signing Bonus. The Company will pay Executive a signing bonus in the gross amount of \$50,000, less applicable tax withholding requirements (the “Signing Bonus”), payable on the Company’s first payroll date following the Effective Date. In the event Executive’s employment is terminated by the Company for Cause or the Executive resigns for any reason (or no reason), in each case, on or prior to the first anniversary of the Effective Date, the Executive shall repay to the Company the Signing Bonus. The Executive acknowledges and agrees that, to the extent the Signing Bonus remains subject to the repayment obligation contained in this Section 3(c), the Signing Bonus shall be deemed to remain unearned by the Executive. The Company will have the right to offset such amount against any compensation otherwise payable to Executive in connection with Executive’s termination of employment.

(d) Benefits. Executive shall be entitled to participate in benefits under the Company’s benefit plans and arrangements, including, without limitation, any employee benefit plan or arrangement made available in the future by the Company to its senior executives, subject to and on a basis consistent with the terms, conditions and overall administration of such plans and arrangements. The Company shall have the right to amend or delete any such benefit plan or arrangement made available by the Company to its senior executives and not otherwise specifically provided for herein; provided, that any reduction of Executive’s benefits such that Executive’s benefits are, in the aggregate, materially less favorable to Executive than those benefits offered to Executive as of the Effective Date shall be considered a material breach of this Agreement by the Company.

(e) Expenses. The Company shall reimburse Executive for reasonable out-of-pocket business expenses incurred in connection with the performance of his or her duties hereunder, subject to such policies as the Company may from time to time establish, and Executive furnishing the Company with evidence in the form of receipts satisfactory to the Company substantiating the claimed expenditures.

(f) Paid Time Off. Executive shall be entitled to such periods of paid time off (“PTO”) each year as provided from time to time under the Company’s PTO policy and as otherwise provided for senior executive officers.

(g) Equity Awards.

(i) Executive shall be entitled to participate in any equity or other employee benefit plan that is generally available to senior executive officers, as distinguished from general management, of the Company. Except as otherwise provided in this Agreement, Executive’s participation in and benefits under any such plan shall be on the terms and subject to the conditions specified in the governing document of the particular plan.

(ii) As soon as practicable following the Effective Date and subject to the Board’s approval, Executive will be granted a stock option to purchase 618,160 shares of the Company’s common stock at an exercise price per share equal to the fair market value per share of the Company’s common stock on the date of grant, as determined by the Board (the “Initial Stock Option”). The Initial Stock Option will be granted pursuant to the eFFECTOR Therapeutics, Inc. 2021 Incentive Award Plan (the “Plan”). Executive’s receipt of the Initial Stock Option will be subject to Executive executing the Company’s standard stock option agreement. The Initial Stock Option will be subject to the terms and conditions of the Plan and the stock option agreement. So long as Executive continues in service with the Company, the Initial Stock Option will vest with respect to 25% of the shares on the one-year anniversary of the Effective Date and, with

respect to the balance, in 36 equal successive monthly installments upon Executive's completion of each additional month of service thereafter. The Initial Stock Option will be subject to accelerated vesting under certain circumstances, as described in Section 4(d)(iii) herein and the form of award agreement.

4. End of Employment Payments, Benefits and Severance. Executive shall be entitled to receive benefits upon a termination of employment only as set forth in this Section 4:

(a) At-Will Employment; Termination. The Company and Executive acknowledge that Executive's employment is and shall continue to be at-will, as defined under applicable law, and that Executive's employment with the Company may be terminated by either party at any time for any or no reason, with or without notice. If Executive's employment terminates for any reason, Executive shall not be entitled to any payments, benefits, damages, awards or compensation other than as provided in this Agreement. Executive's employment under this Agreement shall be terminated immediately on the death of Executive.

(b) End of Employment Payments. Upon Executive's termination of employment with the Company for any reason, or no reason, Executive shall not be entitled to receive any payment or other benefit, except as set forth in Sections 4(c) and 4(d) below, except that Executive shall be entitled to receive (i) Executive's fully earned but unpaid base salary, through the date such termination is effective (the "Separation Date") at the rate then in effect plus all accrued but unused PTO, and (ii) all other amounts or benefits to which Executive is entitled under any compensation, retirement or benefit plan of the Company at the time of the Separation Date in accordance with the terms of such plans, including, without limitation, any continuation of benefits required by COBRA or applicable law (the amounts in clauses (i) and (ii), the "Accrued Obligations").

(c) Severance Upon Involuntary Termination Apart from a Change in Control. Subject to Sections 4(e) and 10(o) below and Executive's continued compliance with Section 5, if Executive's employment is Involuntarily Terminated prior to a Change in Control or more than twelve (12) months following a Change in Control, Executive shall be entitled to receive, in addition to those payments and benefits set forth in Section 4(b) above, but in lieu of any other severance benefits to which Executive may otherwise be entitled under any severance plan or program of the Company, the benefits provided below:

(i) Executive shall be entitled to receive Executive's monthly base salary as in effect immediately prior to the Separation Date for an additional twelve (12) months after the Separation Date in accordance with the Company's usual payroll practices (and in any event no less frequently than monthly, although subject to the provisions of Sections 4(e) and 10(o) below), with the first installment commencing on the first payroll date that is sixty (60) days following the Separation Date (and any installment payments which would otherwise have been paid to Executive before the sixtieth (60th) day following the Separation Date will be paid together with the first installment); and

(ii) for the period beginning on the Separation Date and ending on the date which is twelve (12) full months following the Separation Date (or, if earlier, the date on which the applicable continuation period under COBRA expires), the Company shall arrange to provide or pay the applicable premiums for Executive and his or her eligible dependents who were covered under the Company's health insurance plans as of the Separation Date with health (including medical and dental) insurance benefits substantially similar to those provided to Executive and his

or her dependents immediately prior to the Separation Date. Notwithstanding the previous sentence, with regard to such COBRA continuation coverage, if the Company determines in its sole discretion that it cannot provide the foregoing benefit without potentially violating applicable law (including, without limitation, Section 2716 of the Public Health Service Act), the Company shall in lieu thereof provide to the Executive a taxable monthly payment in an amount equal to the monthly COBRA premium that the Executive would be required to pay to continue the Executive's and his or her covered dependents' group insurance coverages in effect on the Separation Date (which amount shall be based on the premiums for the first month of COBRA coverage).

(d) Severance Upon Involuntary Termination Following a Change in Control. Subject to Sections 4(e) and 10(o) and Executive's continued compliance with Section 5, if Executive's employment is Involuntarily Terminated upon or within twelve (12) months following a Change in Control, Executive shall be entitled to receive, in addition to those payments and benefits set forth in Section 4(b) above, but in lieu of any severance benefits to which Executive may otherwise be entitled under any severance plan or program of the Company (and, for the avoidance of doubt, in the event Executive is eligible for severance benefits under this Section 4(d), Executive shall not be eligible for any severance benefits under Section 4(c) as a result of such Involuntary Termination), the benefits provided below:

(i) Executive shall be entitled to receive Executive's monthly base salary as in effect immediately prior to the Separation Date for an additional twelve (12) months after the Separation Date in accordance with the Company's usual payroll practices (and in any event no less frequently than monthly, although subject to the provisions of Sections 4(e) and 10(o) below), with the first installment commencing on the first payroll date that is sixty (60) days following the Separation Date (and any installment payments which would otherwise have been paid to Executive before the sixtieth (60th) day following the Separation Date will be paid together with the first installment);

(ii) for the period beginning on the Separation Date and ending on the date which is twelve (12) full months following the Separation Date (or, if earlier, the date on which the applicable continuation period under COBRA expires), the Company shall arrange to provide or pay the applicable premiums for Executive and his or her eligible dependents who were covered under the Company's health insurance plans as of the Separation Date with health (including medical and dental) insurance benefits substantially similar to those provided to Executive and his or her dependents immediately prior to the Separation Date. Notwithstanding the previous sentence, with regard to such COBRA continuation coverage, if the Company determines in its sole discretion that it cannot provide the foregoing benefit without potentially violating applicable law (including, without limitation, Section 2716 of the Public Health Service Act), the Company shall in lieu thereof provide to the Executive a taxable monthly payment in an amount equal to the monthly COBRA premium that the Executive would be required to pay to continue the Executive's and his or her covered dependents' group insurance coverages in effect on the Separation Date (which amount shall be based on the premiums for the first month of COBRA coverage);

(iii) Executive shall be entitled to receive an amount equal to (A) the annual Target Bonus amount for the year in which Executive's Separation from Service occurs multiplied by (B) 1.0, with such payment occurring, subject to the provisions of Sections 4(e) and 10(o) below, on the first payroll date that is sixty (60) days following the Separation Date (but no later than March 15 of the calendar year following the calendar year in which the Separation Date occurs); and

(iv) the vesting and/or exercisability of all of Executive's outstanding unvested Stock Awards shall be automatically accelerated in full on the Separation Date. The foregoing provisions are hereby deemed to be a part of each Stock Award and to supersede any less favorable provision in any agreement or plan regarding such Stock Award (and, for the avoidance of doubt, if any Stock Award is subject to more favorable vesting pursuant to any agreement or plan regarding such Stock Award, such more favorable provisions shall continue to apply and shall not be limited by this clause (iv)).

(e) Release. As a condition to Executive's receipt of any post-termination benefits pursuant to Sections 4(c) and 4(d) above (collectively, the "Severance Benefits"), Executive shall execute and not revoke a general release of all claims in favor of the Company (the "Release") in the form attached hereto as Exhibit A. In the event the Release does not become effective within the fifty-five (55) day period following the Separation Date, Executive shall not be entitled to the aforesaid payments and benefits.

(f) Exclusive Remedy. Except as otherwise expressly required by law (e.g., COBRA) or as specifically provided herein, all of Executive's rights to salary, severance, benefits, bonuses and other amounts hereunder (if any) accruing after the Separation Date shall cease upon such date. In the event of Executive's termination of employment with the Company, Executive's sole remedy shall be to receive the payments and benefits described in this Section 4. In addition, Executive acknowledges and agrees that he or she is not entitled to any reimbursement by the Company for any taxes payable by Executive as a result of the payments and benefits received by Executive pursuant to this Section 4, including, without limitation, any excise tax imposed by Section 4999 of the Code. Any payments made to Executive under this Section 4 shall be inclusive of any amounts or benefits to which Executive may be entitled pursuant to the Worker Adjustment and Retraining Notification Act, 29 U.S.C. Sections 2101 et seq., and the Department of Labor regulations thereunder, or any similar state law.

(g) No Mitigation. Except as otherwise provided in Sections 4(c)(ii) and 4(d)(ii) above, Executive shall not be required to mitigate the amount of any payment provided for in this Section 4 by seeking other employment or otherwise, nor shall the amount of any payment or benefit provided for in this Section 4 be reduced by any compensation earned by Executive as the result of employment by another employer or self-employment or by retirement benefits; provided, however, that loans, advances or other amounts owed by Executive to the Company may be offset by the Company against amounts payable to Executive under this Section 4.

(h) Return of the Company's Property. In the event of Executive's termination of employment for any reason, the Company shall have the right, at its option, to require Executive to vacate his or her offices prior to or on the Separation Date and to cease all activities on the Company's behalf. Upon Executive's termination of employment in any manner, as a condition to the Executive's receipt of any severance benefits described in this Agreement, Executive shall immediately surrender to the Company all lists, books and records of, or in connection with, the Company's business, and all other property belonging to the Company, it being distinctly understood that all such lists, books and records, and other documents, are the property of the Company. Executive shall deliver to the Company a signed statement certifying compliance with this Section 4(h) prior to the receipt of any severance benefits described in this Agreement.

5. Certain Covenants.

(a) No Conflicts. Except as may otherwise be approved by the Board, during the term of Executive's employment, Executive shall not have any ownership interest (of record or beneficial) in, or have any interest as an employee, salesman, consultant, officer or director in, or otherwise aid or assist in any manner, any firm, corporation, partnership, proprietorship or other business that engages in any county, city or part thereof in the United States and/or any foreign country in a business which competes directly or indirectly (as determined by the Board) with the Company's business in such county, city or part thereof, so long as the Company, or any successor in interest of the Company to the business and goodwill of the Company, remains engaged in such business in such county, city or part thereof or continues to solicit customers or potential customers therein; provided, however, that Executive may own, directly or indirectly, solely as an investment, securities of any entity if Executive (i) is not a controlling person of, or a member of a group which controls, such entity; or (ii) does not, directly or indirectly, own five percent (5%) or more of any class of securities of any such entity.

(b) Confidential Information. Executive and the Company have entered into the Company's standard employee proprietary information and inventions agreement (the "Proprietary Information and Inventions Agreement"). Executive agrees to perform each and every obligation of Executive therein contained.

(c) Solicitation of Employees. Executive shall not during the term of Executive's employment and for twelve (12) months following any Separation from Service (regardless of whether or not Executive receives any Severance Benefits) (the "Restricted Period"), directly or indirectly, solicit or encourage to leave the employment of the Company or any of its affiliates, any employee of the Company or any of its affiliates.

(d) Rights and Remedies Upon Breach. If Executive breaches or threatens to commit a breach of any of the provisions of this Section 5 (the "Restrictive Covenants"), the Company shall have the following rights and remedies, each of which rights and remedies shall be independent of the other and severally enforceable, and all of which rights and remedies shall be in addition to, and not in lieu of, any other rights and remedies available to the Company under law or in equity:

(i) Specific Performance. The right and remedy to have the Restrictive Covenants specifically enforced by any court having equity jurisdiction, all without the need to post a bond or any other security or to prove any amount of actual damage or that money damages would not provide an adequate remedy, it being acknowledged and agreed that any such breach or threatened breach will cause irreparable injury to the Company and that money damages will not provide adequate remedy to the Company; and

(ii) Accounting and Indemnification. The right and remedy to require Executive (A) to account for and pay over to the Company all compensation, profits, monies, accruals, increments or other benefits derived or received by Executive or any associated party deriving such benefits as a result of any such breach of the Restrictive Covenants; and (B) to indemnify the Company against any other losses, damages (including special and consequential damages), costs and expenses, including actual attorneys' fees and court costs, which may be

incurred by them and which result from or arise out of any such breach or threatened breach of the Restrictive Covenants.

(e) Severability of Covenants/Blue Pencilling. If any court determines that any of the Restrictive Covenants, or any part thereof, is invalid or unenforceable, the remainder of the Restrictive Covenants shall not thereby be affected and shall be given full effect, without regard to the invalid portions. If any court determines that any of the Restrictive Covenants, or any part thereof, are unenforceable because of the duration of such provision or the area covered thereby, such court shall have the power to reduce the duration or area of such provision and, in its reduced form, such provision shall then be enforceable and shall be enforced. Executive hereby waives any and all right to attack the validity of the Restrictive Covenants on the grounds of the breadth of their geographic scope or the length of their term.

(f) Enforceability in Jurisdictions. The Company and Executive intend to and do hereby confer jurisdiction to enforce the Restrictive Covenants upon the courts of any jurisdiction within the geographical scope of such covenants. If the courts of any one or more of such jurisdictions hold the Restrictive Covenants wholly unenforceable by reason of the breadth of such scope or otherwise, it is the intention of the Company and Executive that such determination not bar or in any way affect the right of the Company to the relief provided above in the courts of any other jurisdiction within the geographical scope of such covenants, as to breaches of such covenants in such other respective jurisdictions, such covenants as they relate to each jurisdiction being, for this purpose, severable into diverse and independent covenants.

(g) Definitions. For purposes of this Section 5, the term “Company” means not only the Company, but also any company, partnership or entity which, directly or indirectly, controls, is controlled by or is under common control with the Company.

(h) Defend Trade Secrets Act Notice of Immunity Rights. Executive acknowledges that the Company has provided Executive with the following notice of immunity rights in compliance with the requirements of the Defend Trade Secrets Act: (i) Executive shall not be held criminally or civilly liable under any Federal or State trade secret law for the disclosure of Proprietary Information (as defined in the Proprietary Information and Inventions Agreement) that is made in confidence to a Federal, State, or local government official or to an attorney solely for the purpose of reporting or investigating a suspected violation of law, (ii) Executive shall not be held criminally or civilly liable under any Federal or State trade secret law for the disclosure of Proprietary Information that is made in a complaint or other document filed in a lawsuit or other proceeding, if such filing is made under seal and (iii) if Executive files a lawsuit for retaliation by the Company for reporting a suspected violation of law, Executive may disclose the Proprietary Information to his or her attorney and use the Proprietary Information in the court proceeding, if the Executive files any document containing the Proprietary Information under seal, and does not disclose the Proprietary Information, except pursuant to court order.

6. Insurance; Indemnification.

(a) Insurance. The Company shall have the right to take out life, health, accident, “key-man” or other insurance covering Executive, in the name of the Company and at the Company’s expense in any amount deemed appropriate by the Company. Executive shall assist

the Company in obtaining such insurance, including, without limitation, submitting to any required examinations and providing information and data required by insurance companies.

(b) Indemnification. Executive will be provided with indemnification against third party claims related to his or her work for the Company as required by Delaware law. The Company shall provide Executive with directors and officers liability insurance coverage at least as favorable as that which the Company may maintain from time to time for members of the Board and other executive officers.

7. Arbitration. Any dispute, claim or controversy based on, arising out of or relating to Executive's employment or this Agreement shall be settled by final and binding arbitration in San Diego, California, before a single neutral arbitrator in accordance with the National Rules for the Resolution of Employment Disputes (the "Rules") of the American Arbitration Association ("AAA"), and judgment on the award rendered by the arbitrator may be entered in any court having jurisdiction. The Rules may be found online at www.adr.org. Arbitration may be compelled pursuant to the California Arbitration Act (Code of Civil Procedure §§ 1280 et seq.). If the parties are unable to agree upon an arbitrator, one shall be appointed by the AAA in accordance with its Rules. Each party shall pay the fees of its own attorneys, the expenses of its witnesses and all other expenses connected with presenting its case; however, Executive and the Company agree that, to the extent permitted by law, the arbitrator may, in his or her discretion, award reasonable attorneys' fees to the prevailing party. Other costs of the arbitration, including the cost of any record or transcripts of the arbitration, AAA's administrative fees, the fee of the arbitrator, and all other fees and costs, shall be borne by the Company. This Section 7 is intended to be the exclusive method for resolving any and all claims by the parties against each other for payment of damages under this Agreement or relating to Executive's employment; provided, however, that Executive shall retain the right to file administrative charges with or seek relief through any government agency of competent jurisdiction, and to participate in any government investigation, including but not limited to (i) claims for workers' compensation, state disability insurance or unemployment insurance; (ii) claims for unpaid wages or waiting time penalties brought before the California Division of Labor Standards Enforcement; provided, however, that any appeal from an award or from denial of an award of wages and/or waiting time penalties shall be arbitrated pursuant to the terms of this Agreement; and (iii) claims for administrative relief from the United States Equal Employment Opportunity Commission and/or the California Department of Fair Employment and Housing (or any similar agency in any applicable jurisdiction other than California); provided, further, that Executive shall not be entitled to obtain any monetary relief through such agencies other than workers' compensation benefits or unemployment insurance benefits. This Agreement shall not limit either party's right to obtain any provisional remedy, including, without limitation, injunctive or similar relief, from any court of competent jurisdiction as may be necessary to protect their rights and interests pending the outcome of arbitration, including without limitation injunctive relief, in any court of competent jurisdiction pursuant to California Code of Civil Procedure § 1281.8 or any similar statute of an applicable jurisdiction. Seeking any such relief shall not be deemed to be a waiver of such party's right to compel arbitration. Each party hereby expressly waives his, her or its right to a jury trial.

8. General Relationship. Executive shall be considered an employee of the Company within the meaning of all federal, state and local laws and regulations including, but not limited to, laws and regulations governing unemployment insurance, workers' compensation, industrial accident, labor and taxes.

9. Section 280G of the Code.

(a) Best Pay Provision. In the event that any payment or benefit received or to be received by Executive pursuant to the terms of any plan, arrangement or agreement (including any payment or benefit received in connection with a change in ownership or control or the termination of Executive's employment) (all such payments and benefits being hereinafter referred to as the "Total Payments") would be subject (in whole or part) to the excise tax (the "Excise Tax") imposed under Section 4999 of the Code, then the Total Payments shall be reduced to the extent necessary so that no portion of the Total Payments is subject to the Excise Tax but only if (i) the net amount of such Total Payments, as so reduced (after subtracting the amount of federal, state and local income taxes on such reduced Total Payments and after taking into account the phase out of itemized deductions and personal exemptions attributable to such reduced Total Payments) is greater than or equal to (ii) the net amount of such Total Payments without such reduction (after subtracting the net amount of federal, state and local income taxes on such Total Payments and the amount of Excise Tax to which Executive would be subject in respect of such unreduced Total Payments and after taking into account the phase out of itemized deductions and personal exemptions attributable to such unreduced Total Payments). Except to the extent that an alternative reduction order would result in a greater economic benefit to the Executive on an after-tax basis, the parties intend that the Total Payments shall be reduced in the following order: (w) reduction of any cash severance payments otherwise payable to Executive that are exempt from Section 409A of the Code, (x) reduction of any other cash payments or benefits otherwise payable to Executive that are exempt from Section 409A of the Code, but excluding any payment attributable to the acceleration of vesting or payment with respect to any Stock Award that is exempt from Section 409A of the Code, (y) reduction of any other payments or benefits otherwise payable to Executive on a pro-rata basis or such other manner that complies with Section 409A of the Code, but excluding any payment attributable to the acceleration of vesting and payment with respect to any Stock Award that is exempt from Section 409A of the Code, and (z) reduction of any payments attributable to the acceleration of vesting or payment with respect to any Stock Award that is exempt from Section 409A of the Code; provided, in case of clauses (x), (y) and (z), that reduction of any payments or benefits attributable to the acceleration of vesting of Company Stock Awards shall be first applied to Stock Awards with later vesting dates; provided, further, that, notwithstanding the foregoing, any such reduction shall be undertaken in a manner that complies with and does not result in the imposition of additional taxes on the Executive under Section 409A of the Code. The foregoing reductions shall be made in a manner that results in the maximum economic benefit to Executive on an after-tax basis and, to the extent economically equivalent payments or benefits are subject to reduction, in a pro rata manner.

(b) Determinations. All determinations regarding the application of this Section 9 shall be made by an independent accounting firm or consulting group with nationally recognized standing and substantial expertise and experience in performing calculations regarding the applicability of Section 280G of the Code and the Excise Tax retained by the Company prior to the date of the applicable change in ownership or control (the "280G Firm"). For purposes of determining whether and the extent to which the Total Payments will be subject to the Excise Tax, (i) no portion of the Total Payments shall be taken into account which (x) does not constitute a "parachute payment" within the meaning of Section 280G(b)(2) of the Code (including by reason of Section 280G(b)(4)(A) of the Code) and, in calculating the Excise Tax, or (y) constitutes reasonable compensation for services actually rendered, within the meaning of Section

280G(b)(4)(B) of the Code, in excess of the “base amount” (as defined in Section 280G(b)(3) of the Code) allocable to such reasonable compensation, (ii) no portion of the Total Payments the receipt or enjoyment of which Executive shall have waived at such time and in such manner as not to constitute a “payment” within the meaning of Section 280G(b) of the Code shall be taken into account, and (iii) the value of any non-cash benefit or any deferred payment or benefit included in the Total Payments shall be determined by the 280G Firm in accordance with the principles of Sections 280G(d)(3) and (4) of the Code. All determinations related to the calculations to be performed pursuant to this “Section 280G Treatment” section shall be done by the 280G Firm. The 280G Firm will be directed to submit its determination and detailed supporting calculations to both Executive and the Company within fifteen (15) days after notification from either the Company or Executive that Executive may receive payments which may be “parachute payments.” Executive and the Company will each provide the 280G Firm access to and copies of any books, records, and documents as may be reasonably requested by the 280G Firm, and otherwise cooperate with the 280G Firm in connection with the preparation and issuance of the determinations and calculations contemplated by this Agreement. The fees and expenses of the 280G Firm for its services in connection with the determinations and calculations contemplated by this Agreement will be borne solely by the Company.

10. Miscellaneous.

(a) Modification; Prior Claims. This Agreement and the Proprietary Information and Inventions Agreement set forth the entire understanding of the parties with respect to the subject matter hereof, supersedes all existing agreements between them concerning such subject matter, including, without limitation, the Offer Letter. This Agreement may be amended or modified only with the written consent of Executive and an authorized representative of the Company. No oral waiver, amendment or modification will be effective under any circumstances whatsoever.

(b) Assignment; Assumption by Successor. The rights of the Company under this Agreement may, without the consent of Executive, be assigned by the Company, in its sole and unfettered discretion, to any person, firm, corporation or other business entity which at any time, whether by purchase, merger or otherwise, directly or indirectly, acquires all or substantially all of the assets or business of the Company. The Company will require any successor (whether direct or indirect, by purchase, merger or otherwise) to all or substantially all of the business or assets of the Company expressly to assume and to agree to perform this Agreement in the same manner and to the same extent that the Company would be required to perform it if no such succession had taken place; provided, however, that no such assumption shall relieve the Company of its obligations hereunder. As used in this Agreement, the “Company” shall mean the Company as hereinbefore defined and any successor to its business and/or assets as aforesaid which assumes and agrees to perform this Agreement by operation of law or otherwise.

(c) Survival. The covenants, agreements, representations and warranties contained in or made in Sections 4, 5, 6, 7, 9 and 10 of this Agreement shall survive any Executive’s termination of employment.

(d) Third-Party Beneficiaries. This Agreement does not create, and shall not be construed as creating, any rights enforceable by any person not a party to this Agreement.

(e) Waiver. The failure of either party hereto at any time to enforce performance by the other party of any provision of this Agreement shall in no way affect such party's rights thereafter to enforce the same, nor shall the waiver by either party of any breach of any provision hereof be deemed to be a waiver by such party of any other breach of the same or any other provision hereof.

(f) Section Headings. The headings of the several sections in this Agreement are inserted solely for the convenience of the parties and are not a part of and are not intended to govern, limit or aid in the construction of any term or provision hereof.

(g) Notices. Any notice required or permitted by this Agreement shall be in writing and shall be delivered as follows with notice deemed given as indicated: (i) by personal delivery when delivered personally; (ii) by overnight courier upon written verification of receipt; (iii) by email, telecopy or facsimile transmission upon acknowledgment of receipt of electronic transmission; or (iv) by certified or registered mail, return receipt requested, upon verification of receipt. Notice shall be sent to Executive at the address listed on the Company's personnel records and to the Company at its principal place of business, or such other address as either party may specify in writing.

(h) Severability. All Sections, clauses and covenants contained in this Agreement are severable, and in the event any of them shall be held to be invalid by any court, this Agreement shall be interpreted as if such invalid Sections, clauses or covenants were not contained herein.

(i) Governing Law and Venue. This Agreement is to be governed by and construed in accordance with the laws of the State of California applicable to contracts made and to be performed wholly within such State, and without regard to the conflicts of laws principles thereof. Except as provided in Sections 5 and 7, any suit brought hereon shall be brought in the state or federal courts sitting in San Diego, California, the parties hereto hereby waiving any claim or defense that such forum is not convenient or proper. Each party hereby agrees that any such court shall have in personam jurisdiction over it and consents to service of process in any manner authorized by California law.

(j) Non-transferability of Interest. None of the rights of Executive to receive any form of compensation payable pursuant to this Agreement shall be assignable or transferable except through a testamentary disposition or by the laws of descent and distribution upon the death of Executive. Any attempted assignment, transfer, conveyance, or other disposition (other than as aforesaid) of any interest in the rights of Executive to receive any form of compensation to be made by the Company pursuant to this Agreement shall be void.

(k) Gender. Where the context so requires, the use of the masculine gender shall include the feminine and/or neuter genders and the singular shall include the plural, and vice versa, and the word "person" shall include any corporation, firm, partnership or other form of association.

(l) Counterparts. This Agreement may be executed in one or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same Agreement.

(m) Construction. The language in all parts of this Agreement shall in all cases be construed simply, according to its fair meaning, and not strictly for or against any of the parties hereto. Without limitation, there shall be no presumption against any party on the ground that such party was responsible for drafting this Agreement or any part thereof.

(n) Withholding and other Deductions. All compensation payable to Executive hereunder shall be subject to such deductions as the Company is from time to time required to make pursuant to law, governmental regulation or order.

(o) Code Section 409A.

(i) This Agreement is not intended to provide for any deferral of compensation subject to Section 409A of the Code, and, to the maximum extent permitted by applicable law, amounts payable to Executive pursuant to Sections 4(c)(i), 4(c)(ii), 4(d)(i), 4(d)(ii) and 4(d)(iii) shall be made in reliance upon Treasury Regulation Section 1.409A-1(b)(9) (with respect to separation pay plans) or Treasury Regulation Section 1.409A-1(b)(4) (with respect to short-term deferrals). To the extent applicable, this Agreement shall be interpreted in accordance with Code Section 409A and Department of Treasury regulations and other interpretive guidance issued thereunder. For purposes of Section 409A of the Code, the right to a series of installment payments under this Agreement shall be treated as a right to a series of separate payments. For purposes of this Agreement, all references to Executive's "termination of employment" shall mean Executive's Separation from Service.

(ii) If the Executive is a "specified employee" (as defined in Section 409A of the Code), as determined by the Company in accordance with Section 409A of the Code, on the Separation Date, to the extent that the payments or benefits under this Agreement are subject to Section 409A of the Code and the delayed payment or distribution of all or any portion of such amounts to which Executive is entitled under this Agreement is required in order to avoid a prohibited distribution under Section 409A(a)(2)(B)(i) of the Code, then such portion deferred pursuant to this Section 10(o)(ii) shall be paid or distributed to Executive in a lump sum on the earlier of (A) the date that is six (6)-months following Executive's Separation from Service, (B) the date of Executive's death or (C) the earliest date as is permitted under Section 409A of the Code. Any remaining payments due under the Agreement shall be paid as otherwise provided herein.

(iii) If Executive and the Company determine that any payments or benefits payable under this Agreement intended to comply with Sections 409A(a)(2), (3) and (4) of the Code do not comply with Section 409A of the Code, Executive and the Company agree to amend this Agreement, or take such other actions as Executive and the Company deem reasonably necessary or appropriate, to comply with the requirements of Section 409A of the Code and the Treasury Regulations thereunder (and any applicable transition relief) while preserving the economic agreement of the parties. To the extent that any provision in this Agreement is ambiguous as to its compliance with Section 409A of the Code, the provision shall be read in such a manner that no payments payable under this Agreement shall be subject to an "additional tax" as defined in Section 409A(a)(1)(B) of the Code.

(iv) Any reimbursement of expenses or in-kind benefits payable under this Agreement shall be made in accordance with Treasury Regulation Section 1.409A-3(i)(1)(iv) and shall be paid on or before the last day of Executive's taxable year following the taxable year in

which Executive incurred the expenses. The amount of expenses reimbursed or in-kind benefits payable in one year shall not affect the amount eligible for reimbursement or in-kind benefits payable in any other taxable year of Executive's, and Executive's right to reimbursement for such amounts shall not be subject to liquidation or exchange for any other benefit.

(Signature Page Follows)

IN WITNESS WHEREOF, the parties have executed this Agreement as of the date first set forth above.

EFFECTOR THERAPEUTICS, INC.

By: /s/ Stephen T. Worland
Name: Stephen T. Worland, Ph.D.
Title: President and CEO

EXECUTIVE

/s/ Douglas Warner
Douglas Warner, M.D.

EXHIBIT A

GENERAL RELEASE OF CLAIMS

[The language in this Release may change based on legal developments and evolving best practices; this form is provided as an example of what will be included in the final Release document.]

This General Release of Claims ("Release") is entered into as of this 24th day of July, 2022, between Douglas Warner, M.D. ("Executive"), eFFECTOR Therapeutics, Inc., a Delaware corporation (the "Company") (collectively referred to herein as the "Parties").

WHEREAS, Executive and the Company are parties to that certain Employment Agreement effective as of July 24, 2022 (the "Agreement");

WHEREAS, the Parties agree that were it not for execution and enforceability of this Release, Executive would not be entitled to receive the Severance Benefits (as defined below) set forth in the Agreement; and

WHEREAS, the Parties now wish to fully and finally to resolve all matters between them.

NOW, THEREFORE, in consideration of, and subject to, the severance benefits payable to Executive pursuant to the Agreement, the adequacy of which is hereby acknowledged by Executive, and which Executive acknowledges that he or she would not otherwise be entitled to receive, Executive and the Company hereby agree as follows:

1. General Release of Claims by Executive.

(a) Executive, on behalf of himself or herself and his or her executors, heirs, administrators, representatives and assigns, hereby agrees to release and forever discharge the Company and all predecessors, successors and their respective parent corporations, affiliates,

related, and/or subsidiary entities, and all of their past and present investors, directors, stockholders, officers, general or limited partners, employees, attorneys, agents and representatives, and the employee benefit plans in which Executive is or has been a participant by virtue of his or her employment with or service to the Company (collectively, the “Company Releasees”), from any and all claims, debts, demands, accounts, judgments, rights, causes of action, equitable relief, damages, costs, charges, complaints, obligations, promises, agreements, controversies, suits, expenses, compensation, responsibility and liability of every kind and character whatsoever (including attorneys’ fees and costs), whether in law or equity, known or unknown, asserted or unasserted, suspected or unsuspected (collectively, “Claims”), which Executive has or may have had against such entities based on any events or circumstances arising or occurring on or prior to the date hereof or on or prior to the date hereof, arising directly or indirectly out of, relating to, or in any other way involving in any manner whatsoever Executive’s employment by or service to the Company or the termination thereof, including any and all claims arising under federal, state, or local laws relating to employment, including without limitation claims of wrongful discharge, breach of express or implied contract, fraud, misrepresentation, defamation, or liability in tort, and claims of any kind that may be brought in any court or administrative agency including, without limitation, claims under Title VII of the Civil Rights Act of 1964, as amended, 42 U.S.C. Section 2000, et seq.; the Americans with Disabilities Act, as amended, 42 U.S.C. § 12101 et seq.; the Rehabilitation Act of 1973, as amended, 29 U.S.C. § 701 et seq.; the Civil Rights Act of 1866, and the Civil Rights Act of 1991; 42 U.S.C. Section 1981, et seq.; the Age Discrimination in Employment Act, as amended, 29 U.S.C. Section 621, et seq. (the “ADEA”); the Equal Pay Act, as amended, 29 U.S.C. Section 206(d); regulations of the Office of Federal Contract Compliance, 41 C.F.R. Section 60, et seq.; the Family and Medical Leave Act, as amended, 29 U.S.C. § 2601 et seq.; the Fair Labor Standards Act of 1938, as amended, 29 U.S.C. § 201 et seq.; the Employee Retirement Income Security Act, as amended, 29 U.S.C. § 1001 et seq.; and the California Fair Employment and Housing Act, California Government Code Section 12940, et seq.

Notwithstanding the generality of the foregoing, Executive does not release the following claims:

- (i) Claims for unemployment compensation or any state disability insurance benefits pursuant to the terms of applicable state law;
 - (ii) Claims for workers’ compensation insurance benefits under the terms of any worker’s compensation insurance policy or fund of the Company;
 - (iii) Claims pursuant to the terms and conditions of the federal law known as COBRA;
 - (iv) Claims for indemnity under the bylaws of the Company, as provided for by California law or under any applicable insurance policy with respect to Executive’s liability as an employee, director or officer of the Company;
 - (v) Claims for Executive’s right to bring to the attention of the Equal Employment Opportunity Commission or the California Department of Fair Employment and Housing or any other federal, state or local government agency claims of discrimination, or from
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participating in an investigation or proceeding conducted by the Equal Employment Opportunity Commission or any other federal, state or local government agency; provided, however, that Executive does release his or her right to secure any damages for alleged discriminatory treatment;

(vi) Claims based on any right Executive may have to enforce the Company's executory obligations under the Agreement;

(vii) Claims Executive may have to vested or earned compensation and benefits; and

(viii) Executive's right to communicate or cooperate with any governmental agency.

(b) EXECUTIVE ACKNOWLEDGES THAT HE OR SHE HAS BEEN ADVISED OF AND IS FAMILIAR WITH THE PROVISIONS OF CALIFORNIA CIVIL CODE SECTION 1542, WHICH PROVIDES AS FOLLOWS:

"A GENERAL RELEASE DOES NOT EXTEND TO CLAIMS THAT THE CREDITOR OR RELEASING PARTY DOES NOT KNOW OR SUSPECT TO EXIST IN HIS OR HER FAVOR AT THE TIME OF EXECUTING THE RELEASE AND THAT, IF KNOWN BY HIM OR HER, MUST HAVE MATERIALLY AFFECTED HIS OR HER SETTLEMENT WITH THE DEBTOR OR RELEASED PARTY."

BEING AWARE OF SAID CODE SECTION, EXECUTIVE HEREBY EXPRESSLY WAIVES ANY RIGHTS HE OR SHE MAY HAVE THEREUNDER, AS WELL AS UNDER ANY OTHER STATUTES OR COMMON LAW PRINCIPLES OF SIMILAR EFFECT.

(c) Executive acknowledges that this Release was presented to him or her on the date indicated above and th Executive is entitled to have [twenty-one (21)][forty-five (45)] days' time in which to consider it. Executive further acknowledges that the Company has advised him or her that he or she is waiving his or her rights under the ADEA, and that Executive should consult with an attorney of his or her choice before signing this Release, and Executive has had sufficient time to consider the terms of this Release. Executive represents and acknowledges that if Executive executes this Release before [twenty-one (21)][forty-five (45)] days have elapsed, Executive does so knowingly, voluntarily, and upon the advice and with the approval of Executive's legal counsel (if any), and that Executive voluntarily waives any remaining consideration period.

(d) Executive understands that after executing this Release, Executive has the right to revoke it within seven (7) days after his or her execution of it. Executive understands that this Release will not become effective and enforceable unless the seven (7) day revocation period passes and Executive does not revoke the Release in writing. Executive understands that this Release may not be revoked after the seven (7) day revocation period has passed. Executive also understands that any revocation of this Release must be made in writing and delivered to the Company at its principal place of business within the seven (7) day period.

(e) Executive understands that this Release shall become effective, irrevocable, and binding upon Executive on the eighth (8th) day after his or her execution of it, so long as Executive has not revoked it within the time period and in the manner specified in clause (d) above.

(f) Executive further understands that Executive will not be given any severance benefits under the Agreement unless this Release is effective on or before the date that is fifty-five (55) days following the date of Executive's termination of employment.

2. Defend Trade Secrets Act Notice of Immunity Rights. Executive acknowledges that the Company has provided Executive with the following notice of immunity rights in compliance with the requirements of the Defend Trade Secrets Act: (i) Executive shall not be held criminally or civilly liable under any Federal or State trade secret law for the disclosure of Proprietary Information (as defined in the Proprietary Information and Inventions Agreement (as defined in the Agreement)) that is made in confidence to a Federal, State, or local government official or to an attorney solely for the purpose of reporting or investigating a suspected violation of law, (ii) Executive shall not be held criminally or civilly liable under any Federal or State trade secret law for the disclosure of Proprietary Information that is made in a complaint or other document filed in a lawsuit or other proceeding, if such filing is made under seal and (iii) if Executive files a lawsuit for retaliation by the Company for reporting a suspected violation of law, Executive may disclose the Proprietary Information to his or her attorney and use the Proprietary Information in the court proceeding, if the Executive files any document containing the Proprietary Information under seal, and does not disclose the Proprietary Information, except pursuant to court order.

3. No Assignment. Executive represents and warrants to the Company Releasees that there has been no assignment or other transfer of any interest in any Claim that Executive may have against the Company Releasees. Executive agrees to indemnify and hold harmless the Company Releasees from any liability, claims, demands, damages, costs, expenses and attorneys' fees incurred as a result of any such assignment or transfer from Executive.

4. Severability. In the event any provision of this Release is found to be unenforceable by an arbitrator or court of competent jurisdiction, such provision shall be deemed modified to the extent necessary to allow enforceability of the provision as so limited, it being intended that the Parties shall receive the benefit contemplated herein to the fullest extent permitted by law. If a deemed modification is not satisfactory in the judgment of such arbitrator or court, the unenforceable provision shall be deemed deleted, and the validity and enforceability of the remaining provisions shall not be affected thereby.

5. Interpretation; Construction. The headings set forth in this Release are for convenience only and shall not be used in interpreting this Agreement. This Release has been drafted by legal counsel representing the Company, but Executive has participated in the negotiation of its terms. Furthermore, Executive acknowledges that Executive has had an opportunity to review and revise the Release and have it reviewed by legal counsel, if desired, and, therefore, the normal rule of construction to the effect that any ambiguities are to be resolved against the drafting party shall not be employed in the interpretation of this Release. Either party's failure to enforce any provision of this Release shall not in any way be construed as a waiver of any such provision, or prevent that party thereafter from enforcing each and every other provision of this Release.

6. Governing Law and Venue. This Release will be governed by and construed in accordance with the laws of the United States of America and the State of California applicable to contracts made and to be performed wholly within such State, and without regard to the conflicts of laws principles thereof. Any suit brought hereon shall be brought in the state or federal courts sitting in San Diego County, California, the Parties hereby waiving any claim or defense that such forum is not convenient or proper. Each party hereby agrees that any such court shall have in personam jurisdiction over it and consents to service of process in any manner authorized by California law.

7. Entire Agreement. This Release and the Agreement constitute the entire agreement of the Parties in respect of the subject matter contained herein and therein and supersede all prior or simultaneous representations, discussions, negotiations and agreements, whether written or oral. This Release may be amended or modified only with the written consent of Executive and an authorized representative of the Company. No oral waiver, amendment or modification will be effective under any circumstances whatsoever.

8. Counterparts. This Release may be executed in multiple counterparts, each of which shall be deemed to be an original but all of which together shall constitute one and the same instrument.

(Signature Page Follows)

IN WITNESS WHEREOF, and intending to be legally bound, the Parties have executed the foregoing Release as of the date first written above.

EXECUTIVE

EFFECTOR THERAPEUTICS, INC.

/s/ Douglas Warner

By: /s/ Stephen T. Worland

Print Name: Douglas Warner, M.D.

Print Name: /s/ Stephen T. Worland

Title: President and CEO

EMPLOYMENT AGREEMENT

THIS EMPLOYMENT AGREEMENT (this “Agreement”) is entered into by and among eFFECTOR Therapeutics, Inc., a Delaware corporation (the “Company”) and Mayank J. Gandhi, M.D. (“Executive”), and shall be effective September 1, 2022 (the “Effective Date”).

WHEREAS, the Company and the Executive previously entered into that certain Offer Letter, dated September 1, 2022, (the “Offer Letter”), which sets forth the terms and conditions of the Executive’s employment with the Company; and

WHEREAS, the Company desires to employ Executive, and Executive desires to commence employment with the Company, on the terms and conditions set forth in this Agreement.

NOW, THEREFORE, in consideration of the mutual promises herein contained, the parties agree as follows:

1. Definitions. As used in this Agreement, the following terms shall have the following meanings:

(a) Board. “Board” means the Board of Directors of the Company.

(b) Cause. “Cause” means any of the following:

(i) the commission of an act of fraud, embezzlement or dishonesty by Executive, or the commission of some other illegal act by Executive (other than traffic violations or other offenses or violations outside of the course of Executive’s employment), that has a demonstrable material adverse impact on the Company or any successor or affiliate thereof;

(ii) a conviction of, or plea of “guilty” or “no contest” to, a felony by Executive;

(iii) any unauthorized use or disclosure by Executive of confidential information or trade secrets of the Company or any successor or affiliate thereof that has, or may reasonably be expected to have, a material adverse impact on any such entity;

(iv) Executive’s gross negligence, insubordination or material violation of any duty of loyalty to the Company or any successor or affiliate thereof, or any other demonstrable material misconduct on the part of Executive;

(v) Executive’s ongoing and repeated failure or refusal to perform or neglect of Executive’s duties as required by this Agreement or to comply with the instructions given to him or her by the Chief Executive Officer or the Board; or

(vi) Executive’s willful, material breach of any Company policy or any material provision of this Agreement;

provided, however, that, for the matters set forth in clauses (v) or (vi) above, “Cause” shall additionally mean Executive’s failure to cure such conduct to the reasonable satisfaction of the Board within thirty (30) days of written notice to Executive setting forth in reasonable detail the conduct resulting in such determination of “Cause” and the need for Executive to cure such matter. Prior to the determination “Cause” under this Section 1(b) has occurred, the Company shall provide the Executive an opportunity to be heard prior to the final decision to terminate the Executive’s employment hereunder for such “Cause” and make any decision that such “Cause” exists in good faith.

The foregoing definition shall not in any way preclude or restrict the right of the Company or any successor or affiliate thereof to discharge or dismiss Executive for any other acts or omissions, but such other acts or omissions shall not be deemed, for purposes of this Agreement, to constitute grounds for termination for Cause.

(c) Change in Control. “Change in Control” shall have the meaning given to such term in the eFFECTOR Therapeutics, Inc. 2021 Incentive Award Plan.

(d) Code. “Code” means the Internal Revenue Code of 1986, as amended from time to time, and the Treasury Regulations and other interpretive guidance issued thereunder.

(e) Good Reason. “Good Reason” means the occurrence of any of the following events or conditions without Executive’s written consent:

- (i) a material diminution in Executive’s authority, duties or responsibilities;
- (ii) a material diminution in Executive’s base compensation, unless such a reduction is imposed as part of a generalized reduction in the base salaries of senior management of the Company;
- (iii) a change to the geographic location at which Executive must perform his or her duties on a regular basis to a location that is more than fifty (50) miles from the Company’s then-current offices (excepting reasonable travel on the Company’s business); or
- (iv) a material breach by the Company or any successor or affiliate of its obligations to Executive under this Agreement.

Executive must provide written notice to the Company of the occurrence of any of the foregoing events or conditions without Executive’s written consent within thirty (30) days of the occurrence of such event. The Company or any successor or affiliate shall have a period of thirty (30) days to cure such event or condition after receipt of written notice of such event from Executive. The Executive’s Separation from Service by reason of resignation from employment with the Company for Good Reason must occur within ninety (90) days following the initial existence of the act or failure to act constituting Good Reason.

(f) Involuntary Termination. “Involuntary Termination” means (i) the Executive’s Separation from Service by reason of Executive’s discharge by the Company other than for Cause, or (ii) the Executive’s Separation from Service by reason of Executive’s resignation of employment with the Company for Good Reason. Executive’s Separation from Service by reason of Executive’s death or discharge by the Company following Executive’s disability shall not constitute an Involuntary Termination.

(g) Separation from Service. “Separation from Service,” with respect to the Executive, means the Executive’s “separation from service,” as defined in Treasury Regulation Section 1.409A-1(h).

(h) Stock Awards. “Stock Awards” means all stock options, restricted stock and such other awards granted pursuant to the Company’s stock option and equity incentive award plans or agreements and any shares of stock issued upon exercise thereof.

2. Services to Be Rendered.

(a) Duties and Responsibilities. Executive shall serve as Chief Business Officer of the Company. In the performance of such duties, Executive shall report directly to the Chief Executive Officer. Executive hereby consents to serve as an officer and/or director of the Company or any subsidiary or affiliate thereof without any additional salary or compensation, if so requested by the Chief Executive Officer or the Board. Executive shall be employed by the Company on a full time basis. Executive’s primary place of work shall be the Company’s facility in San Diego, California, or such other location as may be designated by the Chief Executive Officer or the Board from time to time. Executive shall also render services at such other places within or outside the United States as the Chief Executive Officer or the Board may direct from time to time. Executive shall be subject to and comply with the policies and procedures generally applicable to senior executives of the Company to the extent the same are not inconsistent with any term of this Agreement.

(b) Exclusive Services. Executive shall at all times faithfully, industriously and to the best of his or her ability, experience and talent perform to the satisfaction of the Chief Executive Officer or the Board all of the duties that may be assigned to Executive hereunder and shall devote substantially all of his or her productive time and efforts to the performance of such duties. Subject to the terms of the Proprietary Information and Inventions Agreement referred to in Section 5(b), this shall not preclude Executive from devoting time to personal and family investments or serving on community and civic boards, or participating in industry associations, provided such activities do not interfere with his or her duties to the Company, as determined in good faith by the Chief Executive Officer or the Board. Executive agrees that he or she will not join any boards, other than community and civic boards (which do not interfere with his or her duties to the Company), without the prior approval of the Chief Executive Officer or the Board.

3. Compensation and Benefits. The Company shall pay or provide, as the case may be, to Executive the compensation and other benefits and rights set forth in this Section 3.

(a) Base Salary. As of the Effective Date, the Company shall pay to Executive a base salary of \$400,000 per year, payable in accordance with the Company’s usual payroll practices (and in any event no less frequently than monthly). Executive’s base salary shall be subject to review annually by and at the sole discretion of the Board or its designee.

(b) Annual Bonus. Executive shall participate in any bonus plan, program or arrangement that the Board or its designee may approve for the senior executives of the Company. Commencing with the calendar year in which the Effective Date occurs, Executive’s target bonus under the Company’s annual bonus plan shall be forty percent (40%) of Executive’s base salary (the “Target Bonus”). Notwithstanding anything to the contrary contained in this Agreement or any applicable bonus plan, program or arrangement, but except as provided in Section 4(d)(ii) Executive shall not be entitled to receive any such bonus, nor any portion thereof, if Executive is

not employed on the day such bonus is paid. Executive's bonus for 2022 shall be pro-rated to reflect the portion of the year that Executive is employed by the Company.

(c) Benefits. Executive shall be entitled to participate in benefits under the Company's benefit plans and arrangements, including, without limitation, any employee benefit plan or arrangement made available in the future by the Company to its senior executives, subject to and on a basis consistent with the terms, conditions and overall administration of such plans and arrangements. The Company shall have the right to amend or delete any such benefit plan or arrangement made available by the Company to its senior executives and not otherwise specifically provided for herein; provided, that any reduction of Executive's benefits such that Executive's benefits are, in the aggregate, materially less favorable to Executive than those benefits offered to Executive as of the Effective Date shall be considered a material breach of this Agreement by the Company.

(d) Expenses. The Company shall reimburse Executive for reasonable out-of-pocket business expenses incurred in connection with the performance of his or her duties hereunder, subject to such policies as the Company may from time to time establish, and Executive furnishing the Company with evidence in the form of receipts satisfactory to the Company substantiating the claimed expenditures.

(e) Paid Time Off. Executive shall be entitled to such periods of paid time off ("PTO") each year as provided from time to time under the Company's PTO policy and as otherwise provided for senior executive officers.

(f) Equity Awards.

(i) Executive shall be entitled to participate in any equity or other employee benefit plan that is generally available to senior executive officers, as distinguished from general management, of the Company. Except as otherwise provided in this Agreement, Executive's participation in and benefits under any such plan shall be on the terms and subject to the conditions specified in the governing document of the particular plan.

(ii) As soon as practicable following the Effective Date and subject to the Board's approval, Executive will be granted a stock option to purchase 500,000 shares of the Company's common stock at an exercise price per share equal to the fair market value per share of the Company's common stock on the date of grant, as determined by the Board (the "Initial Stock Option"). The Initial Stock Option will be granted pursuant to the eFFECTOR Therapeutics, Inc. 2021 Incentive Award Plan (the "Plan"). Executive's receipt of the Initial Stock Option will be subject to Executive executing the Company's standard stock option agreement. The Initial Stock Option will be subject to the terms and conditions of the Plan and the stock option agreement. So long as Executive continues in service with the Company, the Initial Stock Option will vest with respect to 25% of the shares on the one-year anniversary of the Effective Date and, with respect to the balance, in 36 equal successive monthly installments upon Executive's completion of each additional month of service thereafter. The Initial Stock Option will be subject to accelerated vesting under certain circumstances, as described in Section 4(d)(iii) herein and the form of award agreement.

4. End of Employment Payments, Benefits and Severance. Executive shall be entitled to receive benefits upon a termination of employment only as set forth in this Section 4:

(a) At-Will Employment; Termination. The Company and Executive acknowledge that Executive's employment is and shall continue to be at-will, as defined under applicable law, and that Executive's employment with the Company may be terminated by either party at any time for any or no reason, with or without notice. If Executive's employment terminates for any reason, Executive shall not be entitled to any payments, benefits, damages, awards or compensation other than as provided in this Agreement. Executive's employment under this Agreement shall be terminated immediately on the death of Executive.

(b) End of Employment Payments. Upon Executive's termination of employment with the Company for any reason, or no reason, Executive shall not be entitled to receive any payment or other benefit, except as set forth in Sections 4(c) and 4(d) below, except that Executive shall be entitled to receive (i) Executive's fully earned but unpaid base salary, through the date such termination is effective (the "Separation Date") at the rate then in effect plus all accrued but unused PTO, and (ii) all other amounts or benefits to which Executive is entitled under any compensation, retirement or benefit plan of the Company at the time of the Separation Date in accordance with the terms of such plans, including, without limitation, any continuation of benefits required by COBRA or applicable law (the amounts in clauses (i) and (ii), the "Accrued Obligations").

(c) Severance Upon Involuntary Termination Apart from a Change in Control. Subject to Sections 4(e) and 10(o) below and Executive's continued compliance with Section 5, if Executive's employment is Involuntarily Terminated prior to a Change in Control or more than twelve (12) months following a Change in Control, Executive shall be entitled to receive, in addition to those payments and benefits set forth in Section 4(b) above, but in lieu of any other severance benefits to which Executive may otherwise be entitled under any severance plan or program of the Company, the benefits provided below:

(i) Executive shall be entitled to receive Executive's monthly base salary as in effect immediately prior to the Separation Date for an additional nine (9) months after the Separation Date in accordance with the Company's usual payroll practices (and in any event no less frequently than monthly, although subject to the provisions of Sections 4(e) and 10(o) below), with the first installment commencing on the first payroll date that is sixty (60) days following the Separation Date (and any installment payments which would otherwise have been paid to Executive before the sixtieth (60th) day following the Separation Date will be paid together with the first installment); and

(ii) for the period beginning on the Separation Date and ending on the date which is nine (9) full months following the Separation Date (or, if earlier, the date on which the applicable continuation period under COBRA expires), the Company shall arrange to provide or pay the applicable premiums for Executive and his or her eligible dependents who were covered under the Company's health insurance plans as of the Separation Date with health (including medical and dental) insurance benefits substantially similar to those provided to Executive and his or her dependents immediately prior to the Separation Date. Notwithstanding the previous sentence, with regard to such COBRA continuation coverage, if the Company determines in its sole discretion that it cannot provide the foregoing benefit without potentially violating applicable law (including, without limitation, Section 2716 of the Public Health Service Act), the Company shall in lieu thereof provide to the Executive a taxable monthly payment in an amount equal to the monthly COBRA premium that the Executive would be required to pay to continue the Executive's and his or her covered dependents' group insurance coverages in effect on the Separation Date (which amount shall be based on the premiums for the first month of COBRA coverage).

(d) Severance Upon Involuntary Termination Following a Change in Control. Subject to Sections 4(e) and 10(o) and Executive's continued compliance with Section 5, if Executive's employment is Involuntarily Terminated upon or within twelve (12) months following a Change in Control, Executive shall be entitled to receive, in addition to those payments and benefits set forth in Section 4(b) above, but in lieu of any severance benefits to which Executive may otherwise be entitled under any severance plan or program of the Company (and, for the avoidance of doubt, in the event Executive is eligible for severance benefits under this Section 4(d), Executive shall not be eligible for any severance benefits under Section 4(c) as a result of such Involuntary Termination), the benefits provided below:

(i) Executive shall be entitled to receive Executive's monthly base salary as in effect immediately prior to the Separation Date for an additional twelve (12) months after the Separation Date in accordance with the Company's usual payroll practices (and in any event no less frequently than monthly, although subject to the provisions of Sections 4(e) and 10(o) below), with the first installment commencing on the first payroll date that is sixty (60) days following the Separation Date (and any installment payments which would otherwise have been paid to Executive before the sixtieth (60th) day following the Separation Date will be paid together with the first installment);

(ii) for the period beginning on the Separation Date and ending on the date which is twelve (12) full months following the Separation Date (or, if earlier, the date on which the applicable continuation period under COBRA expires), the Company shall arrange to provide or pay the applicable premiums for Executive and his or her eligible dependents who were covered under the Company's health insurance plans as of the Separation Date with health (including medical and dental) insurance benefits substantially similar to those provided to Executive and his or her dependents immediately prior to the Separation Date. Notwithstanding the previous sentence, with regard to such COBRA continuation coverage, if the Company determines in its sole discretion that it cannot provide the foregoing benefit without potentially violating applicable law (including, without limitation, Section 2716 of the Public Health Service Act), the Company shall in lieu thereof provide to the Executive a taxable monthly payment in an amount equal to the monthly COBRA premium that the Executive would be required to pay to continue the Executive's and his or her covered dependents' group insurance coverages in effect on the Separation Date (which amount shall be based on the premiums for the first month of COBRA coverage);

(iii) Executive shall be entitled to receive an amount equal to (A) the annual Target Bonus amount for the year in which Executive's Separation from Service occurs multiplied by (B) 1.0, with such payment occurring, subject to the provisions of Sections 4(e) and 10(o) below, on the first payroll date that is sixty (60) days following the Separation Date (but no later than March 15 of the calendar year following the calendar year in which the Separation Date occurs); and

(iv) the vesting and/or exercisability of all of Executive's outstanding unvested Stock Awards shall be automatically accelerated in full on the Separation Date. The foregoing provisions are hereby deemed to be a part of each Stock Award and to supersede any less favorable provision in any agreement or plan regarding such Stock Award (and, for the avoidance of doubt, if any Stock Award is subject to more favorable vesting pursuant to any agreement or plan regarding such Stock Award, such more favorable provisions shall continue to apply and shall not be limited by this clause (iv)).

(e) Release. As a condition to Executive's receipt of any post-termination benefits pursuant to Sections 4(c) and 4(d) above (collectively, the "Severance Benefits"),

Executive shall execute and not revoke a general release of all claims in favor of the Company (the “Release”) in the form attached hereto as Exhibit A. In the event the Release does not become effective within the fifty-five (55) day period following the Separation Date, Executive shall not be entitled to the aforesaid payments and benefits.

(f) Exclusive Remedy. Except as otherwise expressly required by law (e.g., COBRA) or as specifically provided herein, all of Executive’s rights to salary, severance, benefits, bonuses and other amounts hereunder (if any) accruing after the Separation Date shall cease upon such date. In the event of Executive’s termination of employment with the Company, Executive’s sole remedy shall be to receive the payments and benefits described in this Section 4. In addition, Executive acknowledges and agrees that he or she is not entitled to any reimbursement by the Company for any taxes payable by Executive as a result of the payments and benefits received by Executive pursuant to this Section 4, including, without limitation, any excise tax imposed by Section 4999 of the Code. Any payments made to Executive under this Section 4 shall be inclusive of any amounts or benefits to which Executive may be entitled pursuant to the Worker Adjustment and Retraining Notification Act, 29 U.S.C. Sections 2101 et seq., and the Department of Labor regulations thereunder, or any similar state law.

(g) No Mitigation. Except as otherwise provided in Sections 4(c)(ii) and 4(d)(ii) above, Executive shall not be required to mitigate the amount of any payment provided for in this Section 4 by seeking other employment or otherwise, nor shall the amount of any payment or benefit provided for in this Section 4 be reduced by any compensation earned by Executive as the result of employment by another employer or self-employment or by retirement benefits; provided, however, that loans, advances or other amounts owed by Executive to the Company may be offset by the Company against amounts payable to Executive under this Section 4.

(h) Return of the Company’s Property. In the event of Executive’s termination of employment for any reason, the Company shall have the right, at its option, to require Executive to vacate his or her offices prior to or on the Separation Date and to cease all activities on the Company’s behalf. Upon Executive’s termination of employment in any manner, as a condition to the Executive’s receipt of any severance benefits described in this Agreement, Executive shall immediately surrender to the Company all lists, books and records of, or in connection with, the Company’s business, and all other property belonging to the Company, it being distinctly understood that all such lists, books and records, and other documents, are the property of the Company. Executive shall deliver to the Company a signed statement certifying compliance with this Section 4(h) prior to the receipt of any severance benefits described in this Agreement.

5. Certain Covenants.

(a) No Conflicts. Except as may otherwise be approved by the Board, during the term of Executive’s employment, Executive shall not have any ownership interest (of record or beneficial) in, or have any interest as an employee, salesman, consultant, officer or director in, or otherwise aid or assist in any manner, any firm, corporation, partnership, proprietorship or other business that engages in any county, city or part thereof in the United States and/or any foreign country in a business which competes directly or indirectly (as determined by the Board) with the Company’s business in such county, city or part thereof, so long as the Company, or any successor in interest of the Company to the business and goodwill of the Company, remains engaged in such business in such county, city or part thereof or continues to solicit customers or potential customers

therein; provided, however, that Executive may own, directly or indirectly, solely as an investment, securities of any entity if Executive (i) is not a controlling person of, or a member of a group which controls, such entity; or (ii) does not, directly or indirectly, own five percent (5%) or more of any class of securities of any such entity.

(b) Confidential Information. Executive and the Company have entered into the Company's standard employee proprietary information and inventions agreement (the "Proprietary Information and Inventions Agreement"). Executive agrees to perform each and every obligation of Executive therein contained.

(c) Solicitation of Employees. Executive shall not during the term of Executive's employment and for twelve (12) months following any Separation from Service (regardless of whether or not Executive receives any Severance Benefits) (the "Restricted Period"), directly or indirectly, solicit or encourage to leave the employment of the Company or any of its affiliates, any employee of the Company or any of its affiliates.

(d) Rights and Remedies Upon Breach. If Executive breaches or threatens to commit a breach of any of the provisions of this Section 5 (the "Restrictive Covenants"), the Company shall have the following rights and remedies, each of which rights and remedies shall be independent of the other and severally enforceable, and all of which rights and remedies shall be in addition to, and not in lieu of, any other rights and remedies available to the Company under law or in equity:

(i) Specific Performance. The right and remedy to have the Restrictive Covenants specifically enforced by any court having equity jurisdiction, all without the need to post a bond or any other security or to prove any amount of actual damage or that money damages would not provide an adequate remedy, it being acknowledged and agreed that any such breach or threatened breach will cause irreparable injury to the Company and that money damages will not provide adequate remedy to the Company; and

(ii) Accounting and Indemnification. The right and remedy to require Executive (A) to account for and pay over to the Company all compensation, profits, monies, accruals, increments or other benefits derived or received by Executive or any associated party deriving such benefits as a result of any such breach of the Restrictive Covenants; and (B) to indemnify the Company against any other losses, damages (including special and consequential damages), costs and expenses, including actual attorneys' fees and court costs, which may be incurred by them and which result from or arise out of any such breach or threatened breach of the Restrictive Covenants.

(e) Severability of Covenants/Blue Pencilling. If any court determines that any of the Restrictive Covenants, or any part thereof, is invalid or unenforceable, the remainder of the Restrictive Covenants shall not thereby be affected and shall be given full effect, without regard to the invalid portions. If any court determines that any of the Restrictive Covenants, or any part thereof, are unenforceable because of the duration of such provision or the area covered thereby, such court shall have the power to reduce the duration or area of such provision and, in its reduced form, such provision shall then be enforceable and shall be enforced. Executive hereby waives

any and all right to attack the validity of the Restrictive Covenants on the grounds of the breadth of their geographic scope or the length of their term.

(f) Enforceability in Jurisdictions. The Company and Executive intend to and do hereby confer jurisdiction to enforce the Restrictive Covenants upon the courts of any jurisdiction within the geographical scope of such covenants. If the courts of any one or more of such jurisdictions hold the Restrictive Covenants wholly unenforceable by reason of the breadth of such scope or otherwise, it is the intention of the Company and Executive that such determination not bar or in any way affect the right of the Company to the relief provided above in the courts of any other jurisdiction within the geographical scope of such covenants, as to breaches of such covenants in such other respective jurisdictions, such covenants as they relate to each jurisdiction being, for this purpose, severable into diverse and independent covenants.

(g) Definitions. For purposes of this Section 5, the term “Company” means not only the Company, but also any company, partnership or entity which, directly or indirectly, controls, is controlled by or is under common control with the Company.

(h) Defend Trade Secrets Act Notice of Immunity Rights. Executive acknowledges that the Company has provided Executive with the following notice of immunity rights in compliance with the requirements of the Defend Trade Secrets Act: (i) Executive shall not be held criminally or civilly liable under any Federal or State trade secret law for the disclosure of Proprietary Information (as defined in the Proprietary Information and Inventions Agreement) that is made in confidence to a Federal, State, or local government official or to an attorney solely for the purpose of reporting or investigating a suspected violation of law, (ii) Executive shall not be held criminally or civilly liable under any Federal or State trade secret law for the disclosure of Proprietary Information that is made in a complaint or other document filed in a lawsuit or other proceeding, if such filing is made under seal and (iii) if Executive files a lawsuit for retaliation by the Company for reporting a suspected violation of law, Executive may disclose the Proprietary Information to his or her attorney and use the Proprietary Information in the court proceeding, if the Executive files any document containing the Proprietary Information under seal, and does not disclose the Proprietary Information, except pursuant to court order.

6. Insurance; Indemnification.

(a) Insurance. The Company shall have the right to take out life, health, accident, “key-man” or other insurance covering Executive, in the name of the Company and at the Company’s expense in any amount deemed appropriate by the Company. Executive shall assist the Company in obtaining such insurance, including, without limitation, submitting to any required examinations and providing information and data required by insurance companies.

(b) Indemnification. Executive will be provided with indemnification against third party claims related to his or her work for the Company as required by Delaware law. The Company shall provide Executive with directors and officers liability insurance coverage at least as favorable as that which the Company may maintain from time to time for members of the Board and other executive officers.

7. Arbitration. Any dispute, claim or controversy based on, arising out of or relating to Executive’s employment or this Agreement shall be settled by final and binding arbitration in San

Diego, California, before a single neutral arbitrator in accordance with the National Rules for the Resolution of Employment Disputes (the “Rules”) of the American Arbitration Association (“AAA”), and judgment on the award rendered by the arbitrator may be entered in any court having jurisdiction. The Rules may be found online at www.adr.org. Arbitration may be compelled pursuant to the California Arbitration Act (Code of Civil Procedure §§ 1280 et seq.). If the parties are unable to agree upon an arbitrator, one shall be appointed by the AAA in accordance with its Rules. Each party shall pay the fees of its own attorneys, the expenses of its witnesses and all other expenses connected with presenting its case; however, Executive and the Company agree that, to the extent permitted by law, the arbitrator may, in his or her discretion, award reasonable attorneys’ fees to the prevailing party. Other costs of the arbitration, including the cost of any record or transcripts of the arbitration, AAA’s administrative fees, the fee of the arbitrator, and all other fees and costs, shall be borne by the Company. This Section 7 is intended to be the exclusive method for resolving any and all claims by the parties against each other for payment of damages under this Agreement or relating to Executive’s employment; provided, however, that Executive shall retain the right to file administrative charges with or seek relief through any government agency of competent jurisdiction, and to participate in any government investigation, including but not limited to (i) claims for workers’ compensation, state disability insurance or unemployment insurance; (ii) claims for unpaid wages or waiting time penalties brought before the California Division of Labor Standards Enforcement; provided, however, that any appeal from an award or from denial of an award of wages and/or waiting time penalties shall be arbitrated pursuant to the terms of this Agreement; and (iii) claims for administrative relief from the United States Equal Employment Opportunity Commission and/or the California Department of Fair Employment and Housing (or any similar agency in any applicable jurisdiction other than California); provided, further, that Executive shall not be entitled to obtain any monetary relief through such agencies other than workers’ compensation benefits or unemployment insurance benefits. This Agreement shall not limit either party’s right to obtain any provisional remedy, including, without limitation, injunctive or similar relief, from any court of competent jurisdiction as may be necessary to protect their rights and interests pending the outcome of arbitration, including without limitation injunctive relief, in any court of competent jurisdiction pursuant to California Code of Civil Procedure § 1281.8 or any similar statute of an applicable jurisdiction. Seeking any such relief shall not be deemed to be a waiver of such party’s right to compel arbitration. Each party hereby expressly waives his, her or its right to a jury trial.

8. General Relationship. Executive shall be considered an employee of the Company within the meaning of all federal, state and local laws and regulations including, but not limited to, laws and regulations governing unemployment insurance, workers’ compensation, industrial accident, labor and taxes.

9. Section 280G of the Code.

(a) Best Pay Provision. In the event that any payment or benefit received or to be received by Executive pursuant to the terms of any plan, arrangement or agreement (including any payment or benefit received in connection with a change in ownership or control or the termination of Executive’s employment) (all such payments and benefits being hereinafter referred to as the “Total Payments”) would be subject (in whole or part) to the excise tax (the “Excise Tax”) imposed under Section 4999 of the Code, then the Total Payments shall be reduced to the extent necessary so that no portion of the Total Payments is subject to the Excise Tax but only if (i) the net amount of such Total Payments, as so reduced (after subtracting the amount of federal, state and local income taxes on such reduced Total Payments and after taking into account the phase out of

itemized deductions and personal exemptions attributable to such reduced Total Payments) is greater than or equal to (ii) the net amount of such Total Payments without such reduction (after subtracting the net amount of federal, state and local income taxes on such Total Payments and the amount of Excise Tax to which Executive would be subject in respect of such unreduced Total Payments and after taking into account the phase out of itemized deductions and personal exemptions attributable to such unreduced Total Payments). Except to the extent that an alternative reduction order would result in a greater economic benefit to the Executive on an after-tax basis, the parties intend that the Total Payments shall be reduced in the following order: (w) reduction of any cash severance payments otherwise payable to Executive that are exempt from Section 409A of the Code, (x) reduction of any other cash payments or benefits otherwise payable to Executive that are exempt from Section 409A of the Code, but excluding any payment attributable to the acceleration of vesting or payment with respect to any Stock Award that is exempt from Section 409A of the Code, (y) reduction of any other payments or benefits otherwise payable to Executive on a pro-rata basis or such other manner that complies with Section 409A of the Code, but excluding any payment attributable to the acceleration of vesting and payment with respect to any Stock Award that is exempt from Section 409A of the Code, and (z) reduction of any payments attributable to the acceleration of vesting or payment with respect to any Stock Award that is exempt from Section 409A of the Code; provided, in case of clauses (x), (y) and (z), that reduction of any payments or benefits attributable to the acceleration of vesting of Company Stock Awards shall be first applied to Stock Awards with later vesting dates; provided, further, that, notwithstanding the foregoing, any such reduction shall be undertaken in a manner that complies with and does not result in the imposition of additional taxes on the Executive under Section 409A of the Code. The foregoing reductions shall be made in a manner that results in the maximum economic benefit to Executive on an after-tax basis and, to the extent economically equivalent payments or benefits are subject to reduction, in a pro rata manner.

(b) Determinations. All determinations regarding the application of this Section 9 shall be made by an independent accounting firm or consulting group with nationally recognized standing and substantial expertise and experience in performing calculations regarding the applicability of Section 280G of the Code and the Excise Tax retained by the Company prior to the date of the applicable change in ownership or control (the “280G Firm”). For purposes of determining whether and the extent to which the Total Payments will be subject to the Excise Tax, (i) no portion of the Total Payments shall be taken into account which (x) does not constitute a “parachute payment” within the meaning of Section 280G(b)(2) of the Code (including by reason of Section 280G(b)(4)(A) of the Code) and, in calculating the Excise Tax, or (y) constitutes reasonable compensation for services actually rendered, within the meaning of Section 280G(b)(4)(B) of the Code, in excess of the “base amount” (as defined in Section 280G(b)(3) of the Code) allocable to such reasonable compensation, (ii) no portion of the Total Payments the receipt or enjoyment of which Executive shall have waived at such time and in such manner as not to constitute a “payment” within the meaning of Section 280G(b) of the Code shall be taken into account, and (iii) the value of any non-cash benefit or any deferred payment or benefit included in the Total Payments shall be determined by the 280G Firm in accordance with the principles of Sections 280G(d)(3) and (4) of the Code. All determinations related to the calculations to be performed pursuant to this “Section 280G Treatment” section shall be done by the 280G Firm. The 280G Firm will be directed to submit its determination and detailed supporting calculations to both Executive and the Company within fifteen (15) days after notification from either the Company or Executive that Executive may receive payments which may be “parachute payments.”

Executive and the Company will each provide the 280G Firm access to and copies of any books, records, and documents as may be reasonably requested by the 280G Firm, and otherwise cooperate with the 280G Firm in connection with the preparation and issuance of the determinations and calculations contemplated by this Agreement. The fees and expenses of the 280G Firm for its services in connection with the determinations and calculations contemplated by this Agreement will be borne solely by the Company.

10. Miscellaneous.

(a) Modification; Prior Claims. This Agreement and the Proprietary Information and Inventions Agreement set forth the entire understanding of the parties with respect to the subject matter hereof, supersedes all existing agreements between them concerning such subject matter, including, without limitation, the Offer Letter. This Agreement may be amended or modified only with the written consent of Executive and an authorized representative of the Company. No oral waiver, amendment or modification will be effective under any circumstances whatsoever.

(b) Assignment; Assumption by Successor. The rights of the Company under this Agreement may, without the consent of Executive, be assigned by the Company, in its sole and unfettered discretion, to any person, firm, corporation or other business entity which at any time, whether by purchase, merger or otherwise, directly or indirectly, acquires all or substantially all of the assets or business of the Company. The Company will require any successor (whether direct or indirect, by purchase, merger or otherwise) to all or substantially all of the business or assets of the Company expressly to assume and to agree to perform this Agreement in the same manner and to the same extent that the Company would be required to perform it if no such succession had taken place; provided, however, that no such assumption shall relieve the Company of its obligations hereunder. As used in this Agreement, the “Company” shall mean the Company as hereinbefore defined and any successor to its business and/or assets as aforesaid which assumes and agrees to perform this Agreement by operation of law or otherwise.

(c) Survival. The covenants, agreements, representations and warranties contained in or made in Sections 4, 5, 6, 7, 9 and 10 of this Agreement shall survive any Executive’s termination of employment.

(d) Third-Party Beneficiaries. This Agreement does not create, and shall not be construed as creating, any rights enforceable by any person not a party to this Agreement.

(e) Waiver. The failure of either party hereto at any time to enforce performance by the other party of any provision of this Agreement shall in no way affect such party’s rights thereafter to enforce the same, nor shall the waiver by either party of any breach of any provision hereof be deemed to be a waiver by such party of any other breach of the same or any other provision hereof.

(f) Section Headings. The headings of the several sections in this Agreement are inserted solely for the convenience of the parties and are not a part of and are not intended to govern, limit or aid in the construction of any term or provision hereof.

(g) Notices. Any notice required or permitted by this Agreement shall be in writing and shall be delivered as follows with notice deemed given as indicated: (i) by personal delivery when delivered personally; (ii) by overnight courier upon written verification of receipt; (iii) by email, telecopy or facsimile transmission upon acknowledgment of receipt of electronic transmission; or (iv) by certified or registered mail, return receipt requested, upon verification of receipt. Notice shall be sent to Executive at the address listed on the Company's personnel records and to the Company at its principal place of business, or such other address as either party may specify in writing.

(h) Severability. All Sections, clauses and covenants contained in this Agreement are severable, and in the event any of them shall be held to be invalid by any court, this Agreement shall be interpreted as if such invalid Sections, clauses or covenants were not contained herein.

(i) Governing Law and Venue. This Agreement is to be governed by and construed in accordance with the laws of the State of California applicable to contracts made and to be performed wholly within such State, and without regard to the conflicts of laws principles thereof. Except as provided in Sections 5 and 7, any suit brought hereon shall be brought in the state or federal courts sitting in San Diego, California, the parties hereto hereby waiving any claim or defense that such forum is not convenient or proper. Each party hereby agrees that any such court shall have in personam jurisdiction over it and consents to service of process in any manner authorized by California law.

(j) Non-transferability of Interest. None of the rights of Executive to receive any form of compensation payable pursuant to this Agreement shall be assignable or transferable except through a testamentary disposition or by the laws of descent and distribution upon the death of Executive. Any attempted assignment, transfer, conveyance, or other disposition (other than as aforesaid) of any interest in the rights of Executive to receive any form of compensation to be made by the Company pursuant to this Agreement shall be void.

(k) Gender. Where the context so requires, the use of the masculine gender shall include the feminine and/or neuter genders and the singular shall include the plural, and vice versa, and the word "person" shall include any corporation, firm, partnership or other form of association.

(l) Counterparts. This Agreement may be executed in one or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same Agreement.

(m) Construction. The language in all parts of this Agreement shall in all cases be construed simply, according to its fair meaning, and not strictly for or against any of the parties hereto. Without limitation, there shall be no presumption against any party on the ground that such party was responsible for drafting this Agreement or any part thereof.

(n) Withholding and other Deductions. All compensation payable to Executive hereunder shall be subject to such deductions as the Company is from time to time required to make pursuant to law, governmental regulation or order.

(o) Code Section 409A.

(i) This Agreement is not intended to provide for any deferral of compensation subject to Section 409A of the Code, and, to the maximum extent permitted by applicable law, amounts payable to Executive pursuant to Sections 4(c)(i), 4(c)(ii), 4(d)(i), 4(d)(ii) and 4(d)(iii) shall be made in reliance upon Treasury Regulation Section 1.409A-1(b)(9) (with respect to separation pay plans) or Treasury Regulation Section 1.409A-1(b)(4) (with respect to short-term deferrals). To the extent applicable, this Agreement shall be interpreted in accordance with Code Section 409A and Department of Treasury regulations and other interpretive guidance issued thereunder. For purposes of Section 409A of the Code, the right to a series of installment payments under this Agreement shall be treated as a right to a series of separate payments. For purposes of this Agreement, all references to Executive's "termination of employment" shall mean Executive's Separation from Service.

(ii) If the Executive is a "specified employee" (as defined in Section 409A of the Code), as determined by the Company in accordance with Section 409A of the Code, on the Separation Date, to the extent that the payments or benefits under this Agreement are subject to Section 409A of the Code and the delayed payment or distribution of all or any portion of such amounts to which Executive is entitled under this Agreement is required in order to avoid a prohibited distribution under Section 409A(a)(2)(B)(i) of the Code, then such portion deferred pursuant to this Section 10(o)(ii) shall be paid or distributed to Executive in a lump sum on the earlier of (A) the date that is six (6)-months following Executive's Separation from Service, (B) the date of Executive's death or (C) the earliest date as is permitted under Section 409A of the Code. Any remaining payments due under the Agreement shall be paid as otherwise provided herein.

(iii) If Executive and the Company determine that any payments or benefits payable under this Agreement intended to comply with Sections 409A(a)(2), (3) and (4) of the Code do not comply with Section 409A of the Code, Executive and the Company agree to amend this Agreement, or take such other actions as Executive and the Company deem reasonably necessary or appropriate, to comply with the requirements of Section 409A of the Code and the Treasury Regulations thereunder (and any applicable transition relief) while preserving the economic agreement of the parties. To the extent that any provision in this Agreement is ambiguous as to its compliance with Section 409A of the Code, the provision shall be read in such a manner that no payments payable under this Agreement shall be subject to an "additional tax" as defined in Section 409A(a)(1)(B) of the Code.

(iv) Any reimbursement of expenses or in-kind benefits payable under this Agreement shall be made in accordance with Treasury Regulation Section 1.409A-3(i)(1)(iv) and shall be paid on or before the last day of Executive's taxable year following the taxable year in which Executive incurred the expenses. The amount of expenses reimbursed or in-kind benefits payable in one year shall not affect the amount eligible for reimbursement or in-kind benefits payable in any other taxable year of Executive's, and Executive's right to reimbursement for such amounts shall not be subject to liquidation or exchange for any other benefit.

(Signature Page Follows)

IN WITNESS WHEREOF, the parties have executed this Agreement as of the date first set forth above.

EFFECTOR THERAPEUTICS, INC.

By: /s/ Stephen T. Worland
Name: Stephen T. Worland, Ph.D.
Title: President and CEO

EXECUTIVE

/s/ Mayank J. Gandhi
Mayank J. Gandhi, M.D.

EXHIBIT A

GENERAL RELEASE OF CLAIMS

[The language in this Release may change based on legal developments and evolving best practices; this form is provided as an example of what will be included in the final Release document.]

This General Release of Claims ("Release") is entered into as of this ____ day of _____, ____, between Mayank J. Gandhi, M.D. ("Executive"), eFFECTOR Therapeutics, Inc., a Delaware corporation (the "Company") (collectively referred to herein as the "Parties").

WHEREAS, Executive and the Company are parties to that certain Employment Agreement effective as of August [___], 2022 (the "Agreement");

WHEREAS, the Parties agree that were it not for execution and enforceability of this Release, Executive would not be entitled to receive the Severance Benefits (as defined below) set forth in the Agreement; and

WHEREAS, the Parties now wish to fully and finally to resolve all matters between them.

NOW, THEREFORE, in consideration of, and subject to, the severance benefits payable to Executive pursuant to the Agreement, the adequacy of which is hereby acknowledged by Executive, and which Executive acknowledges that he or she would not otherwise be entitled to receive, Executive and the Company hereby agree as follows:

1. General Release of Claims by Executive.

(a) Executive, on behalf of himself or herself and his or her executors, heirs, administrators, representatives and assigns, hereby agrees to release and forever discharge the Company and all predecessors, successors and their respective parent corporations, affiliates, related, and/or subsidiary entities, and all of their past and present investors, directors, stockholders, officers, general or limited partners, employees, attorneys, agents and representatives, and the employee benefit plans in which Executive is or has been a participant by virtue of his or her employment with or service to the Company (collectively, the "Company").

Releasees”), from any and all claims, debts, demands, accounts, judgments, rights, causes of action, equitable relief, damages, costs, charges, complaints, obligations, promises, agreements, controversies, suits, expenses, compensation, responsibility and liability of every kind and character whatsoever (including attorneys’ fees and costs), whether in law or equity, known or unknown, asserted or unasserted, suspected or unsuspected (collectively, “Claims”), which Executive has or may have had against such entities based on any events or circumstances arising or occurring on or prior to the date hereof or on or prior to the date hereof, arising directly or indirectly out of, relating to, or in any other way involving in any manner whatsoever Executive’s employment by or service to the Company or the termination thereof, including any and all claims arising under federal, state, or local laws relating to employment, including without limitation claims of wrongful discharge, breach of express or implied contract, fraud, misrepresentation, defamation, or liability in tort, and claims of any kind that may be brought in any court or administrative agency including, without limitation, claims under Title VII of the Civil Rights Act of 1964, as amended, 42 U.S.C. Section 2000, et seq.; the Americans with Disabilities Act, as amended, 42 U.S.C. § 12101 et seq.; the Rehabilitation Act of 1973, as amended, 29 U.S.C. § 701 et seq.; the Civil Rights Act of 1866, and the Civil Rights Act of 1991; 42 U.S.C. Section 1981, et seq.; the Age Discrimination in Employment Act, as amended, 29 U.S.C. Section 621, et seq. (the “ADEA”); the Equal Pay Act, as amended, 29 U.S.C. Section 206(d); regulations of the Office of Federal Contract Compliance, 41 C.F.R. Section 60, et seq.; the Family and Medical Leave Act, as amended, 29 U.S.C. § 2601 et seq.; the Fair Labor Standards Act of 1938, as amended, 29 U.S.C. § 201 et seq.; the Employee Retirement Income Security Act, as amended, 29 U.S.C. § 1001 et seq.; and the California Fair Employment and Housing Act, California Government Code Section 12940, et seq.

Notwithstanding the generality of the foregoing, Executive does not release the following claims:

- (i) Claims for unemployment compensation or any state disability insurance benefits pursuant to the terms of applicable state law;
 - (ii) Claims for workers’ compensation insurance benefits under the terms of any worker’s compensation insurance policy or fund of the Company;
 - (iii) Claims pursuant to the terms and conditions of the federal law known as COBRA;
 - (iv) Claims for indemnity under the bylaws of the Company, as provided for by California law or under any applicable insurance policy with respect to Executive’s liability as an employee, director or officer of the Company;
 - (v) Claims for Executive’s right to bring to the attention of the Equal Employment Opportunity Commission or the California Department of Fair Employment and Housing or any other federal, state or local government agency claims of discrimination, or from participating in an investigation or proceeding conducted by the Equal Employment Opportunity Commission or any other federal, state or local government agency; provided, however, that Executive does release his or her right to secure any damages for alleged discriminatory treatment;
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(vi) Claims based on any right Executive may have to enforce the Company's executory obligations under the Agreement;

(vii) Claims Executive may have to vested or earned compensation and benefits; and

(viii) Executive's right to communicate or cooperate with any governmental agency.

(b) EXECUTIVE ACKNOWLEDGES THAT HE OR SHE HAS BEEN ADVISED OF AND IS FAMILIAR WITH THE PROVISIONS OF CALIFORNIA CIVIL CODE SECTION 1542, WHICH PROVIDES AS FOLLOWS:

"A GENERAL RELEASE DOES NOT EXTEND TO CLAIMS THAT THE CREDITOR OR RELEASING PARTY DOES NOT KNOW OR SUSPECT TO EXIST IN HIS OR HER FAVOR AT THE TIME OF EXECUTING THE RELEASE AND THAT, IF KNOWN BY HIM OR HER, MUST HAVE MATERIALLY AFFECTED HIS OR HER SETTLEMENT WITH THE DEBTOR OR RELEASED PARTY."

BEING AWARE OF SAID CODE SECTION, EXECUTIVE HEREBY EXPRESSLY WAIVES ANY RIGHTS HE OR SHE MAY HAVE THEREUNDER, AS WELL AS UNDER ANY OTHER STATUTES OR COMMON LAW PRINCIPLES OF SIMILAR EFFECT.

(c) Executive acknowledges that this Release was presented to him or her on the date indicated above and th Executive is entitled to have [twenty-one (21)][forty-five (45)] days' time in which to consider it. Executive further acknowledges that the Company has advised him or her that he or she is waiving his or her rights under the ADEA, and that Executive should consult with an attorney of his or her choice before signing this Release, and Executive has had sufficient time to consider the terms of this Release. Executive represents and acknowledges that if Executive executes this Release before [twenty-one (21)][forty-five (45)] days have elapsed, Executive does so knowingly, voluntarily, and upon the advice and with the approval of Executive's legal counsel (if any), and that Executive voluntarily waives any remaining consideration period.

(d) Executive understands that after executing this Release, Executive has the right to revoke it within seven (7) days after his or her execution of it. Executive understands that this Release will not become effective and enforceable unless the seven (7) day revocation period passes and Executive does not revoke the Release in writing. Executive understands that this Release may not be revoked after the seven (7) day revocation period has passed. Executive also understands that any revocation of this Release must be made in writing and delivered to the Company at its principal place of business within the seven (7) day period.

(e) Executive understands that this Release shall become effective, irrevocable, and binding upon Executive on the eighth (8th) day after his or her execution of it, so long as Executive has not revoked it within the time period and in the manner specified in clause (d) above.

(f) Executive further understands that Executive will not be given any severance benefits under the Agreement unless this Release is effective on or before the date that is fifty-five (55) days following the date of Executive's termination of employment.

2. Defend Trade Secrets Act Notice of Immunity Rights. Executive acknowledges that the Company has provided Executive with the following notice of immunity rights in compliance with the requirements of the Defend Trade Secrets Act: (i) Executive shall not be held criminally or civilly liable under any Federal or State trade secret law for the disclosure of Proprietary Information (as defined in the Proprietary Information and Inventions Agreement (as defined in the Agreement)) that is made in confidence to a Federal, State, or local government official or to an attorney solely for the purpose of reporting or investigating a suspected violation of law, (ii) Executive shall not be held criminally or civilly liable under any Federal or State trade secret law for the disclosure of Proprietary Information that is made in a complaint or other document filed in a lawsuit or other proceeding, if such filing is made under seal and (iii) if Executive files a lawsuit for retaliation by the Company for reporting a suspected violation of law, Executive may disclose the Proprietary Information to his or her attorney and use the Proprietary Information in the court proceeding, if the Executive files any document containing the Proprietary Information under seal, and does not disclose the Proprietary Information, except pursuant to court order.

3. No Assignment. Executive represents and warrants to the Company Releasees that there has been no assignment or other transfer of any interest in any Claim that Executive may have against the Company Releasees. Executive agrees to indemnify and hold harmless the Company Releasees from any liability, claims, demands, damages, costs, expenses and attorneys' fees incurred as a result of any such assignment or transfer from Executive.

4. Severability. In the event any provision of this Release is found to be unenforceable by an arbitrator or court of competent jurisdiction, such provision shall be deemed modified to the extent necessary to allow enforceability of the provision as so limited, it being intended that the Parties shall receive the benefit contemplated herein to the fullest extent permitted by law. If a deemed modification is not satisfactory in the judgment of such arbitrator or court, the unenforceable provision shall be deemed deleted, and the validity and enforceability of the remaining provisions shall not be affected thereby.

5. Interpretation; Construction. The headings set forth in this Release are for convenience only and shall not be used in interpreting this Agreement. This Release has been drafted by legal counsel representing the Company, but Executive has participated in the negotiation of its terms. Furthermore, Executive acknowledges that Executive has had an opportunity to review and revise the Release and have it reviewed by legal counsel, if desired, and, therefore, the normal rule of construction to the effect that any ambiguities are to be resolved against the drafting party shall not be employed in the interpretation of this Release. Either party's failure to enforce any provision of this Release shall not in any way be construed as a waiver of any such provision, or prevent that party thereafter from enforcing each and every other provision of this Release.

6. Governing Law and Venue. This Release will be governed by and construed in accordance with the laws of the United States of America and the State of California applicable to contracts made and to be performed wholly within such State, and without regard to the conflicts of laws principles thereof. Any suit brought hereon shall be brought in the state or federal courts

sitting in San Diego County, California, the Parties hereby waiving any claim or defense that such forum is not convenient or proper. Each party hereby agrees that any such court shall have in personam jurisdiction over it and consents to service of process in any manner authorized by California law.

7. Entire Agreement. This Release and the Agreement constitute the entire agreement of the Parties in respect of the subject matter contained herein and therein and supersede all prior or simultaneous representations, discussions, negotiations and agreements, whether written or oral. This Release may be amended or modified only with the written consent of Executive and an authorized representative of the Company. No oral waiver, amendment or modification will be effective under any circumstances whatsoever.

8. Counterparts. This Release may be executed in multiple counterparts, each of which shall be deemed to be an original but all of which together shall constitute one and the same instrument.

(Signature Page Follows)

IN WITNESS WHEREOF, and intending to be legally bound, the Parties have executed the foregoing Release as of the date first written above.

EXECUTIVE

EFFECTOR THERAPEUTICS, INC.

By: _____

Print Name: Mayank J. Ghandhi, M.D.

Print Name: Stephen T. Worland, Ph.D.

Title: President and CEO

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

- (1) Registration Statement (Form S-3 No. 333-267221) of eFFECTOR Therapeutics, Inc.,
- (2) Registration Statement (Form S-8 No. 333-260688) pertaining to the eFFECTOR Therapeutics, Inc. 2021 Incentive Award Plan, the eFFECTOR Therapeutics, Inc. 2021 Employee Stock Purchase Plan and the eFFECTOR Therapeutics, Inc. 2013 Equity Incentive Plan of eFFECTOR Therapeutics, Inc.;

of our report dated March 8, 2023, with respect to the consolidated financial statements of eFFECTOR Therapeutics, Inc., included in this Annual Report (Form 10-K) of eFFECTOR Therapeutics, Inc. for the year ended December 31, 2022.

/s/ Ernst & Young LLP

San Diego, California
March 8, 2023

**CERTIFICATION 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**

I, Stephen T. Worland, certify that:

1. I have reviewed this Annual Report on Form 10-K of eFFECTOR Therapeutics, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
 - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 8, 2023

By: /s/ Stephen Worland
Stephen T. Worland, Ph.D.
President, Chief Executive Officer and Director

**CERTIFICATION 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**

I, Michael Byrnes, certify that:

1. I have reviewed this Annual Report on Form 10-K of eFFECTOR Therapeutics, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
 - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 8, 2023

By: /s/ Michael Byrnes
Michael Byrnes
Chief Financial Officer

- (1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

By: /s/ Stephen Worland
Stephen T. Worland, Ph.D.
President, Chief Executive Officer and Director

**CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report of eFFECTOR Therapeutics, Inc. (the “Company”) on Form 10-K for the period ending December 31, 2022 as filed with the Securities and Exchange Commission on the date hereof (the “Report”), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

- (1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: March 8, 2023

By: /s/ Michael Byrnes
Michael Byrnes
Chief Financial Officer
